Exhibit 52

United States Patent Application 20200282046

United States Patent Application	**20200282046**
Kind Code	**A1**
Ciaramella; Giuseppe ; et al.	**September 10, 2020**

BETACORONAVIRUS MRNA VACCINE

Abstract

The disclosure relates to respiratory virus ribonucleic acid (RNA) vaccines and combination vaccines, as well as methods of using the vaccines and compositions comprising the vaccines.

Inventors: **Ciaramella; Giuseppe**; *(Sudbury, MA)* ; **Himansu; Sunny**; *(Winchester, MA)*

Applicant:

Name	City	State	Country	Type
ModernaTX, Inc.	Cambridge	MA	US	

Assignee: **ModernaTX, Inc.**
Cambridge
MA

Family ID: **58558175**
Appl. No.: **16/880829**
Filed: **May 21, 2020**

Related U.S. Patent Documents

Application Number	Filing Date	Patent Number
16805587	Feb 28, 2020	10702600
16880829		
16368270	Mar 28, 2019	10702599
16805587		
16040981	Jul 20, 2018	10272150
16368270		
15674599	Aug 11, 2017	10064934
16040981		
PCT/US2016/058327	Oct 21, 2016	

15674599	
62247362	Oct 28, 2015
62247394	Oct 28, 2015
62247483	Oct 28, 2015
62247297	Oct 28, 2015
62244802	Oct 22, 2015
62244946	Oct 22, 2015
62244813	Oct 22, 2015
62244837	Oct 22, 2015
62245031	Oct 22, 2015

Current U.S. Class:	**1/1**
Current CPC Class:	A61P 11/00 20180101; C12N 2760/18634 20130101; A61K 2039/55511 20130101; C07K 16/10 20130101; C12N 2770/20034 20130101; C07K 2317/76 20130101; A61K 2039/70 20130101; A61K 39/12 20130101; A61K 39/155 20130101; C12N 2760/18034 20130101; Y02A 50/30 20180101; C12N 2760/18334 20130101; A61K 2039/6018 20130101; A61K 2039/53 20130101; A61K 2039/55555 20130101; A61K 39/215 20130101; C07K 16/1027 20130101; C12N 2760/18434 20130101; C12N 2760/18534 20130101
International Class:	A61K 39/155 20060101 A61K039/155; C07K 16/10 20060101 C07K016/10; A61K 39/12 20060101 A61K039/12; A61K 39/215 20060101 A61K039/215; A61P 11/00 20060101 A61P011/00

Claims

1.-135. (canceled)

136. A method comprising administering to a subject a messenger ribonucleic acid (mRNA) comprising an open reading frame encoding a Betacoronavirus (BetaCoV) S protein or S protein subunit formulated in a lipid nanoparticle in an effective amount to induce in the subject an immune response to the Betacoronavirus S protein or S protein subunit.

137. The method of claim 136, wherein the open reading frame encodes a BetaCoV S protein.

138. The method of claim 137, wherein the immune response is a neutralizing antibody response specific to the BetaCoV S protein.

139. The method of claim 136, wherein the open reading frame encodes a BetaCoV S protein subunit selected from an S1 subunit and an S2 subunit.

140. The method of claim 139, wherein the immune response is a neutralizing antibody response specific to the BetaCoV S protein subunit.

141. The method of claim 136, wherein the mRNA formulated in a lipid nanoparticle is administered intramuscularly.

142. The method of claim 136, wherein the mRNA further comprises a 5' untranslated region and a 3' untranslated region.

143. The method of claim 136, wherein the mRNA further comprises a poly(A) tail.

144. The method of claim 136, wherein the mRNA further comprises a 5' cap analog.

145. The method of claim 144, wherein the 5' cap analog is 7mG(5')ppp(5')N1mpNp.

146. The method of claim 136, wherein the mRNA comprises a chemical modification.

147. The method of claim 146, wherein the chemical modification is a 1-methylpseudouridine modification or a 1-ethylpseudouridine modification.

148. The method of claim 146, wherein at least 80% of the uracil in the open reading frame of the mRNA has a chemical modification.

149. The method of claim 136, wherein the lipid nanoparticle comprises an ionizable cationic lipid, a neutral lipid, a cholesterol, and a PEG-modified lipid.

150. The method of claim 149, wherein the lipid nanoparticle comprises 20-60 mol % ionizable cationic lipid, 5-25 mol % neutral lipid, 25-55 mol % cholesterol, and 0.5-15 mol % polyethylene glycol (PEG)-modified lipid.

151. The method of claim 150, wherein the lipid nanoparticle comprises 50 mol % ionizable cationic lipid, 10 mol % neutral lipid, 38.5 mol % cholesterol, and 1.5 mol % PEG-modified lipid.

152. The method of claim 149, wherein the ionizable cationic lipid is Compound 25.

153. The method of claim 149, wherein the neutral lipid is 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), the sterol is cholesterol, and the PEG-modified lipid is 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 (PEG-DMG).

154. A method comprising administering to a subject an mRNA comprising a 5' cap analog, a 5' untranslated region, an open reading frame encoding a BetaCoV S protein or S protein subunit, a 3' untranslated region, and a poly(A) tail formulated in a lipid nanoparticle in an effective amount to induce in the subject an immune response to the BetaCoV S protein or S protein subunit, wherein the lipid nanoparticle comprises 20-60 mol % ionizable cationic lipid, 5-25 mol % neutral lipid, 25-55 mol % cholesterol, and 0.5-15 mol % PEG-modified lipid.

155. The method of claim 154, wherein the open reading frame encodes a BetaCoV S protein.

156. The method of claim 155, wherein the ionizable cationic lipid is Compound 25, the neutral lipid is DSPC, the sterol is cholesterol, and the PEG-modified lipid is PEG-DMG.

157. The method of claim 155, wherein at least 80% of the uracil in the open reading frame of the mRNA has a 1-methylpseudouridine modification.

158. The method of claim 157, wherein the ionizable cationic lipid is Compound 25, the neutral lipid is DSPC, the sterol is cholesterol, and the PEG-modified lipid is PEG-DMG.

Description

RELATED APPLICATIONS

[0001] This application is a division of U.S. application Ser. No. 16/805,587, filed Feb. 28, 2020, which is a continuation of U.S. application Ser. No. 16/368,270, filed Mar. 28, 2019, which is a continuation of Ser. No. 16/040,981, filed Jul. 20, 2018, now U.S. Pat. No. 10,272,150, which is a continuation of U.S. application Ser. No. 15/674,599, filed Aug. 11, 2017, now U.S. Pat. No. 10,064,934, which is a continuation of International application number PCT/US2016/058327, filed Oct. 21, 2016, which claims the benefit under 35 U.S.C. .sctn. 119(e) of U.S. provisional application No. 62/244,802, filed Oct. 22, 2015, U.S. provisional application No. 62/247,297, filed Oct. 28, 2015, U.S. provisional application No. 62/244,946, filed Oct. 22, 2015, U.S. provisional application No. 62/247,362, filed Oct. 28, 2015, U.S. provisional application No. 62/244,813, filed Oct. 22, 2015, U.S. provisional application No. 62/247,394, filed Oct. 28, 2015, U.S. provisional application No. 62/244,837, filed Oct. 22, 2015, U.S. provisional application No. 62/247,483, filed Oct. 28, 2015, and U.S. provisional application No. 62/245,031, filed Oct. 22, 2015, each of which is incorporated by reference herein in its entirety.

BACKGROUND

[0002] Respiratory disease is a medical term that encompasses pathological conditions affecting the organs and tissues that make gas exchange possible in higher organisms, and includes conditions of the upper respiratory tract, trachea, bronchi, bronchioles, alveoli, pleura and pleural cavity, and the nerves and muscles of breathing. Respiratory diseases range from mild and self-limiting, such as the common cold, to life-threatening entities like bacterial pneumonia, pulmonary embolism, acute asthma and lung cancer. Respiratory disease is a common and significant cause of illness and death around the world. In the US, approximately 1 billion "common colds" occur each year. Respiratory conditions are among the most frequent reasons for hospital stays among children.

[0003] The human Metapneumovirus (hMPV) is a negative-sense, single-stranded RNA virus of the genus Pneumovirinae and of the family Paramyxoviridae and is closely related to the avian Metapneumovirus (AMPV) subgroup C. It was isolated for the first time in 2001 in the Netherlands by using the RAP-PCR (RNA arbitrarily primed PCR) technique for identification of unknown viruses growing in cultured cells. hPMV is second only to RSV as an important cause of viral lower respiratory tract illness (LRI) in young children. The seasonal epidemiology of hMPV appears to be similar to that of RSV, but the incidence of infection and illness appears to be substantially lower.

[0004] Parainfluenza virus type 3 (PIV3), like hMPV, is also a negative-sense, single-stranded sense RNA virus of the genus Pneumovirinae and of the family Paramyxoviridae and is a major cause of ubiquitous acute respiratory infections of infancy and early childhood. Its incidence peaks around 4-12 months of age, and the virus is responsible for 3-10% of hospitalizations, mainly for bronchiolitis and pneumonia. PIV3 can be fatal, and in some instances is associated with neurologic diseases, such as febrile seizures. It can also result in airway remodeling, a significant cause of morbidity. In developing regions of the world, infants and young children are at the highest risk of mortality, either from primary PIV3 viral infection or a secondary consequences, such as bacterial infections. Human parainfluenza viruses (hPIV) types 1, 2 and 3 (hPIV1, hPIV2 and hPIV3, respectively), also like hMPV, are second only to RSV as important causes of viral LRI in young children.

[0005] RSV, too, is a negative-sense, single-stranded RNA virus of the genus Pneumovirinae and of the family Paramyxoviridae. Symptoms in adults typically resemble a sinus infection or the common cold, although the infection may be asymptomatic. In older adults (e.g., >60 years), RSV infection may progress to bronchiolitis or pneumonia. Symptoms in children are often more severe, including bronchiolitis and pneumonia. It is estimated that in the United States, most children are infected with RSV by the age of three. The RSV virion consists of an internal nucleocapsid comprised of the viral RNA bound to nucleoprotein (N), phosphoprotein (P), and large polymerase protein (L). The nucleocapsid is surrounded by matrix protein (M) and is encapsulated by a lipid bilayer into which the viral fusion (F) and attachment (G) proteins as well as the small hydrophobic protein (SH) are incorporated. The viral genome also encodes two nonstructural proteins (NS1 and NS2), which inhibit type I interferon activity as well as the M-2 protein.

[0006] The continuing health problems associated with hMPV, PIV3 and RSV are of concern internationally, reinforcing the importance of developing effective and safe vaccine candidates against these virus.

[0007] Despite decades of research, no vaccines currently exist (Sato and Wright, Pediatr. Infect. Dis. J. 2008; 27(10 Suppl):S123-5). Recombinant technology, however, has been used to target the formation of vaccines for hPIV-1, 2 and 3 serotypes, for example, and has taken the form of several live-attenuated intranasal vaccines. Two vaccines in particular were found to be immunogenic and well tolerated against hPIV-3 in phase I trials. hPIV1 and hPIV2 vaccine candidates remain less advanced (Durbin and Karron, Clinical infectious diseases: an official publication of the Infectious Diseases Society of America 2003; 37(12):1668-77).

[0008] Measles virus (MeV), like hMPV, PIV3 and RSV, is a negative-sense, single-stranded RNA virus that is the cause of measles, an infection of the respiratory system. MeV is of the genus Morbillivirus within the family Paramyxoviridae. Humans are the natural hosts of the virus; no animal reservoirs are known to exist. Symptoms of measles include fever, cough, runny nose, red eyes and a generalized, maculopapular, erythematous rash. The virus is highly contagious and is spread by coughing

[0009] In additional to hMPV, PIV, RSV and MeV, Betacoronaviruses are known to cause respiratory illnesses. Betacoronaviruses (BetaCoVs) are one of four genera of coronaviruses of the subfamily Coronavirinae in the family Coronaviridae, of the order Nidovirales. They are enveloped, positive-sense, single-stranded RNA viruses of zoonotic origin. The coronavirus genera are each composed of varying viral lineages, with the Betacoronavirus genus containing four such lineages. The BetaCoVs of the greatest clinical importance concerning humans are OC43 and HKU1 of the A lineage, ***SARS***-CoV of the B lineage, and MERS-CoV of the C lineage. MERS-CoV is the first Betacoronavirus belonging to lineage C that is known to infect humans.

[0010] The Middle East respiratory syndrome coronavirus (MERS-CoV), or EMC/2012 (HCoV-EMC/2012), initially referred to as novel coronavirus 2012 or simply novel coronavirus, was first reported in 2012 after genome sequencing of a virus isolated from sputum samples from a person who fell ill during a 2012 outbreak of a new flu. As of July 2015, MERS-CoV cases have been reported in over 21 countries. The outbreaks of MERS-CoV have raised serious concerns world-wide, reinforcing the importance of developing effective and safe vaccine candidates against MERS-CoV.

[0011] Severe acute respiratory syndrome (***SARS***) emerged in China in 2002 and spread to other countries before brought under control. Because of a concern for reemergence or a ***deliberate release of the SARS*** coronavirus, vaccine development was initiated.

[0012] Deoxyribonucleic acid (DNA) vaccination is one technique used to stimulate humoral and cellular immune responses to foreign antigens, such as hMPV antigens and/or PIV antigens and/or RSV antigens. The direct injection of genetically engineered DNA (e.g., naked plasmid DNA) into a living host results in a small number of its cells directly producing an antigen, resulting in a protective immunological response. With this technique, however, comes potential problems, including the possibility of insertional mutagenesis, which could lead to the activation of oncogenes or the inhibition of tumor suppressor genes.

SUMMARY

[0013] Provided herein are ribonucleic acid (RNA) vaccines that build on the knowledge that RNA (e.g., messenger RNA (mRNA)) can safely direct the body's cellular machinery to produce nearly any protein of interest, from native proteins to antibodies and other entirely novel protein constructs that can have therapeutic activity inside and outside of cells. The RNA (e.g., mRNA) vaccines of the present disclosure may be used to induce a balanced immune response against hMPV, PIV, RSV, MeV, and/or BetaCoV (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1), or any combination of two or more of the foregoing viruses, comprising both cellular and humoral immunity, without risking the possibility of insertional mutagenesis, for example. hMPV, PIV, RSV, MeV, BetaCoV (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) and combinations thereof are referred to herein as "respiratory viruses." Thus, the term "respiratory virus RNA

vaccines" encompasses hMPV RNA vaccines, PIV RNA vaccines, RSV RNA vaccines, MeV RNA vaccines, BetaCoV RNA vaccines, and any combination of two or more of hMPV RNA vaccines, PIV RNA vaccines, RSV RNA vaccines, MeV RNA vaccines, and BetaCoV RNA vaccines.

[0014] The RNA (e.g., mRNA) vaccines may be utilized in various settings depending on the prevalence of the infection or the degree or level of unmet medical need. The RNA (e.g. mRNA) vaccines may be utilized to treat and/or prevent a hMPV, PIV, RSV, MeV, a BetaCoV (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1), or any combination of two or more of the foregoing viruses, of various genotypes, strains, and isolates. The RNA (e.g., mRNA) vaccines have superior properties in that they produce much larger antibody titers and produce responses earlier than commercially available anti-viral therapeutic treatments. While not wishing to be bound by theory, it is believed that the RNA (e.g., mRNA) vaccines, as mRNA polynucleotides, are better designed to produce the appropriate protein conformation upon translation as the RNA (e.g., mRNA) vaccines co-opt natural cellular machinery. Unlike traditional vaccines, which are manufactured ex vivo and may trigger unwanted cellular responses, RNA (e.g., mRNA) vaccines are presented to the cellular system in a more native fashion.

[0015] In some aspects the invention is a respiratory virus vaccine, comprising at least one RNA polynucleotide having an open reading frame encoding at least one respiratory virus antigenic polypeptide, formulated in a cationic lipid nanoparticle.

[0016] Surprisingly, in some aspects it has also been shown that efficacy of mRNA vaccines can be significantly enhanced when combined with a flagellin adjuvant, in particular, when one or more antigen-encoding mRNAs is combined with an mRNA encoding flagellin.

[0017] RNA (e.g., mRNA) vaccines combined with the flagellin adjuvant (e.g., mRNA-encoded flagellin adjuvant) have superior properties in that they may produce much larger antibody titers and produce responses earlier than commercially available vaccine formulations. While not wishing to be bound by theory, it is believed that the RNA (e.g., mRNA) vaccines, for example, as mRNA polynucleotides, are better designed to produce the appropriate protein conformation upon translation, for both the antigen and the adjuvant, as the RNA (e.g., mRNA) vaccines co-opt natural cellular machinery. Unlike traditional vaccines, which are manufactured ex vivo and may trigger unwanted cellular responses, RNA (e.g., mRNA) vaccines are presented to the cellular system in a more native fashion.

[0018] Some embodiments of the present disclosure provide RNA (e.g., mRNA) vaccines that include at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide or an immunogenic fragment thereof (e.g., an immunogenic fragment capable of inducing an immune response to the antigenic polypeptide) and at least one RNA (e.g., mRNA polynucleotide) having an open reading frame encoding a flagellin adjuvant.

[0019] In some embodiments, at least one flagellin polypeptide (e.g., encoded flagellin polypeptide) is a flagellin protein. In some embodiments, at least one flagellin polypeptide (e.g., encoded flagellin polypeptide) is an immunogenic flagellin fragment. In some embodiments, at least one flagellin polypeptide and at least one antigenic polypeptide are encoded by a single RNA (e.g., mRNA) polynucleotide. In other embodiments, at least one flagellin polypeptide and at least one antigenic polypeptide are each encoded by a different RNA polynucleotide.

[0020] In some embodiments at least one flagellin polypeptide has at least 80%, at least 85%, at least 90%, or at least 95% identity to a flagellin polypeptide having a sequence identified by any one of SEQ ID NO: 54-56.

[0021] Provided herein, in some embodiments, is a ribonucleic acid (RNA) (e.g., mRNA) vaccine, comprising at least one (e.g., at least 2, 3, 4 or 5) RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, or a BetaCoV (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide, or any combination of two or more of the foregoing antigenic polypeptides. Herein, use of the term "antigenic polypeptide" encompasses immunogenic fragments of the antigenic polypeptide (an immunogenic fragment that is induces (or is capable of inducing) an immune response to hMPV, PIV, RSV, MeV, or a BetaCoV), unless otherwise stated.

[0022] Also provided herein, in some embodiments, is a RNA (e.g., mRNA) vaccine comprising at least one (e.g., at least 2, 3, 4 or 5) RNA polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, linked to a signal peptide.

[0023] Further provided herein, in some embodiments, is a nucleic acid (e.g., DNA) encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) RNA (e.g., mRNA) polynucleotide.

[0024] Further still, provided herein, in some embodiments, is a method of inducing an immune response in a subject, the method comprising administering to the subject a vaccine comprising at least one (e.g., at least 2, 3, 4 or 5) RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one (e.g., at least 2, 3, 4 or 5) hMPV, PIV, RSV, MeV, and/or a BetaCoV (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide, or any combination of two or more of the foregoing antigenic polypeptides.

[0025] hMPV/PIV3/RSV

[0026] In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3 or RSV antigenic polypeptide. In some embodiments, at least one antigenic polypeptide is a hMPV, PIV3 or RSV polyprotein. In some embodiments, at least one antigenic polypeptide is major surface glycoprotein G or an immunogenic fragment thereof. In some embodiments, at least one antigenic polypeptide is Fusion (F) glycoprotein (e.g., Fusion glycoprotein F0, F1 or F2) or an immunogenic fragment thereof. In some embodiments, at least one antigenic polypeptide is major surface glycoprotein G or an immunogenic fragment thereof and F glycoprotein or an immunogenic fragment thereof. In some embodiments, the antigenic polypeptide is nucleoprotein (N) or an immunogenic fragment thereof, phosphoprotein (P) or an immunogenic fragment thereof, large polymerase protein (L) or an immunogenic fragment thereof, matrix protein (M) or an immunogenic fragment thereof, small hydrophobic protein (SH) or an immunogenic fragment thereof nonstructural protein 1 (NS1) or an immunogenic fragment thereof, or nonstructural protein 2 (NS2) and an immunogenic fragment thereof.

[0027] In some embodiments, at least one hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 (Table 3; see also amino acid sequences of Table 4). In some embodiments, the amino acid sequence of the hMPV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 5-8 (Table 3; see also amino acid sequences of Table 4).

[0028] In some embodiments, at least one hMPV antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 1-4 (Table 2).

[0029] In some embodiments, at least one hMPV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 1-4 (Table 2). In some embodiments, at least one hMPV RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 57-60 (Table 2).

[0030] In some embodiments, at least one antigenic polypeptide is obtained from hMPV strain CAN98-75 (CAN75) or the hMPV strain CAN97-83 (CAN83).

[0031] In some embodiments, at least one PIV3 antigenic polypeptide comprises hemagglutinin-neuraminidase, Fusion (F) glycoprotein, matrix protein (M), nucleocapsid protein (N), viral replicase (L), non-structural V protein, or an immunogenic fragment thereof.

[0032] In some embodiments, at least one PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7). In some embodiments, the amino acid sequence of the PIV3 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7).

[0033] In some embodiments, at least one PIV3 antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7).

[0034] In some embodiments, at least one PIV3 RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7). In some embodiments, at least one PIV3 RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 61-64 (Table 5).

[0035] In some embodiments, at least one antigenic polypeptide is obtained from PIV3 strain HPIV3/Homo sapiens/PER/FLA4815/2008.

[0036] In some embodiments, at least one RSV antigenic polypeptide comprises at least one antigenic polypeptide that comprises glycoprotein G, glycoprotein F, or an immunogenic fragment thereof. In some embodiments, at least one RSV antigenic polypeptide comprises at least one antigenic polypeptide that comprises glycoprotein F and at least one or at least two antigenic polypeptide selected from G, M, N, P, L, SH, M2, NS1 and NS2.

[0037] MeV

[0038] In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MeV antigenic polypeptide. In some embodiments, at least one antigenic polypeptide is a hemagglutinin (HA) protein or an immunogenic fragment thereof. The HA protein may be from MeV strain D3 or B8, for example. In some embodiments, at least one antigenic polypeptide is a Fusion (F) protein or an immunogenic fragment thereof. The F protein may be from MeV strain D3 or B8, for example. In some embodiments, a MeV RNA (e.g., mRNA) vaccines comprises a least one RNA polynucleotide encoding a HA protein and a F protein. The HA and F proteins may be from MeV strain D3 or B8, for example.

[0039] In some embodiments, at least one MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 (Table 14). In some embodiments, the amino acid sequence of the MeV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 47-50 (Table 14).

[0040] In some embodiments, at least one MeV antigenic polypeptide is encoded by a nucleic acid sequence of SEQ ID NO: 35-46 (Table 13).

[0041] In some embodiments, at least one MeV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 35-46 (Table 13). In some embodiments, at least one MeV RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 69-80 (Table 13).

[0042] In some embodiments, at least one antigenic polypeptide is obtained from MeV strain B3/B3.1, C2, D4, D6, D7, D8, G3, H1, Moraten, Rubeovax, MVi/New Jersey.USA/45.05, MVi/Texas.USA/4.07, AIK-C, MVi/New York.USA/26.09/3, MVi/California.USA/16.03, MVi/Virginia.USA/15.09, MVi/California.USA/8.04, or MVi/Pennsylvania.USA/20.09.

[0043] BetaCoV

[0044] In some embodiments, a RNA (e.g., mRNA) vaccine comprises at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one BetaCoV antigenic polypeptide. In some embodiments, the BetaCoV is MERS-CoV. In some embodiments, the BetaCoV is ***SARS***-CoV. In some embodiments, the BetaCoV is HCoV-OC43. In some embodiments, the BetaCoV is HCoV-229E. In some embodiments, the BetaCoV is HCoV-NL63. In some embodiments, the BetaCoV is HCoV-HKU1. In some embodiments, at least one antigenic polypeptide is a Betacoronavirus structural protein. For example, a Betacoronavirus structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, a Betacoronavirus structural protein is a spike protein (S). In some embodiments, a Betacoronavirus structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

[0045] BetaCoV RNA (e.g., mRNA) polynucleotides of the vaccines provided herein may encode viral protein components of Betacoronaviruses, for example, accessory proteins, replicase proteins and the like are encompassed by the present disclosure. RNA (e.g., mRNA) vaccines may include RNA polynucleotides encoding at least one accessory protein (e.g., protein 3, protein 4a, protein 4b, protein 5), at least one replicase protein (e.g., protein 1a, protein 1b), or a combination of at least one accessory protein and at least one replicase protein. The present disclosure also encompasses RNA (e.g., mRNA) vaccines comprising RNA (e.g., mRNA) polynucleotides encoding an accessory protein and/or a replicase protein in combination with at least one structural protein. Due to their surface expression properties, vaccines featuring RNA polynucleotides encoding structural proteins are believed to have preferred immunogenic activity and, hence, may be most suitable for use in the vaccines of the present disclosure.

[0046] Some embodiments of the present disclosure provide Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1 or a combination thereof) vaccines that include at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH, HCoV-HKU1) antigenic polypeptide. Also provided herein are pan-Betacoronavirus vaccines. Thus, a Betacoronavirus vaccine comprising a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding any one, two, three or four of MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, and HCoV-HKU1, for example, may be effective against any one of, any combination of, or all of, MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1. Other Betacoronaviruses are encompassed by the present disclosure.

[0047] In some embodiments, at least one antigenic polypeptide is a MERS-CoV structural protein. For example, a MERS-CoV structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the MERS-CoV structural protein is a spike protein (S) (see, e.g., Coleman C M et al. Vaccine 2014; 32:3169-74, incorporated herein by reference). In some embodiments, the MERS-CoV structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof (Li J et al. Viral Immunol 2013; 26(2):126-32; He Y et al. Biochem Biophys Res Commun 2004; 324(2):773-81, each of which is incorporated herein by reference).

[0048] In some embodiments, at least one MERS-CoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-28 or 33 (Table 11). In some embodiments, the amino acid sequence of the MERS-CoV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 24-28 or 33 (Table 11).

[0049] In some embodiments, at least one MERS-CoV antigenic polypeptide is encoded by a nucleic acid sequence identified by any one of SEQ ID NO: 20-23 (Table 10).

[0050] In some embodiments, at least one MERS-CoV RNA (e.g., mRNA) polynucleotide is encoded by a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 20-23 (Table 10). In some embodiments, at least one MERS-CoV RNA (e.g., mRNA) polynucleotide comprises a nucleic acid sequence, or a fragment of a nucleotide sequence, identified by any one of SEQ ID NO: 65-68 (Table 10).

[0051] In some embodiments, at least one antigenic polypeptide is obtained from MERS-CoV strain Riyadh_14_2013, 2cEMC/2012, or Hasa_1_2013.

[0052] In some embodiments, at least one antigenic polypeptide is a ***SARS***-CoV structural protein. For example, a ***SARS***-CoV structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the ***SARS***-CoV structural protein is a spike protein (S). In some embodiments, the ***SARS***-CoV structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

[0053] In some embodiments, at least one ***SARS***-CoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11). In some embodiments, the amino acid sequence of the ***SARS***-CoV antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11).

[0054] In some embodiments, at least one antigenic polypeptide is a HCoV-OC43 structural protein. For example, a HCoV-OC43 structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the HCoV-OC43 structural protein is a spike protein (S). In some embodiments, the HCoV-OC43 structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

[0055] In some embodiments, at least one HCoV-OC43 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 30 (Table 11). In some embodiments, the amino acid sequence of the HCoV-OC43 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 30 (Table 11).

[0056] In some embodiments, an antigenic polypeptide is a HCoV-HKU1 structural protein. For example, a HCoV-HKU1 structural protein may be spike protein (S), envelope protein (E), nucleocapsid protein (N), membrane protein (M) or an immunogenic fragment thereof. In some embodiments, the HCoV-HKU1 structural protein is a spike protein (S). In some embodiments, the HCoV-HKU1 structural protein is a S1 subunit or a S2 subunit of spike protein (S) or an immunogenic fragment thereof.

[0057] In some embodiments, at least one HCoV-HKU1 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 31 (Table 11). In some embodiments, the amino acid sequence of the HCoV-HKU1 antigenic polypeptide is, or is a fragment of, or is a homolog or variant having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to, the amino acid sequence identified by any one of SEQ ID NO: 31 (Table 11).

[0058] In some embodiments, an open reading frame of a RNA (e.g., mRNA) vaccine is codon-optimized. In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and is codon optimized mRNA.

[0059] In some embodiments, a RNA (e.g., mRNA) vaccine further comprising an adjuvant.

[0060] Tables 4, 7, 12 and 15 provide National Center for Biotechnology Information (NCBI) accession numbers of interest. It should be understood that the phrase "an amino acid sequence of Tables 4, 7, 12 and 15" refers to an amino acid sequence identified by one or more NCBI accession numbers listed in Tables 4, 7, 12 and 15. Each of the amino acid sequences, and variants having greater than 95% identity or greater than 98% identity to each of the amino acid sequences encompassed by the accession numbers of Tables 4, 7, 12 and 15 are included within the constructs (polynucleotides/polypeptides) of the present disclosure.

[0061] In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 80% identity to wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 75%, 85% or 95% identity to a wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 50-80%, 60-80%, 40-80%, 30-80%, 70-80%, 75-80% or 78-80% identity to wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 40-85%, 50-85%, 60-85%, 30-85%, 70-85%, 75-85% or 80-85% identity to wild-type mRNA sequence. In some embodiments, at least one mRNA polynucleotide is encoded by a nucleic acid having a sequence identified by any one of SEQ ID NO: 1-4, 9-12, 20-23, or 35-46 (Tables 2, 5, 10 and 13; see also nucleic acid sequences of Table 7) and having less than 40-90%, 50-90%, 60-90%, 30-90%, 70-90%, 75-90%, 80-90%, or 85-90% identity to wild-type mRNA sequence.

[0062] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) identity to wild-type mRNA sequence, but does not include wild-type mRNA sequence.

[0063] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and has less than 95%, 90%, 85%, 80% or 75% identity to wild-type mRNA sequence. In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and has 30-80%, 40-80%, 50-80%, 60-80%, 70-80%, 75-80% or 78-80%, 30-85%, 40-85%, 50-805%, 60-85%, 70-85%, 75-85% or 78-85%, 30-90%, 40-90%, 50-90%, 60-90%, 70-90%, 75-90%, 80-90% or 85-90% identity to wild-type mRNA sequence.

[0064] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15). In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having 95%-99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15).

[0065] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having membrane fusion activity. In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide having 95%-99% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, or 47-50 (Tables 3, 6, 11 and 14; see also amino acid sequences of Tables 4, 7, 12 and 15) and having membrane fusion activity.

[0066] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) that attaches to cell receptors.

[0067] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) that causes fusion of viral and cellular membranes.

[0068] In some embodiments, at least one RNA polynucleotide encodes at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) that is responsible for binding of the virus to a cell being infected.

[0069] Some embodiments of the present disclosure provide a vaccine that includes at least one ribonucleic acid (RNA) (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides), at least one 5' terminal cap and at least one chemical modification, formulated within a lipid nanoparticle.

[0070] In some embodiments, a 5' terminal cap is 7mG(5')ppp(5')N1mpNp.

[0071] In some embodiments, at least one chemical modification is selected from pseudouridine, N1-methylpseudouridine, N1-ethylpseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcytosine, 5-methyluridine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine. In some embodiments, the chemical modification is in the 5-position of the uracil. In some embodiments, the chemical modification is a N1-methylpseudouridine. In some embodiments, the chemical modification is a N1-ethylpseudouridine.

[0072] In some embodiments, a lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid. In some embodiments, a cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol. In some embodiments, a cationic lipid is selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), (12Z,15Z)--N,N-dimethyl-2-nonylhenicosa-12,15-dien-1-amine (L608), and N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]heptadecan-8-amine (L530).

[0073] In some embodiments, the lipid is

##STR00001##

[0074] In some embodiments, the lipid is

##STR00002##

[0075] In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), discussed below.

[0076] In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine is formulated in a lipid nanoparticle that comprises a compound selected from Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112 and 122, described below.

[0077] Some embodiments of the present disclosure provide a vaccine that includes at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides), wherein at least 80% (e.g., 85%, 90%, 95%, 98%, 99%) of the uracil in the open reading frame have a chemical modification, optionally wherein the vaccine is formulated in a lipid nanoparticle (e.g., a lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid).

[0078] In some embodiments, 100% of the uracil in the open reading frame have a chemical modification. In some embodiments, a chemical modification is in the 5-position of the uracil. In some embodiments, a chemical modification is a N1-methyl pseudouridine. In some embodiments, 100% of the uracil in the open reading frame have a N1-methyl pseudouridine in the 5-position of the uracil.

[0079] In some embodiments, an open reading frame of a RNA (e.g., mRNA) polynucleotide encodes at least two antigenic polypeptides (e.g., at least two hMPV antigenic polypeptides, at least two PIV3 antigenic polypeptides, at least two RSV antigenic polypeptides, at least two MeV antigenic polypeptides, or at least two BetaCoV antigenic polypeptides, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides). In some embodiments, the open reading frame encodes at least five or at least ten antigenic polypeptides. In some embodiments, the open reading frame encodes at least 100 antigenic polypeptides. In some embodiments, the open reading frame encodes 2-100 antigenic polypeptides.

[0080] In some embodiments, a vaccine comprises at least two RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides). In some embodiments, the vaccine comprises at least five or at least ten RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide or an immunogenic fragment thereof. In some embodiments, the vaccine comprises at least 100 RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide. In some embodiments, the vaccine comprises 2-100 RNA (e.g., mRNA) polynucleotides, each having an open reading frame encoding at least one antigenic polypeptide.

[0081] In some embodiments, at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) is fused to a signal peptide. In some embodiments, the signal peptide is selected from: a HuIgGk signal peptide (METPAQLLFLLLLWLPDTTG; SEQ ID NO: 15); IgE heavy chain epsilon-1 signal peptide (MDWTWILFLVAAATRVHS; SEQ ID NO: 16); Japanese encephalitis PRM signal sequence (MLGSNSGQRVVFTILLLLVAPAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence

(MWLVSLAIVTACAGA; SEQ ID NO: 19).

[0082] In some embodiments, the signal peptide is fused to the N-terminus of at least one antigenic polypeptide. In some embodiments, a signal peptide is fused to the C-terminus of at least one antigenic polypeptide.

[0083] In some embodiments, at least one antigenic polypeptide (e.g., at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, or at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides) comprises a mutated N-linked glycosylation site.

[0084] Also provided herein is a RNA (e.g., mRNA) vaccine of any one of the foregoing paragraphs (e.g., a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a BetaCoV vaccine, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing vaccines), formulated in a nanoparticle (e.g., a lipid nanoparticle).

[0085] In some embodiments, the nanoparticle has a mean diameter of 50-200 nm. In some embodiments, the nanoparticle is a lipid nanoparticle. In some embodiments, the lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid. In some embodiments, the lipid nanoparticle comprises a molar ratio of about 20-60% cationic lipid, 0.5-15% PEG-modified lipid, 25-55% sterol, and 25% non-cationic lipid. In some embodiments, the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol. In some embodiments, the cationic lipid is selected from 2,2-dilinoleyl-4-dimethylaminoethyl[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319).

[0086] In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), as discussed below.

[0087] In some embodiments, a lipid nanoparticle comprises Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122, as discussed below.

[0088] In some embodiments, the nanoparticle has a polydispersity value of less than 0.4 (e.g., less than 0.3, 0.2 or 0.1).

[0089] In some embodiments, the nanoparticle has a net neutral charge at a neutral pH value.

[0090] In some embodiments, the respiratory virus vaccine is multivalent.

[0091] Some embodiments of the present disclosure provide methods of inducing an antigen specific immune response in a subject, comprising administering to the subject any of the RNA (e.g., mRNA) vaccine as provided herein in an amount effective to produce an antigen-specific immune response. In some embodiments, the RNA (e.g., mRNA) vaccine is a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a BetaCoV vaccine, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1 vaccines. In some embodiments, the RNA (e.g., mRNA) vaccine is a combination vaccine comprising a combination of any two or more of the foregoing vaccines.

[0092] In some embodiments, an antigen-specific immune response comprises a T cell response or a B cell response.

[0093] In some embodiments, a method of producing an antigen-specific immune response comprises administering to a subject a single dose (no booster dose) of a RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, the RNA (e.g., mRNA) vaccine is a hMPV vaccine, a PIV3 vaccine, a RSV vaccine, a MeV vaccine, or a BetaCoV vaccine, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1 vaccines. In some embodiments, the RNA (e.g., mRNA) vaccine is a combination vaccine comprising a combination of any two or more of the foregoing vaccines.

[0094] In some embodiments, a method further comprises administering to the subject a second (booster) dose of a RNA (e.g., mRNA) vaccine. Additional doses of a RNA (e.g., mRNA) vaccine may be administered.

[0095] In some embodiments, the subjects exhibit a seroconversion rate of at least 80% (e.g., at least 85%, at least 90%, or at least 95%) following the first dose or the second (booster) dose of the vaccine. Seroconversion is the time period during which a specific antibody develops and becomes detectable in the blood. After seroconversion has occurred, a virus can be detected in blood tests for the antibody. During an infection or immunization, antigens enter the blood, and the immune system begins to produce antibodies in response. Before seroconversion, the antigen itself may or may not be detectable, but antibodies are considered absent. During seroconversion, antibodies are present but not yet detectable. Any time after seroconversion, the antibodies can be detected in the blood, indicating a prior or current infection.

[0096] In some embodiments, a RNA (e.g., mRNA) vaccine is administered to a subject by intradermal or intramuscular injection.

[0097] Some embodiments, of the present disclosure provide methods of inducing an antigen specific immune response in a subject, including administering to a subject a RNA (e.g., mRNA) vaccine in an effective amount to produce an antigen specific immune response in a subject. Antigen-specific immune responses in a subject may be determined, in some embodiments, by assaying for antibody titer (for titer of an antibody that binds to a hMPV, PIV3, RSV, MeV and/or BetaCoV antigenic polypeptide) following administration to the subject of any of the RNA (e.g., mRNA) vaccines of the present disclosure. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by at least 1 log relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1-3 log relative to a control.

[0098] In some embodiments, the anti-antigenic polypeptide antibody titer produced in a subject is increased at least 2 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 5 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased 2-10 times relative to a control.

[0099] In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has not been administered a RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine (see, e.g., Ren J. et al. J of Gen. Virol. 2015; 96: 1515-1520), or wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a hMPV, PIV3, RSV, MeV and/or BetaCoV virus-like particle (VLP) vaccine (see, e.g., Cox R G et al., J Virol. 2014 June; 88(11): 6368-6379).

[0100] A RNA (e.g., mRNA) vaccine of the present disclosure is administered to a subject in an effective amount (an amount effective to induce an immune response). In some embodiments, the effective amount is a dose equivalent to an at least 2-fold, at least 4-fold, at least 10-fold, at least 100-fold, at least 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, wherein the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, an inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, or a hMPV, PIV3, RSV, MeV and/or BetaCoV VLP vaccine. In some embodiments, the effective amount is a dose equivalent to 2-1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, wherein the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, an inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, or a hMPV, PIV3, RSV, MeV and/or BetaCoV VLP vaccine.

[0101] In some embodiments, the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a virus-like particle (VLP) vaccine comprising structural proteins of hMPV, PIV3, RSV, MeV and/or BetaCoV.

[0102] In some embodiments, the RNA (e.g., mRNA) vaccine is formulated in an effective amount to produce an antigen specific immune response in a subject.

[0103] In some embodiments, the effective amount is a total dose of 25 .mu.g to 1000 .mu.g, or 50 .mu.g to 1000 .mu.g. In some embodiments, the effective amount is a total dose of 100 .mu.g. In some embodiments, the effective amount is a dose of 25 .mu.g administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 100 .mu.g administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 400 .mu.g administered to the subject a total of two times. In some embodiments, the effective amount is a dose of 500 .mu.g administered to the subject a total of two times.

[0104] In some embodiments, the efficacy (or effectiveness) of a RNA (e.g., mRNA) vaccine is greater than 60%. In some embodiments, the RNA (e.g., mRNA) polynucleotide of the vaccine at least one hMPV antigenic polypeptide, at least one PIV3 antigenic polypeptide, at least one RSV antigenic polypeptide, at least one MeV antigenic polypeptide, at least one BetaCoV antigenic polypeptide, e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1, or any combination of two or more of the foregoing antigenic polypeptides.

[0105] Vaccine efficacy may be assessed using standard analyses (see, e.g., Weinberg et al., J Infect Dis. 2010 Jun. 1; 201(11):1607-10). For example, vaccine efficacy may be measured by double-blind, randomized, clinical controlled trials. Vaccine efficacy may be expressed as a proportionate reduction in disease attack rate (AR) between the unvaccinated (ARU) and vaccinated (ARV) study cohorts and can be calculated from the relative risk (RR) of disease among the vaccinated group with use of the following formulas:

Efficacy=(ARU-ARV)/ARU.times.100; and

Efficacy=(1-RR).times.100.

[0106] Likewise, vaccine effectiveness may be assessed using standard analyses (see, e.g., Weinberg et al., J Infect Dis. 2010 Jun. 1; 201(11):1607-10). Vaccine effectiveness is an assessment of how a vaccine (which may have already proven to have high vaccine efficacy) reduces disease in a population. This measure can assess the net balance of benefits and adverse effects of a vaccination program, not just the vaccine itself, under natural field conditions rather than in a controlled clinical trial. Vaccine effectiveness is proportional to vaccine efficacy (potency) but is also affected by how well target groups in the population are immunized, as well as by other non-vaccine-related factors that influence the `real-world` outcomes of hospitalizations, ambulatory visits, or costs. For example, a retrospective case control analysis may be used, in which the rates of vaccination among a set of infected cases and appropriate controls are compared. Vaccine effectiveness may be expressed as a rate difference, with use of the odds ratio (OR) for developing infection despite vaccination:

Effectiveness=(1-OR).times.100.

[0107] In some embodiments, the efficacy (or effectiveness) of a RNA (e.g., mRNA) vaccine is at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, or at least 90%.

[0108] In some embodiments, the vaccine immunizes the subject against hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses for up to 2 years. In some embodiments, the vaccine immunizes the subject against hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses for more than 2 years, more than 3 years, more than 4 years, or for 5-10 years.

[0109] In some embodiments, the subject is about 5 years old or younger. For example, the subject may be between the ages of about 1 year and about 5 years (e.g., about 1, 2, 3, 5 or 5 years), or between the ages of about 6 months and about 1 year (e.g., about 6, 7, 8, 9, 10, 11 or 12 months). In some embodiments, the subject is about 12 months or younger (e.g., 12, 11, 10, 9, 8, 7, 6, 5, 4, 3, 2 months or 1 month). In some embodiments, the subject is about 6 months or younger.

[0110] In some embodiments, the subject was born full term (e.g., about 37-42 weeks). In some embodiments, the subject was born prematurely, for example, at about 36 weeks of gestation or earlier (e.g., about 36, 35, 34, 33, 32, 31, 30, 29, 28, 27, 26 or 25 weeks). For example, the subject may have been born at about 32 weeks of gestation or earlier. In some embodiments, the subject was born prematurely between about 32 weeks and about 36 weeks of gestation. In such subjects, a RNA (e.g., mRNA) vaccine may be administered later in life, for example, at the age of about 6 months to about 5 years, or older.

[0111] In some embodiments, the subject is pregnant (e.g., in the first, second or third trimester) when administered an RNA (e.g., mRNA) vaccine. Viruses such as hMPV, PIV3 and RSV causes infections of the lower respiratory tract, mainly in infants and young children. One-third of RSV related deaths, for example, occur in the first year of life, with 99 percent of these deaths occurring in low-resource countries. It's so widespread in the United States that nearly all children become infected with the virus before their second birthdays. Thus, the present disclosure provides RNA (e.g., mRNA) vaccines for maternal immunization to improve mother-to-child transmission of protection against the virus.

[0112] In some embodiments, the subject is a young adult between the ages of about 20 years and about 50 years (e.g., about 20, 25, 30, 35, 40, 45 or 50 years old).

[0113] In some embodiments, the subject is an elderly subject about 60 years old, about 70 years old, or older (e.g., about 60, 65, 70, 75, 80, 85 or 90 years old).

[0114] In some embodiments, the subject is has a chronic pulmonary disease (e.g., chronic obstructive pulmonary disease (COPD) or asthma). Two forms of COPD include chronic bronchitis, which involves a long-term cough with mucus, and emphysema, which involves damage to the lungs over time. Thus, a subject administered a RNA (e.g., mRNA) vaccine may have chronic bronchitis or emphysema.

[0115] In some embodiments, the subject has been exposed to hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses; the subject is infected with hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses; or subject is at risk of infection by hMPV, PIV3, RSV, MeV, BetaCoV (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1), or any combination of two or more of the foregoing viruses.

[0116] In some embodiments, the subject is immunocompromised (has an impaired immune system, e.g., has an immune disorder or autoimmune disorder).

[0117] In some embodiments the nucleic acid vaccines described herein are chemically modified. In other embodiments the nucleic acid vaccines are unmodified.

[0118] Yet other aspects provide compositions for and methods of vaccinating a subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first respiratory virus antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization element, and wherein an adjuvant is not coformulated or co-administered with the vaccine.

[0119] In other aspects the invention is a composition for or method of vaccinating a subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide wherein a dosage of between 10 .mu.g/kg and 400 .mu.g/kg of the nucleic acid vaccine is administered to the subject. In some embodiments the dosage of the RNA polynucleotide is 1-5 .mu.g, 5-10 .mu.g, 10-15 .mu.g, 15-20 .mu.g, 10-25 .mu.g, 20-25 .mu.g, 20-50 .mu.g, 30-50 .mu.g, 40-50 .mu.g, 40-60 .mu.g, 60-80 .mu.g, 60-100 .mu.g, 50-100 .mu.g, 80-120 .mu.g, 40-120 .mu.g, 40-150 .mu.g, 50-150 .mu.g, 50-200 .mu.g, 80-200 .mu.g, 100-200 .mu.g, 120-250 .mu.g, 150-250 .mu.g, 180-280 .mu.g, 200-300 .mu.g, 50-300 .mu.g, 80-300 .mu.g, 100-300 .mu.g, 40-300 .mu.g, 50-350 .mu.g, 100-350 .mu.g, 200-350 .mu.g, 300-350 .mu.g, 320-400 .mu.g, 40-380 .mu.g, 40-100 .mu.g, 100-400 .mu.g, 200-400 .mu.g, or 300-400 .mu.g per dose. In some embodiments, the nucleic acid vaccine is administered to the subject by intradermal or intramuscular injection. In some embodiments, the nucleic acid vaccine is administered to the subject on day zero. In some embodiments, a second dose of the nucleic acid vaccine is administered to the subject on day twenty one.

[0120] In some embodiments, a dosage of 25 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 100 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 50 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 75 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 150 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 400 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, a dosage of 200 micrograms of the RNA polynucleotide is included in the nucleic acid vaccine administered to the subject. In some embodiments, the RNA polynucleotide accumulates at a 100 fold higher level in the local lymph node in comparison with the distal lymph node. In other embodiments the nucleic acid vaccine is chemically modified and in other embodiments the nucleic acid vaccine is not chemically modified.

[0121] Aspects of the invention provide a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization element, and a pharmaceutically acceptable carrier or excipient, wherein an adjuvant is not included in the vaccine. In some embodiments, the stabilization element is a histone stem-loop. In some embodiments, the stabilization element is a nucleic acid sequence having increased GC content relative to wild type sequence.

[0122] Aspects of the invention provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide is present in the formulation for in vivo administration to a host, which confers an antibody titer superior to the criterion for seroprotection for the first antigen for an acceptable percentage of human subjects. In some embodiments, the antibody titer produced by the mRNA vaccines of the invention is a neutralizing antibody titer. In some embodiments the neutralizing antibody titer is greater than a protein vaccine. In other embodiments the neutralizing antibody titer produced by the mRNA vaccines of the invention is greater than an adjuvanted protein vaccine. In yet other embodiments the neutralizing antibody titer produced by the mRNA vaccines of the invention is 1,000-10,000, 1,200-10,000, 1,400-10,000, 1,500-10,000, 1,000-5,000, 1,000-4,000, 1,800-10,000, 2000-10,000, 2,000-5,000, 2,000-3,000, 2,000-4,000, 3,000-5,000, 3,000-4,000, or 2,000-2,500. A neutralization titer is typically expressed as the highest serum dilution required to achieve a 50% reduction in the number of plaques.

[0123] Also provided are nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide is present in a formulation for in vivo administration to a host for eliciting a longer lasting high antibody titer than an antibody titer elicited by an mRNA vaccine having a stabilizing element or formulated with an adjuvant and encoding the first antigenic polypeptide. In some embodiments, the RNA polynucleotide is formulated to produce a neutralizing antibodies within one week of a single administration. In some embodiments, the adjuvant is selected from a cationic peptide and an immunostimulatory nucleic acid. In some embodiments, the cationic peptide is protamine.

[0124] Aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide is present in the formulation for in vivo administration to a host such that the level of antigen expression in the host significantly exceeds a level of antigen expression produced by an mRNA vaccine having a stabilizing element or formulated with an adjuvant and encoding the first antigenic polypeptide.

[0125] Other aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified mRNA vaccine to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0126] Aspects of the invention also provide a unit of use vaccine, comprising between 10 ug and 400 ug of one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification or optionally no nucleotide modification, the open reading frame encoding a first antigenic polypeptide, and a pharmaceutically acceptable carrier or excipient, formulated for delivery to a human subject. In some embodiments, the vaccine further comprises a cationic lipid nanoparticle.

[0127] Aspects of the invention provide methods of creating, maintaining or restoring antigenic memory to a respiratory virus strain in an individual or population of individuals comprising administering to said individual or population an antigenic memory booster nucleic acid vaccine comprising (a) at least one RNA polynucleotide, said polynucleotide comprising at least one chemical modification or optionally no nucleotide modification and two or more codon-optimized open reading frames, said open reading frames encoding a set of reference antigenic polypeptides, and (b) optionally a pharmaceutically acceptable carrier or excipient. In some embodiments, the vaccine is administered to the individual via a route selected from the group consisting of intramuscular administration, intradermal administration and subcutaneous administration. In some embodiments, the administering step comprises contacting a muscle tissue of the subject with a device suitable for injection of the composition. In some embodiments, the administering step comprises contacting a muscle tissue of the subject with a device suitable for injection of the composition in combination with electroporation.

[0128] Aspects of the invention provide methods of vaccinating a subject comprising administering to the subject a single dosage of between 25 ug/kg and 400 ug/kg of a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a first antigenic polypeptide in an effective amount to vaccinate the subject.

[0129] Other aspects provide nucleic acid vaccines comprising one or more RNA polynucleotides having an open reading frame comprising at least one chemical modification, the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified mRNA vaccine to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0130] Other aspects provide nucleic acid vaccines comprising an LNP formulated RNA polynucleotide having an open reading frame comprising no nucleotide modifications (unmodified), the open reading frame encoding a first antigenic polypeptide, wherein the vaccine has at least 10 fold less RNA polynucleotide than is required for an unmodified mRNA vaccine not formulated in a LNP to produce an equivalent antibody titer. In some embodiments, the RNA polynucleotide is present in a dosage of 25-100 micrograms.

[0131] The data presented in the Examples demonstrate significant enhanced immune responses using the formulations of the invention. Both chemically modified and unmodified RNA vaccines are useful according to the invention. Surprisingly, in contrast to prior art reports that it was preferable to use chemically unmodified mRNA formulated in a carrier for the production of vaccines, it is described herein that chemically modified mRNA-LNP vaccines required a much lower effective mRNA dose than unmodified mRNA, i.e., tenfold less than unmodified mRNA when formulated in carriers other than LNP. Both the chemically modified and unmodified RNA vaccines of the invention produce better immune responses than mRNA vaccines formulated in a different lipid carrier.

[0132] In other aspects the invention encompasses a method of treating an elderly subject age 60 years or older comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

[0133] In other aspects the invention encompasses a method of treating a young subject age 17 years or younger comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

[0134] In other aspects the invention encompasses a method of treating an adult subject comprising administering to the subject a nucleic acid vaccine comprising one or more RNA polynucleotides having an open reading frame encoding a respiratory virus antigenic polypeptide in an effective amount to vaccinate the subject.

[0135] In some aspects the invention is a method of vaccinating a subject with a combination vaccine including at least two nucleic acid sequences encoding respiratory antigens wherein the dosage for the vaccine is a combined therapeutic dosage wherein the dosage of each individual nucleic acid encoding an antigen is a sub therapeutic dosage. In some embodiments, the combined dosage is 25 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 100 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments the combined dosage is 50 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 75 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 150 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the combined dosage is 400 micrograms of the RNA polynucleotide in the nucleic acid vaccine administered to the subject. In some embodiments, the sub therapeutic dosage of each individual nucleic acid encoding an antigen is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 micrograms. In other embodiments the nucleic acid vaccine is chemically modified and in other embodiments the nucleic acid vaccine is not chemically modified.

[0136] The RNA polynucleotide is one of SEQ ID NO: 1-4, 9-12, 20-23, 35-46, 57-61, and 64-80 and includes at least one chemical modification. In other embodiments the RNA polynucleotide is one of SEQ ID NO: 1-4, 9-12, 20-23, 35-46, 57-61, and 64-80 and does not include any nucleotide modifications, or is unmodified. In yet other embodiments the at least one RNA polynucleotide encodes an antigenic protein of any of SEQ ID NO: 5-8, 12-13, 24-34, and 47-50 and includes at least one chemical modification. In other embodiments the RNA polynucleotide encodes an antigenic protein of any of SEQ ID NO: 5-8, 12-13, 24-34, and 47-50 and does not include any nucleotide modifications, or is unmodified.

[0137] In preferred aspects, vaccines of the invention (e.g., LNP-encapsulated mRNA vaccines) produce prophylactically- and/or therapeutically-efficacious levels, concentrations and/or titers of antigen-specific antibodies in the blood or serum of a vaccinated subject. As defined herein, the term antibody titer refers to the amount of antigen-specific antibody produces in s subject, e.g., a human subject. In exemplary embodiments, antibody titer is expressed as the inverse of the greatest dilution (in a serial dilution) that still gives a positive result. In exemplary embodiments, antibody titer is determined or measured by enzyme-linked immunosorbent assay (ELISA). In exemplary embodiments, antibody titer is determined or measured by neutralization assay, e.g., by microneutralization assay. In certain aspects, antibody titer measurement is expressed as a ratio, such as 1:40, 1:100, etc.

[0138] In exemplary embodiments of the invention, an efficacious vaccine produces an antibody titer of greater than 1:40, greater that 1:100, greater than 1:400, greater than 1:1000, greater than 1:2000, greater than 1:3000, greater than 1:4000, greater than 1:500, greater than 1:6000, greater than 1:7500, greater than 1:10000. In exemplary embodiments, the antibody titer is produced or reached by 10 days following vaccination, by 20 days following vaccination, by 30 days following vaccination, by 40 days following vaccination, or by 50 or more days following vaccination. In exemplary embodiments, the titer is produced or reached following a single dose of vaccine administered to the subject. In other embodiments, the titer is produced or reached following multiple doses, e.g., following a first and a second dose (e.g., a booster dose.)

[0139] In exemplary aspects of the invention, antigen-specific antibodies are measured in units of .mu.g/ml or are measured in units of IU/L (International Units per liter) or mIU/ml (milli International Units per ml). In exemplary embodiments of the invention, an efficacious vaccine produces >0.5 .mu.g/ml, >0.1 .mu.g/ml, >0.2 .mu.g/ml, >0.35 .mu.g/ml, >0.5 .mu.g/ml, >1 .mu.g/ml, >2 .mu.g/ml, >5 .mu.g/ml or >10 .mu.g/ml. In exemplary embodiments of the invention, an efficacious vaccine produces >10 mIU/ml, >20 mIU/ml, >50 mIU/ml, >100 mIU/ml, >200 mIU/ml, >500 mIU/ml or >1000 mIU/ml. In exemplary embodiments, the antibody level or concentration is produced or reached by 10 days following vaccination, by 20 days following vaccination, by 30 days following vaccination, by 40 days following vaccination, or by 50 or more days following vaccination. In exemplary embodiments, the level or concentration is produced or reached following a single dose of vaccine administered to the subject. In other embodiments, the level or concentration is produced or reached following multiple doses, e.g., following a first and a second dose (e.g., a booster dose.) In exemplary embodiments, antibody level or concentration is determined or measured by enzyme-linked immunosorbent assay (ELISA). In exemplary embodiments, antibody level or concentration is determined or measured by neutralization assay, e.g., by microneutralization assay.

[0140] The details of various embodiments of the disclosure are set forth in the description below. Other features, objects, and advantages of the disclosure will be apparent from the description and from the claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0141] The foregoing and other objects, features and advantages will be apparent from the following description of particular embodiments of the disclosure, as illustrated in the accompanying drawings in which like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of various embodiments of the disclosure.

[0142] FIG. 1 shows a schematic of one example of a RNA (e.g. mRNA) vaccine construct of the present disclosure. The construct depicts a human Metapneumovirus and human respiratory syncytial virus full length fusion protein obtained from wild-type strains (The Journal of General Virology. 2008; 89(Pt 12): 3113-3118, incorporated herein by reference).

[0143] FIGS. 2A-2C are graphs showing the levels of anti-hMPV fusion protein-specific antibodies in the serum of mice immunized with hMPV mRNA vaccines on day 0 (FIG. 2A), day 14 (FIG. 2B) and day 35 (FIG. 2C) post immunization. The mice were immunized with a single dose (2 .mu.g or 10 .mu.g) on day 0 and were given a boost dose (2 .mu.g or 10 .mu.g) on day 21, hMPV fusion protein-specific antibodies were detected at up to 1:10000 dilution of serum on day 35 for both doses.

[0144] FIGS. 3A-3C are graphs showing the result of IgG isotyping in the serum of mice immunized with hMPV mRNA vaccines. The levels of hMPV fusion protein-specific IgG2a (FIG. 3A) and IgG1 (FIG. 3B) antibodies in the serum are measured by ELISA. FIG. 3C shows that hMPV fusion protein mRNA vaccine induced a mixed Th1/Th2 cytokine response with a Th1 bias.

[0145] FIG. 4 is a graph showing in vitro neutralization of a hMPV B2 strain (TN/91-316) using the sera of mice immunized with a mRNA vaccine encoding hMPV fusion protein. Mouse serum obtained from mice receiving a 10 .mu.g or a 2 .mu.g dose contained hMPV-neutralizing antibodies.

[0146] FIGS. 5A-5C are graphs showing a Th1 cytokine response induced by a hMPV fusion peptide pool (15-mers-50 (overlap)) in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A (ConA, a positive control for splenocyte stimulation) was included. The cytokines tested included IFN-.gamma. (FIG. 5A), IL-2 (FIG. 5B) and IL12 (FIG. 5C).

[0147] FIGS. 6A-6E are graphs showing the Th2 cytokine response induced by a hMPV fusion peptide pool (15-mers-50) in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A was also included. The cytokines tested included IL-10 (FIG. 6A), TNF-.alpha. (FIG. 6B), IL4 (FIG. 6C), IL-5 (FIG. 6D) and IL-6 (FIG. 6E).

[0148] FIGS. 7A-7C are graphs showing the Th1 response induced by inactivated hMPV virus in splenocytes isolated from mice immunized with hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A was included. The cytokines tested included IFN-.gamma. (FIG. 7A), IL-2 (FIG. 7B) and IL12 (FIG. 7C).

[0149] FIGS. 8A-8E are graphs showing the Th2 response induced by inactivated hMPV virus in splenocytes isolated from mice immunized with the hMPV mRNA vaccines. Virus-free media was used as a negative control and Concanavalin A was included. The cytokines tested include IL-10 (FIG. 8A), TNF-.alpha. (FIG. 8B), IL4 (FIG. 8C), IL-5 (FIG. 8D) and IL-6 (FIG. 8E).

[0150] FIGS. 9A-9B are graphs showing the results of cotton rat challenge experiments. Two different doses of the hMPV mRNA vaccines were used (2 .mu.g or 10 .mu.g doses) to immunize the cotton rats before challenge. The hMPV mRNA vaccines reduced the viral titer in the lung and nose of the cotton rat, with the 10 .mu.g dose being more effective in reducing viral titer. Use of a 10 .mu.g dose resulted in 100% protection in the lung and a 2 log reduction in nose viral titer. Use of a 2 .mu.g dose resulted in a 1 log reduction in lung vital titer and no reduction in nose viral titer. The vaccine was administered on Day 0, and a boost was administered on Day 21.

[0151] FIG. 10 is a graph showing the lung histopathology of cotton rats that received hMPV mRNA vaccines. Pathology associated with vaccine-enhanced disease was not observed in immunized groups.

[0152] FIG. 11 is a graph showing hMPV neutralization antibody titers in cotton rats that received hMPV mRNA vaccines (2 .mu.g or 10 .mu.g doses) on days 35 and 42 post immunization.

[0153] FIG. 12 is a graph showing the lung and nose viral load in cotton rats challenged with a hMPV/A2 strain after immunization with the indicated mRNA vaccines (hMPV mRNA vaccine or hMPV/PIV mRNA combination vaccine). Vaccinated cotton rats showed reduced lung and nose viral loads after challenge, compared to control.

[0154] FIG. 13 is a graph showing the lung and nose viral load in cotton rats challenged with PIV3 strain after immunization with indicated mRNA vaccines (PIV mRNA vaccine or hMPV/PIV combination vaccine). Vaccinated cotton rats showed reduced lung and nose viral loads after challenge, compared to control.

[0155] FIG. 14 is a graph showing hMPV neutralizing antibody titers in cotton rats that received different dosages of hMPV mRNA vaccines or hMPV/PIV combination mRNA vaccines on day 42 post immunization.

The dosages of the vaccine are indicated in Table 9.

[0156] FIG. 15 is a graph showing PIV3 neutralizing antibody titers in cotton rats that received different dosages of PIV mRNA vaccines or hMPV/PIV combination mRNA vaccines on day 42 post immunization. The dosages of the vaccine are indicated in Table 9.

[0157] FIG. 16 is a graph showing the lung histopathology score of cotton rats immunized with hMPV mRNA vaccines, PIV mRNA vaccines or hMPV/PIV combination mRNA vaccines as indicated in Table 9. Low occurrence of alevolitis and interstitial pneumonia was observed, indicating no antibody-dependent enhancement (ADE) of hMPV associated diseases.

[0158] FIG. 17 is a graph showing the reciprocal MERS-CoV neutralizing antibody titers in mice immunized with Betacoronavirus mRNA vaccine encoding the MERS-CoV full-length Spike protein, on days 0, 21, 42, and 56 post immunization.

[0159] FIG. 18 is a graph showing the reciprocal MERS-CoV neutralizing antibody titers in mice immunized with Betacoronavirus mRNA vaccine encoding either the MERS-CoV full-length Spike protein, or the S2 subunit of the Spike protein. The full length spike protein induced a stronger immune response compared to the S2 subunit alone.

[0160] FIGS. 19A-19C are graphs showing the viral load in the nose and throat, the bronchoalveolar lavage (BAL), or the lungs of New Zealand white rabbits 4 days post challenge with MERS-CoV. The New Zealand white rabbits were immunized with one 20 .mu.g-dose (on day 0) or two 20 .mu.g-doses (on day 0 and 21) of MERS-CoV mRNA vaccine encoding the full-length Spike protein before challenge. FIG. 19A shows that two doses of MERS-CoV mRNA vaccine resulted in a 3 log reduction of viral load in the nose and led to complete protection in the throat of the New Zealand white rabbits. FIG. 19B shows that two doses of MERS-CoV mRNA vaccine resulted in a 4 log reduction of viral load in the BAL of the New Zealand white rabbits. FIG. 19C show one dose of MERS-CoV mRNA vaccine resulted in a 2 log reduction of viral load, while two doses of MERS-CoV mRNA vaccine resulted in an over 4 log reduction of viral load in the lungs of the New Zealand white rabbits.

[0161] FIGS. 20A-20B are images and graphs showing viral load or replicating virus detected by PCR in the lungs of New Zealand white rabbits 4 days post challenge with MERS-CoV. The New Zealand white rabbits were immunized with a single 20 .mu.g dose (on day 0, Group 1a) of MERS-CoV mRNA vaccine encoding the full-length Spike protein, two 20 .mu.g doses (on day 0 and 21, Group 1b) of MERS-CoV mRNA vaccine encoding the full-length Spike protein, or placebo (Group 2) before challenge. FIG. 20A shows that two doses of 20 .mu.g a MERS-CoV mRNA vaccine reduced over 99% (2 log) of viruses in the lungs of New Zealand white rabbits. FIG. 20B shows that the group of New Zealand white rabbits that received 2 doses of 20 .mu.g MERS-CoV mRNA vaccine did not have any detectable replicating MERS-CoV virus in their lungs.

[0162] FIG. 21 is a graph showing the MERS-CoV neutralizing antibody titers in New Zealand white rabbits immunized with MERS-CoV mRNA vaccine encoding the full-length Spike protein. Immunization of the in New Zealand white rabbits were carried out as described in FIGS. 21A-21C. The results show that two doses of 20 .mu.g MERS-CoV mRNA vaccine induced a significant amount of neutralizing antibodies against MERS-CoV (EC.sub.50 between 500-1000). The MERS-CoV mRNA vaccine induced antibody titer is 3-5 fold better than any other vaccines tested in the same model.

DETAILED DESCRIPTION

[0163] The present disclosure provides, in some embodiments, vaccines that comprise RNA (e.g., mRNA) polynucleotides encoding a human Metapneumovirus (hMPV) antigenic polypeptide, a parainfluenza virus type 3 (PIV3) antigenic polypeptide, a respiratory syncytial virus (RSV) antigenic polypeptide, a measles virus (MeV) antigenic polypeptide, or a Betacoronavirus antigenic polypeptide (e.g., Middle East respiratory syndrome coronavirus (MERS-CoV), ***SARS***-CoV, human coronavirus (HCoV)-OC43, HCoV-229E, HCoV-

NL63, HCoV-NL, HCoV-NH (New Haven) and HCoV-HKU1) (see, e.g., Esper F. et al. Emerging Infectious Diseases, 12(5), 2006; and Pyrc K. et al. Journal of Virology, 81(7):3051-57, 2007, the contents of each of which is here incorporated by reference in their entirety). The present disclosure also provides, in some embodiments, combination vaccines that comprise at least one RNA (e.g., mRNA) polynucleotide encoding at least two antigenic polypeptides selected from hMPV antigenic polypeptides, PIV3 antigenic polypeptides, RSV antigenic polypeptides, MeV antigenic polypeptides and BetaCoV antigenic polypeptides. Also provided herein are methods of administering the RNA (e.g., mRNA) vaccines, methods of producing the RNA (e.g., mRNA) vaccines, compositions (e.g., pharmaceutical compositions) comprising the RNA (e.g., mRNA) vaccines, and nucleic acids (e.g., DNA) encoding the RNA (e.g., mRNA) vaccines. In some embodiments, a RNA (e.g., mRNA) vaccine comprises an adjuvant, such as a flagellin adjuvant, as provided herein.

[0164] The RNA (e.g., mRNA) vaccines (e.g., hMPV, PIV3, RSV, MeV, BetaCoV RNA vaccines and combinations thereof), in some embodiments, may be used to induce a balanced immune response, comprising both cellular and humoral immunity, without many of the risks associated with DNA vaccination.

[0165] The entire contents of International Application No. PCT/US2015/02740 is incorporated herein by reference.

Human Metapneumovirus (hMPV)

[0166] hMPV shares substantial homology with respiratory syncytial virus (RSV) in its surface glycoproteins. hMPV fusion protein (F) is related to other paramyxovirus fusion proteins and appears to have homologous regions that may have similar functions. The hMPV fusion protein amino acid sequence contains features characteristic of other paramyxovirus F proteins, including a putative cleavage site and potential N-linked glycosylation sites. Paramyxovirus fusion proteins are synthesized as inactive precursors (F0) that are cleaved by host cell proteases into the biologically fusion-active F1 and F2 domains (see, e.g., Cseke G. et al. Journal of Virology 2007; 81(2):698-707, incorporated herein by reference). hMPV has one putative cleavage site, in contrast to the two sites established for RSV F, and only shares 34% amino acid sequence identity with RSV F. F2 is extracellular and disulfide linked to F1. Fusion proteins are type I glycoproteins existing as trimers, with two 4-3 heptad repeat domains at the N- and C-terminal regions of the protein (HR1 and HR2), which form coiled-coil alpha-helices. These coiled coils become apposed in an antiparallel fashion when the protein undergoes a conformational change into the fusogenic state. There is a hydrophobic fusion peptide N proximal to the N-terminal heptad repeat, which is thought to insert into the target cell membrane, while the association of the heptad repeats brings the transmembrane domain into close proximity, inducing membrane fusion (see, e.g., Baker, K A et al. Mol. Cell 1999; 3:309-319). This mechanism has been proposed for a number of different viruses, including RSV, influenza virus, and human immunodeficiency virus. Fusion proteins are major antigenic determinants for all known paramyxoviruses and for other viruses that possess similar fusion proteins such as human immunodeficiency virus, influenza virus, and Ebola virus.

[0167] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV fusion protein (F). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding a F1 or F2 subunit of a hMPV F protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV glycoprotein (G). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV matrix protein (M). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV phosphoprotein (P). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV nucleoprotein (N). In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding hMPV SH protein (SH).

[0168] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein, M protein, P protein, N protein and SH protein.

[0169] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and G protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and SH protein.

[0170] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and M protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and P protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and N protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and SH protein.

[0171] In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and P protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and N protein. In some embodiments, a hMPV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and SH protein.

[0172] A hMPV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV antigenic polypeptide identified by any one of SEQ ID NO: 5-8 (Table 3; see also amino acid sequences of Table 4).

[0173] A hMPV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 1-4 (Table 2).

[0174] The present disclosure is not limited by a particular strain of hMPV. The strain of hMPV used in a vaccine may be any strain of hMPV. Non-limiting examples of strains of hMPV for use as provide herein include the CAN98-75 (CAN75) and the CAN97-83 (CAN83) hMPV strains (Skiadopoulos M H et al. J Virol. 20014; 78(13)6927-37, incorporated herein by reference), a hMPV A1, A2, B1 or B2 strain (see, e.g., de Graaf M et al. The Journal of General Virology 2008; 89:975-83; Peret T C T et al. The Journal of Infectious Disease 2002; 185:1660-63, incorporated herein by reference), a hMPV isolate TN/92-4 (e.g., SEQ ID NO: 1 and 5), a hMPV isolate NL/1/99 (e.g., SEQ ID NO: 2 and 6), or a hMPV isolate PER/CFI0497/2010/B (e.g., SEQ ID NO: 3 and 7).

[0175] In some embodiments, at least one hMPV antigenic polypeptide is obtained from a hMPV A1, A2, B1 or B2 strain (see, e.g., de Graaf M et al. The Journal of General Virology 2008; 89:975-83; Peret T C T et al. The Journal of Infectious Disease 2002; 185:1660-63, incorporated herein by reference). In some embodiments, at least one antigenic polypeptide is obtained from the CAN98-75 (CAN75) hMPV strain. In some embodiments, at least one antigenic polypeptide is obtained from the CAN97-83 (CAN83) hMPV strain. In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate TN/92-4 (e.g., SEQ ID NO: 1 and 5). In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate NL/1/99 (e.g., SEQ ID NO: 2 and 6). In some embodiments, at least one antigenic polypeptide is obtained from hMPV isolate PER/CFI0497/2010/B (e.g., SEQ ID NO: 3 and 7).

[0176] In some embodiments, hMPV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding a hMPV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with hMPV F protein and having F protein activity.

[0177] A protein is considered to have F protein activity if, for example, the protein acts to fuse the viral envelope and host cell plasma membrane, mediates viral entry into a host cell via an interaction with arginine-glycine-aspartate RGD-binding integrins, or a combination thereof (see, e.g., Cox R G et al. J Virol. 2012;

88(22):12148-60, incorporated herein by reference).

[0178] In some embodiments, hMPV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding hMPV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with hMPV G protein and having G protein activity.

[0179] A protein is considered to have G protein activity if, for example, the protein acts to modulate (e.g., inhibit) hMPV-induced cellular (immune) responses (see, e.g., Bao X et al. PLoS Pathog. 2008; 4(5):e1000077, incorporated herein by reference).

Human parainfluenza virus type 3 (PIV3)

[0180] Parainfluenza viruses belong to the family Paramyxoviridae. These are enveloped viruses with a negative-sense single-stranded RNA genome. Parainfluenza viruses belong to the subfamily Paramyxoviridae, which is subdivided into three genera: Respirovirus (PIV-1, PIV-3, and Sendai virus (SeV)), Rubulavirus (PIV-2, PIV-4 and mumps virus) and Morbillivirus (measles virus, rinderpest virus and canine distemper virus (CDV)). Their genome, a .about.15 500 nucleotide-long negative-sense RNA molecule, encodes two envelope glycoproteins, the hemagglutinin-neuraminidase (HN), the fusion protein (F or F0), which is cleaved into F1 and F2 subunits, a matrix protein (M), a nucleocapsid protein (N) and several nonstructural proteins including the viral replicase (L). All parainfluenza viruses, except for PIV-1, express a non-structural V protein that blocks IFN signaling in the infected cell and acts therefore as a virulence factor (see, e.g., Nishio M et al. J Virol. 2008; 82(13):6130-38).

[0181] PIV3 hemagglutinin-neuraminidase (HN), a structural protein, is found on the viral envelope, where it is necessary for attachment and cell entry. It recognizes and binds to sialic acid-containing receptors on the host cell's surface. As a neuroaminidase, HN removes sialic acid from virus particles, preventing self-aggregation of the virus, and promoting the efficient spread of the virus. Furthermore, HN promotes the activity of the fusion (F or F0) protein, contributing to the penetration of the host cell's surface.

[0182] PIV3 fusion protein (PIV3 F) is located on the viral envelope, where it facilitates the viral fusion and cell entry. The F protein is initially inactive, but proteolytic cleavage leads to its active forms, F1 and F2, which are linked by disulfide bonds. This occurs when the HN protein binds its receptor on the host cell's surface. During early phases of infection, the F glycoprotein mediates penetration of the host cell by fusion of the viral envelope to the plasma membrane. In later stages of the infection, the F protein facilitates the fusion of the infected cells with neighboring uninfected cells, which leads to the formation of a syncytium and spread of the infection.

[0183] PIV3 matrix protein (M) is found within the viral envelope and assists with viral assembly. It interacts with the nucleocapsid and envelope glycoproteins, where it facilitates the budding of progeny viruses through its interactions with specific sites on the cytoplasmic tail of the viral glycoproteins and nucleocapsid. It also plays a role in transporting viral components to the budding site.

[0184] PIV3 phosphoprotein (P) and PIV3 large polymerase protein (L) are found in the nucleocapsid where they form part of the RNA polymerase complex. The L protein, a viral RNA-dependent RNA polymerase, facilitates genomic transcription, while the host cell's ribosomes translate the viral mRNA into viral proteins.

[0185] PIV3 V is a non-structural protein that blocks IFN signaling in the infected cell, therefore acting as a virulence factor.

[0186] PIV3 nucleoprotein (N) encapsidates the genome in a ratio of 1 N per 6 ribonucleotides, protecting it from nucleases. The nucleocapsid (NC) has a helical structure. The encapsidated genomic RNA is termed the NC and serves as template for transcription and replication. During replication, encapsidation by PIV3 N is coupled to RNA synthesis and all replicative products are resistant to nucleases. PIV3 N homo-multimerizes to form the nucleocapsid and binds to viral genomic RNA. PIV3 N binds the P protein and thereby positions the polymerase on the template.

[0187] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 fusion protein (F). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding a F1 or F2 subunit of a PIV3 F protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 hemagglutinin-neuraminidase (HN) (see, e.g., van Wyke Coelingh K L et al. J Virol. 1987; 61(5):1473-77, incorporated herein by reference). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 matrix protein (M). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 phosphoprotein (P). In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding PIV3 nucleoprotein (N).

[0188] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein, M protein, P protein, and N protein.

[0189] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and HN protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein.

[0190] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HN protein and N protein.

[0191] In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein and M protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein and P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, HN protein and N protein.

[0192] A PIV3 vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one PIV3 antigenic polypeptide identified by any one of SEQ ID NO: 12-13 (Table 6; see also amino acid sequences of Table 7).

[0193] A PIV3 vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 9-12 (Table 5; see also nucleic acid sequences of Table 7).

[0194] The present disclosure is not limited by a particular strain of PIV3. The strain of PIV3 used in a vaccine may be any strain of PIV3. A non-limiting example of a strain of PIV3 for use as provide herein includes HPIV3/Homo sapiens/PER/FLA4815/2008.

[0195] In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding a PIV3 antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with PIV3 F protein and having F protein activity.

[0196] In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding PIV3 antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with PIV3 hemagglutinin-neuraminidase (HN) and having hemagglutinin-neuraminidase activity.

[0197] A protein is considered to have hemagglutinin-neuraminidase activity if, for example, it is capable of both receptor binding and receptor cleaving. Such proteins are major surface glycoproteins that have functional sites for cell attachment and for neuraminidase activity. They are able to cause red blood cells to agglutinate and to cleave the glycosidic linkages of neuraminic acids, so they have the potential to both bind a potential host cell and then release the cell if necessary, for example, to prevent self-aggregation of the virus.

[0198] In some embodiments, PIV3 vaccines comprise RNA (e.g., mRNA) polynucleotides encoding PIV3 antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with PIV3 HN, F (e.g., F, F1 or F2), M, N, L or V and having HN, F (e.g., F, F1 or F2), M, N, L or V activity, respectively.

Respiratory Syncytial Virus (RSV)

[0199] RSV is a negative-sense, single-stranded RNA virus of the genus Pneumovirinae. The virus is present in at least two antigenic subgroups, known as Group A and Group B, primarily resulting from differences in the surface G glycoproteins. Two RSV surface glycoproteins--G and F--mediate attachment with and attachment to cells of the respiratory epithelium. F surface glycoproteins mediate coalescence of neighboring cells. This results in the formation of syncytial cells. RSV is the most common cause of bronchiolitis. Most infected adults develop mild cold-like symptoms such as congestion, low-grade fever, and wheezing. Infants and small children may suffer more severe symptoms such as bronchiolitis and pneumonia. The disease may be transmitted among humans via contact with respiratory secretions.

[0200] The genome of RSV encodes at least three surface glycoproteins, including F, G, and SH, four nucleocapsid proteins, including L, P, N, and M2, and one matrix protein, M. Glycoprotein F directs viral penetration by fusion between the virion and the host membrane. Glycoprotein G is a type II transmembrane glycoprotein and is the major attachment protein. SH is a short integral membrane protein. Matrix protein M is found in the inner layer of the lipid bilayer and assists virion formation. Nucleocapsid proteins L, P, N, and M2 modulate replication and transcription of the RSV genome. It is thought that glycoprotein G tethers and stabilizes the virus particle at the surface of bronchial epithelial cells, while glycoprotein F interacts with cellular glycosaminoglycans to mediate fusion and delivery of the RSV virion contents into the host cell (Krzyzaniak M A et al. PLoS Pathog 2013; 9(4)).

[0201] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding L protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding P protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding N protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M2 protein. In some embodiments, a PIV3 vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M protein.

[0202] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein, L protein, P protein, N protein, M2 protein and M protein.

[0203] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and G protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and L protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and M protein.

[0204] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and L protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and P protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding G protein and M protein.

[0205] In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and L protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and P protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and N protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M2 protein. In some embodiments, a RSV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein, G protein and M protein.

[0206] The present disclosure is not limited by a particular strain of RSV. The strain of RSV used in a vaccine may be any strain of RSV.

[0207] In some embodiments, RSV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding a RSV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with RSV F protein and having F protein activity.

[0208] In some embodiments, RSV vaccines comprise RNA (e.g., mRNA) polynucleotides encoding RSV antigenic polypeptides having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with RSV G protein and having G protein activity.

[0209] A protein is considered to have G protein activity if, for example, the protein acts to modulate (e.g., inhibit) hMPV-induced cellular (immune) responses (see, e.g., Bao X et al. PLoS Pathog. 2008; 4(5):e1000077, incorporated herein by reference).

Measles Virus (MeV)

[0210] Molecular epidemiologic investigations and virologic surveillance contribute notably to the control and prevention of measles. Nearly half of measles-related deaths worldwide occur in India, yet virologic surveillance data are incomplete for many regions of the country. Previous studies have documented the presence of measles virus genotypes D4, D7, and D8 in India, and genotypes D5, D9, D11, H1, and G3 have been detected in neighboring countries. Recently, MeV genotype B3 was detected in India (Kuttiatt V S et al. Emerg Infect Dis. 2014; 20(10): 1764-66).

[0211] The glycoprotein complex of paramyxoviruses mediates receptor binding and membrane fusion. In particular, the MeV fusion (F) protein executes membrane fusion, after receptor binding by the hemagglutinin (HA) protein (Muhlebach M D et al. Journal of Virology 2008; 82(22):11437-45). The MeV P gene codes for three proteins: P, an essential polymerase cofactor, and V and C, which have multiple functions but are not strictly required for viral propagation in cultured cells. V shares the amino-terminal domain with P but has a zinc-binding carboxyl-terminal domain, whereas C is translated from an overlapping reading frame. The MeV C protein is an infectivity factor. During replication, the P protein binds incoming monomeric nucleocapsid (N) proteins with its amino-terminal domain and positions them for assembly into the nascent ribonucleocapsid. The P protein amino-terminal domain is natively unfolded (Deveaux P et al. Journal of Virology 2004; 78(21):11632-40).

[0212] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding C protein.

[0213] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein, P protein, V protein and C protein.

[0214] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and F protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein and C protein.

[0215] some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding F protein and C protein.

[0216] In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and P protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and V protein. In some embodiments, a MeV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding HA protein, F protein and C protein.

[0217] In some embodiments, MeV vaccines comprise RNA (e.g., mRNA) encoding a MeV antigenic polypeptide having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with MeV HA protein and having MeV HA protein activity.

[0218] In some embodiments, MeV vaccines comprise RNA (e.g., mRNA) encoding a MeV antigenic polypeptide having at least 95%, at least 96%, at least 97%, at least 98% or at least 99% identity with MeV F protein and having MeV F protein activity.

[0219] A protein is considered to have HA protein activity if the protein mediates receptor binding and/or membrane fusion. MeV F protein executes membrane fusion, after receptor binding by the MeV HA protein.

[0220] A MeV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MeV antigenic polypeptide identified by any one of SEQ ID NO: 47-50 (Table 14; see also amino acid sequences of Table 15).

[0221] A MeV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide identified by any one of SEQ ID NO: 37, 40, 43, 46 (Table 13).

[0222] A MeV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 35, 36, 38, 39, 41, 42, 44 and 45 (Table 13).

[0223] The present disclosure is not limited by a particular strain of MeV. The strain of MeV used in a vaccine may be any strain of MeV. Non-limiting examples of strains of MeV for use as provide herein include B3/B3.1, C2, D4, D6, D7, D8, G3, H1, Moraten, Rubeovax, MVi/New Jersey.USA/45.05, MVi/Texas.USA/4.07, AIK-C, MVi/New York.USA/26.09/3, MVi/California.USA/16.03, MVi/Virginia.USA/15.09, MVi/California.USA/8.04, and MVi/Pennsylvania.USA/20.09.

[0224] MeV proteins may be from MeV genotype D4, D5, D7, D8, D9, D11, H1, G3 or B3. In some embodiments, a MeV HA protein or a MeV F protein is from MeV genotype D8. In some embodiments, a MeV HA protein or a MeV F protein is from MeV genotype B3.

Betacoronaviruses (BetaCoV)

[0225] MERS-Co V. MERS-CoV is a positive-sense, single-stranded RNA virus of the genus Betacoronavirus. The genomes are phylogenetically classified into two clades, clade A and clade B. It has a strong tropism for non-ciliated bronchial epithelial cells, evades the innate immune response and antagonizes interferon (IFN) production in infected cells. Dipeptyl peptidase 4 (DDP4, also known as CD26) has been identified as a functional cellular receptor for MERS-CoV. Its enzymatic activity is not required for infection, although its amino acid sequence is highly conserved across species and is expressed in the human bronchial epithelium and kidneys. Most infected individuals develop severe acute respiratory illnesses, including fever, cough, and shortness of breath, and the virus can be fatal. The disease may be transmitted among humans, generally among those in close contact.

[0226] The genome of MERS-CoV encodes at least four unique accessory proteins, such as 3, 4a, 4b and 5, two replicase proteins (open reading frame 1a and 1b), and four major structural proteins, including spike (S), envelope (E), nucleocapsid (N), and membrane (M) proteins (Almazan F et al. MBio 2013; 4(5):e00650-13). The accessory proteins play nonessential roles in MERS-CoV replication, but they are likely structural proteins or interferon antagonists, modulating in vivo replication efficiency and/or pathogenesis, as in the case of ***SARS***-CoV (Almazan F et al. MBio 2013; 4(5):e00650-13; Totura A L et al. Curr Opin Virol 2012; 2(3):264-75; Scobey T et al. Proc Natl Acad Sci USA 2013; 110(40):16157-62). The other proteins of MERS-CoV maintain different functions in virus replication. The E protein, for example, involves in virulence, and deleting the E-coding gene results in replication-competent and propagation-defective viruses or attenuated viruses (Almazan F et al. MBio 2013; 4(5):e00650-13). The S protein is particularly essential in mediating virus binding to cells expressing receptor dipeptidyl peptidase-4 (DPP4) through receptor-binding domain (RBD) in the S1 subunit, whereas the S2 subunit subsequently mediates virus entry via fusion of the virus and target cell membranes (Li F. J Virol 2015; 89(4):1954-64; Raj V S et al. Nature 2013; 495(7440):251-4).

[0227] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding the S1 subunit of the S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding the S2 subunit of the S protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding M protein.

[0228] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein, N protein and M protein.

[0229] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and E protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and M protein.

[0230] In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and M protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), M protein and N protein. In some embodiments, a MERS-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein, M protein and N protein.

[0231] A MERS-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one MERS-CoV antigenic polypeptide identified by any one of SEQ ID NO: 24-38 or 33 (Table 11; see also amino acid sequences of Table 12).

[0232] A MERS-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide encoded by a nucleic acid (e.g., DNA) identified by any one of SEQ ID NO: 20-23 (Table 10).

[0233] The present disclosure is not limited by a particular strain of MERS-CoV. The strain of MERS-CoV used in a vaccine may be any strain of MERS-CoV. Non-limiting examples of strains of MERS-CoV for use as provide herein include Riyadh_14_2013, and 2cEMC/2012, Hasa_1_2013.

[0234] ***SARS***-CoV. The genome of ***SARS***-CoV includes of a single, positive-strand RNA that is approximately 29,700 nucleotides long. The overall genome organization of ***SARS***-CoV is similar to that of other coronaviruses. The reference genome includes 13 genes, which encode at least 14 proteins. Two large overlapping reading frames (ORFs) encompass 71% of the genome. The remainder has 12 potential ORFs, including genes for structural proteins S (spike), E (small envelope), M (membrane), and N (nucleocapsid). Other potential ORFs code for unique putative ***SARS***-CoV-specific polypeptides that lack obvious sequence similarity to known proteins. A detailed analysis of the ***SARS***-CoV genome has been published in J Mol Biol 2003; 331: 991-1004.

[0235] In some embodiments, a ***SARS***-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein, N protein and M protein.

[0236] In some embodiments, a ***SARS***-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and E protein. In some embodiments, a ***SARS***-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and N protein. In some embodiments, a ***SARS***-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2) and M protein.

[0237] In some embodiments, a ***SARS***-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and M protein. In some embodiments, a ***SARS***-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), E protein and N protein. In some embodiments, a ***SARS***-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding S protein (S, S1 and/or S2), M protein and N protein. In some embodiments, a ***SARS***-CoV vaccine of the present disclosure comprises a RNA (e.g., mRNA) polynucleotide encoding E protein, M protein and N protein.

[0238] A ***SARS***-CoV vaccine may comprise, for example, at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one ***SARS***-CoV antigenic polypeptide identified by any one of SEQ ID NO: 29, 32 or 34 (Table 11; see also amino acid sequences of Table 12).

[0239] The present disclosure is not limited by a particular strain of ***SARS***-CoV. The strain of ***SARS***-CoV used in a vaccine may be any strain of ***SARS***-CoV.

[0240] HCoV-OC43. Human coronavirus OC43 is an enveloped, positive-sense, single-stranded RNA virus in the species Betacoronavirus-1 (genus Betacoronavirus, subfamily Coronavirinae, family Coronaviridae, order Nidovirales). Four HCoV-OC43 genotypes (A to D), have been identified with genotype D most likely arising from recombination. The complete genome sequencing of two genotype C and D strains and bootscan analysis shows recombination events between genotypes B and C in the generation of genotype D. Of 29 strains identified, none belong to the more ancient genotype A. Along with HCoV-229E, a species in the Alphacoronavirus genus, HCoV-OC43 are among the known viruses that cause the common cold. Both viruses can cause severe lower respiratory tract infections, including pneumonia in infants, the elderly, and immunocompromised individuals such as those undergoing chemotherapy and those with HIV-AIDS.

[0241] HCoV-HKU1. Human coronavirus HKU1 (HCoV-HKU1) is a positive-sense, single-stranded RNA virus with the HE gene, which distinguishes it as a group 2, or Betacoronavirus. It was discovered in January 2005 in two patients in Hong Kong. The genome of HCoV-HKU1 is a 29,926-nucleotide, polyadenylated RNA. The GC content is 32%, the lowest among all known coronaviruses. The genome organization is the same as that of other group II coronaviruses, with the characteristic gene order 1a, 1b, HE, S, E, M, and N. Furthermore, accessory protein genes are present between the S and E genes (ORF4) and at the position of the N gene (ORF8). The TRS is presumably located within the AAUCUAAAC sequence, which precedes each ORF except E. As in sialodacryoadenitis virus and mouse hepatitis virus (MHV), translation of the E protein possibly occurs via an internal ribosomal entry site. The 3' untranslated region contains a predicted stem-loop structure immediately downstream of the N ORF (nucleotide position 29647 to 29711). Further downstream, a pseudoknot structure is present at nucleotide position 29708 to 29760. Both RNA structures are conserved in group II coronaviruses and are critical for virus replication.

[0242] HCoV-NL63. The RNA genome of human coronavirus NL63 (HCoV-NL63) is 27,553 nucleotides, with a poly(A) tail (FIG. 1). With a GC content of 34%, HCoV-NL63 has one of the lowest GC contents of the coronaviruses, for which GC content ranges from 32 to 42%. Untranslated regions of 286 and 287 nucleotides are present at the 5' and 3' termini, respectively. Genes predicted to encode the S, E, M, and N proteins are found in the 3' part of the HCoV-NL63 genome. The HE gene, which is present in some group II coronaviruses, is absent, and there is only a single, monocistronic accessory protein ORF (ORF3) located between the S and E genes. Subgenomic mRNAs are generated for all ORFs (S, ORF3, E, M, and N), and the core sequence of the TRS of HCoV-NL63 is defined as AACUAAA. This sequence is situated upstream of every ORF except for the E ORF, which contains the suboptimal core sequence AACUAUA. Interestingly, a 13-nucleotide sequence with perfect homology to the leader sequence is situated upstream of the suboptimal E TRS. Annealing of this 13-nucleotide sequence to the leader sequence may act as a compensatory mechanism for the disturbed leader-TRS/body-TRS interaction.

[0243] HCoV-229E. Human coronavirus 229E (HCoV-229E) is a single-stranded, positive-sense, RNA virus species in the Alphacoronavirus genus of the subfamily Coronavirinae, in the family Coronaviridae, of the order Nidovirales. Along with Human coronavirus OC43, it is responsible for the common cold. HCoV-NL63 and HCoV-229E are two of the four human coronaviruses that circulate worldwide. These two viruses are unique in their relationship towards each other. Phylogenetically, the viruses are more closely related to each other than to any other human coronavirus, yet they only share 65% sequence identity. Moreover, the viruses use different receptors to enter their target cell. HCoV-NL63 is associated with croup in children, whereas all signs suggest that the virus probably causes the common cold in healthy adults. HCoV-229E is a proven common cold virus in healthy adults, so it is probable that both viruses induce comparable symptoms in adults, even though their mode of infection differs (HCoV-NL63 and HCoV-229E are two of the four human coronaviruses that circulate worldwide. These two viruses are unique in their relationship towards each other. Phylogenetically, the viruses are more closely related to each other than to any other human coronavirus, yet they only share 65% sequence identity. Moreover, the viruses use different receptors to enter their target cell. HCoV-NL63 is associated with croup in children, whereas all signs suggest that the virus probably causes the common cold in healthy adults. HCoV-229E is a proven common cold virus in healthy adults, so it is probable that both viruses induce comparable symptoms in adults, even though their mode of infection differs (Dijkman R. et al. J Formos Med Assoc. 2009 April; 108(4):270-9, the contents of which is incorporated herein by reference in their entirety).

Combination Vaccines

[0244] Embodiments of the present disclosure also provide combination RNA (e.g., mRNA) vaccines. A "combination RNA (e.g., mRNA) vaccine" of the present disclosure refers to a vaccine comprising at least one (e.g., at least 2, 3, 4, or 5) RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a combination of any two or more (or all of) antigenic polypeptides selected from hMPV antigenic polypeptides, PIV3 antigenic polypeptides, RSV antigenic polypeptides, MeV antigenic polypeptides, and BetaCoV antigenic polypeptides (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0245] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a RSV antigenic polypeptide, a MeV antigenic polypeptide, and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0246] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a PIV3 antigenic polypeptide.

[0247] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a RSV antigenic polypeptide.

[0248] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a MeV antigenic polypeptide.

[0249] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide and a BetaCoV antigenic polypeptide.

[0250] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide and a RSV antigenic polypeptide.

[0251] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide and a MeV antigenic polypeptide.

[0252] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0253] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0254] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0255] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0256] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0257] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0258] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0259] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0260] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0261] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a RSV antigenic polypeptide.

[0262] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a MeV antigenic polypeptide.

[0263] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a PIV3 antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0264] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0265] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0266] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a hMPV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0267] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0268] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a PIV3 antigenic polypeptide, a RSV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0269] In some embodiments, a combination RNA (e.g., mRNA) vaccine comprises a RNA (e.g., mRNA) polynucleotide encoding a RSV antigenic polypeptide, a MeV antigenic polypeptide and a BetaCoV antigenic polypeptide (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1).

[0270] Other combination respiratory virus RNA (e.g., mRNA) vaccines are encompassed by the present disclosure.

[0271] It has been discovered that the mRNA vaccines described herein are superior to current vaccines in several ways. First, the lipid nanoparticle (LNP) delivery is superior to other formulations including a protamine base approach described in the literature and no additional adjuvants are to be necessary. The use of LNPs enables the effective delivery of chemically modified or unmodified mRNA vaccines. Additionally it has been demonstrated herein that both modified and unmodified LNP formulated mRNA vaccines were superior to conventional vaccines by a significant degree. In some embodiments the mRNA vaccines of the invention are superior to conventional vaccines by a factor of at least 10 fold, 20 fold, 40 fold, 50 fold, 100 fold, 500 fold or 1,000 fold.

[0272] Although attempts have been made to produce functional RNA vaccines, including mRNA vaccines and self-replicating RNA vaccines, the therapeutic efficacy of these RNA vaccines have not yet been fully established. Quite surprisingly, the inventors have discovered, according to aspects of the invention a class of formulations for delivering mRNA vaccines in vivo that results in significantly enhanced, and in many respects synergistic, immune responses including enhanced antigen generation and functional antibody production with neutralization capability. These results can be achieved even when significantly lower doses of the mRNA are administered in comparison with mRNA doses used in other classes of lipid based formulations. The formulations of the invention have demonstrated significant unexpected in vivo immune responses sufficient to establish the efficacy of functional mRNA vaccines as prophylactic and therapeutic agents. Additionally, self-replicating RNA vaccines rely on viral replication pathways to deliver enough RNA to a cell to produce an immunogenic response. The formulations of the invention do not require viral replication to produce enough protein to result in a strong immune response. Thus, the mRNA of the invention are not self-replicating RNA and do not include components necessary for viral replication.

[0273] The invention involves, in some aspects, the surprising finding that lipid nanoparticle (LNP) formulations significantly enhance the effectiveness of mRNA vaccines, including chemically modified and unmodified mRNA vaccines. The efficacy of mRNA vaccines formulated in LNP was examined in vivo using several distinct antigens. The results presented herein demonstrate the unexpected superior efficacy of the mRNA vaccines formulated in LNP over other commercially available vaccines.

[0274] In addition to providing an enhanced immune response, the formulations of the invention generate a more rapid immune response with fewer doses of antigen than other vaccines tested. The mRNA-LNP formulations of the invention also produce quantitatively and qualitatively better immune responses than vaccines formulated in a different carriers.

[0275] The data described herein demonstrate that the formulations of the invention produced significant unexpected improvements over existing antigen vaccines. Additionally, the mRNA-LNP formulations of the invention are superior to other vaccines even when the dose of mRNA is lower than other vaccines. Mice immunized with either 10 .mu.g or 2 .mu.g doses of an hMPV fusion protein mRNA LNP vaccine or a PIV3 mRNA LNP vaccine produced neutralizing antibodies which for instance, successfully neutralized the hMPV B2 virus. A 10 .mu.g dose of mRNA vaccine protected 100% of mice from lethal challenge and drastically reduced the viral titer after challenge (.about.2 log reduction).

[0276] Two 20 .mu.g doses of MERS-CoV mRNA LNP vaccine significantly reduced viral load and induced significant amount of neutralizing antibodies against MERS-CoV (EC.sub.50 between 500-1000). The MERS-CoV mRNA vaccine induced antibody titer was 3-5 fold better than any other vaccines tested in the same model.

[0277] The LNP used in the studies described herein has been used previously to deliver siRNA in various animal models as well as in humans. In view of the observations made in association with the siRNA delivery of LNP formulations, the fact that LNP is useful in vaccines is quite surprising. It has been observed that therapeutic delivery of siRNA formulated in LNP causes an undesirable inflammatory response associated with a transient IgM response, typically leading to a reduction in antigen production and a compromised immune response. In contrast to the findings observed with siRNA, the LNP-mRNA formulations of the invention are demonstrated herein to generate enhanced IgG levels, sufficient for prophylactic and therapeutic methods rather than transient IgM responses.

Nucleic Acids/Polynucleotides

[0278] Respiratory virus vaccines, as provided herein, comprise at least one (one or more) ribonucleic acid (RNA) (e.g., mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide selected from hMPV, PIV3, RSV, MeV and BetaCoV (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) antigenic polypeptides. The term "nucleic acid" includes any compound and/or substance that comprises a polymer of nucleotides (nucleotide monomer). These polymers are referred to as polynucleotides. Thus, the terms "nucleic acid" and "polynucleotide" are used interchangeably.

[0279] Nucleic acids may be or may include, for example, ribonucleic acids (RNAs), deoxyribonucleic acids (DNAs), threose nucleic acids (TNAs), glycol nucleic acids (GNAs), peptide nucleic acids (PNAs), locked nucleic acids (LNAs, including LNA having a .beta.-D-ribo configuration, .alpha.-LNA having an .alpha.-L-ribo configuration (a diastereomer of LNA), 2'-amino-LNA having a 2'-amino functionalization, and 2'-amino-.alpha.-LNA having a 2'-amino functionalization), ethylene nucleic acids (ENA), cyclohexenyl nucleic acids (CeNA) or chimeras or combinations thereof.

[0280] In some embodiments, polynucleotides of the present disclosure function as messenger RNA (mRNA). "Messenger RNA" (mRNA) refers to any polynucleotide that encodes a (at least one) polypeptide (a naturally-occurring, non-naturally-occurring, or modified polymer of amino acids) and can be translated to produce the encoded polypeptide in vitro, in vivo, in situ or ex vivo. The skilled artisan will appreciate that, except where otherwise noted, polynucleotide sequences set forth in the instant application will recite "T"s in a representative DNA sequence but where the sequence represents RNA (e.g., mRNA), the "T"s would be substituted for "U"s. Thus, any of the RNA polynucleotides encoded by a DNA identified by a particular sequence identification number may also comprise the corresponding RNA (e.g., mRNA) sequence encoded by the DNA, where each "T" of the DNA sequence is substituted with "U."

[0281] The basic components of an mRNA molecule typically include at least one coding region, a 5' untranslated region (UTR), a 3' UTR, a 5' cap and a poly-A tail. Polynucleotides of the present disclosure may function as mRNA but can be distinguished from wild-type mRNA in their functional and/or structural design features, which serve to overcome existing problems of effective polypeptide expression using nucleic-acid based therapeutics.

[0282] In some embodiments, a RNA polynucleotide of an RNA (e.g., mRNA) vaccine encodes 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, 2-3, 3-10, 3-9, 3-8, 3-7, 3-6, 3-5, 3-4, 4-10, 4-9, 4-8, 4-7, 4-6, 4-5, 5-10, 5-9, 5-8, 5-7, 5-6, 6-10, 6-9, 6-8, 6-7, 7-10, 7-9, 7-8, 8-10, 8-9 or 9-10 antigenic polypeptides. In some embodiments, a RNA (e.g., mRNA) polynucleotide of a respiratory virus vaccine encodes at least 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 antigenic polypeptides. In some embodiments, a RNA (e.g., mRNA) polynucleotide of a respiratory virus vaccine encodes at least 100 or at least 200 antigenic polypeptides. In some embodiments, a RNA polynucleotide of an respiratory virus vaccine encodes 1-10, 5-15, 10-20, 15-25, 20-30, 25-35, 30-40, 35-45, 40-50, 1-50, 1-100, 2-50 or 2-100 antigenic polypeptides.

[0283] Polynucleotides of the present disclosure, in some embodiments, are codon optimized. Codon optimization methods are known in the art and may be used as provided herein. Codon optimization, in some embodiments, may be used to match codon frequencies in target and host organisms to ensure proper folding; bias GC content to increase mRNA stability or reduce secondary structures; minimize tandem repeat codons or base runs that may impair gene construction or expression; customize transcriptional and translational control regions; insert or remove protein trafficking sequences; remove/add post translation modification sites in encoded protein (e.g. glycosylation sites); add, remove or shuffle protein domains; insert or delete restriction sites; modify ribosome binding sites and mRNA degradation sites; adjust translational rates to allow the various domains of the protein to fold properly; or to reduce or eliminate problem secondary structures within the polynucleotide. Codon optimization tools, algorithms and services are known in the art--non-limiting examples include services from GeneArt (Life Technologies), DNA2.0 (Menlo Park Calif.) and/or proprietary methods. In some embodiments, the open reading frame (ORF) sequence is optimized using optimization algorithms.

[0284] In some embodiments, a codon optimized sequence shares less than 95% sequence identity, less than 90% sequence identity, less than 85% sequence identity, less than 80% sequence identity, or less than 75% sequence identity to a naturally-occurring or wild-type sequence (e.g., a naturally-occurring or wild-type mRNA sequence encoding a polypeptide or protein of interest (e.g., an antigenic protein or antigenic polypeptide)).

[0285] In some embodiments, a codon-optimized sequence shares between 65% and 85% (e.g., between about 67% and about 85%, or between about 67% and about 80%) sequence identity to a naturally-occurring sequence or a wild-type sequence (e.g., a naturally-occurring or wild-type mRNA sequence encoding a polypeptide or protein of interest (e.g., an antigenic protein or polypeptide)). In some embodiments, a codon-optimized sequence shares between 65% and 75%, or about 80% sequence identity to a naturally-occurring sequence or wild-type sequence (e.g., a naturally-occurring or wild-type mRNA sequence encoding a polypeptide or protein of interest (e.g., an antigenic protein or polypeptide)).

[0286] In some embodiments a codon-optimized RNA (e.g., mRNA) may, for instance, be one in which the levels of G/C are enhanced. The G/C-content of nucleic acid molecules may influence the stability of the RNA. RNA having an increased amount of guanine (G) and/or cytosine (C) residues may be functionally more stable than nucleic acids containing a large amount of adenine (A) and thymine (T) or uracil (U) nucleotides. WO02/098443 discloses a pharmaceutical composition containing an mRNA stabilized by sequence modifications in the translated region. Due to the degeneracy of the genetic code, the modifications work by substituting existing codons for those that promote greater RNA stability without changing the resulting amino acid. The approach is limited to coding regions of the RNA.

Antigens/Antigenic Polypeptides

[0287] In some embodiments, an antigenic polypeptide (e.g., a hMPV, PIV3, RSV, MeV or BetaCoV antigenic polypeptide) is longer than 25 amino acids and shorter than 50 amino acids. Polypeptides include gene products, naturally occurring polypeptides, synthetic polypeptides, homologs, orthologs, paralogs, fragments and other equivalents, variants, and analogs of the foregoing. A polypeptide may be a single molecule or may be a multi-molecular complex such as a dimer, trimer or tetramer. Polypeptides may also comprise single chain polypeptides or multichain polypeptides, such as antibodies or insulin, and may be associated or linked to each other. Most commonly, disulfide linkages are found in multichain polypeptides. The term "polypeptide" may also apply to amino acid polymers in which at least one amino acid residue is an artificial chemical analogue of a corresponding naturally-occurring amino acid.

[0288] A "polypeptide variant" is a molecule that differs in its amino acid sequence relative to a native sequence or a reference sequence. Amino acid sequence variants may possess substitutions, deletions, insertions, or a combination of any two or three of the foregoing, at certain positions within the amino acid sequence, as compared to a native sequence or a reference sequence. Ordinarily, variants possess at least 50% identity to a native sequence or a reference sequence. In some embodiments, variants share at least 80% identity or at least 90% identity with a native sequence or a reference sequence.

[0289] In some embodiments "variant mimics" are provided. A "variant mimic" contains at least one amino acid that would mimic an activated sequence. For example, glutamate may serve as a mimic for phosphoro-threonine and/or phosphoro-serine. Alternatively, variant mimics may result in deactivation or in an inactivated product containing the mimic. For example, phenylalanine may act as an inactivating substitution for tyrosine, or alanine may act as an inactivating substitution for serine.

[0290] "Orthologs" refers to genes in different species that evolved from a common ancestral gene by speciation. Normally, orthologs retain the same function in the course of evolution. Identification of orthologs is important for reliable prediction of gene function in newly sequenced genomes.

[0291] "Analogs" is meant to include polypeptide variants that differ by one or more amino acid alterations, for example, substitutions, additions or deletions of amino acid residues that still maintain one or more of the properties of the parent or starting polypeptide.

[0292] The present disclosure provides several types of compositions that are polynucleotide or polypeptide based, including variants and derivatives. These include, for example, substitutional, insertional, deletion and covalent variants and derivatives. The term "derivative" is synonymous with the term "variant" and generally refers to a molecule that has been modified and/or changed in any way relative to a reference molecule or a starting molecule.

[0293] As such, polynucleotides encoding peptides or polypeptides containing substitutions, insertions and/or additions, deletions and covalent modifications with respect to reference sequences, in particular the polypeptide sequences disclosed herein, are included within the scope of this disclosure. For example, sequence tags or amino acids, such as one or more lysines, can be added to peptide sequences (e.g., at the N-terminal or C-terminal ends). Sequence tags can be used for peptide detection, purification or localization. Lysines can be used to increase peptide solubility or to allow for biotinylation. Alternatively, amino acid residues located at the carboxy and amino terminal regions of the amino acid sequence of a peptide or protein may optionally be deleted providing for truncated sequences. Certain amino acids (e.g., C-terminal residues or N-terminal residues) alternatively may be deleted depending on the use of the sequence, as for example, expression of the sequence as part of a larger sequence that is soluble, or linked to a solid support.

[0294] "Substitutional variants" when referring to polypeptides are those that have at least one amino acid residue in a native or starting sequence removed and a different amino acid inserted in its place at the same position. Substitutions may be single, where only one amino acid in the molecule has been substituted, or they may be multiple, where two or more (e.g., 3, 4 or 5) amino acids have been substituted in the same molecule.

[0295] As used herein the term "conservative amino acid substitution" refers to the substitution of an amino acid that is normally present in the sequence with a different amino acid of similar size, charge, or polarity. Examples of conservative substitutions include the substitution of a non-polar (hydrophobic) residue such as isoleucine, valine and leucine for another non-polar residue. Likewise, examples of conservative substitutions include the substitution of one polar (hydrophilic) residue for another such as between arginine and lysine, between glutamine and asparagine, and between glycine and serine. Additionally, the substitution of a basic residue such as lysine, arginine or histidine for another, or the substitution of one acidic residue such as aspartic acid or glutamic acid for another acidic residue are additional examples of conservative substitutions. Examples of non-conservative substitutions include the substitution of a non-polar (hydrophobic) amino acid residue such as isoleucine, valine, leucine, alanine, methionine for a polar (hydrophilic) residue such as cysteine, glutamine, glutamic acid or lysine and/or a polar residue for a non-polar residue.

[0296] "Features" when referring to polypeptide or polynucleotide are defined as distinct amino acid sequence-based or nucleotide-based components of a molecule respectively. Features of the polypeptides encoded by the polynucleotides include surface manifestations, local conformational shape, folds, loops, half-loops, domains, half-domains, sites, termini and any combination(s) thereof.

[0297] As used herein when referring to polypeptides the term "domain" refers to a motif of a polypeptide having one or more identifiable structural or functional characteristics or properties (e.g., binding capacity, serving as a site for protein-protein interactions).

[0298] As used herein when referring to polypeptides the terms "site" as it pertains to amino acid based embodiments is used synonymously with "amino acid residue" and "amino acid side chain." As used herein when referring to polynucleotides the terms "site" as it pertains to nucleotide based embodiments is used synonymously with "nucleotide." A site represents a position within a peptide or polypeptide or polynucleotide that may be modified, manipulated, altered, derivatized or varied within the polypeptide-based or polynucleotide-based molecules.

[0299] As used herein the terms "termini" or "terminus" when referring to polypeptides or polynucleotides refers to an extremity of a polypeptide or polynucleotide respectively. Such extremity is not limited only to the first or final site of the polypeptide or polynucleotide but may include additional amino acids or nucleotides in the terminal regions. Polypeptide-based molecules may be characterized as having both an N-terminus (terminated by an amino acid with a free amino group (NH2)) and a C-terminus (terminated by an amino acid with a free carboxyl group (COOH)). Proteins are in some cases made up of multiple polypeptide chains brought together by disulfide bonds or by non-covalent forces (multimers, oligomers). These proteins have multiple N- and C-termini. Alternatively, the termini of the polypeptides may be modified such that they begin or end, as the case may be, with a non-polypeptide based moiety such as an organic conjugate.

[0300] As recognized by those skilled in the art, protein fragments, functional protein domains, and homologous proteins are also considered to be within the scope of polypeptides of interest. For example, provided herein is any protein fragment (meaning a polypeptide sequence at least one amino acid residue shorter than a reference polypeptide sequence but otherwise identical) of a reference protein having a length of 10, 20, 30, 40, 50, 60, 70, 80, 90, 100 or longer than 100 amino acids. In another example, any protein that includes a stretch of 20, 30, 40, 50, or 100 (contiguous) amino acids that are 40%, 50%, 60%, 70%, 80%, 90%, 95%, or 100% identical to any of the sequences described herein can be utilized in accordance with the disclosure. In some embodiments, a polypeptide includes 2, 3, 4, 5, 6, 7, 8, 9, 10, or more mutations as shown in any of the sequences provided herein or referenced herein. In another example, any protein that includes a stretch of 20, 30, 40, 50, or 100 amino acids that are greater than 80%, 90%, 95%, or 100% identical to any of the sequences described herein, wherein the protein has a stretch of 5, 10, 15, 20, 25, or 30 amino acids that are less than 80%, 75%, 70%, 65% to 60% identical to any of the sequences described herein can be utilized in accordance with the disclosure.

[0301] Polypeptide or polynucleotide molecules of the present disclosure may share a certain degree of sequence similarity or identity with the reference molecules (e.g., reference polypeptides or reference polynucleotides), for example, with art-described molecules (e.g., engineered or designed molecules or wild-type molecules). The term "identity," as known in the art, refers to a relationship between the sequences of two or more polypeptides or polynucleotides, as determined by comparing the sequences. In the art, identity also means the degree of sequence relatedness between two sequences as determined by the number of matches between strings of two or more amino acid residues or nucleic acid residues. Identity measures the percent of identical matches between the smaller of two or more sequences with gap alignments (if any) addressed by a particular mathematical model or computer program (e.g., "algorithms"). Identity of related peptides can be readily calculated by known methods. "% identity" as it applies to polypeptide or polynucleotide sequences is defined as the percentage of residues (amino acid residues or nucleic acid residues) in the candidate amino acid or nucleic acid sequence that are identical with the residues in the amino acid sequence or nucleic acid sequence of a second sequence after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent identity. Methods and computer programs for the alignment are well known in the art. Identity depends on a calculation of percent identity but may differ in value due to gaps and penalties introduced in the calculation. Generally, variants of a particular polynucleotide or polypeptide have at least 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% but less than 100% sequence identity to that particular reference polynucleotide or polypeptide as determined by sequence alignment programs and parameters described herein and known to those skilled in the art. Such tools for alignment include those of the BLAST suite (Stephen F. Altschul, et al. (1997)." Gapped BLAST and PSI-BLAST: a new generation of protein database search programs," Nucleic Acids Res. 25:3389-3402). Another popular local alignment technique is based on the Smith-Waterman algorithm (Smith, T. F. & Waterman, M. S. (1981) "Identification of common molecular subsequences." J. Mol. Biol. 147:195-197). A general global alignment technique based on dynamic programming is the Needleman-Wunsch algorithm (Needleman, S. B. & Wunsch, C. D. (1970) "A general method applicable to the search for similarities in the amino acid sequences of two proteins." J. Mol. Biol. 48:443-453). More recently, a Fast Optimal Global Sequence Alignment Algorithm (FOGSAA) was developed that purportedly produces global alignment of nucleotide and protein sequences faster than other optimal global alignment methods, including the Needleman-Wunsch algorithm. Other tools are described herein, specifically in the definition of "identity" below.

[0302] As used herein, the term "homology" refers to the overall relatedness between polymeric molecules, e.g. between nucleic acid molecules (e.g. DNA molecules and/or RNA molecules) and/or between polypeptide molecules. Polymeric molecules (e.g. nucleic acid molecules (e.g. DNA molecules and/or RNA molecules) and/or polypeptide molecules) that share a threshold level of similarity or identity determined by alignment of matching residues are termed homologous. Homology is a qualitative term that describes a relationship between molecules and can be based upon the quantitative similarity or identity. Similarity or identity is a quantitative term that defines the degree of sequence match between two compared sequences. In some embodiments, polymeric molecules are considered to be "homologous" to one another if their sequences are at least 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% identical or similar. The term "homologous" necessarily refers to a comparison between at least two sequences (polynucleotide or polypeptide sequences). Two polynucleotide sequences are considered homologous if the polypeptides they encode are at least 50%, 60%, 70%, 80%, 90%, 95%, or even 99% for at least one stretch of at least 20 amino acids. In some embodiments, homologous polynucleotide sequences are characterized by the ability to encode a stretch of at least 4-5 uniquely specified amino acids. For polynucleotide sequences less than 60 nucleotides in length, homology is determined by the ability to encode a stretch of at least 4-5 uniquely specified amino acids. Two protein sequences are considered homologous if the proteins are at least 50%, 60%, 70%, 80%, or 90% identical for at least one stretch of at least 20 amino acids.

[0303] Homology implies that the compared sequences diverged in evolution from a common origin. The term "homolog" refers to a first amino acid sequence or nucleic acid sequence (e.g., gene (DNA or RNA) or protein sequence) that is related to a second amino acid sequence or nucleic acid sequence by descent from a common ancestral sequence. The term "homolog" may apply to the relationship between genes and/or proteins separated by the event of speciation or to the relationship between genes and/or proteins separated by the event of genetic duplication. "Orthologs" are genes (or proteins) in different species that evolved from a common ancestral gene (or protein) by speciation. Typically, orthologs retain the same function in the course of evolution. "Paralogs" are genes (or proteins) related by duplication within a genome. Orthologs retain the same function in the course of evolution, whereas paralogs evolve new functions, even if these are related to the original one.

[0304] The term "identity" refers to the overall relatedness between polymeric molecules, for example, between polynucleotide molecules (e.g. DNA molecules and/or RNA molecules) and/or between polypeptide molecules. Calculation of the percent identity of two polynucleic acid sequences, for example, can be performed by aligning the two sequences for optimal comparison purposes (e.g., gaps can be introduced in one or both of a first and a second nucleic acid sequences for optimal alignment and non-identical sequences can be disregarded for comparison purposes). In certain embodiments, the length of a sequence aligned for comparison purposes is at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or 100% of the length of the reference sequence. The nucleotides at corresponding nucleotide positions are then compared. When a position in the first sequence is occupied by the same nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking into account the number of gaps, and the length of each gap, which needs to be introduced for optimal alignment of the two sequences. The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. For example, the percent identity between two nucleic acid sequences can be determined using methods such as those described in Computational Molecular Biology, Lesk, A. M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D. W., ed., Academic Press, New York, 1993; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; Computer Analysis of Sequence Data, Part I, Griffin, A. M., and Griffin, H. G., eds., Humana Press, New Jersey, 1994; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991; each of which is incorporated herein by reference. For example, the percent identity between two nucleic acid sequences can be determined using the algorithm of Meyers and Miller (CABIOS, 1989, 4:11-17), which has been incorporated into the ALIGN program (version 2.0) using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. The percent identity between two nucleic acid sequences can, alternatively, be determined using the GAP program in the GCG software package using an NWSgapdna.CMP matrix. Methods commonly employed to determine percent identity between sequences include, but are not limited to those disclosed in Carillo, H., and Lipman, D., SIAM J Applied Math., 48:1073 (1988); incorporated herein by reference. Techniques for determining identity are codified in publicly available computer programs. Exemplary computer software to determine homology between two sequences include, but are not limited to, GCG program package, Devereux, J., et al., Nucleic Acids Research, 12(1), 387 (1984)), BLASTP, BLASTN, and FASTA Altschul, S. F. et al., J. Molec. Biol., 215, 403 (1990)).

Multiprotein and Multicomponent Vaccines

[0305] The present disclosure encompasses respiratory virus vaccines comprising multiple RNA (e.g., mRNA) polynucleotides, each encoding a single antigenic polypeptide, as well as respiratory virus vaccines comprising a single RNA polynucleotide encoding more than one antigenic polypeptide (e.g., as a fusion polypeptide). Thus, a vaccine composition comprising a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a first antigenic polypeptide and a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a second antigenic polypeptide encompasses (a) vaccines that comprise a first RNA polynucleotide encoding a first antigenic polypeptide and a second RNA polynucleotide encoding a second antigenic polypeptide, and (b) vaccines that comprise a single RNA polynucleotide encoding a first and second antigenic polypeptide (e.g., as a fusion polypeptide). RNA (e.g., mRNA) vaccines of the present disclosure, in some embodiments, comprise 2-10 (e.g., 2, 3, 4, 5, 6, 7, 8, 9 or 10), or more, RNA polynucleotides having an open reading frame, each of which encodes a different antigenic polypeptide (or a single RNA polynucleotide encoding 2-10, or more, different antigenic polypeptides). The antigenic polypeptides may be selected from hMPV, PIV3, RSV, MEV and BetaCoV (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) antigenic polypeptides.

[0306] In some embodiments, a respiratory virus vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral capsid protein, a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral premembrane/membrane protein, and a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral envelope protein. In some embodiments, a respiratory virus vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral fusion (F) protein and a RNA polynucleotide having an open reading frame encoding a viral major surface glycoprotein (G protein). In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral F protein. In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a viral G protein. In some embodiments, a vaccine comprises a RNA (e.g., mRNA) polynucleotide having an open reading frame encoding a HN protein.

[0307] In some embodiments, a multicomponent vaccine comprises at least one RNA (e.g., mRNA) polynucleotide encoding at least one antigenic polypeptide fused to a signal peptide (e.g., any one of SEQ ID NO: 15-19). The signal peptide may be fused at the N-terminus or the C-terminus of an antigenic polypeptide. An antigenic polypeptide fused to a signal peptide may be selected from hMPV, PIV3, RSV, MEV and BetaCoV (e.g., selected from MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and HCoV-HKU1) antigenic polypeptides.

Signal Peptides

[0308] In some embodiments, antigenic polypeptides encoded by respiratory virus RNA (e.g., mRNA) polynucleotides comprise a signal peptide. Signal peptides, comprising the N-terminal 15-60 amino acids of proteins, are typically needed for the translocation across the membrane on the secretory pathway and, thus, universally control the entry of most proteins both in eukaryotes and prokaryotes to the secretory pathway. Signal peptides generally include three regions: an N-terminal region of differing length, which usually comprises positively charged amino acids; a hydrophobic region; and a short carboxy-terminal peptide region. In eukaryotes, the signal peptide of a nascent precursor protein (pre-protein) directs the ribosome to the rough endoplasmic reticulum (ER) membrane and initiates the transport of the growing peptide chain across it for processing. ER processing produces mature proteins, wherein the signal peptide is cleaved from precursor proteins, typically by a ER-resident signal peptidase of the host cell, or they remain uncleaved and function as a membrane anchor. A signal peptide may also facilitate the targeting of the protein to the cell membrane. The signal peptide, however, is not responsible for the final destination of the mature protein. Secretory proteins devoid of additional address tags in their sequence are by default secreted to the external environment. During recent years, a more advanced view of signal peptides has evolved, showing that the functions and immunodominance of certain signal peptides are much more versatile than previously anticipated.

[0309] Respiratory virus vaccines of the present disclosure may comprise, for example, RNA (e.g., mRNA) polynucleotides encoding an artificial signal peptide, wherein the signal peptide coding sequence is operably linked to and is in frame with the coding sequence of the antigenic polypeptide. Thus, respiratory virus vaccines of the present disclosure, in some embodiments, produce an antigenic polypeptide comprising an antigenic polypeptide (e.g., hMPV, PIV3, RSV, MeV or BetaCoV) fused to a signal peptide. In some embodiments, a signal peptide is fused to the N-terminus of the antigenic polypeptide. In some embodiments, a signal peptide is fused to the C-terminus of the antigenic polypeptide.

[0310] In some embodiments, the signal peptide fused to the antigenic polypeptide is an artificial signal peptide. In some embodiments, an artificial signal peptide fused to the antigenic polypeptide encoded by the RNA (e.g., mRNA) vaccine is obtained from an immunoglobulin protein, e.g., an IgE signal peptide or an IgG signal peptide. In some embodiments, a signal peptide fused to the antigenic polypeptide encoded by a RNA (e.g., mRNA) vaccine is an Ig heavy chain epsilon-1 signal peptide (IgE HC SP) having the sequence of: MDWTWILFLVAAATRVHS (SEQ ID NO: 16). In some embodiments, a signal peptide fused to the antigenic polypeptide encoded by the (e.g., mRNA) RNA (e.g., mRNA) vaccine is an IgGk chain V-III region HAH signal peptide (IgGk SP) having the sequence of METPAQLLFLLLLWLPDTTG (SEQ ID NO: 15). In some embodiments, the signal peptide is selected from: Japanese encephalitis PRM signal sequence (MLGSNSGQRVVFTILLLLVAPAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVSLAIVTACAGA; SEQ ID NO: 19).

[0311] In some embodiments, the antigenic polypeptide encoded by a RNA (e.g., mRNA) vaccine comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8, 12-13, 24-34, 47-50 or 54-56 (Tables 3, 6, 11, 14 or 17; see also amino acid sequences of Tables 4, 7, 12 or 15) fused to a signal peptide identified by any one of SEQ ID NO: 15-19 (Table 8). The examples disclosed herein are not meant to be limiting and any signal peptide that is known in the art to facilitate targeting of a protein to ER for processing and/or targeting of a protein to the cell membrane may be used in accordance with the present disclosure.

[0312] A signal peptide may have a length of 15-60 amino acids. For example, a signal peptide may have a length of 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, or 60 amino acids. In some embodiments, a signal peptide has a length of 20-60, 25-60, 30-60, 35-60, 40-60, 45-60, 50-60, 55-60, 15-55, 20-55, 25-55, 30-55, 35-55, 40-55, 45-55, 50-55, 15-50, 20-50, 25-50, 30-50, 35-50, 40-50, 45-50, 15-45, 20-45, 25-45, 30-45, 35-45, 40-45, 15-40, 20-40, 25-40, 30-40, 35-40, 15-35, 20-35, 25-35, 30-35, 15-30, 20-30, 25-30, 15-25, 20-25, or 15-20 amino acids.

[0313] A signal peptide is typically cleaved from the nascent polypeptide at the cleavage junction during ER processing. The mature antigenic polypeptide produce by a respiratory virus RNA (e.g., mRNA) vaccine of the present disclosure typically does not comprise a signal peptide.

Chemical Modifications

[0314] Respiratory virus vaccines of the present disclosure, in some embodiments, comprise at least RNA (e.g. mRNA) polynucleotide having an open reading frame encoding at least one antigenic polypeptide that comprises at least one chemical modification.

[0315] The terms "chemical modification" and "chemically modified" refer to modification with respect to adenosine (A), guanosine (G), uridine (U), thymidine (T) or cytidine (C) ribonucleosides or deoxyribnucleosides in at least one of their position, pattern, percent or population. Generally, these terms do not refer to the ribonucleotide modifications in naturally occurring 5'-terminal mRNA cap moieties. With respect to a polypeptide, the term "modification" refers to a modification relative to the canonical set 20 amino acids. Polypeptides, as provided herein, are also considered "modified" of they contain amino acid substitutions, insertions or a combination of substitutions and insertions.

[0316] Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides), in some embodiments, comprise various (more than one) different modifications. In some embodiments, a particular region of a polynucleotide contains one, two or more (optionally different) nucleoside or nucleotide modifications. In some embodiments, a modified RNA polynucleotide (e.g., a modified mRNA polynucleotide), introduced to a cell or organism, exhibits reduced degradation in the cell or organism, respectively, relative to an unmodified polynucleotide. In some embodiments, a modified RNA polynucleotide (e.g., a modified mRNA polynucleotide), introduced into a cell or organism, may exhibit reduced immunogenicity in the cell or organism, respectively (e.g., a reduced innate response).

[0317] Modifications of polynucleotides include, without limitation, those described herein. Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) may comprise modifications that are naturally-occurring, non-naturally-occurring or the polynucleotide may comprise a combination of naturally-occurring and non-naturally-occurring modifications. Polynucleotides may include any useful modification, for example, of a sugar, a nucleobase, or an internucleoside linkage (e.g., to a linking phosphate, to a phosphodiester linkage or to the phosphodiester backbone).

[0318] Polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides), in some embodiments, comprise non-natural modified nucleotides that are introduced during synthesis or post-synthesis of the polynucleotides to achieve desired functions or properties. The modifications may be present on an internucleotide linkages, purine or pyrimidine bases, or sugars. The modification may be introduced with chemical synthesis or with a polymerase enzyme at the terminal of a chain or anywhere else in the chain. Any of the regions of a polynucleotide may be chemically modified.

[0319] The present disclosure provides for modified nucleosides and nucleotides of a polynucleotide (e.g., RNA polynucleotides, such as mRNA polynucleotides). A "nucleoside" refers to a compound containing a sugar molecule (e.g., a pentose or ribose) or a derivative thereof in combination with an organic base (e.g., a purine or pyrimidine) or a derivative thereof (also referred to herein as "nucleobase"). A nucleotide" refers to a nucleoside, including a phosphate group. Modified nucleotides may by synthesized by any useful method, such as, for example, chemically, enzymatically, or recombinantly, to include one or more modified or non-natural nucleosides. Polynucleotides may comprise a region or regions of linked nucleosides. Such regions may have variable backbone linkages. The linkages may be standard phosphdioester linkages, in which case the polynucleotides would comprise regions of nucleotides.

[0320] Modified nucleotide base pairing encompasses not only the standard adenosine-thymine, adenosine-uracil, or guanosine-cytosine base pairs, but also base pairs formed between nucleotides and/or modified nucleotides comprising non-standard or modified bases, wherein the arrangement of hydrogen bond donors and hydrogen bond acceptors permits hydrogen bonding between a non-standard base and a standard base or between two complementary non-standard base structures. One example of such non-standard base pairing is the base pairing between the modified nucleotide inosine and adenine, cytosine or uracil. Any combination of base/sugar or linker may be incorporated into polynucleotides of the present disclosure.

[0321] Modifications of polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) that are useful in the vaccines of the present disclosure include, but are not limited to the following: 2-methylthio-N6-(cis-hydroxyisopentenyl)adenosine; 2-methylthio-N6-methyladenosine; 2-methylthio-N6-threonyl carbamoyladenosine; N6-glycinylcarbamoyladenosine; N6-isopentenyladenosine; N6-methyladenosine; N6-threonylcarbamoyladeno sine; 1,2'-O-dimethyladenosine; 1-methyladenosine; 2'-O-methyladenosine; 2'-O-ribosyladenosine (phosphate); 2-methyladenosine; 2-methylthio-N6 isopentenyladenosine; 2-methylthio-N6-hydroxynorvalyl carbamoyladenosine; 2'-O-methyladenosine; 2'-O-ribosyladenosine (phosphate); Isopentenyladenosine; N6-(cis-hydroxyisopentenyl)adenosine; N6,2'-O-dimethyladenosine; N6,2'-O-dimethyladenosine; N6,N6,2'-O-trimethyladenosine; N6,N6-dimethyladenosine; N6-acetyladenosine; N6-hydroxynorvalylcarbamoyladenosine; N6-methyl-N6-threonylcarbamoyladenosine; 2-methyladenosine; 2-methylthio-N6-isopentenyladenosine; 7-deaza-adenosine; N1-methyl-adenosine; N6,N6 (dimethyl)adenine; N6-cis-hydroxy-isopentenyl-adenosine; .alpha.-thio-adenosine; 2 (amino)adenine; 2 (aminopropyl)adenine; 2 (methylthio) N6 (isopentenyl)adenine; 2-(alkyl)adenine; 2-(aminoalkyl)adenine; 2-(aminopropyl)adenine; 2-(halo)adenine; 2-(halo)adenine; 2-(propyl)adenine; 2'-Amino-2'-deoxy-ATP; 2'-Azido-2'-deoxy-ATP; 2'-Deoxy-2'-a-aminoadenosine TP; 2'-Deoxy-2'-a-azidoadenosine TP; 6 (alkyl)adenine; 6 (methyl)adenine; 6-(alkyl)adenine; 6-(methyl)adenine; 7 (deaza)adenine; 8 (alkenyl)adenine; 8 (alkynyl)adenine; 8 (amino)adenine; 8 (thioalkyl)adenine; 8-(alkenyl)adenine; 8-(alkyl)adenine; 8-(alkynyl)adenine; 8-(amino)adenine; 8-(halo)adenine; 8-(hydroxyl)adenine; 8-(thioalkyl)adenine; 8-(thiol)adenine; 8-azido-adeno sine; aza adenine; deaza adenine; N6 (methyl)adenine; N6-(isopentyl)adenine; 7-deaza-8-aza-adenosine; 7-methyladenine; 1-Deazaadenosine TP; 2'Fluoro-N6-Bz-deoxyadenosine TP; 2'-OMe-2-Amino-ATP; 2'O-methyl-N6-Bz-deoxyadenosine TP; 2'-a-Ethynyladenosine TP; 2-aminoadenine; 2-Aminoadenosine TP; 2-Amino-ATP; 2'-a-Trifluoromethyladenosine TP; 2-Azidoadenosine TP; 2'-b-Ethynyladenosine TP; 2-Bromoadenosine TP; 2'-b-Trifluoromethyladenosine TP; 2-Chloroadenosine TP; 2'-Deoxy-2',2'-difluoroadenosine TP; 2'-Deoxy-2'-a-mercaptoadenosine TP; 2'-Deoxy-2'-a-thiomethoxyadenosine TP; 2'-Deoxy-2'-b-aminoadenosine TP; 2'-Deoxy-2'-b-azidoadenosine TP; 2'-Deoxy-2'-b-bromoadenosine TP; 2'-Deoxy-2'-b-chloroadenosine TP; 2'-Deoxy-2'-b-fluoroadenosine TP; 2'-Deoxy-2'-b-iodoadenosine TP; 2'-Deoxy-2'-b-mercaptoadenosine TP; 2'-Deoxy-2'-b-thiomethoxyadenosine TP; 2-Fluoroadenosine TP; 2-Iodoadenosine TP; 2-Mercaptoadenosine TP; 2-methoxy-adenine; 2-methylthio-adenine; 2-Trifluoromethyladenosine TP; 3-Deaza-3-bromoadenosine TP; 3-Deaza-3-chloroadenosine TP; 3-Deaza-3-fluoroadenosine TP; 3-Deaza-3-iodoadenosine TP; 3-Deazaadenosine TP; 4'-Azidoadenosine TP; 4'-Carbocyclic adenosine TP; 4'-Ethynyladenosine TP; 5'-Homo-adenosine TP; 8-Aza-ATP; 8-bromo-adenosine TP; 8-Trifluoromethyladenosine TP; 9-Deazaadenosine TP; 2-aminopurine; 7-deaza-2,6-diaminopurine; 7-deaza-8-aza-2,6-diaminopurine; 7-deaza-8-aza-2-aminopurine; 2,6-diaminopurine; 7-deaza-8-aza-adenine, 7-deaza-2-aminopurine; 2-thiocytidine; 3-methylcytidine; 5-formylcytidine; 5-hydroxymethylcytidine; 5-methylcytidine; N4-acetylcytidine; 2'-O-methylcytidine; 2'-O-methylcytidine; 5,2'-O-dimethylcytidine; 5-formyl-2'-O-methylcytidine; Lysidine; N4,2'-O-dimethylcytidine; N4-acetyl-2'-O-methylcytidine; N4-methylcytidine; N4,N4-Dimethyl-2'-OMe-Cytidine TP; 4-methylcytidine; 5-aza-cytidine; Pseudo-iso-cytidine; pyrrolo-cytidine; .alpha.-thio-cytidine; 2-(thio)cytosine; 2'-Amino-2'-deoxy-CTP; 2'-Azido-2'-deoxy-CTP; 2'-Deoxy-2'-a-aminocytidine TP; 2'-Deoxy-2'-a-azidocytidine TP; 3 (deaza) 5 (aza)cytosine; 3 (methyl)cytosine; 3-(alkyl)cytosine; 3-(deaza) 5 (aza)cytosine; 3-(methyl)cytidine; 4,2'-O-dimethylcytidine; 5 (halo)cytosine; 5 (methyl)cytosine; 5 (propynyl)cytosine; 5 (trifluoromethyl)cytosine; 5-(alkyl)cytosine; 5-(alkynyl)cytosine; 5-(halo)cytosine; 5-(propynyl)cytosine; 5-(trifluoromethyl)cytosine; 5-bromo-cytidine; 5-iodo-cytidine; 5-propynyl cytosine; 6-(azo)cytosine; 6-aza-cytidine; aza cytosine; deaza cytosine; N4 (acetyl)cytosine; 1-methyl-1-deaza-pseudoisocytidine; 1-methyl-pseudoisocytidine; 2-methoxy-5-methyl-cytidine; 2-methoxy-cytidine; 2-thio-5-methyl-cytidine; 4-methoxy-1-methyl-pseudoisocytidine; 4-methoxy-pseudoisocytidine; 4-thio-1-methyl-1-deaza-pseudoisocytidine; 4-thio-1-methyl-pseudoisocytidine; 4-thio-pseudoisocytidine; 5-aza-zebularine; 5-methyl-zebularine; pyrrolo-pseudoisocytidine; Zebularine; (E)-5-(2-Bromo-vinyl)cytidine TP; 2,2'-anhydro-cytidine TP hydrochloride; 2'Fluor-N4-Bz-cytidine TP; 2'Fluoro-N4-Acetyl-cytidine TP; 2'-O-Methyl-N4-Acetyl-cytidine TP; 2'O-methyl-N4-Bz-cytidine TP; 2'-a-Ethynylcytidine TP; 2'-a-Trifluoromethylcytidine TP; 2'-b-Ethynylcytidine TP; 2'-b-Trifluoromethylcytidine TP; 2'-Deoxy-2',2'-difluorocytidine TP; 2'-Deoxy-2'-a-mercaptocytidine TP; 2'-Deoxy-2'-a-thiomethoxycytidine TP; 2'-Deoxy-2'-b-aminocytidine TP; 2'-Deoxy-2'-b-azidocytidine TP; 2'-Deoxy-2'-b-bromocytidine TP; 2'-Deoxy-2'-b-chlorocytidine TP; 2'-Deoxy-2'-b-fluorocytidine TP; 2'-Deoxy-2'-b-iodocytidine TP; 2'-Deoxy-2'-b-mercaptocytidine TP; 2'-Deoxy-2'-b-thiomethoxycytidine TP; 2'-O-Methyl-5-(1-propynyl)cytidine TP; 3'-Ethynylcytidine TP; 4'-Azidocytidine TP; 4'-Carbocyclic cytidine TP; 4'-Ethynylcytidine TP; 5-(1-Propynyl)ara-cytidine TP; 5-(2-Chloro-phenyl)-2-thiocytidine TP; 5-(4-Amino-phenyl)-2-thiocytidine TP; 5-Aminoallyl-CTP; 5-Cyanocytidine TP; 5-Ethynylara-cytidine TP; 5-Ethynylcytidine TP; 5'-Homo-cytidine TP; 5-Methoxycytidine TP; 5-Trifluoromethyl-Cytidine TP; N4-Amino-cytidine TP; N4-Benzoyl-cytidine TP; Pseudoisocytidine; 7-methylguanosine; N2,2'-O-dimethylguanosine; N2-methylguanosine; Wyosine; 1,2'-O-dimethylguanosine; 1-methylguanosine; 2'-O-methylguanosine; 2'-O-ribosylguanosine (phosphate); 2'-O-methylguanosine; 2'-O-ribosylguanosine (phosphate); 7-aminomethyl-7-deazaguanosine; 7-cyano-7-deazaguanosine; Archaeosine; Methylwyo sine; N2,7-dimethylguanosine; N2,N2,2'-O-trimethylguanosine; N2,N2,7-trimethylguanosine; N2,N2-dimethylguanosine; N2,7,2'-O-trimethylguanosine; 6-thio-guanosine; 7-deaza-guanosine; 8-oxo-guanosine; N1-methyl-guanosine; .alpha.-thio-guanosine; 2 (propyl)guanine; 2-(alkyl)guanine; 2'-Amino-2'-deoxy-GTP; 2'-Azido-2'-deoxy-GTP; 2'-Deoxy-2'-a-aminoguanosine TP; 2'-Deoxy-2'-a-azidoguanosine TP; 6 (methyl)guanine; 6-(alkyl)guanine; 6-(methyl)guanine; 6-methyl-guanosine; 7 (alkyl)guanine; 7 (deaza)guanine; 7 (methyl)guanine; 7-(alkyl)guanine; 7-(deaza)guanine; 7-(methyl)guanine; 8 (alkyl)guanine; 8 (alkynyl)guanine; 8 (halo)guanine; 8 (thioalkyl)guanine; 8-(alkenyl)guanine; 8-(alkyl)guanine; 8-(alkynyl)guanine; 8-(amino)guanine; 8-(halo)guanine; 8-(hydroxyl)guanine; 8-(thioalkyl)guanine; 8-(thiol)guanine; aza guanine; deaza guanine; N (methyl)guanine; N-(methyl)guanine; 1-methyl-6-thio-guanosine; 6-methoxy-guanosine; 6-thio-7-deaza-8-aza-guanosine; 6-thio-7-deaza-guanosine; 6-thio-7-methyl-guanosine; 7-deaza-8-aza-guanosine; 7-methyl-8-oxo-guanosine; N2,N2-dimethyl-6-thio-guanosine; N2-methyl-6-thio-guanosine; 1-Me-GTP; 2'Fluoro-N2-isobutyl-guanosine TP; 2'O-methyl-N2-isobutyl-guanosine TP; 2'-a-Ethynylguanosine TP; 2'-a-Trifluoromethylguanosine TP; 2'-b-Ethynylguano sine TP; 2'-b-Trifluoromethylguanosine TP; 2'-Deoxy-2',2'-difluoroguanosine TP; 2'-Deoxy-2'-a-mercaptoguanosine TP; 2'-Deoxy-2'-a-thiomethoxyguanosine TP; 2'-Deoxy-2'-b-aminoguanosine TP; 2'-Deoxy-2'-b-azidoguanosine TP; 2'-Deoxy-2'-b-bromoguanosine TP; 2'-Deoxy-2'-b-chloroguanosine TP; 2'-Deoxy-2'-b-fluoroguanosine TP; 2'-Deoxy-2'-b-iodoguanosine TP; 2'-Deoxy-2'-b-mercaptoguanosine TP; 2'-Deoxy-2'-b-thiomethoxyguanosine TP; 4'-Azidoguanosine TP; 4'-Carbocyclic guanosine TP; 4'-Ethynylguanosine TP; 5'-Homo-guanosine TP; 8-bromo-guanosine TP; 9-Deazaguanosine TP; N2-isobutyl-guanosine TP; 1-methylinosine; Inosine; 1,2'-O-dimethylinosine; 2'-O-methylinosine; 7-methylinosine; 2'-O-methylinosine; Epoxyqueuosine; galactosyl-queuosine; Mannosylqueuosine; Queuosine; allyamino-thymidine; aza thymidine; deaza thymidine; deoxy-thymidine; 2'-O-methyluridine; 2-thiouridine; 3-methyluridine; 5-carboxymethyluridine; 5-hydroxyuridine; 5-methyluridine; 5-taurinomethyl-2-thiouridine; 5-taurinomethyluridine; Dihydrouridine; Pseudouridine; (3-(3-amino-3-carboxypropyl)uridine; 1-methyl-3-(3-amino-5-carboxypropyl)pseudouridine; 1-methylpseduouridine; 1-methyl-pseudouridine; 2'-O-methyluridine; 2'-O-methylpseudouridine; 2'-O-methyluridine; 2-thio-2'-O-methyluridine; 3-(3-amino-3-carboxypropyl)uridine; 3,2'-O-dimethyluridine; 3-Methyl-pseudo-Uridine TP; 4-thiouridine; 5-(carboxyhydroxymethyl)uridine; 5-(carboxyhydroxymethyl)uridine methyl ester; 5,2'-O-dimethyluridine; 5,6-dihydro-uridine; 5-aminomethyl-2-thiouridine; 5-carbamoylmethyl-2'-O-methyluridine; 5-carbamoylmethyluridine; 5-carboxyhydroxymethyluridine; 5-carboxyhydroxymethyluridine methyl ester; 5-carboxymethylaminomethyl-2'-O-methyluridine; 5-carboxymethylaminomethyl-2-thiouridine; 5-carboxymethylaminomethyl-2-thiouridine; 5-carboxymethylaminomethyluridine; 5-carboxymethylaminomethyluridine; 5-Carbamoylmethyluridine TP; 5-methoxycarbonylmethyl-2'-O-methyluridine; 5-methoxycarbonylmethyl-2-thiouridine; 5-methoxycarbonylmethyluridine; 5-methoxyuridine; 5-methyl-2-thiouridine; 5-methylaminomethyl-2-selenouridine; 5-methylaminomethyl-2-thiouridine; 5-methylaminomethyluridine; 5-Methyldihydrouridine; 5-Oxyacetic acid-Uridine TP; 5-Oxyacetic acid-methyl ester-Uridine TP; N1-methyl-pseudo-uridine; uridine 5-oxyacetic acid; uridine 5-oxyacetic acid methyl ester; 3-(3-Amino-3-carboxypropyl)-Uridine TP; 5-(iso-Pentenylaminomethyl)-2-thiouridine TP; 5-(iso-Pentenylaminomethyl)-2'-O-methyluridine TP; 5-(iso-Pentenylaminomethyl)uridine TP; 5-propynyl uracil; .alpha.-thio-uridine; 1 (aminoalkylamino-carbonylethylenyl)-2(thio)-pseudouracil; 1 (aminoalkylaminocarbonylethylenyl)-2,4-(dithio)pseudouracil; 1 (aminoalkylaminocarbonylethylenyl)-4 (thio)pseudouracil; 1 (aminoalkylaminocarbonylethylenyl)-pseudouracil; 1 (aminocarbonylethylenyl)-2(thio)-pseudouracil; 1 (aminocarbonylethylenyl)-2,4-(dithio)pseudouracil; 1 (aminocarbonylethylenyl)-4 (thio)pseudouracil; 1 (aminocarbonylethylenyl)-pseudouracil; 1 substituted 2(thio)-pseudouracil; 1 substituted 2,4-(dithio)pseudouracil; 1 substituted 4 (thio)pseudouracil; 1 substituted pseudouracil; 1-(aminoalkylamino-carbonylethylenyl)-2-(thio)-pseudouracil; 1-Methyl-3-(3-amino-3-carboxypropyl) pseudouridine TP; 1-Methyl-3-(3-amino-3-carboxypropyl)pseudo-UTP; 1-Methyl-pseudo-UTP; 2 (thio)pseudouracil; 2' deoxy uridine; 2' fluorouridine; 2-(thio)uracil; 2,4-(dithio)psuedouracil; 2' methyl, 2'amino, 2'azido, 2'fluro-guanosine; 2'-Amino-2'-deoxy-UTP; 2'-Azido-2'-deoxy-UTP; 2'-Azido-deoxyuridine TP; 2'-O-methylpseudouridine; 2' deoxy uridine; 2' fluorouridine; 2'-Deoxy-2'-a-aminouridine TP; 2'-Deoxy-2'-a-azidouridine TP; 2-methylpseudouridine; 3 (3 amino-3 carboxypropyl)uracil; 4 (thio)pseudouracil; 4-(thio)pseudouracil; 4-(thio)uracil; 4-thiouracil; 5 (1,3-diazole-1-alkyl)uracil; 5 (2-aminopropyl)uracil; 5 (aminoalkyl)uracil; 5 (dimethylaminoalkyl)uracil; 5 (guanidiniumalkyl)uracil; 5 (methoxycarbonylmethyl)-2-(thio)uracil; 5 (methoxycarbonyl-methyl)uracil; 5 (methyl) 2 (thio)uracil; 5 (methyl) 2,4 (dithio)uracil; 5 (methyl) 4 (thio)uracil; 5 (methylaminomethyl)-2 (thio)uracil; 5 (methylaminomethyl)-2,4 (dithio)uracil; 5 (methylaminomethyl)-4 (thio)uracil; 5 (propynyl)uracil; 5 (trifluoromethyl)uracil; 5-(2-aminopropyl)uracil; 5-(alkyl)-2-(thio)pseudouracil; 5-(alkyl)-2,4 (dithio)pseudouracil; 5-(alkyl)-4 (thio)pseudouracil; 5-(alkyl)pseudouracil; 5-(alkyl)uracil; 5-

(alkynyl)uracil; 5-(allylamino)uracil; 5-(cyanoalkyl)uracil; 5-(dialkylaminoalkyl)uracil; 5-(dimethylaminoalkyl)uracil; 5-(guanidiniumalkyl)uracil; 5-(halo)uracil; 5-(1,3-diazole-1-alkyl)uracil; 5-(methoxy)uracil; 5-(methoxycarbonylmethyl)-2-(thio)uracil; 5-(methoxycarbonyl-methyl)uracil; 5-(methyl) 2(thio)uracil; 5-(methyl) 2,4 (dithio)uracil; 5-(methyl) 4 (thio)uracil; 5-(methyl)-2-(thio)pseudouracil; 5-(methyl)-2,4 (dithio)pseudouracil; 5-(methyl)-4 (thio)pseudouracil; 5-(methyl)pseudouracil; 5-(methylaminomethyl)-2 (thio)uracil; 5-(methylaminomethyl)-2,4(dithio)uracil; 5-(methylaminomethyl)-4-(thio)uracil; 5-(propynyl)uracil; 5-(trifluoromethyl)uracil; 5-aminoallyl-uridine; 5-bromo-uridine; 5-iodo-uridine; 5-uracil; 6 (azo)uracil; 6-(azo)uracil; 6-aza-uridine; allyamino-uracil; aza uracil; deaza uracil; N3 (methyl)uracil; Pseudo-UTP-1-2-ethanoic acid; Pseudouracil; 4-Thio-pseudo-UTP; 1-carboxymethyl-pseudouridine; 1-methyl-1-deaza-pseudouridine; 1-propynyl-uridine; 1-taurinomethyl-1-methyl-uridine; 1-taurinomethyl-4-thio-uridine; 1-taurinomethyl-pseudouridine; 2-methoxy-4-thio-pseudouridine; 2-thio-1-methyl-1-deaza-pseudouridine; 2-thio-1-methyl-pseudouridine; 2-thio-5-aza-uridine; 2-thio-dihydropseudouridine; 2-thio-dihydrouridine; 2-thio-pseudouridine; 4-methoxy-2-thio-pseudouridine; 4-methoxy-pseudouridine; 4-thio-1-methyl-pseudouridine; 4-thio-pseudouridine; 5-aza-uridine; Dihydropseudouridine; (.+-.)1-(2-Hydroxypropyl)pseudouridine TP; (2R)-1-(2-Hydroxypropyl)pseudouridine TP; (2S)-1-(2-Hydroxypropyl)pseudouridine TP; (E)-5-(2-Bromo-vinyl)ara-uridine TP; (E)-5-(2-Bromo-vinyl)uridine TP; (Z)-5-(2-Bromo-vinyl)ara-uridine TP; (Z)-5-(2-Bromo-vinyl)uridine TP; 1-(2,2,2-Trifluoroethyl)-pseudo-UTP; 1-(2,2,3,3,3-Pentafluoropropyl)pseudouridine TP; 1-(2,2-Diethoxyethyl)pseudouridine TP; 1-(2,4,6-Trimethylbenzyl)pseudouridine TP; 1-(2,4,6-Trimethyl-benzyl)pseudo-UTP; 1-(2,4,6-Trimethyl-phenyl)pseudo-UTP; 1-(2-Amino-2-carboxyethyl)pseudo-UTP; 1-(2-Amino-ethyl)pseudo-UTP; 1-(2-Hydroxyethyl)pseudouridine TP; 1-(2-Methoxyethyl)pseudouridine TP; 1-(3,4-Bis-trifluoromethoxybenzyl)pseudouridine TP; 1-(3,4-Dimethoxybenzyl)pseudouridine TP; 1-(3-Amino-3-carboxypropyl)pseudo-UTP; 1-(3-Amino-propyl)pseudo-UTP; 1-(3-Cyclopropyl-prop-2-ynyl)pseudouridine TP; 1-(4-Amino-4-carboxybutyl)pseudo-UTP; 1-(4-Amino-benzyl)pseudo-UTP; 1-(4-Amino-butyl)pseudo-UTP; 1-(4-Amino-phenyl)pseudo-UTP; 1-(4-Azidobenzyl)pseudouridine TP; 1-(4-Bromobenzyl)pseudouridine TP; 1-(4-Chlorobenzyl)pseudouridine TP; 1-(4-Fluorobenzyl)pseudouridine TP; 1-(4-Iodobenzyl)pseudouridine TP; 1-(4-Methanesulfonylbenzyl)pseudouridine TP; 1-(4-Methoxybenzyl)pseudouridine TP; 1-(4-Methoxy-benzyl)pseudo-UTP; 1-(4-Methoxy-phenyl)pseudo-UTP; 1-(4-Methylbenzyl)pseudouridine TP; 1-(4-Methyl-benzyl)pseudo-UTP; 1-(4-Nitrobenzyl)pseudouridine TP; 1-(4-Nitro-benzyl)pseudo-UTP; 1(4-Nitro-phenyl)pseudo-UTP; 1-(4-Thiomethoxybenzyl)pseudouridine TP; 1-(4-Trifluoromethoxybenzyl)pseudouridine TP; 1-(4-Trifluoromethylbenzyl)pseudouridine TP; 1-(5-Amino-pentyl)pseudo-UTP; 1-(6-Amino-hexyl)pseudo-UTP; 1,6-Dimethyl-pseudo-UTP; 1-[3-(2-{2-[2-(2-Aminoethoxy)-ethoxy]-ethoxy}-ethoxy)-propionyl]pseudouri- dine TP; 1-{3-[2-(2-Aminoethoxy)-ethoxy]-propionyl}pseudouridine TP; 1-Acetylpseudouridine TP; 1-Alkyl-6-(1-propynyl)-pseudo-UTP; 1-Alkyl-6-(2-propynyl)-pseudo-UTP; 1-Alkyl-6-allyl-pseudo-UTP; 1-Alkyl-6-ethynyl-pseudo-UTP; 1-Alkyl-6-homoallyl-pseudo-UTP;

1-Alkyl-6-vinyl-pseudo-UTP; 1-Allylpseudouridine TP; 1-Aminomethyl-pseudo-UTP; 1-Benzoylpseudouridine TP; 1-Benzyloxymethylpseudouridine TP; 1-Benzyl-pseudo-UTP; 1-Biotinyl-PEG2-pseudouridine TP; 1-Biotinylpseudouridine TP; 1-Butyl-pseudo-UTP; 1-Cyanomethylpseudouridine TP; 1-Cyclobutylmethyl-pseudo-UTP; 1-Cyclobutyl-pseudo-UTP; 1-Cycloheptylmethyl-pseudo-UTP; 1-Cycloheptyl-pseudo-UTP; 1-Cyclohexylmethyl-pseudo-UTP; 1-Cyclohexyl-pseudo-UTP; 1-Cyclooctylmethyl-pseudo-UTP; 1-Cyclooctyl-pseudo-UTP; 1-Cyclopentylmethyl-pseudo-UTP; 1-Cyclopentyl-pseudo-UTP; 1-Cyclopropylmethyl-pseudo-UTP; 1-Cyclopropyl-pseudo-UTP; 1-Ethyl-pseudo-UTP; 1-Hexyl-pseudo-UTP; 1-Homoallylpseudouridine TP; 1-Hydroxymethylpseudouridine TP; 1-iso-propyl-pseudo-UTP; 1-Me-2-thio-pseudo-UTP; 1-Me-4-thio-pseudo-UTP; 1-Me-alpha-thio-pseudo-UTP; 1-Methanesulfonylmethylpseudouridine TP; 1-Methoxymethylpseudouridine TP; 1-Methyl-6-(2,2,2-Trifluoroethyl)pseudo-UTP; 1-Methyl-6-(4-morpholino)-pseudo-UTP; 1-Methyl-6-(4-thiomorpholino)-pseudo-UTP; 1-Methyl-6-(substituted phenyl)pseudo-UTP; 1-Methyl-6-amino-pseudo-UTP; 1-Methyl-6-azido-pseudo-UTP; 1-Methyl-6-bromo-pseudo-UTP; 1-Methyl-6-butyl-pseudo-UTP; 1-Methyl-6-chloro-pseudo-UTP; 1-Methyl-6-cyano-pseudo-UTP; 1-Methyl-6-dimethylamino-pseudo-UTP; 1-Methyl-6-ethoxy-pseudo-UTP; 1-Methyl-6-ethylcarboxylate-pseudo-UTP; 1-Methyl-6-ethyl-pseudo-UTP; 1-Methyl-6-fluoro-pseudo-UTP; 1-Methyl-6-formyl-pseudo-UTP; 1-Methyl-6-hydroxyamino-pseudo-UTP; 1-Methyl-6-hydroxy-pseudo-UTP; 1-Methyl-6-iodo-pseudo-UTP; 1-Methyl-6-iso-propyl-pseudo-UTP; 1-Methyl-6-methoxy-pseudo-UTP; 1-Methyl-6-methylamino-pseudo-UTP; 1-Methyl-6-phenyl-pseudo-UTP; 1-Methyl-6-propyl-pseudo-UTP; 1-Methyl-6-tert-butyl-pseudo-UTP; 1-Methyl-6-

trifluoromethoxy-pseudo-UTP; 1-Methyl-6-trifluoromethyl-pseudo-UTP; 1-Morpholinomethylpseudouridine TP; 1-Pentyl-pseudo-UTP; 1-Phenyl-pseudo-UTP; 1-Pivaloylpseudouridine TP; 1-Propargylpseudouridine TP; 1-Propyl-pseudo-UTP; 1-propynyl-pseudouridine; 1-p-tolyl-pseudo-UTP; 1-tert-Butyl-pseudo-UTP; 1-Thiomethoxymethylpseudouridine TP; 1-Thiomorpholinomethylpseudouridine TP; 1-Trifluoroacetylpseudouridine TP; 1-Trifluoromethyl-pseudo-UTP; 1-Vinylpseudouridine TP; 2,2'-anhydro-uridine TP; 2'-bromo-deoxyuridine TP; 2'-F-5-Methyl-2'-deoxy-UTP; 2'-OMe-5-Me-UTP; 2'-OMe-pseudo-UTP; 2'-a-Ethynyluridine TP; 2'-a-Trifluoromethyluridine TP; 2'-b-Ethynyluridine TP; 2'-b-Trifluoromethyluridine TP; 2'-Deoxy-2',2'-difluorouridine TP; 2'-Deoxy-2'-a-mercaptouridine TP; 2'-Deoxy-2'-a-thiomethoxyuridine TP; 2'-Deoxy-2'-b-aminouridine TP; 2'-Deoxy-2'-b-azidouridine TP; 2'-Deoxy-2'-b-bromouridine TP; 2'-Deoxy-2'-b-chlorouridine TP; 2'-Deoxy-2'-b-fluorouridine TP; 2'-Deoxy-2'-b-iodouridine TP; 2'-Deoxy-2'-b-mercaptouridine TP; 2'-Deoxy-2'-b-thiomethoxyuridine TP; 2-methoxy-4-thio-uridine; 2-methoxyuridine; 2'-O-Methyl-5-(1-propynyl)uridine TP; 3-Alkyl-pseudo-UTP; 4'-Azidouridine TP; 4'-Carbocyclic uridine TP; 4'-Ethynyluridine TP; 5-(1-Propynyl)ara-uridine TP; 5-(2-Furanyl)uridine TP; 5-Cyanouridine TP; 5-Dimethylaminouridine TP; 5'-Homo-uridine TP; 5-iodo-2'-fluoro-deoxyuridine TP; 5-Phenylethynyluridine TP; 5-Trideuteromethyl-6-deuterouridine TP; 5-Trifluoromethyl-Uridine TP; 5-Vinylarauridine TP; 6-(2,2,2-Trifluoroethyl)-pseudo-UTP; 6-(4-Morpholino)-pseudo-UTP; 6-(4-Thiomorpholino)-pseudo-UTP; 6-(Substituted-Phenyl)-pseudo-UTP; 6-Amino-pseudo-UTP; 6-Azido-pseudo-UTP; 6-Bromo-pseudo-UTP; 6-Butyl-pseudo-UTP; 6-Chloro-pseudo-UTP; 6-Cyano-pseudo-UTP; 6-Dimethylamino-pseudo-UTP; 6-Ethoxy-pseudo-UTP; 6-Ethylcarboxylate-pseudo-UTP; 6-Ethyl-pseudo-UTP; 6-Fluoro-pseudo-UTP; 6-Formyl-pseudo-UTP; 6-Hydroxyamino-pseudo-UTP; 6-Hydroxy-pseudo-UTP; 6-Iodo-pseudo-UTP; 6-iso-Propyl-pseudo-UTP; 6-Methoxy-pseudo-UTP; 6-Methylamino-pseudo-UTP; 6-Methyl-pseudo-UTP; 6-Phenyl-pseudo-UTP; 6-Phenyl-pseudo-UTP; 6-Propyl-pseudo-UTP; 6-tert-Butyl-pseudo-UTP; 6-Trifluoromethoxy-pseudo-UTP; 6-Trifluoromethyl-pseudo-UTP; Alpha-thio-pseudo-UTP; Pseudouridine 1-(4-methylbenzenesulfonic acid) TP; Pseudouridine 1-(4-methylbenzoic acid) TP; Pseudouridine TP 1-[3-(2-ethoxy)]propionic acid; Pseudouridine TP 1-[3-{2-(2-[2-(2-ethoxy)-ethoxy]-ethoxy)-ethoxy}]propionic acid; Pseudouridine TP 1-[3-{2-(2-[2-{2(2-ethoxy)-ethoxy}-ethoxy]-ethoxy)-ethoxy}]propionic acid; Pseudouridine TP 1-[3-{2-(2-[2-ethoxy]-ethoxy)-ethoxy}]propionic acid; Pseudouridine TP 1-[3-{2-(2-ethoxy)-ethoxy}] propionic acid; Pseudouridine TP 1-methylphosphonic acid; Pseudouridine TP 1-methylphosphonic acid diethyl ester; Pseudo-UTP-N1-3-propionic acid; Pseudo-UTP-N1-4-butanoic acid; Pseudo-UTP-N1-5-pentanoic acid; Pseudo-UTP-N1-6-hexanoic acid; Pseudo-UTP-N1-7-heptanoic acid; Pseudo-UTP-N1-methyl-p-benzoic acid; Pseudo-UTP-N1-p-benzoic acid; Wybutosine; Hydroxywybutosine; Isowyosine; Peroxywybutosine; undermodified hydroxywybutosine; 4-demethylwyosine; 2,6-(diamino)purine; 1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl: 1,3-(diaza)-2-(oxo)-phenthiazin-1-yl; 1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 1,3,5-(triaza)-2,6-(dioxa)-naphthalene; 2 (amino)purine; 2,4,5-(trimethyl)phenyl; 2' methyl, 2'amino, 2'azido, 2'fluro-cytidine; 2' methyl, 2'amino, 2'azido, 2'fluro-adenine; 2'methyl, 2'amino, 2'azido, 2'fluro-uridine; 2'-amino-2'-deoxyribose; 2-amino-6-Chloro-purine; 2-aza-inosinyl; 2'-azido-2'-deoxyribose; 2'fluoro-2'-deoxyribose; 2'-fluoro-modified bases; 2'-O-methyl-ribose; 2-oxo-7-aminopyridopyrimidin-3-yl; 2-oxo-pyridopyrimidine-3-yl; 2-pyridinone; 3 nitropyrrole; 3-(methyl)-7-(propynyl)isocarbostyrilyl; 3-(methyl)isocarbostyrilyl; 4-(fluoro)-6-(methyl)benzimidazole; 4-(methyl)benzimidazole; 4-(methyl)indolyl; 4,6-(dimethyl)indolyl; 5 nitroindole; 5 substituted pyrimidines; 5-(methyl)isocarbostyrilyl; 5-nitroindole; 6-(aza)pyrimidine; 6-(azo)thymine; 6-(methyl)-7-(aza)indolyl; 6-chloro-purine; 6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; 7-(aminoalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenthiazin-1-yl; 7-(aminoalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 7-(aminoalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 7-(aminoalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenthiazin-1-yl; 7-(aminoalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 7-(aza)indolyl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenoxazinl-yl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenthiazin-1-yl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 7-(guanidiniumalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 7-(guanidiniumalkyl-hydroxy)-1,3-(diaza)-2-(oxo)-phenthiazin-1-yl; 7-(guanidiniumalkylhydroxy)-1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 7-(propynyl)isocarbostyrilyl; 7-(propynyl)isocarbostyrilyl, propynyl-7-(aza)indolyl; 7-deaza-inosinyl; 7-substituted 1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 7-substituted 1,3-(diaza)-2-(oxo)-phenoxazin-1-yl; 9-(methyl)-imidizopyridinyl; Aminoindolyl; Anthracenyl; bis-ortho-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; bis-ortho-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Difluorotolyl; Hypoxanthine; Imidizopyridinyl; Inosinyl; Isocarbostyrilyl; Isoguanisine; N2-substituted purines; N6-methyl-2-amino-purine; N6-substituted purines; N-alkylated derivative; Napthalenyl; Nitrobenzimidazolyl; Nitroimidazolyl; Nitroindazolyl; Nitropyrazolyl;

Nubularine; 06-substituted purines; O-alkylated derivative; ortho-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; ortho-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Oxoformycin TP; para-(aminoalkylhydroxy)-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; para-substituted-6-phenyl-pyrrolo-pyrimidin-2-on-3-yl; Pentacenyl; Phenanthracenyl; Phenyl; propynyl-7-(aza)indolyl; Pyrenyl; pyridopyrimidin-3-yl; pyridopyrimidin-3-yl, 2-oxo-7-amino-pyridopyrimidin-3-yl; pyrrolo-pyrimidin-2-on-3-yl; Pyrrolopyrimidinyl; Pyrrolopyrizinyl; Stilbenzyl; substituted 1,2,4-triazoles; Tetracenyl; Tubercidine; Xanthine; Xanthosine-5'-TP; 2-thio-zebularine; 5-aza-2-thio-zebularine; 7-deaza-2-amino-purine; pyridin-4-one ribonucleoside; 2-Amino-riboside-TP; Formycin A TP; Formycin B TP; Pyrrolosine TP; 2'-OH-ara-adenosine TP; 2'-OH-ara-cytidine TP; 2'-OH-ara-uridine TP; 2'-OH-ara-guanosine TP; 5-(2-carbomethoxyvinyl)uridine TP; and N6-(19-Amino-pentaoxanonadecyl)adenosine TP.

[0322] In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) include a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

[0323] In some embodiments, modified nucleobases in polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are selected from the group consisting of pseudouridine (.psi.), N1-methylpseudouridine (m.sup.1.psi.), N1-ethylpseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcytosine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine. In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) include a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

[0324] In some embodiments, modified nucleobases in polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are selected from the group consisting of 1-methyl-pseudouridine (m.sup.1.psi.), 5-methoxy-uridine (mo.sup.5U), 5-methyl-cytidine (m.sup.5C), pseudouridine (.psi.), .alpha.-thio-guanosine and .alpha.-thio-adenosine. In some embodiments, polynucleotides includes a combination of at least two (e.g., 2, 3, 4 or more) of the aforementioned modified nucleobases.

[0325] In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise pseudouridine (.psi.) and 5-methyl-cytidine (m.sup.5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 1-methyl-pseudouridine (m.sup.1.psi.). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 1-methyl-pseudouridine (m.sup.1.psi.) and 5-methyl-cytidine (m.sup.5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2-thiouridine (s.sup.2U). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2-thiouridine and 5-methyl-cytidine (m.sup.5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise methoxy-uridine (mo.sup.5U). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 5-methoxy-uridine (mo.sup.5U) and 5-methyl-cytidine (m.sup.5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2'-O-methyl uridine. In some embodiments polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise 2'-O-methyl uridine and 5-methyl-cytidine (m.sup.5C). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise N6-methyl-adenosine (m.sup.6A). In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise N6-methyl-adenosine (m.sup.6A) and 5-methyl-cytidine (m.sup.5C).

[0326] In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) are uniformly modified (e.g., fully modified, modified throughout the entire sequence) for a particular modification. For example, a polynucleotide can be uniformly modified with 5-methyl-cytidine (m.sup.5C), meaning that all cytosine residues in the mRNA sequence are replaced with 5-methyl-cytidine (m.sup.5C). Similarly, a polynucleotide can be uniformly modified for any type of nucleoside residue present in the sequence by replacement with a modified residue such as those set forth above.

[0327] Exemplary nucleobases and nucleosides having a modified cytosine include N4-acetyl-cytidine (ac4C), 5-methyl-cytidine (m5C), 5-halo-cytidine (e.g., 5-iodo-cytidine), 5-hydroxymethyl-cytidine (hm5C), 1-methyl-pseudoisocytidine, 2-thio-cytidine (s2C), and 2-thio-5-methyl-cytidine.

[0328] In some embodiments, a modified nucleobase is a modified uridine. Exemplary nucleobases and In some embodiments, a modified nucleobase is a modified cytosine. nucleosides having a modified uridine include 5-cyano uridine, and 4'-thio uridine.

[0329] In some embodiments, a modified nucleobase is a modified adenine. Exemplary nucleobases and nucleosides having a modified adenine include 7-deaza-adenine, 1-methyl-adenosine (m1A), 2-methyl-adenine (m2A), and N6-methyl-adenosine (m6A).

[0330] In some embodiments, a modified nucleobase is a modified guanine. Exemplary nucleobases and nucleosides having a modified guanine include inosine (I), 1-methyl-inosine (m1I), wyosine (imG), methylwyosine (mimG), 7-deaza-guanosine, 7-cyano-7-deaza-guanosine (preQ0), 7-aminomethyl-7-deaza-guanosine (preQ1), 7-methyl-guanosine (m7G), 1-methyl-guanosine (m1G), 8-oxo-guanosine, 7-methyl-8-oxo-guanosine.

[0331] The polynucleotides of the present disclosure may be partially or fully modified along the entire length of the molecule. For example, one or more or all or a given type of nucleotide (e.g., purine or pyrimidine, or any one or more or all of A, G, U, C) may be uniformly modified in a polynucleotide of the disclosure, or in a given predetermined sequence region thereof (e.g., in the mRNA including or excluding the polyA tail). In some embodiments, all nucleotides X in a polynucleotide of the present disclosure (or in a given sequence region thereof) are modified nucleotides, wherein X may any one of nucleotides A, G, U, C, or any one of the combinations A+G, A+U, A+C, G+U, G+C, U+C, A+G+U, A+G+C, G+U+C or A+G+C.

[0332] The polynucleotide may contain from about 1% to about 100% modified nucleotides (either in relation to overall nucleotide content, or in relation to one or more types of nucleotide, i.e., any one or more of A, G, U or C) or any intervening percentage (e.g., from 1% to 20%, from 1% to 25%, from 1% to 50%, from 1% to 60%, from 1% to 70%, from 1% to 80%, from 1% to 90%, from 1% to 95%, from 10% to 20%, from 10% to 25%, from 10% to 50%, from 10% to 60%, from 10% to 70%, from 10% to 80%, from 10% to 90%, from 10% to 95%, from 10% to 100%, from 20% to 25%, from 20% to 50%, from 20% to 60%, from 20% to 70%, from 20% to 80%, from 20% to 90%, from 20% to 95%, from 20% to 100%, from 50% to 60%, from 50% to 70%, from 50% to 80%, from 50% to 90%, from 50% to 95%, from 50% to 100%, from 70% to 80%, from 70% to 90%, from 70% to 95%, from 70% to 100%, from 80% to 90%, from 80% to 95%, from 80% to 100%, from 90% to 95%, from 90% to 100%, and from 95% to 100%). Any remaining percentage is accounted for by the presence of unmodified A, G, U, or C.

[0333] The polynucleotides may contain at a minimum 1% and at maximum 100% modified nucleotides, or any intervening percentage, such as at least 5% modified nucleotides, at least 10% modified nucleotides, at least 25% modified nucleotides, at least 50% modified nucleotides, at least 80% modified nucleotides, or at least 90% modified nucleotides. For example, the polynucleotides may contain a modified pyrimidine such as a modified uracil or cytosine. In some embodiments, at least 5%, at least 10%, at least 25%, at least 50%, at least 80%, at least 90% or 100% of the uracil in the polynucleotide is replaced with a modified uracil (e.g., a 5-substituted uracil). The modified uracil can be replaced by a compound having a single unique structure, or can be replaced by a plurality of compounds having different structures (e.g., 2, 3, 4 or more unique structures). n some embodiments, at least 5%, at least 10%, at least 25%, at least 50%, at least 80%, at least 90% or 100% of the cytosine in the polynucleotide is replaced with a modified cytosine (e.g., a 5-substituted cytosine). The modified cytosine can be replaced by a compound having a single unique structure, or can be replaced by a plurality of compounds having different structures (e.g., 2, 3, 4 or more unique structures).

[0334] Thus, in some embodiments, the RNA (e.g., mRNA) vaccines comprise a 5'UTR element, an optionally codon optimized open reading frame, and a 3'UTR element, a poly(A) sequence and/or a polyadenylation signal wherein the RNA is not chemically modified.

[0335] In some embodiments, the modified nucleobase is a modified uracil. Exemplary nucleobases and nucleosides having a modified uracil include pseudouridine (.psi.), pyridin-4-one ribonucleoside, 5-aza-uridine, 6-aza-uridine, 2-thio-5-aza-uridine, 2-thio-uridine (s.sup.2U), 4-thio-uridine (s.sup.4U), 4-thio-pseudouridine, 2-thio-pseudouridine, 5-hydroxy-uridine (ho.sup.5U), 5-aminoallyl-uridine, 5-halo-uridine (e.g., 5-iodo-uridineor 5-bromo-uridine), 3-methyl-uridine (m.sup.3U), 5-methoxy-uridine (mo.sup.5U), uridine 5-oxyacetic acid (cmo.sup.5U), uridine 5-oxyacetic acid methyl ester (mcmo.sup.5U), 5-carboxymethyl-uridine (cm.sup.5U), 1-carboxymethyl-pseudouridine, 5-carboxyhydroxymethyl-uridine (chm.sup.5U), 5-carboxyhydroxymethyl-uridine methyl ester (mchm.sup.5U), 5-methoxycarbonylmethyl-uridine (mcm.sup.5U), 5-methoxycarbonylmethyl-2-thio-uridine (mcm.sup.5s.sup.2U), 5-aminomethyl-2-thio-uridine (nm.sup.5s.sup.2U), 5-methylaminomethyl-uridine (mnm.sup.5U), 5-methylaminomethyl-2-thio-uridine (mnm.sup.5s.sup.2U), 5-methylaminomethyl-2-seleno-uridine (mnm.sup.5se.sup.2U), 5-carbamoylmethyl-uridine (ncm.sup.5U), 5-carboxymethylaminomethyl-uridine (cmnm.sup.5U), 5-carboxymethylaminomethyl-2-thio-uridine (cmnm.sup.5s.sup.2U), 5-propynyl-uridine, 1-propynyl-pseudouridine, 5-taurinomethyl-uridine (.tau.m.sup.5U), 1-taurinomethyl-pseudouridine, 5-taurinomethyl-2-thio-uridine (.tau.m.sup.5s.sup.2U), 1-taurinomethyl-4-thio-pseudouridine, 5-methyl-uridine (m.sup.5U, i.e., having the nucleobase deoxythymine), 1-methyl-pseudouridine (m.sup.1.psi.), 5-methyl-2-thio-uridine (m.sup.5s.sup.2U), 1-methyl-4-thio-pseudouridine (m.sup.1s.sup.4.psi.), 4-thio-1-methyl-pseudouridine, 3-methyl-pseudouridine (m.sup.3.psi.), 2-thio-1-methyl-pseudouridine, 1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-1-deaza-pseudouridine, dihydrouridine (D), dihydropseudouridine, 5,6-dihydrouridine, 5-methyl-dihydrouridine (m.sup.5D), 2-thio-dihydrouridine, 2-thio-dihydropseudouridine, 2-methoxy-uridine, 2-methoxy-4-thio-uridine, 4-methoxy-pseudouridine, 4-methoxy-2-thio-pseudouridine, N1-methyl-pseudouridine, 3-(3-amino-3-carboxypropyl)uridine (acp.sup.3U), 1-methyl-3-(3-amino-3-carboxypropyl)pseudouridine (acp.sup.3 .psi.), 5-(isopentenylaminomethyl)uridine (inm.sup.5U), 5-(isopentenylaminomethyl)-2-thio-uridine (inm.sup.5s.sup.2U), .alpha.-thio-uridine, 2'-O-methyl-uridine (Urn), 5,2'-O-dimethyl-uridine (m.sup.5Um), 2'-O-methyl-pseudouridine (.psi.m), 2-thio-2'-O-methyl-uridine (s.sup.2Um), 5-methoxycarbonylmethyl-2'-O-methyl-uridine (mcm.sup.5Um), 5-carbamoylmethyl-2'-O-methyl-uridine (ncm.sup.5Um), 5-carboxymethylaminomethyl-2'-O-methyl-uridine (cmnm.sup.5Um), 3,2'-O-dimethyl-uridine (m.sup.3Um), and 5-(isopentenylaminomethyl)-2'-O-methyl-uridine (inm.sup.5Um), 1-thio-uridine, deoxythymidine, 2'-F-ara-uridine, 2'-F-uridine, 2'-0H-ara-uridine, 5-(2-carbomethoxyvinyl) uridine, and 5-[3-(1-E-propenylamino)]uridine.

[0336] In some embodiments, the modified nucleobase is a modified cytosine. Exemplary nucleobases and nucleosides having a modified cytosine include 5-aza-cytidine, 6-aza-cytidine, pseudoisocytidine, 3-methyl-cytidine (m.sup.3C), N4-acetyl-cytidine (ac.sup.4C), 5-formyl-cytidine (f.sup.5C), N4-methyl-cytidine (m.sup.4C), 5-methyl-cytidine (m.sup.5C), 5-halo-cytidine (e.g., 5-iodo-cytidine), 5-hydroxymethyl-cytidine (hm.sup.5C), 1-methyl-pseudoisocytidine, pyrrolo-cytidine, pyrrolo-pseudoisocytidine, 2-thio-cytidine (s.sup.2C), 2-thio-5-methyl-cytidine, 4-thio-pseudoisocytidine, 4-thio-1-methyl-pseudoisocytidine, 4-thio-1-methyl-1-deaza-pseudoisocytidine, 1-methyl-1-deaza-pseudoisocytidine, zebularine, 5-aza-zebularine, 5-methyl-zebularine, 5-aza-2-thio-zebularine, 2-thio-zebularine, 2-methoxy-cytidine, 2-methoxy-5-methyl-cytidine, 4-methoxy-pseudoisocytidine, 4-methoxy-1-methyl-pseudoisocytidine, lysidine (k.sub.2C), .alpha.-thio-cytidine, 2'-O-methyl-cytidine (Cm), 5,2'-O-dimethyl-cytidine (m.sup.5Cm), N4-acetyl-2'-O-methyl-cytidine (ac.sup.4Cm), N4,2'-O-dimethyl-cytidine (m.sup.4Cm), 5-formyl-2'-O-methyl-cytidine (f.sup.5Cm), N4,N4,2'-O-trimethyl-cytidine (m.sup.4.sub.2 Cm), 1-thio-cytidine, 2'-F-ara-cytidine, 2'-F-cytidine, and 2'-0H-ara-cytidine.

[0337] In some embodiments, the modified nucleobase is a modified adenine. Exemplary nucleobases and nucleosides having a modified adenine include 2-amino-purine, 2,6-diaminopurine, 2-amino-6-halo-purine (e.g., 2-amino-6-chloro-purine), 6-halo-purine (e.g., 6-chloro-purine), 2-amino-6-methyl-purine, 8-azido-adenosine, 7-deaza-adenine, 7-deaza-8-aza-adenine, 7-deaza-2-amino-purine, 7-deaza-8-aza-2-amino-purine, 7-deaza-2,6-diaminopurine, 7-deaza-8-aza-2,6-diaminopurine, 1-methyl-adenosine (m.sup.1A), 2-methyl-adenine (m.sup.2A), N6-methyl-adenosine (m.sup.6A), 2-methylthio-N6-methyl-adenosine (ms.sup.2 m.sup.6A), N6-isopentenyl-adenosine (i.sup.6A), 2-methylthio-N6-isopentenyl-adenosine (ms.sup.2i.sup.6A), N6-(cis-hydroxyisopentenyl)adenosine (io.sup.6A), 2-methylthio-N6-(cis-hydroxyisopentenyl)adenosine (ms.sup.2io.sup.6A), N6-glycinylcarbamoyl-adenosine (g.sup.6A), N6-threonylcarbamoyl-adenosine (t.sup.6A), N6-methyl-N6-threonylcarbamoyl-adenosine (m.sup.6t.sup.6A), 2-methylthio-N6-threonylcarbamoyl-adenosine (ms.sup.2g.sup.6A), N6,N6-dimethyl-adenosine (m.sup.6.sub.2 A), N6-hydroxynorvalylcarbamoyl-adenosine (hn.sup.6A), 2-methylthio-N6-hydroxynorvalylcarbamoyl-adenosine (ms.sup.2hn.sup.6A), N6-acetyl-adenosine (ac.sup.6A), 7-methyl-adenine, 2-methylthio-adenine, 2-methoxy-adenine, .alpha.-thio-adenosine, 2'-O-methyl-adenosine (Am), N6,2'-O-dimethyl-adenosine (m.sup.6Am), N6,N6,2'-O-trimethyl-adenosine (m.sup.6.sub.2 Am), 1,2'-O-dimethyl-adenosine (m.sup.1Am), 2'-O-ribosyladenosine (phosphate) (Ar(p)), 2-amino-N6-methyl-purine, 1-thio-adenosine, 8-azido-adenosine, 2'-F-ara-adenosine, 2'-F-adenosine, 2'-0H-ara-adenosine, and N6-(19-amino-pentaoxanonadecyl)-adenosine.

[0338] In some embodiments, the modified nucleobase is a modified guanine. Exemplary nucleobases and nucleosides having a modified guanine include inosine (I), 1-methyl-inosine (m.sup.1I), wyosine (imG), methylwyosine (mimG), 4-demethyl-wyosine (imG-14), isowyosine (imG2), wybutosine (yW), peroxywybutosine (o2yW), hydroxywybutosine (OhyW), undermodified hydroxywybutosine (OhyW*), 7-deaza-guanosine, queuosine (Q), epoxyqueuosine (oQ), galactosyl-queuosine (galQ), mannosyl-queuosine (manQ), 7-cyano-7-deaza-guanosine (preQ.sub.0), 7-aminomethyl-7-deaza-guanosine (preQ.sub.1), archaeosine (G.+-.), 7-deaza-8-aza-guanosine, 6-thio-guanosine, 6-thio-7-deaza-guanosine, 6-thio-7-deaza-8-aza-guanosine, 7-methyl-guanosine (m.sup.7G), 6-thio-7-methyl-guanosine, 7-methyl-inosine, 6-methoxy-guanosine, 1-methyl-guanosine (m.sup.1G), N2-methyl-guanosine (m.sup.2G), N2,N2-dimethyl-guanosine (m.sup.2.sub.2 G), N2,7-dimethyl-guano sine (m.sup.2,7G), N2,N2,7-dimethyl-guanosine (m.sup.2,2,7G), 8-oxo-guanosine, 7-methyl-8-oxo-guanosine, 1-methyl-6-thio-guanosine, N2-methyl-6-thio-guanosine, N2,N2-dimethyl-6-thio-guanosine, .alpha.-thio-guanosine, 2'-O-methyl-guanosine (Gm), N2-methyl-2'-O-methyl-guanosine (m.sup.2Gm), N2,N2-dimethyl-2'-O-methyl-guanosine (m.sup.2.sub.2 Gm), 1-methyl-2'-O-methyl-guanosine (m.sup.1Gm), N2,7-dimethyl-2'-O-methyl-guanosine (m.sup.2,7Gm), 2'-O-methyl-inosine (Im), 1,2'-O-dimethyl-inosine (m.sup.1Im), 2'-O-ribosylguanosine (phosphate) (Gr(p)), 1-thio-guanosine, 06-methyl-guanosine, 2'-F-ara-guanosine, and 2'-F-guanosine.

N-Linked Glycosylation Site Mutants

[0339] N-linked glycans of viral proteins play important roles in modulating the immune response. Glycans can be important for maintaining the appropriate antigenic conformations, shielding potential neutralization epitopes, and may alter the proteolytic susceptibility of proteins. Some viruses have putative N-linked glycosylation sites. Deletion or modification of an N-linked glycosylation site may enhance the immune response. Thus, the present disclosure provides, in some embodiments, RNA (e.g., mRNA) vaccines comprising nucleic acids (e.g., mRNA) encoding antigenic polypeptides that comprise a deletion or modification at one or more N-linked glycosylation sites.

In Vitro Transcription of RNA (e.g., mRNA)

[0340] Respiratory virus vaccines of the present disclosure comprise at least one RNA polynucleotide, such as a mRNA (e.g., modified mRNA). mRNA, for example, is transcribed in vitro from template DNA, referred to as an "in vitro transcription template." In some embodiments, an in vitro transcription template encodes a 5' untranslated (UTR) region, contains an open reading frame, and encodes a 3' UTR and a polyA tail. The particular nucleic acid sequence composition and length of an in vitro transcription template will depend on the mRNA encoded by the template.

[0341] A "5' untranslated region" (5'UTR) refers to a region of an mRNA that is directly upstream (i.e., 5') from the start codon (i.e., the first codon of an mRNA transcript translated by a ribosome) that does not encode a polypeptide.

[0342] A "3' untranslated region" (3'UTR) refers to a region of an mRNA that is directly downstream (i.e., 3') from the stop codon (i.e., the codon of an mRNA transcript that signals a termination of translation) that does not encode a polypeptide.

[0343] An "open reading frame" is a continuous stretch of DNA beginning with a start codon (e.g., methionine (ATG)), and ending with a stop codon (e.g., TAA, TAG or TGA) and encodes a polypeptide.

[0344] A "polyA tail" is a region of mRNA that is downstream, e.g., directly downstream (i.e., 3'), from the 3' UTR that contains multiple, consecutive adenosine monophosphates. A polyA tail may contain 10 to 300 adenosine monophosphates. For example, a polyA tail may contain 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260, 270, 280, 290 or 300 adenosine monophosphates. In some embodiments, a polyA tail contains 50 to 250 adenosine monophosphates. In a relevant biological setting (e.g., in cells, in vivo) the poly(A) tail functions to protect mRNA from enzymatic degradation, e.g., in the cytoplasm, and aids in transcription termination, export of the mRNA from the nucleus and translation.

[0345] In some embodiments, a polynucleotide includes 200 to 3,000 nucleotides. For example, a polynucleotide may include 200 to 500, 200 to 1000, 200 to 1500, 200 to 3000, 500 to 1000, 500 to 1500, 500 to 2000, 500 to 3000, 1000 to 1500, 1000 to 2000, 1000 to 3000, 1500 to 3000, or 2000 to 3000 nucleotides.

Flagellin Adjuvants

[0346] Flagellin is an approximately 500 amino acid monomeric protein that polymerizes to form the flagella associated with bacterial motion. Flagellin is expressed by a variety of flagellated bacteria (Salmonella typhimurium for example) as well as non-flagellated bacteria (such as Escherichia coli). Sensing of flagellin by cells of the innate immune system (dendritic cells, macrophages, etc.) is mediated by the Toll-like receptor 5 (TLR5) as well as by Nod-like receptors (NLRs) Ipaf and Naip5. TLRs and NLRs have been identified as playing a role in the activation of innate immune response and adaptive immune response. As such, flagellin provides an adjuvant effect in a vaccine.

[0347] The nucleotide and amino acid sequences encoding known flagellin polypeptides are publicly available in the NCBI GenBank database. The flagellin sequences from S. Typhimurium, H. Pylori, V. Cholera, S. marcesens, S. flexneri, T. Pallidum, L. pneumophila, B. burgdorferei, C. difficile, R. meliloti, A. tumefaciens, R. lupini, B. clarridgeiae, P. Mirabilis, B. subtilus, L. monocytogenes, P. aeruginosa, and E. coli, among others are known.

[0348] A flagellin polypeptide, as used herein, refers to a full length flagellin protein, immunogenic fragments thereof, and peptides having at least 50% sequence identify to a flagellin protein or immunogenic fragments thereof. Exemplary flagellin proteins include flagellin from Salmonella typhi (UniPro Entry number: Q56086), Salmonella typhimurium (A0A0C9DG09), Salmonella enteritidis (A0A0C9BAB7), and Salmonella choleraesuis (Q6V2X8), and SEQ ID NO: 54-56 (Table 17). In some embodiments, the flagellin polypeptide has at least 60%, 70%, 75%, 80%, 90%, 95%, 97%, 98%, or 99% sequence identify to a flagellin protein or immunogenic fragments thereof.

[0349] In some embodiments, the flagellin polypeptide is an immunogenic fragment. An immunogenic fragment is a portion of a flagellin protein that provokes an immune response. In some embodiments, the immune response is a TLR5 immune response. An example of an immunogenic fragment is a flagellin protein in which all or a portion of a hinge region has been deleted or replaced with other amino acids. For example, an antigenic polypeptide may be inserted in the hinge region. Hinge regions are the hypervariable regions of a flagellin. Hinge regions of a flagellin are also referred to as "D3 domain or region, "propeller domain or region," "hypervariable domain or region" and "variable domain or region." "At least a portion of a hinge region," as used herein, refers to any part of the hinge region of the flagellin, or the entirety of the hinge region. In other embodiments an immunogenic fragment of flagellin is a 20, 25, 30, 35, or 40 amino acid C-terminal fragment of flagellin.

[0350] The flagellin monomer is formed by domains D0 through D3. D0 and D1, which form the stem, are composed of tandem long alpha helices and are highly conserved among different bacteria. The D1 domain includes several stretches of amino acids that are useful for TLR5 activation. The entire D1 domain or one or more of the active regions within the domain are immunogenic fragments of flagellin. Examples of immunogenic regions within the D1 domain include residues 88-114 and residues 411-431 (in Salmonella typhimurium FliC flagellin. Within the 13 amino acids in the 88-100 region, at least 6 substitutions are permitted between Salmonella flagellin and other flagellins that still preserve TLR5 activation. Thus, immunogenic fragments of flagellin include flagellin like sequences that activate TLR5 and contain a 13 amino acid motif that is 53% or more identical to the Salmonella sequence in 88-100 of FliC (LQRVRELAVQSAN; SEQ ID NO: 84).

[0351] In some embodiments, the RNA (e.g., mRNA) vaccine includes an RNA that encodes a fusion protein of flagellin and one or more antigenic polypeptides. A "fusion protein" as used herein, refers to a linking of two components of the construct. In some embodiments, a carboxy-terminus of the antigenic polypeptide is fused or linked to an amino terminus of the flagellin polypeptide. In other embodiments, an amino-terminus of the antigenic polypeptide is fused or linked to a carboxy-terminus of the flagellin polypeptide. The fusion protein may include, for example, one, two, three, four, five, six or more flagellin polypeptides linked to one, two, three, four, five, six or more antigenic polypeptides. When two or more flagellin polypeptides and/or two or more antigenic polypeptides are linked such a construct may be referred to as a "multimer."

[0352] Each of the components of a fusion protein may be directly linked to one another or they may be connected through a linker. For instance, the linker may be an amino acid linker. The amino acid linker encoded for by the RNA (e.g., mRNA) vaccine to link the components of the fusion protein may include, for instance, at least one member selected from the group consisting of a lysine residue, a glutamic acid residue, a serine residue and an arginine residue. In some embodiments the linker is 1-30, 1-25, 1-25, 5-10, 5, 15, or 5-20 amino acids in length.

[0353] In other embodiments the RNA (e.g., mRNA) vaccine includes at least two separate RNA polynucleotides, one encoding one or more antigenic polypeptides and the other encoding the flagellin polypeptide. The at least two RNA polynucleotides may be co-formulated in a carrier such as a lipid nanoparticle.

Broad Spectrum RNA (e.g., mRNA) Vaccines

[0354] There may be situations where persons are at risk for infection with more than one strain of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). RNA (e.g., mRNA) therapeutic vaccines are particularly amenable to combination vaccination approaches due to a number of factors including, but not limited to, speed of manufacture, ability to rapidly tailor vaccines to accommodate perceived geographical threat, and the like. Moreover, because the vaccines utilize the human body to produce the antigenic protein, the vaccines are amenable to the production of larger, more complex antigenic proteins, allowing for proper folding, surface expression, antigen presentation, etc. in the human subject. To protect against more than one strain of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1), a combination vaccine can be administered that includes RNA (e.g., mRNA) encoding at least one antigenic polypeptide protein (or antigenic portion thereof) of a first respiratory virus and further includes RNA encoding at least one antigenic polypeptide protein (or antigenic portion thereof) of a second respiratory virus. RNA (e.g., mRNA) can be co-formulated, for example, in a single lipid nanoparticle (LNP) or can be formulated in separate LNPs for co-administration.

Methods of Treatment

[0355] Provided herein are compositions (e.g., pharmaceutical compositions), methods, kits and reagents for prevention and/or treatment of respiratory diseases/infections in humans and other mammals. Respiratory virus RNA (e.g. mRNA) vaccines can be used as therapeutic or prophylactic agents, alone or in combination with other vaccine(s). They may be used in medicine to prevent and/or treat respiratory disease/infection. In exemplary aspects, the RNA (e.g., mRNA) vaccines of the present disclosure are used to provide prophylactic protection from hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). Prophylactic protection from hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) can be achieved following administration of a RNA (e.g., mRNA) vaccine of the present disclosure. Respiratory virus RNA (e.g., mRNA) vaccines of the present disclosure may be used to treat or prevent viral "co-infections" containing two or more respiratory infections. Vaccines can be administered once, twice, three times, four times or more, but it is likely sufficient to administer the vaccine once (optionally followed by a single booster). It is possible, although less desirable, to administer the vaccine to an infected individual to achieve a therapeutic response. Dosing may need to be adjusted accordingly.

[0356] A method of eliciting an immune response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) is provided in aspects of the present disclosure. The method involves administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide thereof, thereby inducing in the subject an immune response specific to hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, wherein anti-antigenic polypeptide antibody titer in the subject is increased following vaccination relative to anti-antigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). An "anti-antigenic polypeptide antibody" is a serum antibody the binds specifically to the antigenic polypeptide.

[0357] In some embodiments, a RNA (e.g., mRNA) vaccine (e.g., a hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1 RNA vaccine) capable of eliciting an immune response is administered intramuscularly via a composition including a compound according to Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) (e.g., Compound 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122).

[0358] A prophylactically effective dose is a therapeutically effective dose that prevents infection with the virus at a clinically acceptable level. In some embodiments the therapeutically effective dose is a dose listed in a package insert for the vaccine. A traditional vaccine, as used herein, refers to a vaccine other than the RNA (e.g., mRNA) vaccines of the present disclosure. For instance, a traditional vaccine includes but is not limited to live/attenuated microorganism vaccines, killed/inactivated microorganism vaccines, subunit vaccines, protein antigen vaccines, DNA vaccines, VLP vaccines, etc. In exemplary embodiments, a traditional vaccine is a vaccine that has achieved regulatory approval and/or is registered by a national drug regulatory body, for example the Food and Drug Administration (FDA) in the United States or the European Medicines Agency (EMA).

[0359] In some embodiments the anti-antigenic polypeptide antibody titer in the subject is increased 1 log to 10 log following vaccination relative to anti-antigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

[0360] In some embodiments the anti-antigenic polypeptide antibody titer in the subject is increased 1 log, 2 log, 3 log, 5 log or 10 log following vaccination relative to anti-antigenic polypeptide antibody titer in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

[0361] A method of eliciting an immune response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or

HCoV-HKU1) is provided in other aspects of the disclosure. The method involves administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, thereby inducing in the subject an immune response specific to hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide or an immunogenic fragment thereof, wherein the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine against the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) at 2 times to 100 times the dosage level relative to the RNA (e.g., mRNA) vaccine.

[0362] In some embodiments, the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine at 2, 3, 4, 5, 10, 50, 100 times the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine.

[0363] In some embodiments the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine at 10-100 times, or 100-1000 times, the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine.

[0364] In some embodiments the immune response is assessed by determining [protein] antibody titer in the subject.

[0365] Some aspects of the present disclosure provide a method of eliciting an immune response in a subject against a In some embodiments the immune response in the subject is equivalent to an immune response in a subject vaccinated with a traditional vaccine at 2, 3, 4, 5, 10, 50, 100 times the dosage level relative to the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) RNA (e.g., mRNA) vaccine by administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine comprising at least one RNA (e.g., mRNA) polynucleotide having an open reading frame encoding at least one hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) antigenic polypeptide, thereby inducing in the subject an immune response specific to the antigenic polypeptide or an immunogenic fragment thereof, wherein the immune response in the subject is induced 2 days to 10 weeks earlier relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine against the hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1). In some embodiments, the immune response in the subject is induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine at 2 times to 100 times the dosage level relative to the RNA (e.g., mRNA) vaccine.

[0366] In some embodiments, the immune response in the subject is induced 2 days earlier, or 3 days earlier, relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine.

[0367] In some embodiments the immune response in the subject is induced 1 week, 2 weeks, 3 weeks, 5 weeks, or 10 weeks earlier relative to an immune response induced in a subject vaccinated with a prophylactically effective dose of a traditional vaccine.

[0368] Also provided herein is a method of eliciting an immune response in a subject against hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) by administering to the subject a respiratory virus RNA (e.g., mRNA) vaccine having an open reading frame encoding a first antigenic polypeptide, wherein the RNA polynucleotide does not include a stabilization element, and wherein an adjuvant is not co-formulated or co-administered with the vaccine.

Therapeutic and Prophylactic Compositions

[0369] Provided herein are compositions (e.g., pharmaceutical compositions), methods, kits and reagents for prevention, treatment or diagnosis of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1) in humans and other mammals, for example. Respiratory virus RNA (e.g. mRNA) vaccines can be used as therapeutic or prophylactic agents. They may be used in medicine to prevent and/or treat infectious disease. In some embodiments, the respiratory RNA (e.g., mRNA) vaccines of the present disclosure are used fin the priming of immune effector cells, for example, to activate peripheral blood mononuclear cells (PBMCs) ex vivo, which are then infused (re-infused) into a subject.

[0370] In some embodiments, respiratory virus vaccine containing RNA (e.g., mRNA) polynucleotides as described herein can be administered to a subject (e.g., a mammalian subject, such as a human subject), and the RNA (e.g., mRNA) polynucleotides are translated in vivo to produce an antigenic polypeptide.

[0371] The respiratory virus RNA (e.g., mRNA) vaccines may be induced for translation of a polypeptide (e.g., antigen or immunogen) in a cell, tissue or organism. In some embodiments, such translation occurs in vivo, although such translation may occur ex vivo, in culture or in vitro. In some embodiments, the cell, tissue or organism is contacted with an effective amount of a composition containing a respiratory virus RNA (e.g., mRNA) vaccine that contains a polynucleotide that has at least one a translatable region encoding an antigenic polypeptide.

[0372] An "effective amount" of an respiratory virus RNA (e.g. mRNA) vaccine is provided based, at least in part, on the target tissue, target cell type, means of administration, physical characteristics of the polynucleotide (e.g., size, and extent of modified nucleosides) and other components of the vaccine, and other determinants. In general, an effective amount of the respiratory virus RNA (e.g., mRNA) vaccine composition provides an induced or boosted immune response as a function of antigen production in the cell, preferably more efficient than a composition containing a corresponding unmodified polynucleotide encoding the same antigen or a peptide antigen. Increased antigen production may be demonstrated by increased cell transfection (the percentage of cells transfected with the RNA, e.g., mRNA, vaccine), increased protein translation from the polynucleotide, decreased nucleic acid degradation (as demonstrated, for example, by increased duration of protein translation from a modified polynucleotide), or altered antigen specific immune response of the host cell.

[0373] In some embodiments, RNA (e.g. mRNA) vaccines (including polynucleotides their encoded polypeptides) in accordance with the present disclosure may be used for treatment of hMPV, PIV3, RSV, MeV and/or BetaCoV (including MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH and/or HCoV-HKU1).

[0374] Respiratory RNA (e.g. mRNA) vaccines may be administered prophylactically or therapeutically as part of an active immunization scheme to healthy individuals or early in infection during the incubation phase or during active infection after onset of symptoms. In some embodiments, the amount of RNA (e.g., mRNA) vaccine of the present disclosure provided to a cell, a tissue or a subject may be an amount effective for immune prophylaxis.

[0375] Respiratory virus RNA (e.g. mRNA) vaccines may be administrated with other prophylactic or therapeutic compounds. As a non-limiting example, a prophylactic or therapeutic compound may be an adjuvant or a booster. As used herein, when referring to a prophylactic composition, such as a vaccine, the term "booster" refers to an extra administration of the prophylactic (vaccine) composition. A booster (or booster vaccine) may be given after an earlier administration of the prophylactic composition. The time of administration between the initial administration of the prophylactic composition and the booster may be, but is not limited to, 1 minute, 2 minutes, 3 minutes, 4 minutes, 5 minutes, 6 minutes, 7 minutes, 8 minutes, 9 minutes, 10 minutes, 15 minutes, 20 minutes 35 minutes, 40 minutes, 45 minutes, 50 minutes, 55 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, 6 hours, 7 hours, 8 hours, 9 hours, 10 hours, 11 hours, 12 hours, 13 hours, 14 hours, 15 hours, 16 hours, 17 hours, 18 hours, 19 hours, 20 hours, 21 hours, 22 hours, 23 hours, 1 day, 36 hours, 2 days, 3 days, 4 days, 5 days, 6 days, 1 week, 10 days, 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 10 months, 11 months, 1 year, 18 months, 2 years, 3 years, 4 years, 5 years, 6 years, 7 years, 8 years, 9 years, 10 years, 11 years, 12 years, 13 years, 14 years, 15 years, 16 years, 17 years, 18 years, 19 years, 20 years, 25 years, 30 years, 35 years, 40 years, 45 years, 50 years, 55 years, 60 years, 65 years, 70 years, 75 years, 80 years, 85 years, 90 years, 95 years or more than 99 years. In some embodiments, the time of administration between the initial administration of the prophylactic composition and the booster may be, but is not limited to, 1 week, 2 weeks, 3 weeks, 1 month, 2 months, 3 months, 6 months or 1 year.

[0376] In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines may be administered intramuscularly or intradermally, similarly to the administration of inactivated vaccines known in the art.

[0377] Respiratory virus RNA (e.g. mRNA) vaccines may be utilized in various settings depending on the prevalence of the infection or the degree or level of unmet medical need. As a non-limiting example, the RNA (e.g., mRNA) vaccines may be utilized to treat and/or prevent a variety of respiratory infections. RNA (e.g., mRNA) vaccines have superior properties in that they produce much larger antibody titers and produce responses early than commercially available anti-viral agents/compositions.

[0378] Provided herein are pharmaceutical compositions including respiratory virus RNA (e.g. mRNA) vaccines and RNA (e.g. mRNA) vaccine compositions and/or complexes optionally in combination with one or more pharmaceutically acceptable excipients.

[0379] Respiratory virus RNA (e.g. mRNA) vaccines may be formulated or administered alone or in conjunction with one or more other components. For instance, hMPV/PIV3/RSV RNA (e.g., mRNA) vaccines (vaccine compositions) may comprise other components including, but not limited to, adjuvants.

[0380] In some embodiments, respiratory virus (e.g. mRNA) vaccines do not include an adjuvant (they are adjuvant free).

[0381] Respiratory virus RNA (e.g. mRNA) vaccines may be formulated or administered in combination with one or more pharmaceutically-acceptable excipients. In some embodiments, vaccine compositions comprise at least one additional active substances, such as, for example, a therapeutically-active substance, a prophylactically-active substance, or a combination of both. Vaccine compositions may be sterile, pyrogen-free or both sterile and pyrogen-free. General considerations in the formulation and/or manufacture of pharmaceutical agents, such as vaccine compositions, may be found, for example, in Remington: The Science and Practice of Pharmacy 21st ed., Lippincott Williams & Wilkins, 2005 (incorporated herein by reference in its entirety).

[0382] In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are administered to humans, human patients or subjects. For the purposes of the present disclosure, the phrase "active ingredient" generally refers to the RNA (e.g., mRNA) vaccines or the polynucleotides contained therein, for example, RNA polynucleotides (e.g., mRNA polynucleotides) encoding antigenic polypeptides.

[0383] Formulations of the respiratory virus vaccine compositions described herein may be prepared by any method known or hereafter developed in the art of pharmacology. In general, such preparatory methods include the step of bringing the active ingredient (e.g., mRNA polynucleotide) into association with an excipient and/or one or more other accessory ingredients, and then, if necessary and/or desirable, dividing, shaping and/or packaging the product into a desired single- or multi-dose unit.

[0384] Relative amounts of the active ingredient, the pharmaceutically acceptable excipient, and/or any additional ingredients in a pharmaceutical composition in accordance with the disclosure will vary, depending upon the identity, size, and/or condition of the subject treated and further depending upon the route by which the composition is to be administered. By way of example, the composition may comprise between 0.1% and 100%, e.g., between 0.5 and 50%, between 1-30%, between 5-80%, at least 80% (w/w) active ingredient.

[0385] Respiratory virus RNA (e.g. mRNA) vaccines can be formulated using one or more excipients to: (1) increase stability; (2) increase cell transfection; (3) permit the sustained or delayed release (e.g., from a depot formulation); (4) alter the biodistribution (e.g., target to specific tissues or cell types); (5) increase the translation of encoded protein in vivo; and/or (6) alter the release profile of encoded protein (antigen) in vivo. In addition to traditional excipients such as any and all solvents, dispersion media, diluents, or other liquid vehicles, dispersion or suspension aids, surface active agents, isotonic agents, thickening or emulsifying agents, preservatives, excipients can include, without limitation, lipidoids, liposomes, lipid nanoparticles, polymers, lipoplexes, core-shell nanoparticles, peptides, proteins, cells transfected with respiratory virus RNA (e.g. mRNA) vaccines (e.g., for transplantation into a subject), hyaluronidase, nanoparticle mimics and combinations thereof.

Stabilizing Elements

[0386] Naturally-occurring eukaryotic mRNA molecules have been found to contain stabilizing elements, including, but not limited to untranslated regions (UTR) at their 5'-end (5'UTR) and/or at their 3'-end (3'UTR), in addition to other structural features, such as a 5'-cap structure or a 3'-poly(A) tail. Both the 5'UTR and the 3'UTR are typically transcribed from the genomic DNA and are elements of the premature mRNA. Characteristic structural features of mature mRNA, such as the 5'-cap and the 3'-poly(A) tail are usually added to the transcribed (premature) mRNA during mRNA processing. The 3'-poly(A) tail is typically a stretch of adenine nucleotides added to the 3'-end of the transcribed mRNA. It can comprise up to about 400 adenine nucleotides. In some embodiments the length of the 3'-poly(A) tail may be an essential element with respect to the stability of the individual mRNA.

[0387] In some embodiments the RNA (e.g., mRNA) vaccine may include one or more stabilizing elements. Stabilizing elements may include for instance a histone stem-loop. A stem-loop binding protein (SLBP), a 32 kDa protein has been identified. It is associated with the histone stem-loop at the 3'-end of the histone messages in both the nucleus and the cytoplasm. Its expression level is regulated by the cell cycle; it peaks during the S-phase, when histone mRNA levels are also elevated. The protein has been shown to be essential for efficient 3'-end processing of histone pre-mRNA by the U7 snRNP. SLBP continues to be associated with the stem-loop after processing, and then stimulates the translation of mature histone mRNAs into histone proteins in the cytoplasm. The RNA binding domain of SLBP is conserved through metazoa and protozoa; its binding to the histone stem-loop depends on the structure of the loop. The minimum binding site includes at least three nucleotides 5' and two nucleotides 3' relative to the stem-loop.

[0388] In some embodiments, the RNA (e.g., mRNA) vaccines include a coding region, at least one histone stem-loop, and optionally, a poly(A) sequence or polyadenylation signal. The poly(A) sequence or polyadenylation signal generally should enhance the expression level of the encoded protein. The encoded protein, in some embodiments, is not a histone protein, a reporter protein (e.g. Luciferase, GFP, EGFP, .beta.-Galactosidase, EGFP), or a marker or selection protein (e.g. alpha-Globin, Galactokinase and Xanthine:guanine phosphoribosyl transferase (GPT)).

[0389] In some embodiments, the combination of a poly(A) sequence or polyadenylation signal and at least one histone stem-loop, even though both represent alternative mechanisms in nature, acts synergistically to increase the protein expression beyond the level observed with either of the individual elements. It has been found that the synergistic effect of the combination of poly(A) and at least one histone stem-loop does not depend on the order of the elements or the length of the poly(A) sequence.

[0390] In some embodiments, the RNA (e.g., mRNA) vaccine does not comprise a histone downstream element (HDE). "Histone downstream element" (HDE) includes a purine-rich polynucleotide stretch of approximately 15 to 20 nucleotides 3' of naturally occurring stem-loops, representing the binding site for the U7 snRNA, which is involved in processing of histone pre-mRNA into mature histone mRNA. Ideally, the inventive nucleic acid does not include an intron.

[0391] In some embodiments, the RNA (e.g., mRNA) vaccine may or may not contain a enhancer and/or promoter sequence, which may be modified or unmodified or which may be activated or inactivated. In some embodiments, the histone stem-loop is generally derived from histone genes, and includes an intramolecular base pairing of two neighbored partially or entirely reverse complementary sequences separated by a spacer, including (e.g., consisting of) a short sequence, which forms the loop of the structure. The unpaired loop region is typically unable to base pair with either of the stem loop elements. It occurs more often in RNA, as is a key component of many RNA secondary structures, but may be present in single-stranded DNA as well. Stability of the stem-loop structure generally depends on the length, number of mismatches or bulges, and base composition of the paired region. In some embodiments, wobble base pairing (non-Watson-Crick base pairing) may result. In some embodiments, the at least one histone stem-loop sequence comprises a length of 15 to 45 nucleotides.

[0392] In other embodiments the RNA (e.g., mRNA) vaccine may have one or more AU-rich sequences removed. These sequences, sometimes referred to as AURES are destabilizing sequences found in the 3'UTR. The AURES may be removed from the RNA (e.g., mRNA) vaccines. Alternatively the AURES may remain in the RNA (e.g., mRNA) vaccine.

Nanoparticle Formulations

[0393] In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are formulated in a nanoparticle. In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are formulated in a lipid nanoparticle. In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines are formulated in a lipid-polycation complex, referred to as a cationic lipid nanoparticle. As a non-limiting example, the polycation may include a cationic peptide or a polypeptide such as, but not limited to, polylysine, polyornithine and/or polyarginine. In some embodiments, respiratory virus RNA (e.g., mRNA) vaccines are formulated in a lipid nanoparticle that includes a non-cationic lipid such as, but not limited to, cholesterol or dioleoyl phosphatidylethanolamine (DOPE).

[0394] A lipid nanoparticle formulation may be influenced by, but not limited to, the selection of the cationic lipid component, the degree of cationic lipid saturation, the nature of the PEGylation, ratio of all components and biophysical parameters such as size. In one example by Semple et al. (Nature Biotech. 2010 28:172-176), the lipid nanoparticle formulation is composed of 57.1% cationic lipid, 7.1% dipalmitoylphosphatidylcholine, 34.3% cholesterol, and 1.4% PEG-c-DMA. As another example, changing the composition of the cationic lipid can more effectively deliver siRNA to various antigen presenting cells (Basha et al. Mol Ther. 2011 19:2186-2200).

[0395] In some embodiments, lipid nanoparticle formulations may comprise 35 to 45% cationic lipid, 40% to 50% cationic lipid, 50% to 60% cationic lipid and/or 55% to 65% cationic lipid. In some embodiments, the ratio of lipid to RNA (e.g., mRNA) in lipid nanoparticles may be 5:1 to 20:1, 10:1 to 25:1, 15:1 to 30:1 and/or at least 30:1.

[0396] In some embodiments, the ratio of PEG in the lipid nanoparticle formulations may be increased or decreased and/or the carbon chain length of the PEG lipid may be modified from C14 to C18 to alter the pharmacokinetics and/or biodistribution of the lipid nanoparticle formulations. As a non-limiting example, lipid nanoparticle formulations may contain 0.5% to 3.0%, 1.0% to 3.5%, 1.5% to 4.0%, 2.0% to 4.5%, 2.5% to 5.0% and/or 3.0% to 6.0% of the lipid molar ratio of PEG-c-DOMG (R-3-[(.omega.-methoxy-poly(ethyleneglycol)2000)carbamoyl)]-1,2-dimyristy- loxypropyl-3-amine) (also referred to herein as PEG-DOMG) as compared to the cationic lipid, DSPC and cholesterol. In some embodiments, the PEG-c-DOMG may be replaced with a PEG lipid such as, but not limited to, PEG-DSG (1,2-Distearoyl-sn-glycerol, methoxypolyethylene glycol), PEG-DMG (1,2-Dimyristoyl-sn-glycerol) and/or PEG-DPG (1,2-Dipalmitoyl-sn-glycerol, methoxypolyethylene glycol). The cationic lipid may be selected from any lipid known in the art such as, but not limited to, DLin-MC3-DMA, DLin-DMA, C12-200 and DLin-KC2-DMA.

[0397] In some embodiments, an respiratory virus RNA (e.g. mRNA) vaccine formulation is a nanoparticle that comprises at least one lipid. The lipid may be selected from, but is not limited to, DLin-DMA, DLin-K-DMA, 98N12-5, C12-200, DLin-MC3-DMA, DLin-KC2-DMA, DODMA, PLGA, PEG, PEG-DMG, PEGylated lipids and amino alcohol lipids. In some embodiments, the lipid may be a cationic lipid such as, but not limited to, DLin-DMA, DLin-D-DMA, DLin-MC3-DMA, DLin-KC2-DMA, DODMA and amino alcohol lipids. The amino alcohol cationic lipid may be the lipids described in and/or made by the methods described in U.S. Patent Publication No. US20130150625, herein incorporated by reference in its entirety. As a non-limiting example, the cationic lipid may be 2-amino-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-{[(9Z,2Z)-octadeca-9,12- -dien-1-yloxy]methyl}propan-1-ol (Compound 1 in US20130150625); 2-amino-3-[(9Z)-octadec-9-en-1-yloxy]-2-{[(9Z)-octadec-9-en-1-yloxy]methy- l}propan-1-ol (Compound 2 in US20130150625); 2-amino-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-[(octyloxy)methyl]propa- n-1-ol (Compound 3 in US20130150625); and 2-(dimethylamino)-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-{[(9Z,12Z)-oc- tadeca-9,12-dien-1-yloxy]methyl}propan-1-ol (Compound 4 in US20130150625); or any pharmaceutically acceptable salt or stereoisomer thereof.

[0398] Lipid nanoparticle formulations typically comprise a lipid, in particular, an ionizable cationic lipid, for example, 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), or di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), and further comprise a neutral lipid, a sterol and a molecule capable of reducing particle aggregation, for example a PEG or PEG-modified lipid.

[0399] In some embodiments, a lipid nanoparticle formulation consists essentially of (i) at least one lipid selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319); (ii) a neutral lipid selected from DSPC, DPPC, POPC, DOPE and SM; (iii) a sterol, e.g., cholesterol; and (iv) a PEG-lipid, e.g., PEG-DMG or PEG-cDMA, in a molar ratio of 20-60% cationic lipid:5-25% neutral lipid:25-55% sterol; 0.5-15% PEG-lipid.

[0400] In some embodiments, a lipid nanoparticle formulation includes 25% to 75% on a molar basis of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), e.g., 35 to 65%, 45 to 65%, 60%, 57.5%, 50% or 40% on a molar basis.

[0401] In some embodiments, a lipid nanoparticle formulation includes 0.5% to 15% on a molar basis of the neutral lipid, e.g., 3 to 12%, 5 to 10% or 15%, 10%, or 7.5% on a molar basis. Examples of neutral lipids include, without limitation, DSPC, POPC, DPPC, DOPE and SM. In some embodiments, the formulation includes 5% to 50% on a molar basis of the sterol (e.g., 15 to 45%, 20 to 40%, 40%, 38.5%, 35%, or 31% on a molar basis. A non-limiting example of a sterol is cholesterol. In some embodiments, a lipid nanoparticle formulation includes 0.5% to 20% on a molar basis of the PEG or PEG-modified lipid (e.g., 0.5 to 10%, 0.5 to 5%, 1.5%, 0.5%, 1.5%, 3.5%, or 5% on a molar basis. In some embodiments, a PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of 2,000 Da. In some embodiments, a PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of less than 2,000, for example around 1,500 Da, around 1,000 Da, or around 500 Da. Non-limiting examples of PEG-modified lipids include PEG-distearoyl glycerol (PEG-DMG) (also referred herein as PEG-C14 or C14-PEG), PEG-cDMA (further discussed in Reyes et al. J. Controlled Release, 107, 276-287 (2005) the contents of which are herein incorporated by reference in their entirety).

[0402] In some embodiments, lipid nanoparticle formulations include 25-75% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 0.5-15% of the neutral lipid, 5-50% of the sterol, and 0.5-20% of the PEG or PEG-modified lipid on a molar basis.

[0403] In some embodiments, lipid nanoparticle formulations include 35-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-

dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 3-12% of the neutral lipid, 15-45% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

[0404] In some embodiments, lipid nanoparticle formulations include 45-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 5-10% of the neutral lipid, 25-40% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

[0405] In some embodiments, lipid nanoparticle formulations include 60% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 7.5% of the neutral lipid, 31% of the sterol, and 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0406] In some embodiments, lipid nanoparticle formulations include 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 10% of the neutral lipid, 38.5% of the sterol, and 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0407] In some embodiments, lipid nanoparticle formulations include 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 10% of the neutral lipid, 35% of the sterol, 4.5% or 5% of the PEG or PEG-modified lipid, and 0.5% of the targeting lipid on a molar basis.

[0408] In some embodiments, lipid nanoparticle formulations include 40% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 15% of the neutral lipid, 40% of the sterol, and 5% of the PEG or PEG-modified lipid on a molar basis.

[0409] In some embodiments, lipid nanoparticle formulations include 57.2% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 7.1% of the neutral lipid, 34.3% of the sterol, and 1.4% of the PEG or PEG-modified lipid on a molar basis.

[0410] In some embodiments, lipid nanoparticle formulations include 57.5% of a cationic lipid selected from the PEG lipid is PEG-cDMA (PEG-cDMA is further discussed in Reyes et al. (J. Controlled Release, 107, 276-287 (2005), the contents of which are herein incorporated by reference in their entirety), 7.5% of the neutral lipid, 31.5% of the sterol, and 3.5% of the PEG or PEG-modified lipid on a molar basis.

[0411] In some embodiments, lipid nanoparticle formulations consists essentially of a lipid mixture in molar ratios of 20-70% cationic lipid:5-45% neutral lipid:20-55% cholesterol: 0.5-15% PEG-modified lipid. In some embodiments, lipid nanoparticle formulations consists essentially of a lipid mixture in a molar ratio of 20-60% cationic lipid:5-25% neutral lipid: 25-55% cholesterol: 0.5-15% PEG-modified lipid.

[0412] In some embodiments, the molar lipid ratio is 50/10/38.5/1.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG, PEG-DSG or PEG-DPG), 57.2/7.1134.3/1.4 (mol % cationic lipid/neutral lipid, e.g., DPPC/Chol/PEG-modified lipid, e.g., PEG-cDMA), 40/15/40/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG), 50/10/35/4.5/0.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DSG), 50/10/35/5 (cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG), 40/10/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA), 35/15/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA) or 52/13/30/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA).

[0413] Non-limiting examples of lipid nanoparticle compositions and methods of making them are described, for example, in Semple et al. (2010) Nat. Biotechnol. 28:172-176; Jayarama et al. (2012), Angew. Chem. Int. Ed., 51: 8529-8533; and Maier et al. (2013) Molecular Therapy 21, 1570-1578 (the contents of each of which are incorporated herein by reference in their entirety).

[0414] In some embodiments, lipid nanoparticle formulations may comprise a cationic lipid, a PEG lipid and a structural lipid and optionally comprise a non-cationic lipid. As a non-limiting example, a lipid nanoparticle may comprise 40-60% of cationic lipid, 5-15% of a non-cationic lipid, 1-2% of a PEG lipid and 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise 50% cationic lipid, 10% non-cationic lipid, 1.5% PEG lipid and 38.5% structural lipid. As yet another non-limiting example, a lipid nanoparticle may comprise 55% cationic lipid, 10% non-cationic lipid, 2.5% PEG lipid and 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and L319.

[0415] In some embodiments, the lipid nanoparticle formulations described herein may be 4 component lipid nanoparticles. The lipid nanoparticle may comprise a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle may comprise 40-60% of cationic lipid, 5-15% of a non-cationic lipid, 1-2% of a PEG lipid and 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise 50% cationic lipid, 10% non-cationic lipid, 1.5% PEG lipid and 38.5% structural lipid. As yet another non-limiting example, the lipid nanoparticle may comprise 55% cationic lipid, 10% non-cationic lipid, 2.5% PEG lipid and 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and L319.

[0416] In some embodiments, the lipid nanoparticle formulations described herein may comprise a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle comprise 50% of the cationic lipid DLin-KC2-DMA, 10% of the non-cationic lipid DSPC, 1.5% of the PEG lipid PEG-DOMG and 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise 50% of the cationic lipid DLin-MC3-DMA, 10% of the non-cationic lipid DSPC, 1.5% of the PEG lipid PEG-DOMG and 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise 50% of the cationic lipid DLin-MC3-DMA, 10% of the non-cationic lipid DSPC, 1.5% of the PEG lipid PEG-DMG and 38.5% of the structural lipid cholesterol. As yet another non-limiting example, the lipid nanoparticle comprise 55% of the cationic lipid L319, 10% of the non-cationic lipid DSPC, 2.5% of the PEG lipid PEG-DMG and 32.5% of the structural lipid cholesterol.

[0417] Relative amounts of the active ingredient, the pharmaceutically acceptable excipient, and/or any additional ingredients in a vaccine composition may vary, depending upon the identity, size, and/or condition of the subject being treated and further depending upon the route by which the composition is to be administered. For example, the composition may comprise between 0.1% and 99% (w/w) of the active ingredient. By way of example, the composition may comprise between 0.1% and 100%, e.g., between 0.5 and 50%, between 1-30%, between 5-80%, at least 80% (w/w) active ingredient.

[0418] In some embodiments, the respiratory virus RNA (e.g. mRNA) vaccine composition may comprise the polynucleotide described herein, formulated in a lipid nanoparticle comprising MC3, Cholesterol, DSPC and PEG2000-DMG, the buffer trisodium citrate, sucrose and water for injection. As a non-limiting example, the composition comprises: 2.0 mg/mL of drug substance (e.g., polynucleotides encoding H10N8 hMPV), 21.8 mg/mL of MC3, 10.1 mg/mL of cholesterol, 5.4 mg/mL of DSPC, 2.7 mg/mL of PEG2000-DMG, 5.16 mg/mL of trisodium citrate, 71 mg/mL of sucrose and 1.0 mL of water for injection.

[0419] In some embodiments, a nanoparticle (e.g., a lipid nanoparticle) has a mean diameter of 10-500 nm, 20-400 nm, 30-300 nm, 40-200 nm. In some embodiments, a nanoparticle (e.g., a lipid nanoparticle) has a mean diameter of 50-150 nm, 50-200 nm, 80-100 nm or 80-200 nm.

Liposomes, Lipoplexes, and Lipid Nanoparticles

[0420] The RNA (e.g., mRNA) vaccines of the disclosure can be formulated using one or more liposomes, lipoplexes, or lipid nanoparticles. In some embodiments, pharmaceutical compositions of RNA (e.g., mRNA) vaccines include liposomes. Liposomes are artificially-prepared vesicles which may primarily be composed of a lipid bilayer and may be used as a delivery vehicle for the administration of nutrients and pharmaceutical formulations. Liposomes can be of different sizes such as, but not limited to, a multilamellar vesicle (MLV) which may be hundreds of nanometers in diameter and may contain a series of concentric bilayers separated by narrow aqueous compartments, a small unicellular vesicle (SUV) which may be smaller than 50 nm in diameter, and a large unilamellar vesicle (LUV) which may be between 50 and 500 nm in diameter. Liposome design may include, but is not limited to, opsonins or ligands in order to improve the attachment of liposomes to unhealthy tissue or to activate events such as, but not limited to, endocytosis. Liposomes may contain a low or a high pH in order to improve the delivery of the pharmaceutical formulations.

[0421] The formation of liposomes may depend on the physicochemical characteristics such as, but not limited to, the pharmaceutical formulation entrapped and the liposomal ingredients, the nature of the medium in which the lipid vesicles are dispersed, the effective concentration of the entrapped substance and its potential toxicity, any additional processes involved during the application and/or delivery of the vesicles, the optimization size, polydispersity and the shelf-life of the vesicles for the intended application, and the batch-to-batch reproducibility and possibility of large-scale production of safe and efficient liposomal products.

[0422] In some embodiments, pharmaceutical compositions described herein may include, without limitation, liposomes such as those formed from 1,2-dioleyloxy-N,N-dimethylaminopropane (DODMA) liposomes, DiLa2 liposomes from Marina Biotech (Bothell, Wash.), 1,2-dilinoleyloxy-3-dimethylaminopropane (DLin-DMA), 2,2-dilinoleyl-4-(2-dimethylaminoethyl)-[1,3]-dioxolane (DLin-KC2-DMA), and MC3 (US20100324120; herein incorporated by reference in its entirety) and liposomes which may deliver small molecule drugs such as, but not limited to, DOXIL.RTM. from Janssen Biotech, Inc. (Horsham, Pa.).

[0423] In some embodiments, pharmaceutical compositions described herein may include, without limitation, liposomes such as those formed from the synthesis of stabilized plasmid-lipid particles (SPLP) or stabilized nucleic acid lipid particle (SNALP) that have been previously described and shown to be suitable for oligonucleotide delivery in vitro and in vivo (see Wheeler et al. Gene Therapy. 1999 6:271-281; Zhang et al. Gene Therapy. 1999 6:1438-1447; Jeffs et al. Pharm Res. 2005 22:362-372; Morrissey et al., Nat Biotechnol. 2005 2:1002-1007; Zimmermann et al., Nature. 2006 441:111-114; Heyes et al. J Contr Rel. 2005 107:276-287; Semple et al. Nature Biotech. 2010 28:172-176; Judge et al. J Clin Invest. 2009 119:661-673; deFougerolles Hum Gene Ther. 2008 19:125-132; U.S. Patent Publication No US20130122104; all of which are incorporated herein in their entireties). The original manufacture method by Wheeler et al. was a detergent dialysis method, which was later improved by Jeffs et al. and is referred to as the spontaneous vesicle formation method. The liposome formulations are composed of 3 to 4 lipid components in addition to the polynucleotide. As an example a liposome can contain, but is not limited to, 55% cholesterol, 20% disteroylphosphatidyl choline (DSPC), 10% PEG-S-DSG, and 15% 1,2-dioleyloxy-N,N-dimethylaminopropane (DODMA), as described by Jeffs et al. As another example, certain liposome formulations may contain, but are not limited to, 48% cholesterol, 20% DSPC, 2% PEG-c-DMA, and 30% cationic lipid, where the cationic lipid can be 1,2-distearloxy-N,N-dimethylaminopropane (DSDMA), DODMA, DLin-DMA, or 1,2-dilinolenyloxy-3-dimethylaminopropane (DLenDMA), as described by Heyes et al.

[0424] In some embodiments, liposome formulations may comprise from about 25.0% cholesterol to about 40.0% cholesterol, from about 30.0% cholesterol to about 45.0% cholesterol, from about 35.0% cholesterol to about 50.0% cholesterol and/or from about 48.5% cholesterol to about 60% cholesterol. In some embodiments, formulations may comprise a percentage of cholesterol selected from the group consisting of 28.5%, 31.5%, 33.5%, 36.5%, 37.0%, 38.5%, 39.0% and 43.5%. In some embodiments, formulations may comprise from about 5.0% to about 10.0% DSPC and/or from about 7.0% to about 15.0% DSPC.

[0425] In some embodiments, the RNA (e.g., mRNA) vaccine pharmaceutical compositions may be formulated in liposomes such as, but not limited to, DiLa2 liposomes (Marina Biotech, Bothell, Wash.), SMARTICLES.RTM. (Marina Biotech, Bothell, Wash.), neutral DOPC (1,2-dioleoyl-sn-glycero-3-phosphocholine) based liposomes (e.g., siRNA delivery for ovarian cancer (Landen et al. Cancer Biology & Therapy 2006 5(12)1708-1713); herein incorporated by reference in its entirety) and hyaluronan-coated liposomes (Quiet Therapeutics, Israel).

[0426] In some embodiments, the cationic lipid may be a low molecular weight cationic lipid such as those described in U.S. Patent Application No. 20130090372, the contents of which are herein incorporated by reference in their entirety.

[0427] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid vesicle, which may have crosslinks between functionalized lipid bilayers.

[0428] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid-polycation complex. The formation of the lipid-polycation complex may be accomplished by methods known in the art and/or as described in U.S. Pub. No. 20120178702, herein incorporated by reference in its entirety. As a non-limiting example, the polycation may include a cationic peptide or a polypeptide such as, but not limited to, polylysine, polyornithine and/or polyarginine. In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid-polycation complex, which may further include a non-cationic lipid such as, but not limited to, cholesterol or dioleoyl phosphatidylethanolamine (DOPE).

[0429] In some embodiments, the ratio of PEG in the lipid nanoparticle (LNP) formulations may be increased or decreased and/or the carbon chain length of the PEG lipid may be modified from C14 to C18 to alter the pharmacokinetics and/or biodistribution of the LNP formulations. As a non-limiting example, LNP formulations may contain from about 0.5% to about 3.0%, from about 1.0% to about 3.5%, from about 1.5% to about 4.0%, from about 2.0% to about 4.5%, from about 2.5% to about 5.0% and/or from about 3.0% to about 6.0% of the lipid molar ratio of PEG-c-DOMG (R-3-[(.omega.-methoxy-poly(ethyleneglycol)2000)carbamoyl)]-1,2-dimyristy- loxypropyl-3-amine) (also referred to herein as PEG-DOMG) as compared to the cationic lipid, DSPC and cholesterol. In some embodiments, the PEG-c-DOMG may be replaced with a PEG lipid such as, but not limited to, PEG-DSG (1,2-Distearoyl-sn-glycerol, methoxypolyethylene glycol), PEG-DMG (1,2-Dimyristoyl-sn-glycerol) and/or PEG-DPG (1,2-Dipalmitoyl-sn-glycerol, methoxypolyethylene glycol). The cationic lipid may be selected from any lipid known in the art such as, but not limited to, DLin-MC3-DMA, DLin-DMA, C12-200 and DLin-KC2-DMA.

[0430] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid nanoparticle.

[0431] In some embodiments, the RNA (e.g., mRNA) vaccine formulation comprising the polynucleotide is a nanoparticle which may comprise at least one lipid. The lipid may be selected from, but is not limited to, DLin-DMA, DLin-K-DMA, 98N12-5, C12-200, DLin-MC3-DMA, DLin-KC2-DMA, DODMA, PLGA, PEG, PEG-DMG, PEGylated lipids and amino alcohol lipids. In another aspect, the lipid may be a cationic lipid such as, but not limited to, DLin-DMA, DLin-D-DMA, DLin-MC3-DMA, DLin-KC2-DMA, DODMA and amino alcohol lipids. The amino alcohol cationic lipid may be the lipids described in and/or made by the methods described in U.S. Patent Publication No. US20130150625, herein incorporated by reference in its entirety. As a non-limiting example, the cationic lipid may be 2-amino-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-{[(9Z,2Z)-octadeca-9,12- -dien-1-yloxy]methyl}propan-1-ol (Compound 1 in US20130150625); 2-amino-3-[(9Z)-octadec-9-en-1-yloxy]-2-{[(9Z)-octadec-9-en-1-yloxy]methy- l}propan-1-ol (Compound 2 in US20130150625); 2-amino-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-[(octyloxy)methyl]propa- n-1-ol (Compound 3 in US20130150625); and 2-(dimethylamino)-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-2-{[(9Z,12Z)-oc- tadeca-9,12-dien-1-yloxy]methyl}propan-1-ol (Compound 4 in US20130150625); or any pharmaceutically acceptable salt or stereoisomer thereof.

[0432] Lipid nanoparticle formulations typically comprise a lipid, in particular, an ionizable cationic lipid, for example, 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), or di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), and further comprise a neutral lipid, a sterol and a molecule capable of reducing particle aggregation, for example a PEG or PEG-modified lipid.

[0433] In some embodiments, the lipid nanoparticle formulation consists essentially of (i) at least one lipid selected from the group consisting of 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319); (ii) a neutral lipid selected from DSPC, DPPC, POPC, DOPE and SM; (iii) a sterol, e.g., cholesterol; and (iv) a PEG-lipid, e.g., PEG-DMG or PEG-cDMA, in a molar ratio of about 20-60% cationic lipid:5-25% neutral lipid:25-55% sterol; 0.5-15% PEG-lipid.

[0434] In some embodiments, the formulation includes from about 25% to about 75% on a molar basis of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), e.g., from about 35 to about 65%, from about 45 to about 65%, about 60%, about 57.5%, about 50% or about 40% on a molar basis.

[0435] In some embodiments, the formulation includes from about 0.5% to about 15% on a molar basis of the neutral lipid e.g., from about 3 to about 12%, from about 5 to about 10% or about 15%, about 10%, or about 7.5% on a molar basis. Examples of neutral lipids include, but are not limited to, DSPC, POPC, DPPC, DOPE and SM. In some embodiments, the formulation includes from about 5% to about 50% on a molar basis of the sterol (e.g., about 15 to about 45%, about 20 to about 40%, about 40%, about 38.5%, about 35%, or about 31% on a molar basis. An exemplary sterol is cholesterol. In some embodiments, the formulation includes from about 0.5% to about 20% on a molar basis of the PEG or PEG-modified lipid (e.g., about 0.5 to about 10%, about 0.5 to about 5%, about 1.5%, about 0.5%, about 1.5%, about 3.5%, or about 5% on a molar basis. In some embodiments, the PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of 2,000 Da. In other embodiments, the PEG or PEG modified lipid comprises a PEG molecule of an average molecular weight of less than 2,000, for example around 1,500 Da, around 1,000 Da, or around 500 Da. Examples of PEG-modified lipids include, but are not limited to, PEG-distearoyl glycerol (PEG-DMG) (also referred herein as PEG-C14 or C14-PEG), PEG-cDMA (further discussed in Reyes et al. J. Controlled Release, 107, 276-287 (2005) the contents of which are herein incorporated by reference in their entirety)

[0436] In some embodiments, the formulations of the present disclosure include 25-75% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 0.5-15% of the neutral lipid, 5-50% of the sterol, and 0.5-20% of the PEG or PEG-modified lipid on a molar basis.

[0437] In some embodiments, the formulations of the present disclosure include 35-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 3-12% of the neutral lipid, 15-45% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

[0438] In some embodiments, the formulations of the present disclosure include 45-65% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), 5-10% of the neutral lipid, 25-40% of the sterol, and 0.5-10% of the PEG or PEG-modified lipid on a molar basis.

[0439] In some embodiments, the formulations of the present disclosure include about 60% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 7.5% of the neutral lipid, about 31% of the sterol, and about 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0440] In some embodiments, the formulations of the present disclosure include about 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 10% of the neutral lipid, about 38.5% of the sterol, and about 1.5% of the PEG or PEG-modified lipid on a molar basis.

[0441] In some embodiments, the formulations of the present disclosure include about 50% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 10% of the neutral lipid, about 35% of the sterol, about 4.5% or about 5% of the PEG or PEG-modified lipid, and about 0.5% of the targeting lipid on a molar basis.

[0442] In some embodiments, the formulations of the present disclosure include about 40% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 15% of the neutral lipid, about 40% of the sterol, and about 5% of the PEG or PEG-modified lipid on a molar basis.

[0443] In some embodiments, the formulations of the present disclosure include about 57.2% of a cationic lipid selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319), about 7.1% of the neutral lipid, about 34.3% of the sterol, and about 1.4% of the PEG or PEG-modified lipid on a molar basis.

[0444] In some embodiments, the formulations of the present disclosure include about 57.5% of a cationic lipid selected from the PEG lipid is PEG-cDMA (PEG-cDMA is further discussed in Reyes et al. (J. Controlled Release, 107, 276-287 (2005), the contents of which are herein incorporated by reference in their entirety), about 7.5% of the neutral lipid, about 31.5% of the sterol, and about 3.5% of the PEG or PEG-modified lipid on a molar basis.

[0445] In some embodiments, lipid nanoparticle formulation consists essentially of a lipid mixture in molar ratios of about 20-70% cationic lipid:5-45% neutral lipid:20-55% cholesterol: 0.5-15% PEG-modified lipid; more preferably in a molar ratio of about 20-60% cationic lipid:5-25% neutral lipid:25-55% cholesterol: 0.5-15% PEG-modified lipid.

[0446] In some embodiments, the molar lipid ratio is approximately 50/10/38.5/1.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG, PEG-DSG or PEG-DPG), 57.2/7.1134.3/1.4 (mol % cationic lipid/neutral lipid, e.g., DPPC/Chol/PEG-modified lipid, e.g., PEG-cDMA), 40/15/40/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG), 50/10/35/4.5/0.5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DSG), 50/10/35/5 (cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG), 40/10/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA), 35/15/40/10 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA) or 52/13/30/5 (mol % cationic lipid/neutral lipid, e.g., DSPC/Chol/PEG-modified lipid, e.g., PEG-DMG or PEG-cDMA).

[0447] Examples of lipid nanoparticle compositions and methods of making same are described, for example, in Semple et al. (2010) Nat. Biotechnol. 28:172-176; Jayarama et al. (2012), Angew. Chem. Int. Ed., 51: 8529-8533; and Maier et al. (2013) Molecular Therapy 21, 1570-1578 (the contents of each of which are incorporated herein by reference in their entirety).

[0448] In some embodiments, the lipid nanoparticle formulations described herein may comprise a cationic lipid, a PEG lipid and a structural lipid and optionally comprise a non-cationic lipid. As a non-limiting example, the lipid nanoparticle may comprise about 40-60% of cationic lipid, about 5-15% of a non-cationic lipid, about 1-2% of a PEG lipid and about 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise about 50% cationic lipid, about 10% non-cationic lipid, about 1.5% PEG lipid and about 38.5% structural lipid. As yet another non-limiting example, the lipid nanoparticle may comprise about 55% cationic lipid, about 10% non-cationic lipid, about 2.5% PEG lipid and about 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and L319.

[0449] In some embodiments, the lipid nanoparticle formulations described herein may be 4 component lipid nanoparticles. The lipid nanoparticle may comprise a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle may comprise about 40-60% of cationic lipid, about 5-15% of a non-cationic lipid, about 1-2% of a PEG lipid and about 30-50% of a structural lipid. As another non-limiting example, the lipid nanoparticle may comprise about 50% cationic lipid, about 10% non-cationic lipid, about 1.5% PEG lipid and about 38.5% structural lipid. As yet another non-limiting example, the lipid nanoparticle may comprise about 55% cationic lipid, about 10% non-cationic lipid, about 2.5% PEG lipid and about 32.5% structural lipid. In some embodiments, the cationic lipid may be any cationic lipid described herein such as, but not limited to, DLin-KC2-DMA, DLin-MC3-DMA and L319.

[0450] In some embodiments, the lipid nanoparticle formulations described herein may comprise a cationic lipid, a non-cationic lipid, a PEG lipid and a structural lipid. As a non-limiting example, the lipid nanoparticle comprise about 50% of the cationic lipid DLin-KC2-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of the PEG lipid PEG-DOMG and about 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise about 50% of the cationic lipid DLin-MC3-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of the PEG lipid PEG-DOMG and about 38.5% of the structural lipid cholesterol. As a non-limiting example, the lipid nanoparticle comprise about 50% of the cationic lipid DLin-MC3-DMA, about 10% of the non-cationic lipid DSPC, about 1.5% of the PEG lipid PEG-DMG and about 38.5% of the structural lipid cholesterol. As yet another non-limiting example, the lipid nanoparticle comprise about 55% of the cationic lipid L319, about 10% of the non-cationic lipid DSPC, about 2.5% of the PEG lipid PEG-DMG and about 32.5% of the structural lipid cholesterol.

[0451] As a non-limiting example, the cationic lipid may be selected from (20Z,23Z)--N,N-dimethylnonacosa-20,23-dien-10-amine, (17Z,20Z)--N,N-dimemylhexacosa-17,20-dien-9-amine, (1Z,19Z)--N5N-dimethylpentacosa-16, 19-dien-8-amine, (13Z,16Z)--N,N-dimethyldocosa-13,16-dien-5-amine, (12Z,15Z)--N,N-dimethylhenicosa-12,15-dien-4-amine, (14Z,17Z)--N,N-dimethyltricosa-14,17-dien-6-amine, (15Z,18Z)--N,N-dimethyltetracosa-15,18-dien-7-amine, (18Z,21Z)--N,N-dimethylheptacosa-18,21-dien-10-amine, (15Z,18Z)--N,N-dimethyltetracosa-15,18-dien-5-amine, (14Z,17Z)--N,N-dimethyltricosa-14,17-dien-4-amine, (19Z,22Z)--N,N-dimeihyloctacosa-19,22-dien-9-amine, (18Z,21 Z)--N,N-dimethylheptacosa-18,21-dien-8 amine, (17Z,20Z)--N,N-dimethylhexacosa-17,20-dien-7-amine, (16Z,19Z)--N,N-dimethylpentacosa-16,19-dien-6-amine, (22Z,25Z)--N,N-dimethylhentriaconta-22,25-dien-10-amine, (21 Z,24Z)--N,N-dimethyltriaconta-21,24-dien-9-amine, (18Z)--N,N-dimetylheptacos-18-en-10-amine, (17Z)--N,N-dimethylhexacos-17-en-9-amine, (19Z,22Z)--N,N-dimethyloctacosa-19,22-dien-7-amine, N,N-dimethylheptacosan-10-amine, (20Z,23Z)--N-ethyl-N-methylnonacosa-20,23-dien-10-amine, 1-[(11Z,14Z)-1-nonylicosa-11,14-dien-1-yl]pyrrolidine, (20Z)--N,N-dimethylheptacos-20-en-10-amine, (15Z)--N,N-dimethyl eptacos-15-en-10-amine, (14Z)--N,N-dimethylnonacos-14-en-10-amine, (17Z)--N,N-dimethylnonacos-17-en-10-amine, (24Z)--N,N-dimethyltritriacont-24-en-10-amine, (20Z)--N,N-dimethylnonacos-20-en-10-amine, (22Z)--N,N-dimethylhentriacont-22-en-10-amine, (16Z)--N,N-dimethylpentacos-16-en-8-amine, (12Z,15Z)--N,N-dimethyl-2-nonylhenicosa-12,15-dien-1-amine, (13Z,16Z)--N,N-dimethyl-3-nonyldocosa-13,16-dien-1 amine, N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]eptadecan-8-amine, 1-[(1S,2R)-2-hexylcyclopropyl]-N,N-dimethylnonadecan-10-amine, N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]nonadecan-10-amine, N,N-dimethyl-21-[(1S,2R)-2-octylcyclopropyl]henicosan-10-amine, N,N-dimethyl-1-[(1S,2S)-2-{[(1R,2R)-2-

pentylcycIopropyl]methyl}cyclopropy- l]nonadecan-10-amine,N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]hexadecan-- 8-amine, N,N-dimethyl-[(1R,2S)-2-undecyIcyclopropyl]tetradecan-5-amine, N,N-dimethyl-3-{7- [(1S,2R)-2-octylcyclopropyl]heptyl}dodecan-1-amine, 1-[(1R,2S)-2-heptylcyclopropyl]-N,N-dimethyloctadecan-9-amine, 1-[(1S,2R)-2-decylcyclopropyl]-N,N-dimethylpentadecan-6-amine, N,N-dimethyl-1-R1S,2R)-2-octylcyclopropyllpentadecan-8-amine, R--N,N-dimethyl-1-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-3-(octyloxy)propa- n-2-amine, S--N,N-dimethyl-1-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-3-(octy-loxy)propan-2-amine, 1-{2-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-1-[(octyloxy)methyl]ethyl}pyrr- olidine, (2S)--N,N-dimethyl-1-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-3-[(5Z-)-oct-5-en-1-yloxy]propan-2-amine, 1-{2-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-1-[(octyloxy)methyl]ethyl}azet- idine, (2S)-1-(hexyloxy)-N,N-dimethyl-3-R9Z,12Z)-octadeca-9,12-dien-1-ylox- ylpropan-2-amine, (2S)-1-(heptyloxy)-N,N-dimethyl-3-R9Z,12Z)-octadeca-9,12-dien-1-yloxylpro- pan-2-amine, N,N-dimethyl-1-(nonyloxy)-3-R9Z,12Z)-octadeca-9,12-dien-1-yloxylpropan-2-- amine, N,N-dimethyl-1-[(9Z)-octadec-9-en-1-yloxy]-3-(octyloxy)propan-2-ami- ne; (2S)-N,N-dimethyl-1-[(6Z,9Z,12Z)-octadeca-6,9,12-trien-1-yloxy]-3-(oct- yloxy)propan-2-amine, (2S)-1-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,N-dimethyl-3-(pentyloxy)pro- pan-2-amine, (2S)-1-(hexyloxy)-3-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,N-dimethylprop- an-2-amine, 1-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-- amine, 1-[(13Z,16Z)-docosa-13,16-dien-1-yloxy]-N,N-dimethyl-3-(octyloxy)pr- opan-2-amine, (2S)-1-[(13Z,16Z)-docosa-13,16-dien-1-yloxy]-3-(hexyloxy)-N,N-dimethylpro- pan-2-amine, (2S)-1-[(13Z)-docos-13-en-1-yloxy]-3-(hexyloxy)-N,N-dimethylpropan-2-amin- e, 1-[(13Z)-docos-13-en-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, 1-[(9Z)-hexadec-9-en-1-yloxy]-N,N-dimethyl-3-(octyloxy)propan-2-amine, (2R)-N,N-dimethyl-H(1-metoyloctyl)oxy]-3-[(9Z,12Z)-octadeca-9,12-dien-1-y- loxy]propan-2-amine, (2R)-1-[(3,7-dimethyloctyl)oxy]-N,N-dimethyl-3-R9Z,12Z)-octadeca-9,12-die- n-1-yloxylpropan-2-amine, N,N-dimethyl-1-(octyloxy)-3-({8-R1S,25)-2-{[(1R,2R)-2-pentylcyclopropyl]m-ethyl}cyclopropyl]octyl}oxy)propan-2-amine, N,N-dimethyl-1-1 [8-(2-oc1ylcyclopropyl)octyl]oxy}-3-(octyloxy)propan-2-amine and (11E,20Z,23Z)--N,N-dimethylnonacosa-11,20,2-trien-10-amine or a pharmaceutically acceptable salt or stereoisomer thereof.

[0452] In some embodiments, the LNP formulations of the RNA (e.g., mRNA) vaccines may contain PEG-c-DOMG at 3% lipid molar ratio. In some embodiments, the LNP formulations of the RNA (e.g., mRNA) vaccines may contain PEG-c-DOMG at 1.5% lipid molar ratio.

[0453] In some embodiments, the pharmaceutical compositions of the RNA (e.g., mRNA) vaccines may include at least one of the PEGylated lipids described in International Publication No. WO2012099755, the contents of which are herein incorporated by reference in their entirety.

[0454] In some embodiments, the LNP formulation may contain PEG-DMG 2000 (1,2-dimyristoyl-sn-glycero-3-phophoethanolamine-N-[methoxy(polyethylene glycol)-2000). In some embodiments, the LNP formulation may contain PEG-DMG 2000, a cationic lipid known in the art and at least one other component. In some embodiments, the LNP formulation may contain PEG-DMG 2000, a cationic lipid known in the art, DSPC and cholesterol. As a non-limiting example, the LNP formulation may contain PEG-DMG 2000, DLin-DMA, DSPC and cholesterol. As another non-limiting example the LNP formulation may contain PEG-DMG 2000, DLin-DMA, DSPC and cholesterol in a molar ratio of 2:40:10:48 (see e.g., Geall et al., Nonviral delivery of self-amplifying RNA (e.g., mRNA) vaccines, PNAS 2012; PMID: 22908294, the contents of each of which are herein incorporated by reference in their entirety).

[0455] The lipid nanoparticles described herein may be made in a sterile environment.

[0456] In some embodiments, the LNP formulation may be formulated in a nanoparticle such as a nucleic acid-lipid particle. As a non-limiting example, the lipid particle may comprise one or more active agents or therapeutic agents; one or more cationic lipids comprising from about 50 mol % to about 85 mol % of the total lipid present in the particle; one or more non-cationic lipids comprising from about 13 mol % to about 49.5 mol % of the total lipid present in the particle; and one or more conjugated lipids that inhibit aggregation of particles comprising from about 0.5 mol % to about 2 mol % of the total lipid present in the particle.

[0457] The nanoparticle formulations may comprise a phosphate conjugate. The phosphate conjugate may increase in vivo circulation times and/or increase the targeted delivery of the nanoparticle. As a non-limiting example, the phosphate conjugates may include a compound of any one of the formulas described in International Application No. WO2013033438, the contents of which are herein incorporated by reference in its entirety.

[0458] The nanoparticle formulation may comprise a polymer conjugate. The polymer conjugate may be a water soluble conjugate. The polymer conjugate may have a structure as described in U.S. Patent Application No. 20130059360, the contents of which are herein incorporated by reference in its entirety. In some embodiments, polymer conjugates with the polynucleotides of the present disclosure may be made using the methods and/or segmented polymeric reagents described in U.S. Patent Application No. 20130072709, the contents of which are herein incorporated by reference in its entirety. In some embodiments, the polymer conjugate may have pendant side groups comprising ring moieties such as, but not limited to, the polymer conjugates described in U.S. Patent Publication No. US20130196948, the contents which are herein incorporated by reference in its entirety.

[0459] The nanoparticle formulations may comprise a conjugate to enhance the delivery of nanoparticles of the present disclosure in a subject. Further, the conjugate may inhibit phagocytic clearance of the nanoparticles in a subject. In one aspect, the conjugate may be a "self" peptide designed from the human membrane protein CD47 (e.g., the "self" particles described by Rodriguez et al. (Science 2013 339, 971-975), herein incorporated by reference in its entirety). As shown by Rodriguez et al., the self peptides delayed macrophage-mediated clearance of nanoparticles which enhanced delivery of the nanoparticles. In another aspect, the conjugate may be the membrane protein CD47 (e.g., see Rodriguez et al. Science 2013 339, 971-975, herein incorporated by reference in its entirety). Rodriguez et al. showed that, similarly to "self" peptides, CD47 can increase the circulating particle ratio in a subject as compared to scrambled peptides and PEG coated nanoparticles.

[0460] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure are formulated in nanoparticles which comprise a conjugate to enhance the delivery of the nanoparticles of the present disclosure in a subject. The conjugate may be the CD47 membrane or the conjugate may be derived from the CD47 membrane protein, such as the "self" peptide described previously. In some embodiments, the nanoparticle may comprise PEG and a conjugate of CD47 or a derivative thereof. In some embodiments, the nanoparticle may comprise both the "self" peptide described above and the membrane protein CD47.

[0461] In some embodiments, a "self" peptide and/or CD47 protein may be conjugated to a virus-like particle or pseudovirion, as described herein for delivery of the RNA (e.g., mRNA) vaccines of the present disclosure.

[0462] In some embodiments, RNA (e.g., mRNA) vaccine pharmaceutical compositions comprising the polynucleotides of the present disclosure and a conjugate that may have a degradable linkage. Non-limiting examples of conjugates include an aromatic moiety comprising an ionizable hydrogen atom, a spacer moiety, and a water-soluble polymer. As a non-limiting example, pharmaceutical compositions comprising a conjugate with a degradable linkage and methods for delivering such pharmaceutical compositions are described in U.S. Patent Publication No. US20130184443, the contents of which are herein incorporated by reference in their entirety.

[0463] The nanoparticle formulations may be a carbohydrate nanoparticle comprising a carbohydrate carrier and a RNA (e.g., mRNA) vaccine. As a non-limiting example, the carbohydrate carrier may include, but is not limited to, an anhydride-modified phytoglycogen or glycogen-type material, phtoglycogen octenyl succinate, phytoglycogen beta-dextrin, anhydride-modified phytoglycogen beta-dextrin. (See e.g., International Publication No. WO2012109121; the contents of which are herein incorporated by reference in their entirety).

[0464] Nanoparticle formulations of the present disclosure may be coated with a surfactant or polymer in order to improve the delivery of the particle. In some embodiments, the nanoparticle may be coated with a hydrophilic coating such as, but not limited to, PEG coatings and/or coatings that have a neutral surface charge. The hydrophilic coatings may help to deliver nanoparticles with larger payloads such as, but not limited to, RNA (e.g., mRNA) vaccines within the central nervous system. As a non-limiting example nanoparticles comprising a hydrophilic coating and methods of making such nanoparticles are described in U.S. Patent Publication No.

US20130183244, the contents of which are herein incorporated by reference in their entirety.

[0465] In some embodiments, the lipid nanoparticles of the present disclosure may be hydrophilic polymer particles. Non-limiting examples of hydrophilic polymer particles and methods of making hydrophilic polymer particles are described in U.S. Patent Publication No. US20130210991, the contents of which are herein incorporated by reference in their entirety.

[0466] In some embodiments, the lipid nanoparticles of the present disclosure may be hydrophobic polymer particles.

[0467] Lipid nanoparticle formulations may be improved by replacing the cationic lipid with a biodegradable cationic lipid which is known as a rapidly eliminated lipid nanoparticle (reLNP). Ionizable cationic lipids, such as, but not limited to, DLinDMA, DLin-KC2-DMA, and DLin-MC3-DMA, have been shown to accumulate in plasma and tissues over time and may be a potential source of toxicity. The rapid metabolism of the rapidly eliminated lipids can improve the tolerability and therapeutic index of the lipid nanoparticles by an order of magnitude from a 1 mg/kg dose to a 10 mg/kg dose in rat. Inclusion of an enzymatically degraded ester linkage can improve the degradation and metabolism profile of the cationic component, while still maintaining the activity of the reLNP formulation. The ester linkage can be internally located within the lipid chain or it may be terminally located at the terminal end of the lipid chain. The internal ester linkage may replace any carbon in the lipid chain.

[0468] In some embodiments, the internal ester linkage may be located on either side of the saturated carbon.

[0469] In some embodiments, an immune response may be elicited by delivering a lipid nanoparticle which may include a nanospecies, a polymer and an immunogen. (U.S. Publication No. 20120189700 and International Publication No. WO2012099805; each of which is herein incorporated by reference in their entirety). The polymer may encapsulate the nanospecies or partially encapsulate the nanospecies. The immunogen may be a recombinant protein, a modified RNA and/or a polynucleotide described herein. In some embodiments, the lipid nanoparticle may be formulated for use in a vaccine such as, but not limited to, against a pathogen.

[0470] Lipid nanoparticles may be engineered to alter the surface properties of particles so the lipid nanoparticles may penetrate the mucosal barrier. Mucus is located on mucosal tissue such as, but not limited to, oral (e.g., the buccal and esophageal membranes and tonsil tissue), ophthalmic, gastrointestinal (e.g., stomach, small intestine, large intestine, colon, rectum), nasal, respiratory (e.g., nasal, pharyngeal, tracheal and bronchial membranes), genital (e.g., vaginal, cervical and urethral membranes). Nanoparticles larger than 10-200 nm which are preferred for higher drug encapsulation efficiency and the ability to provide the sustained delivery of a wide array of drugs have been thought to be too large to rapidly diffuse through mucosal barriers. Mucus is continuously secreted, shed, discarded or digested and recycled so most of the trapped particles may be removed from the mucosa tissue within seconds or within a few hours. Large polymeric nanoparticles (200 nm-500 nm in diameter) which have been coated densely with a low molecular weight polyethylene glycol (PEG) diffused through mucus only 4 to 6-fold lower than the same particles diffusing in water (Lai et al. PNAS 2007 104(5):1482-487; Lai et al. Adv Drug Deliv Rev. 2009 61(2): 158-171; each of which is herein incorporated by reference in their entirety). The transport of nanoparticles may be determined using rates of permeation and/or fluorescent microscopy techniques including, but not limited to, fluorescence recovery after photobleaching (FRAP) and high resolution multiple particle tracking (MPT). As a non-limiting example, compositions which can penetrate a mucosal barrier may be made as described in U.S. Pat. No. 8,241,670 or International Patent Publication No. WO2013110028, the contents of each of which are herein incorporated by reference in its entirety.

[0471] The lipid nanoparticle engineered to penetrate mucus may comprise a polymeric material (i.e. a polymeric core) and/or a polymer-vitamin conjugate and/or a tri-block co-polymer. The polymeric material may include, but is not limited to, polyamines, polyethers, polyamides, polyesters, polycarbamates, polyureas, polycarbonates, poly(styrenes), polyimides, polysulfones, polyurethanes, polyacetylenes, polyethylenes, polyethyeneimines, polyisocyanates, polyacrylates, polymethacrylates, polyacrylonitriles, and polyarylates. The polymeric material may be biodegradable and/or biocompatible. Non-limiting examples of biocompatible polymers are described in International Patent Publication No. WO2013116804, the contents of which are herein incorporated by reference in their entirety. The polymeric material may additionally be irradiated. As a non-limiting example, the polymeric material may be gamma irradiated (see e.g., International App. No. WO201282165, herein incorporated by reference in its entirety). Non-limiting examples of specific polymers include poly(caprolactone) (PCL), ethylene vinyl acetate polymer (EVA), poly(lactic acid) (PLA), poly(L-lactic acid) (PLLA), poly(glycolic acid) (PGA), poly(lactic acid-co-glycolic acid) (PLGA), poly(L-lactic acid-co-glycolic acid) (PLLGA), poly(D,L-lactide) (PDLA), poly(L-lactide) (PLLA), poly(D,L-lactide-co-caprolactone), poly(D,L-lactide-co-caprolactone-co-glycolide), poly(D,L-lactide-co-PEO-co-D,L-lactide), poly(D,L-lactide-co-PPO-co-D,L-lactide), polyalkyl cyanoacralate, polyurethane, poly-L-lysine (PLL), hydroxypropyl methacrylate (HPMA), polyethyleneglycol, poly-L-glutamic acid, poly(hydroxy acids), polyanhydrides, polyorthoesters, poly(ester amides), polyamides, poly(ester ethers), polycarbonates, polyalkylenes such as polyethylene and polypropylene, polyalkylene glycols such as poly(ethylene glycol) (PEG), polyalkylene oxides (PEO), polyalkylene terephthalates such as poly(ethylene terephthalate), polyvinyl alcohols (PVA), polyvinyl ethers, polyvinyl esters such as poly(vinyl acetate), polyvinyl halides such as poly(vinyl chloride) (PVC), polyvinylpyrrolidone, polysiloxanes, polystyrene (PS), polyurethanes, derivatized celluloses such as alkyl celluloses, hydroxyalkyl celluloses, cellulose ethers, cellulose esters, nitro celluloses, hydroxypropylcellulose, carboxymethylcellulose, polymers of acrylic acids, such as poly(methyl(meth)acrylate) (PMMA), poly(ethyl(meth)acrylate), poly(butyl(meth)acrylate), poly(isobutyl(meth)acrylate), poly(hexyl(meth)acrylate), poly(isodecyl(meth)acrylate), poly(lauryl(meth)acrylate), poly(phenyl(meth)acrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), poly(octadecyl acrylate) and copolymers and mixtures thereof, polydioxanone and its copolymers, polyhydroxyalkanoates, polypropylene fumarate, polyoxymethylene, poloxamers, poly(ortho)esters, poly(butyric acid), poly(valeric acid), poly(lactide-co-caprolactone), PEG-PLGA-PEG and trimethylene carbonate, polyvinylpyrrolidone. The lipid nanoparticle may be coated or associated with a co-polymer such as, but not limited to, a block co-polymer (such as a branched polyether-polyamide block copolymer described in International Publication No. WO2013012476, herein incorporated by reference in its entirety), and (poly(ethylene glycol))-(poly(propylene oxide))-(poly(ethylene glycol)) triblock copolymer (see e.g., U.S. Publication 20120121718 and U.S. Publication 20100003337 and U.S. Pat. No. 8,263,665, the contents of each of which is herein incorporated by reference in their entirety). The co-polymer may be a polymer that is generally regarded as safe (GRAS) and the formation of the lipid nanoparticle may be in such a way that no new chemical entities are created. For example, the lipid nanoparticle may comprise poloxamers coating PLGA nanoparticles without forming new chemical entities which are still able to rapidly penetrate human mucus (Yang et al. Angew. Chem. Int. Ed. 2011 50:2597-2600; the contents of which are herein incorporated by reference in their entirety). A non-limiting scalable method to produce nanoparticles which can penetrate human mucus is described by Xu et al. (see, e.g., J Control Release 2013, 170(2):279-86; the contents of which are herein incorporated by reference in their entirety).

[0472] The vitamin of the polymer-vitamin conjugate may be vitamin E. The vitamin portion of the conjugate may be substituted with other suitable components such as, but not limited to, vitamin A, vitamin E, other vitamins, cholesterol, a hydrophobic moiety, or a hydrophobic component of other surfactants (e.g., sterol chains, fatty acids, hydrocarbon chains and alkylene oxide chains).

[0473] The lipid nanoparticle engineered to penetrate mucus may include surface altering agents such as, but not limited to, polynucleotides, anionic proteins (e.g., bovine serum albumin), surfactants (e.g., cationic surfactants such as for example dimethyldioctadecyl-ammonium bromide), sugars or sugar derivatives (e.g., cyclodextrin), nucleic acids, polymers (e.g., heparin, polyethylene glycol and poloxamer), mucolytic agents (e.g., N-acetylcysteine, mugwort, bromelain, papain, clerodendrum, acetylcysteine, bromhexine, carbocisteine, eprazinone, mesna, ambroxol, sobrerol, domiodol, letosteine, stepronin, tiopronin, gelsolin, thymosin .beta.4 dornase alfa, neltenexine, erdosteine) and various DNases including rhDNase. The surface altering agent may be embedded or enmeshed in the particle's surface or disposed (e.g., by coating, adsorption, covalent linkage, or other process) on the surface of the lipid nanoparticle. (see e.g., U.S. Publication 20100215580 and U.S. Publication 20080166414 and US20130164343; the contents of each of which are herein incorporated by reference in their entirety).

[0474] In some embodiments, the mucus penetrating lipid nanoparticles may comprise at least one polynucleotide described herein. The polynucleotide may be encapsulated in the lipid nanoparticle and/or disposed on the surface of the particle. The polynucleotide may be covalently coupled to the lipid nanoparticle. Formulations of mucus penetrating lipid nanoparticles may comprise a plurality of nanoparticles. Further, the formulations may contain particles which may interact with the mucus and alter the structural and/or adhesive properties of the surrounding mucus to decrease mucoadhesion, which may increase the delivery of the mucus penetrating lipid nanoparticles to the mucosal tissue.

[0475] In some embodiments, the mucus penetrating lipid nanoparticles may be a hypotonic formulation comprising a mucosal penetration enhancing coating. The formulation may be hypotonice for the epithelium to which it is being delivered. Non-limiting examples of hypotonic formulations may be found in International Patent Publication No. WO2013110028, the contents of which are herein incorporated by reference in their entirety.

[0476] In some embodiments, in order to enhance the delivery through the mucosal barrier the RNA (e.g., mRNA) vaccine formulation may comprise or be a hypotonic solution. Hypotonic solutions were found to increase the rate at which mucoinert particles such as, but not limited to, mucus-penetrating particles, were able to reach the vaginal epithelial surface (see e.g., Ensign et al. Biomaterials 2013 34(28):6922-9, the contents of which are herein incorporated by reference in their entirety).

[0477] In some embodiments, the RNA (e.g., mRNA) vaccine is formulated as a lipoplex, such as, without limitation, the ATUPLEX.TM. system, the DACC system, the DBTC system and other siRNA-lipoplex technology from Silence Therapeutics (London, United Kingdom), STEMFECT.TM. from STEMGENT.RTM. (Cambridge, Mass.), and polyethylenimine (PEI) or protamine-based targeted and non-targeted delivery of nucleic acids acids (Aleku et al. Cancer Res. 2008 68:9788-9798; Strumberg et al. Int J Clin Pharmacol Ther 2012 50:76-78; Santel et al., Gene Ther 2006 13:1222-1234; Santel et al., Gene Ther 2006 13:1360-1370; Gutbier et al., Pulm Pharmacol. Ther. 2010 23:334-344; Kaufmann et al. Microvasc Res 2010 80:286-293 Weide et al. J Immunother. 2009 32:498-507; Weide et al. J Immunother. 2008 31:180-188; Pascolo Expert Opin. Biol. Ther. 4:1285-1294; Fotin-Mleczek et al., 2011 J. Immunother. 34:1-15; Song et al., Nature Biotechnol. 2005, 23:709-717; Peer et al., Proc Natl Acad Sci USA. 2007 6; 104:4095-4100; deFougerolles Hum Gene Ther. 2008 19:125-132, the contents of each of which are incorporated herein by reference in their entirety).

[0478] In some embodiments, such formulations may also be constructed or compositions altered such that they passively or actively are directed to different cell types in vivo, including but not limited to hepatocytes, immune cells, tumor cells, endothelial cells, antigen presenting cells, and leukocytes (Akinc et al. Mol Ther. 2010 18:1357-1364; Song et al., Nat Biotechnol. 2005 23:709-717; Judge et al., J Clin Invest. 2009 119:661-673; Kaufmann et al., Microvasc Res 2010 80:286-293; Santel et al., Gene Ther 2006 13:1222-1234; Santel et al., Gene Ther 2006 13:1360-1370; Gutbier et al., Pulm Pharmacol. Ther. 2010 23:334-344; Basha et al., Mol. Ther. 2011 19:2186-2200; Fenske and Cullis, Expert Opin Drug Deliv. 2008 5:25-44; Peer et al., Science. 2008 319:627-630; Peer and Lieberman, Gene Ther. 2011 18:1127-1133, the contents of each of which are incorporated herein by reference in their entirety). One example of passive targeting of formulations to liver cells includes the DLin-DMA, DLin-KC2-DMA and DLin-MC3-DMA-based lipid nanoparticle formulations, which have been shown to bind to apolipoprotein E and promote binding and uptake of these formulations into hepatocytes in vivo (Akinc et al. Mol Ther. 2010 18:1357-1364, the contents of which are incorporated herein by reference in their entirety). Formulations can also be selectively targeted through expression of different ligands on their surface as exemplified by, but not limited by, folate, transferrin, N-acetylgalactosamine (GalNAc), and antibody targeted approaches (Kolhatkar et al., Curr Drug Discov Technol. 2011 8:197-206; Musacchio and Torchilin, Front Biosci. 2011 16:1388-1412; Yu et al., Mol Membr Biol. 2010 27:286-298; Patil et al., Crit Rev Ther Drug Carrier Syst. 2008 25:1-61; Benoit et al., Biomacromolecules. 2011 12:2708-2714; Zhao et al., Expert Opin Drug Deliv. 2008 5:309-319; Akinc et al., Mol Ther. 2010 18:1357-1364; Srinivasan et al., Methods Mol Biol. 2012 820:105-116; Ben-Arie et al., Methods Mol Biol. 2012 757:497-507; Peer 2010 J Control Release. 20:63-68; Peer et al., Proc Natl Acad Sci USA. 2007 104:4095-4100; Kim et al., Methods Mol Biol. 2011 721:339-353; Subramanya et al., Mol Ther. 2010 18:2028-2037; Song et al., Nat Biotechnol. 2005 23:709-717; Peer et al., Science. 2008 319:627-630; Peer and Lieberman, Gene Ther. 2011 18:1127-1133, the contents of each of which are incorporated herein by reference in their entirety).

[0479] In some embodiments, the RNA (e.g., mRNA) vaccine is formulated as a solid lipid nanoparticle. A solid lipid nanoparticle (SLN) may be spherical with an average diameter between 10 to 1000 nm. SLN possess a solid lipid core matrix that can solubilize lipophilic molecules and may be stabilized with surfactants and/or emulsifiers. In some embodiments, the lipid nanoparticle may be a self-assembly lipid-polymer nanoparticle (see Zhang et al., ACS Nano, 2008, 2 (8), pp 1696-1702; the contents of which are herein incorporated by reference in their entirety). As a non-limiting example, the SLN may be the SLN described in International Patent Publication No. WO2013105101, the contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the SLN may be made by the methods or processes described in International Patent Publication No. WO2013105101, the contents of which are herein incorporated by reference in their entirety.

[0480] Liposomes, lipoplexes, or lipid nanoparticles may be used to improve the efficacy of polynucleotides directed protein production as these formulations may be able to increase cell transfection by the RNA (e.g., mRNA) vaccine; and/or increase the translation of encoded protein. One such example involves the use of lipid encapsulation to enable the effective systemic delivery of polyplex plasmid DNA (Heyes et al., Mol Ther. 2007 15: 713-720; the contents of which are incorporated herein by reference in their entirety). The liposomes, lipoplexes, or lipid nanoparticles may also be used to increase the stability of the polynucleotide.

[0481] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure can be formulated for controlled release and/or targeted delivery. As used herein, "controlled release" refers to a pharmaceutical composition or compound release profile that conforms to a particular pattern of release to effect a therapeutic outcome. In some embodiments, the RNA (e.g., mRNA) vaccines may be encapsulated into a delivery agent described herein and/or known in the art for controlled release and/or targeted delivery. As used herein, the term "encapsulate" means to enclose, surround or encase. As it relates to the formulation of the compounds of the disclosure, encapsulation may be substantial, complete or partial. The term "substantially encapsulated" means that at least greater than 50, 60, 70, 80, 85, 90, 95, 96, 97, 98, 99, 99.9, 99.9 or greater than 99.999% of the pharmaceutical composition or compound of the disclosure may be enclosed, surrounded or encased within the delivery agent. "Partially encapsulation" means that less than 10, 10, 20, 30, 40 50 or less of the pharmaceutical composition or compound of the disclosure may be enclosed, surrounded or encased within the delivery agent. Advantageously, encapsulation may be determined by measuring the escape or the activity of the pharmaceutical composition or compound of the disclosure using fluorescence and/or electron micrograph. For example, at least 1, 5, 10, 20, 30, 40, 50, 60, 70, 80, 85, 90, 95, 96, 97, 98, 99, 99.9, 99.99 or greater than 99.99% of the pharmaceutical composition or compound of the disclosure are encapsulated in the delivery agent.

[0482] In some embodiments, the controlled release formulation may include, but is not limited to, tri-block co-polymers. As a non-limiting example, the formulation may include two different types of tri-block co-polymers (International Pub. No. WO2012131104 and

[0483] WO2012131106, the contents of each of which are incorporated herein by reference in their entirety).

[0484] In some embodiments, the RNA (e.g., mRNA) vaccines may be encapsulated into a lipid nanoparticle or a rapidly eliminated lipid nanoparticle and the lipid nanoparticles or a rapidly eliminated lipid nanoparticle may then be encapsulated into a polymer, hydrogel and/or surgical sealant described herein and/or known in the art. As a non-limiting example, the polymer, hydrogel or surgical sealant may be PLGA, ethylene vinyl acetate (EVAc), poloxamer, GELSITE.RTM. (Nanotherapeutics, Inc. Alachua, Fla.), HYLENEX.RTM. (Halozyme Therapeutics, San Diego Calif.), surgical sealants such as fibrinogen polymers (Ethicon Inc. Cornelia, Ga.), TISSELL.RTM. (Baxter International, Inc Deerfield, Ill.), PEG-based sealants, and COSEAL.RTM. (Baxter International, Inc Deerfield, Ill.).

[0485] In some embodiments, the lipid nanoparticle may be encapsulated into any polymer known in the art which may form a gel when injected into a subject. As another non-limiting example, the lipid nanoparticle may be encapsulated into a polymer matrix which may be biodegradable.

[0486] In some embodiments, the RNA (e.g., mRNA) vaccine formulation for controlled release and/or targeted delivery may also include at least one controlled release coating. Controlled release coatings include, but are not limited to, OPADRY.RTM., polyvinylpyrrolidone/vinyl acetate copolymer, polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, EUDRAGIT RL.RTM., EUDRAGIT RS.RTM. and cellulose derivatives such as ethylcellulose aqueous dispersions (AQUACOAT.RTM. and SURELEASE.RTM.).

[0487] In some embodiments, the RNA (e.g., mRNA) vaccine controlled release and/or targeted delivery formulation may comprise at least one degradable polyester which may contain polycationic side chains. Degradable polyesters include, but are not limited to, poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester), and combinations thereof. In some embodiments, the degradable polyesters may include a PEG conjugation to form a PEGylated polymer.

[0488] In some embodiments, the RNA (e.g., mRNA) vaccine controlled release and/or targeted delivery formulation comprising at least one polynucleotide may comprise at least one PEG and/or PEG related polymer derivatives as described in U.S. Pat. No. 8,404,222, the contents of which are incorporated herein by reference in their entirety.

[0489] In some embodiments, the RNA (e.g., mRNA) vaccine controlled release delivery formulation comprising at least one polynucleotide may be the controlled release polymer system described in US20130130348, the contents of which are incorporated herein by reference in their entirety.

[0490] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be encapsulated in a therapeutic nanoparticle, referred to herein as "therapeutic nanoparticle RNA (e.g., mRNA) vaccines." Therapeutic nanoparticles may be formulated by methods described herein and known in the art such as, but not limited to, International Pub Nos. WO2010005740, WO2010030763, WO2010005721, WO2010005723, WO2012054923, U.S. Publication Nos. US20110262491, US20100104645, US20100087337, US20100068285, US20110274759, US20100068286, US20120288541, US20130123351 and US20130230567 and U.S. Pat. Nos. 8,206,747, 8,293,276, 8,318,208 and 8,318,211; the contents of each of which are herein incorporated by reference in their entirety. In some embodiments, therapeutic polymer nanoparticles may be identified by the methods described in US Pub No. US20120140790, the contents of which are herein incorporated by reference in their entirety.

[0491] In some embodiments, the therapeutic nanoparticle RNA (e.g., mRNA) vaccine may be formulated for sustained release. As used herein, "sustained release" refers to a pharmaceutical composition or compound that conforms to a release rate over a specific period of time. The period of time may include, but is not limited to, hours, days, weeks, months and years. As a non-limiting example, the sustained release nanoparticle may comprise a polymer and a therapeutic agent such as, but not limited to, the polynucleotides of the present disclosure (see International Pub No. 2010075072 and US Pub No. US20100216804, US20110217377 and US20120201859, the contents of each of which are incorporated herein by reference in their entirety). In another non-limiting example, the sustained release formulation may comprise agents which permit persistent bioavailability such as, but not limited to, crystals, macromolecular gels and/or particulate suspensions (see U.S. Patent Publication No US20130150295, the contents of each of which are incorporated herein by reference in their entirety).

[0492] In some embodiments, the therapeutic nanoparticle RNA (e.g., mRNA) vaccines may be formulated to be target specific. As a non-limiting example, the therapeutic nanoparticles may include a corticosteroid (see International Pub. No. WO2011084518, the contents of which are incorporated herein by reference in their entirety). As a non-limiting example, the therapeutic nanoparticles may be formulated in nanoparticles described in International Pub No. WO2008121949, WO2010005726, WO2010005725, WO2011084521 and US Pub No. US20100069426, US20120004293 and US20100104655, the contents of each of which are incorporated herein by reference in their entirety.

[0493] In some embodiments, the nanoparticles of the present disclosure may comprise a polymeric matrix. As a non-limiting example, the nanoparticle may comprise two or more polymers such as, but not limited to, polyethylenes, polycarbonates, polyanhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyacetals, polyethers, polyesters, poly(orthoesters), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polylysine, poly(ethylene imine), poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester) or combinations thereof.

[0494] In some embodiments, the therapeutic nanoparticle comprises a diblock copolymer. In some embodiments, the diblock copolymer may include PEG in combination with a polymer such as, but not limited to, polyethylenes, polycarbonates, polyanhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyacetals, polyethers, polyesters, poly(orthoesters), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polylysine, poly(ethylene imine), poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester) or combinations thereof. In yet another embodiment, the diblock copolymer may be a high-X diblock copolymer such as those described in International Patent Publication No. WO2013120052, the contents of which are incorporated herein by reference in their entirety.

[0495] As a non-limiting example the therapeutic nanoparticle comprises a PLGA-PEG block copolymer (see U.S. Publication No. US20120004293 and U.S. Pat. No. 8,236,330, each of which is herein incorporated by reference in their entirety). In another non-limiting example, the therapeutic nanoparticle is a stealth nanoparticle comprising a diblock copolymer of PEG and PLA or PEG and PLGA (see U.S. Pat. No. 8,246,968 and International Publication No. WO2012166923, the contents of each of which are herein incorporated by reference in their entirety). In yet another non-limiting example, the therapeutic nanoparticle is a stealth nanoparticle or a target-specific stealth nanoparticle as described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

[0496] In some embodiments, the therapeutic nanoparticle may comprise a multiblock copolymer (see e.g., U.S. Pat. Nos. 8,263,665 and 8,287,910 and U.S. Patent Pub. No. US20130195987, the contents of each of which are herein incorporated by reference in their entirety).

[0497] In yet another non-limiting example, the lipid nanoparticle comprises the block copolymer PEG-PLGA-PEG (see e.g., the thermosensitive hydrogel (PEG-PLGA-PEG) was used as a TGF-beta1 gene delivery vehicle in Lee et al. Thermosensitive Hydrogel as a Tgf-.beta.1 Gene Delivery Vehicle Enhances Diabetic Wound Healing. Pharmaceutical Research, 2003 20(12): 1995-2000; as a controlled gene delivery system in Li et al. Controlled Gene Delivery System Based on Thermosensitive Biodegradable Hydrogel. Pharmaceutical Research 2003 20(6):884-888; and Chang et al., Non-ionic amphiphilic biodegradable PEG-PLGA-PEG copolymer enhances gene delivery efficiency in rat skeletal muscle. J Controlled Release. 2007 118:245-253, the contents of each of which are herein incorporated by reference in their entirety). The RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles comprising the PEG-PLGA-PEG block copolymer.

[0498] In some embodiments, the therapeutic nanoparticle may comprise a multiblock copolymer (see e.g., U.S. Pat. Nos. 8,263,665 and 8,287,910 and U.S. Patent Pub. No. US20130195987, the contents of each of which are herein incorporated by reference in their entirety).

[0499] In some embodiments, the block copolymers described herein may be included in a polyion complex comprising a non-polymeric micelle and the block copolymer. (see e.g., U.S. Publication No. 20120076836, the contents of which are herein incorporated by reference in their entirety).

[0500] In some embodiments, the therapeutic nanoparticle may comprise at least one acrylic polymer. Acrylic polymers include but are not limited to, acrylic acid, methacrylic acid, acrylic acid and methacrylic acid copolymers, methyl methacrylate copolymers, ethoxyethyl methacrylates, cyanoethyl methacrylate, amino alkyl methacrylate copolymer, poly(acrylic acid), poly(methacrylic acid), polycyanoacrylates and combinations thereof.

[0501] In some embodiments, the therapeutic nanoparticles may comprise at least one poly(vinyl ester) polymer. The poly(vinyl ester) polymer may be a copolymer such as a random copolymer. As a non-limiting example, the random copolymer may have a structure such as those described in International Application No. WO2013032829 or U.S. Patent Publication No US20130121954, the contents of each of which are herein incorporated by reference in their entirety. In some embodiments, the poly(vinyl ester) polymers may be conjugated to the polynucleotides described herein.

[0502] In some embodiments, the therapeutic nanoparticle may comprise at least one diblock copolymer. The diblock copolymer may be, but it not limited to, a poly(lactic) acid-poly(ethylene)glycol copolymer (see, e.g., International Patent Publication No. WO2013044219, the contents of which are herein incorporated by reference in their entirety). As a non-limiting example, the therapeutic nanoparticle may be used to treat cancer (see International publication No. WO2013044219, the contents of which are herein incorporated by reference in their entirety).

[0503] In some embodiments, the therapeutic nanoparticles may comprise at least one cationic polymer described herein and/or known in the art.

[0504] In some embodiments, the therapeutic nanoparticles may comprise at least one amine-containing polymer such as, but not limited to polylysine, polyethylene imine, poly(amidoamine) dendrimers, poly(beta-amino esters) (see, e.g., U.S. Pat. No. 8,287,849, the contents of which are herein incorporated by reference in their entirety) and combinations thereof.

[0505] In some embodiments, the nanoparticles described herein may comprise an amine cationic lipid such as those described in International Patent Application No. WO2013059496, the contents of which are herein incorporated by reference in their entirety. In some embodiments, the cationic lipids may have an amino-amine or an amino-amide moiety.

[0506] In some embodiments, the therapeutic nanoparticles may comprise at least one degradable polyester which may contain polycationic side chains. Degradeable polyesters include, but are not limited to, poly(serine ester), poly(L-lactide-co-L-lysine), poly(4-hydroxy-L-proline ester), and combinations thereof. In some embodiments, the degradable polyesters may include a PEG conjugation to form a PEGylated polymer.

[0507] In some embodiments, the synthetic nanocarriers may contain an immunostimulatory agent to enhance the immune response from delivery of the synthetic nanocarrier. As a non-limiting example, the synthetic nanocarrier may comprise a Th1 immunostimulatory agent, which may enhance a Th1-based response of the immune system (see International Pub No. WO2010123569 and U.S. Publication No. US20110223201, the contents of each of which are herein incorporated by reference in their entirety).

[0508] In some embodiments, the synthetic nanocarriers may be formulated for targeted release. In some embodiments, the synthetic nanocarrier is formulated to release the polynucleotides at a specified pH and/or after a desired time interval. As a non-limiting example, the synthetic nanoparticle may be formulated to release the RNA (e.g., mRNA) vaccines after 24 hours and/or at a pH of 4.5 (see International Publication Nos. WO2010138193 and WO2010138194 and US Pub Nos. US20110020388 and US20110027217, each of which is herein incorporated by reference in their entireties).

[0509] In some embodiments, the synthetic nanocarriers may be formulated for controlled and/or sustained release of the polynucleotides described herein. As a non-limiting example, the synthetic nanocarriers for sustained release may be formulated by methods known in the art, described herein and/or as described in International Pub No. WO2010138192 and US Pub No. 20100303850, each of which is herein incorporated by reference in their entirety.

[0510] In some embodiments, the RNA (e.g., mRNA) vaccine may be formulated for controlled and/or sustained release wherein the formulation comprises at least one polymer that is a crystalline side chain (CYSC) polymer.

CYSC polymers are described in U.S. Pat. No. 8,399,007, herein incorporated by reference in its entirety.

[0511] In some embodiments, the synthetic nanocarrier may be formulated for use as a vaccine. In some embodiments, the synthetic nanocarrier may encapsulate at least one polynucleotide which encode at least one antigen. As a non-limiting example, the synthetic nanocarrier may include at least one antigen and an excipient for a vaccine dosage form (see International Publication No. WO2011150264 and U.S. Publication No. US20110293723, the contents of each of which are herein incorporated by reference in their entirety). As another non-limiting example, a vaccine dosage form may include at least two synthetic nanocarriers with the same or different antigens and an excipient (see International Publication No. WO2011150249 and U.S. Publication No. US20110293701, the contents of each of which are herein incorporated by reference in their entirety). The vaccine dosage form may be selected by methods described herein, known in the art and/or described in International Publication No. WO2011150258 and U.S. Publication No. US20120027806, the contents of each of which are herein incorporated by reference in their entirety).

[0512] In some embodiments, the synthetic nanocarrier may comprise at least one polynucleotide which encodes at least one adjuvant. As non-limiting example, the adjuvant may comprise dimethyldioctadecylammonium-bromide, dimethyldioctadecylammonium-chloride, dimethyldioctadecylammonium-phosphate or dimethyldioctadecylammonium-acetate (DDA) and an apolar fraction or part of said apolar fraction of a total lipid extract of a mycobacterium (see, e.g., U.S. Pat. No. 8,241,610, the content of which is herein incorporated by reference in its entirety). In some embodiments, the synthetic nanocarrier may comprise at least one polynucleotide and an adjuvant. As a non-limiting example, the synthetic nanocarrier comprising and adjuvant may be formulated by the methods described in International Publication No. WO2011150240 and U.S. Publication No. US20110293700, the contents of each of which are herein incorporated by reference in their entirety.

[0513] In some embodiments, the synthetic nanocarrier may encapsulate at least one polynucleotide that encodes a peptide, fragment or region from a virus. As a non-limiting example, the synthetic nanocarrier may include, but is not limited to, any of the nanocarriers described in International Publication No. WO2012024621, WO201202629, WO2012024632 and U.S. Publication No. US20120064110, US20120058153 and US20120058154, the contents of each of which are herein incorporated by reference in their entirety.

[0514] In some embodiments, the synthetic nanocarrier may be coupled to a polynucleotide which may be able to trigger a humoral and/or cytotoxic T lymphocyte (CTL) response (see, e.g., International Publication No. WO2013019669, the contents of which are herein incorporated by reference in their entirety).

[0515] In some embodiments, the RNA (e.g., mRNA) vaccine may be encapsulated in, linked to and/or associated with zwitterionic lipids. Non-limiting examples of zwitterionic lipids and methods of using zwitterionic lipids are described in U.S. Patent Publication No. US20130216607, the contents of which are herein incorporated by reference in their entirety. In some aspects, the zwitterionic lipids may be used in the liposomes and lipid nanoparticles described herein.

[0516] In some embodiments, the RNA (e.g., mRNA) vaccine may be formulated in colloid nanocarriers as described in U.S. Patent Publication No. US20130197100, the contents of which are herein incorporated by reference in their entirety.

[0517] In some embodiments, the nanoparticle may be optimized for oral administration. The nanoparticle may comprise at least one cationic biopolymer such as, but not limited to, chitosan or a derivative thereof. As a non-limiting example, the nanoparticle may be formulated by the methods described in U.S. Publication No. 20120282343, the contents of which are herein incorporated by reference in their entirety.

[0518] In some embodiments, LNPs comprise the lipid KL52 (an amino-lipid disclosed in U.S. Application Publication No. 2012/0295832, the contents of which are herein incorporated by reference in their entirety. Activity and/or safety (as measured by examining one or more of ALT/AST, white blood cell count and cytokine induction, for example) of LNP administration may be improved by incorporation of such lipids. LNPs comprising KL52 may be administered intravenously and/or in one or more doses. In some embodiments, administration of LNPs comprising KL52 results in equal or improved mRNA and/or protein expression as compared to LNPs comprising MC3.

[0519] In some embodiments, RNA (e.g., mRNA) vaccine may be delivered using smaller LNPs. Such particles may comprise a diameter from below 0.1 um up to 100 nm such as, but not limited to, less than 0.1 um, less than 1.0 um, less than 5 um, less than 10 um, less than 15 um, less than 20 um, less than 25 um, less than 30 um, less than 35 um, less than 40 um, less than 50 um, less than 55 um, less than 60 um, less than 65 um, less than 70 um, less than 75 um, less than 80 um, less than 85 um, less than 90 um, less than 95 um, less than 100 um, less than 125 um, less than 150 um, less than 175 um, less than 200 um, less than 225 um, less than 250 um, less than 275 um, less than 300 um, less than 325 um, less than 350 um, less than 375 um, less than 400 um, less than 425 um, less than 450 um, less than 475 um, less than 500 um, less than 525 um, less than 550 um, less than 575 um, less than 600 um, less than 625 um, less than 650 um, less than 675 um, less than 700 um, less than 725 um, less than 750 um, less than 775 um, less than 800 um, less than 825 um, less than 850 um, less than 875 um, less than 900 um, less than 925 um, less than 950 um, less than 975 um, or less than 1000 um.

[0520] In some embodiments, RNA (e.g., mRNA) vaccines may be delivered using smaller LNPs, which may comprise a diameter from about 1 nm to about 100 nm, from about 1 nm to about 10 nm, about 1 nm to about 20 nm, from about 1 nm to about 30 nm, from about 1 nm to about 40 nm, from about 1 nm to about 50 nm, from about 1 nm to about 60 nm, from about 1 nm to about 70 nm, from about 1 nm to about 80 nm, from about 1 nm to about 90 nm, from about 5 nm to about from 100 nm, from about 5 nm to about 10 nm, about 5 nm to about 20 nm, from about 5 nm to about 30 nm, from about 5 nm to about 40 nm, from about 5 nm to about 50 nm, from about 5 nm to about 60 nm, from about 5 nm to about 70 nm, from about 5 nm to about 80 nm, from about 5 nm to about 90 nm, about 10 to about 50 nm, from about 20 to about 50 nm, from about 30 to about 50 nm, from about 40 to about 50 nm, from about 20 to about 60 nm, from about 30 to about 60 nm, from about 40 to about 60 nm, from about 20 to about 70 nm, from about 30 to about 70 nm, from about 40 to about 70 nm, from about 50 to about 70 nm, from about 60 to about 70 nm, from about 20 to about 80 nm, from about 30 to about 80 nm, from about 40 to about 80 nm, from about 50 to about 80 nm, from about 60 to about 80 nm, from about 20 to about 90 nm, from about 30 to about 90 nm, from about 40 to about 90 nm, from about 50 to about 90 nm, from about 60 to about 90 nm and/or from about 70 to about 90 nm.

[0521] In some embodiments, such LNPs are synthesized using methods comprising microfluidic mixers. Examples of microfluidic mixers may include, but are not limited to, a slit interdigital micromixer including, but not limited to those manufactured by Microinnova (Allerheiligen bei Wildon, Austria) and/or a staggered herringbone micromixer (SHM) (Zhigaltsev, I. V. et al., Bottom-up design and synthesis of limit size lipid nanoparticle systems with aqueous and triglyceride cores using millisecond microfluidic mixing have been published (Langmuir. 2012. 28:3633-40; Belliveau, N. M. et al., Microfluidic synthesis of highly potent limit-size lipid nanoparticles for in vivo delivery of siRNA. Molecular Therapy-Nucleic Acids. 2012. 1:e37; Chen, D. et al., Rapid discovery of potent siRNA-containing lipid nanoparticles enabled by controlled microfluidic formulation. J Am Chem Soc. 2012. 134(16):6948-51, the contents of each of which are herein incorporated by reference in their entirety). In some embodiments, methods of LNP generation comprising SHM, further comprise the mixing of at least two input streams wherein mixing occurs by microstructure-induced chaotic advection (MICA). According to this method, fluid streams flow through channels present in a herringbone pattern causing rotational flow and folding the fluids around each other. This method may also comprise a surface for fluid mixing wherein the surface changes orientations during fluid cycling. Methods of generating LNPs using SHM include those disclosed in U.S. Application Publication Nos. 2004/0262223 and 2012/0276209, the contents of each of which are herein incorporated by reference in their entirety.

[0522] In some embodiments, the RNA (e.g., mRNA) vaccine of the present disclosure may be formulated in lipid nanoparticles created using a micromixer such as, but not limited to, a Slit Interdigital Microstructured Mixer (SIMM-V2) or a Standard Slit Interdigital Micro Mixer (SSIMM) or Caterpillar (CPMM) or Impinging-jet (IJMM) from the Institut fur Mikrotechnik Mainz GmbH, Mainz Germany).

[0523] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles created using microfluidic technology (see, e.g., Whitesides, George M. The Origins and the Future of Microfluidics. Nature, 2006 442: 368-373; and Abraham et al. Chaotic Mixer for Microchannels. Science, 2002 295: 647-651; each of which is herein incorporated by reference in its entirety). As a non-limiting example, controlled microfluidic formulation includes a passive method for mixing streams of steady pressure-driven flows in micro channels at a low Reynolds number (see, e.g., Abraham et al. Chaotic Mixer for Microchannels. Science, 2002 295: 647-651, the contents of which are herein incorporated by reference in their entirety).

[0524] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in lipid nanoparticles created using a micromixer chip such as, but not limited to, those from Harvard Apparatus (Holliston, Mass.) or Dolomite Microfluidics (Royston, UK). A micromixer chip can be used for rapid mixing of two or more fluid streams with a split and recombine mechanism.

[0525] In some embodiments, the RNA (e.g., mRNA) vaccines of the disclosure may be formulated for delivery using the drug encapsulating microspheres described in International Patent Publication No. WO2013063468 or U.S. Pat. No. 8,440,614, the contents of each of which are herein incorporated by reference in their entirety. The microspheres may comprise a compound of the formula (I), (II), (III), (IV), (V) or (VI) as described in International Patent Publication No. WO2013063468, the contents of which are herein incorporated by reference in their entirety. In some embodiments, the amino acid, peptide, polypeptide, lipids (APPL) are useful in delivering the RNA (e.g., mRNA) vaccines of the disclosure to cells (see International Patent Publication No. WO2013063468, the contents of which are herein incorporated by reference in their entirety).

[0526] In some embodiments, the RNA (e.g., mRNA) vaccines of the disclosure may be formulated in lipid nanoparticles having a diameter from about 10 to about 100 nm such as, but not limited to, about 10 to about 20 nm, about 10 to about 30 nm, about 10 to about 40 nm, about 10 to about 50 nm, about 10 to about 60 nm, about 10 to about 70 nm, about 10 to about 80 nm, about 10 to about 90 nm, about 20 to about 30 nm, about 20 to about 40 nm, about 20 to about 50 nm, about 20 to about 60 nm, about 20 to about 70 nm, about 20 to about 80 nm, about 20 to about 90 nm, about 20 to about 100 nm, about 30 to about 40 nm, about 30 to about 50 nm, about 30 to about 60 nm, about 30 to about 70 nm, about 30 to about 80 nm, about 30 to about 90 nm, about 30 to about 100 nm, about 40 to about 50 nm, about 40 to about 60 nm, about 40 to about 70 nm, about 40 to about 80 nm, about 40 to about 90 nm, about 40 to about 100 nm, about 50 to about 60 nm, about 50 to about 70 nm about 50 to about 80 nm, about 50 to about 90 nm, about 50 to about 100 nm, about 60 to about 70 nm, about 60 to about 80 nm, about 60 to about 90 nm, about 60 to about 100 nm, about 70 to about 80 nm, about 70 to about 90 nm, about 70 to about 100 nm, about 80 to about 90 nm, about 80 to about 100 nm and/or about 90 to about 100 nm.

[0527] In some embodiments, the lipid nanoparticles may have a diameter from about 10 to 500 nm.

[0528] In some embodiments, the lipid nanoparticle may have a diameter greater than 100 nm, greater than 150 nm, greater than 200 nm, greater than 250 nm, greater than 300 nm, greater than 350 nm, greater than 400 nm, greater than 450 nm, greater than 500 nm, greater than 550 nm, greater than 600 nm, greater than 650 nm, greater than 700 nm, greater than 750 nm, greater than 800 nm, greater than 850 nm, greater than 900 nm, greater than 950 nm or greater than 1000 nm.

[0529] In some embodiments, the lipid nanoparticle may be a limit size lipid nanoparticle described in International Patent Publication No. WO2013059922, the contents of which are herein incorporated by reference in their entirety. The limit size lipid nanoparticle may comprise a lipid bilayer surrounding an aqueous core or a hydrophobic core; where the lipid bilayer may comprise a phospholipid such as, but not limited to, diacylphosphatidylcholine, a diacylphosphatidylethanolamine, a ceramide, a sphingomyelin, a dihydrosphingomyelin, a cephalin, a cerebroside, a C8-C20 fatty acid diacylphophatidylcholine, and 1-palmitoyl-2-oleoyl phosphatidylcholine (POPC). In some embodiments, the limit size lipid nanoparticle may comprise a polyethylene glycol-lipid such as, but not limited to, DLPE-PEG, DMPE-PEG, DPPC-PEG and DSPE-PEG.

[0530] In some embodiments, the RNA (e.g., mRNA) vaccines may be delivered, localized and/or concentrated in a specific location using the delivery methods described in International Patent Publication No. WO2013063530, the contents of which are herein incorporated by reference in their entirety. As a non-limiting example, a subject may be administered an empty polymeric particle prior to, simultaneously with or after delivering the RNA (e.g., mRNA) vaccines to the subject. The empty polymeric particle undergoes a change in volume once in contact with the subject and becomes lodged, embedded, immobilized or entrapped at a specific location in the subject.

[0531] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in an active substance release system (see, e.g., U.S. Patent Publication No. US20130102545, the contents of which are herein incorporated by reference in their entirety). The active substance release system may comprise 1) at least one nanoparticle bonded to an oligonucleotide inhibitor strand which is hybridized with a catalytically active nucleic acid and 2) a compound bonded to at least one substrate molecule bonded to a therapeutically active substance (e.g., polynucleotides described herein), where the therapeutically active substance is released by the cleavage of the substrate molecule by the catalytically active nucleic acid.

[0532] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a nanoparticle comprising an inner core comprising a non-cellular material and an outer surface comprising a cellular membrane. The cellular membrane may be derived from a cell or a membrane derived from a virus. As a non-limiting example, the nanoparticle may be made by the methods described in International Patent Publication No. WO2013052167, the contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the nanoparticle described in International Patent Publication No. WO2013052167, the contents of which are herein incorporated by reference in their entirety, may be used to deliver the RNA (e.g., mRNA) vaccines described herein.

[0533] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in porous nanoparticle-supported lipid bilayers (protocells). Protocells are described in International Patent Publication No. WO2013056132, the contents of which are herein incorporated by reference in their entirety.

[0534] In some embodiments, the RNA (e.g., mRNA) vaccines described herein may be formulated in polymeric nanoparticles as described in or made by the methods described in U.S. Pat. Nos. 8,420,123 and 8,518,963 and European Patent No. EP2073848B1, the contents of each of which are herein incorporated by reference in their entirety. As a non-limiting example, the polymeric nanoparticle may have a high glass transition temperature such as the nanoparticles described in or nanoparticles made by the methods described in U.S. Pat. No. 8,518,963, the contents of which are herein incorporated by reference in their entirety. As another non-limiting example, the polymer nanoparticle for oral and parenteral formulations may be made by the methods described in European Patent No. EP2073848B1, the contents of which are herein incorporated by reference in their entirety.

[0535] In some embodiments, the RNA (e.g., mRNA) vaccines described herein may be formulated in nanoparticles used in imaging. The nanoparticles may be liposome nanoparticles such as those described in U.S. Patent Publication No US20130129636, herein incorporated by reference in its entirety. As a non-limiting example, the liposome may comprise gadolinium(III)2-{4,7-bis-carboxymethyl-10-[(N,N-distearylamidomethyl-N'-- amido-methyl]-1,4,7,10-tetra-azacyclododec-1-yl}-acetic acid and a neutral, fully saturated phospholipid component (see, e.g., U.S. Patent Publication No US20130129636, the contents of which are herein incorporated by reference in their entirety).

[0536] In some embodiments, the nanoparticles which may be used in the present disclosure are formed by the methods described in U.S. Patent Application No. US20130130348, the contents of which are herein incorporated by reference in their entirety.

[0537] The nanoparticles of the present disclosure may further include nutrients such as, but not limited to, those which deficiencies can lead to health hazards from anemia to neural tube defects (see, e.g., the nanoparticles described in International Patent Publication No WO2013072929, the contents of which are herein incorporated by reference in their entirety). As a non-limiting example, the nutrient may be iron in the form of ferrous, ferric salts or elemental iron, iodine, folic acid, vitamins or micronutrients.

[0538] In some embodiments, the RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in a swellable nanoparticle. The swellable nanoparticle may be, but is not limited to, those described in U.S. Pat. No. 8,440,231, the contents of which are herein incorporated by reference in their entirety. As a non-limiting embodiment, the swellable nanoparticle may be used for delivery of the RNA (e.g., mRNA) vaccines of the present disclosure to the pulmonary system (see, e.g., U.S. Pat. No. 8,440,231, the contents of which are herein incorporated by reference in their entirety).

[0539] The RNA (e.g., mRNA) vaccines of the present disclosure may be formulated in polyanhydride nanoparticles such as, but not limited to, those described in U.S. Pat. No. 8,449,916, the contents of which are herein incorporated by reference in their entirety.

[0540] The nanoparticles and microparticles of the present disclosure may be geometrically engineered to modulate macrophage and/or the immune response. In some embodiments, the geometrically engineered particles may have varied shapes, sizes and/or surface charges in order to incorporated the polynucleotides of the present disclosure for targeted delivery such as, but not limited to, pulmonary delivery (see, e.g., International Publication No WO2013082111, the contents of which are herein incorporated by reference in their entirety). Other physical features the geometrically engineering particles may have include, but are not limited to, fenestrations, angled arms, asymmetry and surface roughness, charge which can alter the interactions with cells and tissues. As a non-limiting example, nanoparticles of the present disclosure may be made by the methods described in International Publication No WO2013082111, the contents of which are herein incorporated by reference in their entirety.

[0541] In some embodiments, the nanoparticles of the present disclosure may be water soluble nanoparticles such as, but not limited to, those described in International Publication No. WO2013090601, the contents of which are herein incorporated by reference in their entirety. The nanoparticles may be inorganic nanoparticles which have a compact and zwitterionic ligand in order to exhibit good water solubility. The nanoparticles may also have small hydrodynamic diameters (HD), stability with respect to time, pH, and salinity and a low level of non-specific protein binding.

[0542] In some embodiments the nanoparticles of the present disclosure may be developed by the methods described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

[0543] In some embodiments, the nanoparticles of the present disclosure are stealth nanoparticles or target-specific stealth nanoparticles such as, but not limited to, those described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety. The nanoparticles of the present disclosure may be made by the methods described in U.S. Patent Publication No. US20130172406, the contents of which are herein incorporated by reference in their entirety.

[0544] In some embodiments, the stealth or target-specific stealth nanoparticles may comprise a polymeric matrix. The polymeric matrix may comprise two or more polymers such as, but not limited to, polyethylenes, polycarbonates, polyanhydrides, polyhydroxyacids, polypropylfumerates, polycaprolactones, polyamides, polyacetals, polyethers, polyesters, poly(orthoesters), polycyanoacrylates, polyvinyl alcohols, polyurethanes, polyphosphazenes, polyacrylates, polymethacrylates, polycyanoacrylates, polyureas, polystyrenes, polyamines, polyesters, polyanhydrides, polyethers, polyurethanes, polymethacrylates, polyacrylates, polycyanoacrylates or combinations thereof.

[0545] In some embodiments, the nanoparticle may be a nanoparticle-nucleic acid hybrid structure having a high density nucleic acid layer. As a non-limiting example, the nanoparticle-nucleic acid hybrid structure may made by the methods described in U.S. Patent Publication No. US20130171646, the contents of which are herein incorporated by reference in their entirety. The nanoparticle may comprise a nucleic acid such as, but not limited to, polynucleotides described herein and/or known in the art.

[0546] At least one of the nanoparticles of the present disclosure may be embedded in in the core a nanostructure or coated with a low density porous 3-D structure or coating which is capable of carrying or associating with at least one payload within or on the surface of the nanostructure. Non-limiting examples of the nanostructures comprising at least one nanoparticle are described in International Patent Publication No. WO2013123523, the contents of which are herein incorporated by reference in their entirety.

[0547] In some embodiments the RNA (e.g., mRNA) vaccine may be associated with a cationic or polycationic compounds, including protamine, nucleoline, spermine or spermidine, or other cationic peptides or proteins, such as poly-L-lysine (PLL), polyarginine, basic polypeptides, cell penetrating peptides (CPPs), including HIV-binding peptides, HIV-1 Tat (HIV), Tat-derived peptides, Penetratin, VP.sup.22 derived or analog peptides, Pestivirus Ems, HSV, VP.sup.22 (Herpes simplex), MAP, KALA or protein transduction domains (PTDs), PpT620, prolin-rich peptides, arginine-rich peptides, lysine-rich peptides, MPG-peptide(s), Pep-1, L-oligomers, Calcitonin peptide(s), Antennapedia-derived peptides (particularly from Drosophila antennapedia), pAntp, plsl, FGF, Lactoferrin, Transportan, Buforin-2, Bac715-24, SynB, SynB(1), pVEC, hCT-derived peptides, SAP, histones, cationic polysaccharides, for example chitosan, polybrene, cationic polymers, e.g. polyethyleneimine (PEI), cationic lipids, e.g. DOTMA: [1-(2,3-sioleyloxy)propyl)]-N,N,N-trimethylammonium chloride, DMRIE, di-C14-amidine, DOTIM, SAINT, DC-Chol, BGTC, CTAP, DOPC, DODAP, DOPE: Dioleyl phosphatidylethanol-amine, DOSPA, DODAB, DOIC, DMEPC, DOGS: Dioctadecylamidoglicylspermin, DIMRI: Dimyristooxypropyl dimethyl hydroxyethyl ammonium bromide, DOTAP: dioleoyloxy-3-(trimethylammonio)propane, DC-6-14: O,O-ditetradecanoyl-N-.alpha.-trimethylammonioacetyl)diethanolamine chloride, CLIP 1: rac-[(2,3-dioctadecyloxypropyl)(2-hydroxyethyl)]-dimethylammonium chloride, CLIP6: rac-[2(2,3-dihexadecyloxypropyloxymethyloxy)ethyl]-trimethylammonium, CLIP9: rac-[2(2,3-dihexadecyloxypropyloxysuccinyloxy)ethyl]-trimethylammo- nium, oligofectamine, or cationic or polycationic polymers, e.g. modified polyaminoacids, such as beta-aminoacid-polymers or reversed polyamides, etc., modified polyethylenes, such as PVP (poly(N-ethyl-4-vinylpyridinium bromide)), etc., modified acrylates, such as pDMAEMA (poly(dimethylaminoethyl methylacrylate)), etc., modified amidoamines such as pAMAM (poly(amidoamine)), etc., modified polybetaminoester (PBAE), such as diamine end modified 1,4 butanediol diacrylate-co-5-amino-1-pentanol polymers, etc., dendrimers, such as polypropylamine dendrimers or pAMAM based dendrimers, etc., polyimine(s), such as PEI: poly(ethyleneimine), poly(propyleneimine), etc., polyallylamine, sugar backbone based polymers, such as cyclodextrin based polymers, dextran based polymers, chitosan, etc., silan backbone based polymers, such as PMOXA-PDMS copolymers, etc., blockpolymers consisting of a combination of one or more cationic blocks (e.g. selected from a cationic polymer as mentioned above) and of one or more hydrophilic or hydrophobic blocks (e.g. polyethyleneglycole), etc.

[0548] In other embodiments the RNA (e.g., mRNA) vaccine is not associated with a cationic or polycationic compounds.

[0549] In some embodiments, a nanoparticle comprises compounds of Formula (I):

##STR00003##

[0550] or a salt or isomer thereof, wherein:

[0551] R.sub.1 is selected from the group consisting of C.sub.5-30 alkyl, C.sub.5-20 alkenyl, --R*YR", --YR", and --R"M'R';

[0552] R.sub.2 and R.sub.3 are independently selected from the group consisting of H, C.sub.1-14 alkyl, C.sub.2-14 alkenyl, --R*YR", --YR", and --R*OR", or R.sub.2 and R.sub.3, together with the atom to which they are attached, form a heterocycle or carbocycle;

[0553] R.sub.4 is selected from the group consisting of a C.sub.3-6 carbocycle, --(CH.sub.2).sub.nQ, --(CH.sub.2).sub.nCHQR, --CHQR, --CQ(R).sub.2, and unsubstituted C.sub.1-6 alkyl, where Q is selected from a carbocycle, heterocycle, --OR, --O(CH.sub.2).sub.nN(R).sub.2, --C(O)OR, --OC(O)R, --CX.sub.3, --CX.sub.2H, --CXH.sub.2, --CN, --N(R).sub.2, --C(O)N(R).sub.2, --N(R)C(O)R, --N(R)S(O).sub.2R, --N(R)C(O)N(R).sub.2, --N(R)C(S)N(R).sub.2, --N(R)R.sub.8, --O(CH.sub.2).sub.nOR, --N(R)C(.dbd.NR.sub.9)N(R).sub.2, --N(R)C(.dbd.CHR.sub.9)N(R).sub.2, --OC(O)N(R).sub.2, --N(R)C(O)OR, --N(OR)C(O)R, --N(OR)S(O).sub.2R, --N(OR)C(O)OR, --N(OR)C(O)N(R).sub.2, --N(OR)C(S)N(R).sub.2, --N(OR)C(.dbd.NR.sub.9)N(R).sub.2, --N(OR)C(.dbd.CHR.sub.9)N(R).sub.2, --C(.dbd.NR.sub.9)N(R).sub.2, --C(.dbd.NR.sub.9)R, --C(O)N(R)O R, and C(R)N(R).sub.2C(O)OR, and each n is independently selected from 1, 2, 3, 4, and 5;

[0554] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0555] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0556] M and M' are independently selected from --C(O)O--, --OC(O)--, --C(O)N(R')--,

[0557] --N(R')C(O)--, --C(O)--, --C(S)--, --C(S)S--, --SC(S)--, --CH(OH)--, --P(O)(OR')O--, --S(O).sub.2--, --S--S--, an aryl group, and a heteroaryl group;

[0558] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0559] R.sub.8 is selected from the group consisting of C.sub.3-6 carbocycle and heterocycle;

[0560] R.sub.9 is selected from the group consisting of H, CN, NO.sub.2, C.sub.1-6 alkyl, --OR, --S(O).sub.2R, --S(O).sub.2N(R).sub.2, C.sub.2-6 alkenyl, C.sub.3-6 carbocycle and heterocycle;

[0561] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0562] each R' is independently selected from the group consisting of C.sub.1-18 alkyl, C.sub.2-18 alkenyl, --R*YR", --YR", and H;

[0563] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0564] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.2-12 alkenyl;

[0565] each Y is independently a C.sub.3-6 carbocycle;

[0566] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0567] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13.

[0568] In some embodiments, a subset of compounds of Formula (I) includes those in which when R.sub.4 is --(CH.sub.2).sub.nQ, --(CH.sub.2).sub.nCHQR, --CHQR, or --CQ(R).sub.2, then (i) Q is not --N(R).sub.2 when n is 1, 2, 3, 4 or 5, or (ii) Q is not 5, 6, or 7-membered heterocycloalkyl when n is 1 or 2.

[0569] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0570] R.sub.1 is selected from the group consisting of C.sub.5-30 alkyl, C.sub.5-20 alkenyl, --R*YR", --YR", and --R"M'R';

[0571] R.sub.2 and R.sub.3 are independently selected from the group consisting of H, C.sub.1-14 alkyl, C.sub.2-14 alkenyl, --R*YR", --YR", and --R*OR", or R.sub.2 and R.sub.3, together with the atom to which they are attached, form a heterocycle or carbocycle;

[0572] R.sub.4 is selected from the group consisting of a C.sub.3-6 carbocycle, --(CH.sub.2).sub.nQ, --(CH.sub.2).sub.nCHQR, --CHQR, --CQ(R).sub.2, and unsubstituted C.sub.1-6 alkyl, where Q is selected from a C.sub.3-6 carbocycle, a 5- to 14-membered heteroaryl having one or more heteroatoms selected from N, O, and S, --OR, --O(CH.sub.2).sub.nN(R).sub.2, --C(O)OR, --OC(O)R, --CX.sub.3, --CX.sub.2H, --CXH.sub.2, --CN, --C(O)N(R).sub.2, --N(R)C(O)R, --N(R)S(O).sub.2R, --N(R)C(O)N(R).sub.2, --N(R)C(S)N(R).sub.2, --CRN(R).sub.2C(O)OR, --N(R)R.sub.8, --O(CH.sub.2).sub.nOR, --N(R)C(.dbd.NR.sub.9)N(R).sub.2, --N(R)C(.dbd.CHR.sub.9)N(R).sub.2, --OC(O)N(R).sub.2, --N(R)C(O)OR, --N(OR)C(O)R, --N(OR)S(O).sub.2R, --N(OR)C(O)OR, --N(OR)C(O)N(R).sub.2, --N(OR)C(S)N(R).sub.2, --N(OR)C(.dbd.NR.sub.9)N(R).sub.2, --N(OR)C(.dbd.CHR.sub.9)N(R).sub.2, --C(.dbd.NR.sub.9)N(R).sub.2, --C(.dbd.NR.sub.9)R, --C(O)N(R)O R, and a 5- to 14-membered heterocycloalkyl having one or more heteroatoms selected from N, O, and S which is substituted with one or more substituents selected from oxo (.dbd.O), OH, amino, mono- or di-alkylamino, and C.sub.1-3 alkyl, and each n is independently selected from 1, 2, 3, 4, and 5;

[0573] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0574] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0575] M and M' are independently selected from --C(O)O--, --OC(O)--, --C(O)N(R')--, --N(R')C(O)--, --C(O)--, --C(S)--, --C(S)S--, --SC(S)--, --CH(OH)--, --P(O)(OR')O--, --S(O).sub.2--, --S--S--, an aryl group, and a heteroaryl group;

[0576] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0577] R.sub.8 is selected from the group consisting of C.sub.3-6 carbocycle and heterocycle;

[0578] R.sub.9 is selected from the group consisting of H, CN, NO.sub.2, C.sub.1-6 alkyl, --OR, --S(O).sub.2R, --S(O).sub.2N(R).sub.2, C.sub.2-6 alkenyl, C.sub.3-6 carbocycle and heterocycle;

[0579] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0580] each R' is independently selected from the group consisting of C.sub.1-18 alkyl, C.sub.2-18 alkenyl, --R*YR", --YR", and H;

[0581] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0582] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.2-12 alkenyl;

[0583] each Y is independently a C.sub.3-6 carbocycle;

[0584] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0585] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0586] or salts or isomers thereof.

[0587] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0588] R.sub.1 is selected from the group consisting of C.sub.5-30 alkyl, C.sub.5-20 alkenyl, --R*YR", --YR", and --R"M'R';

[0589] R.sub.2 and R.sub.3 are independently selected from the group consisting of H, C.sub.1-14 alkyl, C.sub.2-14 alkenyl, --R*YR", --YR", and --R*OR", or R.sub.2 and R.sub.3, together with the atom to which they are attached, form a heterocycle or carbocycle;

[0590] R.sub.4 is selected from the group consisting of a C.sub.3-6 carbocycle, --(CH.sub.2).sub.nQ, --(CH.sub.2).sub.nCHQR, --CHQR, --CQ(R).sub.2, and unsubstituted C.sub.1-6 alkyl, where Q is selected from a C.sub.3-6 carbocycle, a 5- to 14-membered heterocycle having one or more heteroatoms selected from N, O, and S, --OR, --O(CH.sub.2).sub.nN(R).sub.2, --C(O)OR, --OC(O)R, --CX.sub.3, --CX.sub.2H, --CXH.sub.2, --CN, --C(O)N(R).sub.2, --N(R)C(O)R, --N(R)S(O).sub.2R, --N(R)C(O)N(R).sub.2, --N(R)C(S)N(R).sub.2, --CRN(R).sub.2C(O)OR, --N(R)R.sub.8, --O(CH.sub.2).sub.nOR, --N(R)C(.dbd.NR.sub.9)N(R).sub.2, --N(R)C(.dbd.CHR.sub.9)N(R).sub.2, --OC(O)N(R).sub.2, --N(R)C(O)OR, --N(OR)C(O)R, --N(OR)S(O).sub.2R, --N(OR)C(O)OR, --N(OR)C(O)N(R).sub.2, --N(OR)C(S)N(R).sub.2, --N(OR)C(.dbd.NR.sub.9)N(R).sub.2, --N(OR)C(.dbd.CHR.sub.9)N(R).sub.2, --C(.dbd.NR.sub.9)R, --C(O)N(R)OR,

and --C(.dbd.NR.sub.9)N(R).sub.2, and each n is independently selected from 1, 2, 3, 4, and 5; and when Q is a 5- to 14-membered heterocycle and (i) R.sub.4 is --(CH.sub.2).sub.nQ in which n is 1 or 2, or (ii) R.sub.4 is --(CH.sub.2).sub.nCHQR in which n is 1, or (iii) R.sub.4 is --CHQR, and --CQ(R).sub.2, then Q is either a 5- to 14-membered heteroaryl or 8- to 14-membered heterocycloalkyl;

[0591] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0592] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0593] M and M' are independently selected from --C(O)O--, --OC(O)--, --C(O)N(R')--, --N(R')C(O)--, --C(O)--, --C(S)--, --C(S)S--, --SC(S)--, --CH(OH)--, --P(O)(OR')O--, --S(O).sub.2--, --S--S--, an aryl group, and a heteroaryl group;

[0594] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0595] R.sub.8 is selected from the group consisting of C.sub.3-6 carbocycle and heterocycle;

[0596] R.sub.9 is selected from the group consisting of H, CN, NO.sub.2, C.sub.1-6 alkyl, --OR, --S(O).sub.2R, --S(O).sub.2N(R).sub.2, C.sub.2-6 alkenyl, C.sub.3-6 carbocycle and heterocycle;

[0597] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0598] each R' is independently selected from the group consisting of C.sub.1-18 alkyl, C.sub.2-18 alkenyl, --R*YR", --YR", and H;

[0599] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0600] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.2-12 alkenyl;

[0601] each Y is independently a C.sub.3-6 carbocycle;

[0602] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0603] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0604] or salts or isomers thereof.

[0605] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0606] R.sub.1 is selected from the group consisting of C.sub.5-30 alkyl, C.sub.5-20 alkenyl, --R*YR", --YR", and --R"M'R';

[0607] R.sub.2 and R.sub.3 are independently selected from the group consisting of H, C.sub.1-14 alkyl, C.sub.2-14 alkenyl, --R*YR", --YR", and --R*OR", or R.sub.2 and R.sub.3, together with the atom to which they are attached, form a heterocycle or carbocycle;

[0608] R.sub.4 is selected from the group consisting of a C.sub.3-6

carbocycle, --(CH.sub.2).sub.nQ, --(CH.sub.2).sub.nCHQR, --CHQR, --CQ(R).sub.2, and unsubstituted C.sub.1-6 alkyl, where Q is selected from a C.sub.3-6 carbocycle, a 5- to 14-membered heteroaryl having one or more heteroatoms selected from N, O, and S, --OR, --O(CH.sub.2).sub.nN(R).sub.2, --C(O)OR, --OC(O)R, --CX.sub.3, --CX.sub.2H, --CXH.sub.2, --CN, --C(O)N(R).sub.2, --N(R)C(O)R, --N(R)S(O).sub.2R, --N(R)C(O)N(R).sub.2, --N(R)C(S)N(R).sub.2, --CRN(R).sub.2C(O)OR, --N(R)R.sub.8, --O(CH.sub.2).sub.nOR, --N(R)C(.dbd.NR.sub.9)N(R).sub.2, --N(R)C(.dbd.CHR.sub.9)N(R).sub.2, --OC(O)N(R).sub.2, --N(R)C(O)OR, --N(OR)C(O)R, --N(OR)S(O).sub.2R, --N(OR)C(O)OR, --N(OR)C(O)N(R).sub.2, --N(OR)C(S)N(R).sub.2, --N(OR)C(.dbd.NR.sub.9)N(R).sub.2, --N(OR)C(.dbd.CHR.sub.9)N(R).sub.2, --C(.dbd.NR.sub.9)R, --C(O)N(R)OR, and --C(.dbd.NR.sub.9)N(R).sub.2, and each n is independently selected from 1, 2, 3, 4, and 5;

[0609] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0610] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0611] M and M' are independently selected from --C(O)O--, --OC(O)--, --C(O)N(R')--, --N(R')C(O)--, --C(O)--, --C(S)--, --C(S)S--, --SC(S)--, --CH(OH)--, --P(O)(OR')O--, --S(O).sub.2--, --S--S--, an aryl group, and a heteroaryl group;

[0612] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0613] R.sub.8 is selected from the group consisting of C.sub.3-6 carbocycle and heterocycle;

[0614] R.sub.9 is selected from the group consisting of H, CN, NO.sub.2, C.sub.1-6 alkyl, --OR, --S(O).sub.2R, --S(O).sub.2N(R).sub.2, C.sub.2-6 alkenyl, C.sub.3-6 carbocycle and heterocycle; [0615] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0616] each R' is independently selected from the group consisting of C.sub.1-18 alkyl, C.sub.2-18 alkenyl, --R*YR", --YR", and H;

[0617] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0618] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.2-12 alkenyl;

[0619] each Y is independently a C.sub.3-6 carbocycle;

[0620] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0621] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0622] or salts or isomers thereof.

[0623] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0624] R.sub.1 is selected from the group consisting of C.sub.5-30 alkyl, C.sub.5-20 alkenyl, --R*YR", --YR", and --R"M'R';

[0625] R.sub.2 and R.sub.3 are independently selected from the group consisting of H, C.sub.2-14 alkyl, C.sub.2-14 alkenyl, --R*YR", --YR", and --R*OR", or R.sub.2 and R.sub.3, together with the atom to which they are attached, form a heterocycle or carbocycle;

[0626] R.sub.4 is --(CH.sub.2).sub.nQ or --(CH.sub.2).sub.nCHQR, where Q is --N(R).sub.2, and n is selected from 3, 4, and 5;

[0627] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0628] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0629] M and M' are independently selected from --C(O)O--, --OC(O)--, --C(O)N(R')--, --N(R')C(O)--, --C(O)--, --C(S)--, --C(S)S--, --SC(S)--, --CH(OH)--, --P(O)(OR')O--, --S(O).sub.2--, --S--S--, an aryl group, and a heteroaryl group;

[0630] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0631] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0632] each R' is independently selected from the group consisting of C.sub.1-18 alkyl, C.sub.2-18 alkenyl, --R*YR", --YR", and H;

[0633] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0634] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.1-12 alkenyl;

[0635] each Y is independently a C.sub.3-6 carbocycle;

[0636] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0637] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0638] or salts or isomers thereof.

[0639] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0640] R.sub.1 is selected from the group consisting of C.sub.5-30 alkyl, C.sub.5-20 alkenyl, --R*YR", --YR", and --R"M'R';

[0641] R.sub.2 and R.sub.3 are independently selected from the group consisting of C.sub.1-14 alkyl, C.sub.2-14 alkenyl, --R*YR", --YR", and --R*OR", or R.sub.2 and R.sub.3, together with the atom to which they are attached, form a heterocycle or carbocycle;

[0642] R.sub.4 is selected from the group consisting of --(CH.sub.2).sub.nQ, --(CH.sub.2).sub.nCHQR, --CHQR, and --CQ(R).sub.2, where Q is --N(R).sub.2, and n is selected from 1, 2, 3, 4, and 5;

[0643] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0644] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0645] M and M' are independently selected from --C(O)O--, --OC(O)--, --C(O)N(R')--, --N(R')C(O)--, --C(O)--, --C(S)--, --C(S)S--, --SC(S)--, --CH(OH)--, --P(O)(OR')O--, --S(O).sub.2--, --S--S--, an aryl group, and a heteroaryl group;

[0646] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0647] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0648] each R' is independently selected from the group consisting of C.sub.1-18 alkyl, C.sub.2-18 alkenyl, --R*YR", --YR", and H;

[0649] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0650] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.1-12 alkenyl;

[0651] each Y is independently a C.sub.3-6 carbocycle;

[0652] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0653] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0654] or salts or isomers thereof.

[0655] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IA):

##STR00004##

[0656] or a salt or isomer thereof, wherein 1 is selected from 1, 2, 3, 4, and 5; m is selected from 5, 6, 7, 8, and 9; M.sub.1 is a bond or M'; R.sub.4 is unsubstituted C.sub.1-3 alkyl, or --(CH.sub.2).sub.nQ, in which Q is OH, --NHC(S)N(R).sub.2, --NHC(O)N(R).sub.2, --N(R)C(O)R, --N(R)S(O).sub.2R, --N(R)R.sub.8, --NHC(.dbd.NR.sub.9)N(R).sub.2, --NHC(.dbd.CHR.sub.9)N(R).sub.2, --OC(O)N(R).sub.2, --N(R)C(O)OR, heteroaryl or heterocycloalkyl; M and M' are independently selected

from --C(O)O--, --OC(O)--, --C(O)N(R')--, --P(O)(OR')O--, --S--S--, an aryl group, and a heteroaryl group; and R.sub.2 and R.sub.3 are independently selected from the group consisting of H, C.sub.1-14 alkyl, and C.sub.2-14 alkenyl.

[0657] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (II):

##STR00005##

or a salt or isomer thereof, wherein 1 is selected from 1, 2, 3, 4, and 5; M.sub.1 is a bond or M'; R.sub.4 is unsubstituted C.sub.1-3 alkyl, or --(CH.sub.2).sub.nQ, in which n is 2, 3, or 4, and Q is OH, --NHC(S)N(R).sub.2, --NHC(O)N(R).sub.2, --N(R)C(O)R, --N(R)S(O).sub.2R, --N(R)R.sub.8, --NHC(.dbd.NR.sub.9)N(R).sub.2, --NHC(.dbd.CHR.sub.9)N(R).sub.2, --OC(O)N(R).sub.2, --N(R)C(O)OR, heteroaryl or heterocycloalkyl; M and M' are independently selected from --C(O)O--, --OC(O)--, --C(O)N(R')--, --P(O)(OR')O--, --S--S--, an aryl group, and a heteroaryl group; and R.sub.2 and R.sub.3 are independently selected from the group consisting of H, C.sub.1-14 alkyl, and C.sub.2-14 alkenyl.

[0658] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (IIe):

##STR00006##

[0659] or a salt or isomer thereof, wherein R.sub.4 is as described herein.

[0660] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IId):

##STR00007##

[0661] or a salt or isomer thereof, wherein n is 2, 3, or 4; and m, R', R", and R.sub.2 through R.sub.6 are as described herein. For example, each of R.sub.2 and R.sub.3 may be independently selected from the group consisting of C.sub.5-14 alkyl and C.sub.5-14 alkenyl.

[0662] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (IIe):

##STR00008##

[0663] or a salt or isomer thereof, wherein R.sub.4 is as described herein.

[0664] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IId):

##STR00009##

[0665] or a salt or isomer thereof, wherein n is 2, 3, or 4; and m, R', R", and R.sub.2 through R.sub.6 are as described herein. For example, each of R.sub.2 and R.sub.3 may be independently selected from the group consisting of C.sub.5-14 alkyl and C.sub.5-14 alkenyl.

[0666] In some embodiments, the compound of Formula (I) is selected from the group consisting of:

##STR00010## ##STR00011## ##STR00012## ##STR00013## ##STR00014## ##STR00015## ##STR00016## ##STR00017## ##STR00018##

[0667] In further embodiments, the compound of Formula (I) is selected from the group consisting of:

##STR00019##

[0668] In some embodiments, the compound of Formula (I) is selected from the group consisting of:

##STR00020## ##STR00021## ##STR00022## ##STR00023## ##STR00024## ##STR00025## ##STR00026## ##STR00027## ##STR00028## ##STR00029## ##STR00030## ##STR00031## ##STR00032## ##STR00033## ##STR00034## ##STR00035## ##STR00036## ##STR00037## ##STR00038## ##STR00039## ##STR00040## ##STR00041## ##STR00042## ##STR00043## ##STR00044## ##STR00045## ##STR00046## ##STR00047##

and salts and isomers thereof.

[0669] In some embodiments, a nanoparticle comprises the following compound:

##STR00048##

or salts and isomers thereof.

[0670] In some embodiments, the disclosure features a nanoparticle composition including a lipid component comprising a compound as described herein (e.g., a compound according to Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe)).

[0671] In some embodiments, the disclosure features a pharmaceutical composition comprising a nanoparticle composition according to the preceding embodiments and a pharmaceutically acceptable carrier. For example, the pharmaceutical composition is refrigerated or frozen for storage and/or shipment (e.g., being stored at a temperature of 4.degree. C. or lower, such as a temperature between about -150.degree. C. and about 0.degree. C. or between about -80.degree. C. and about -20.degree. C. (e.g., about -5.degree. C., -10.degree. C., -15.degree. C., -20.degree. C., -25.degree. C., -30.degree. C., -40.degree. C., -50.degree. C., -60.degree. C., -70.degree. C., -80.degree. C., -90.degree. C., -130.degree. C. or -150.degree. C.). For example, the pharmaceutical composition is a solution that is refrigerated for storage and/or shipment at, for example, about -20.degree. C., -30.degree. C., -40.degree. C., -50.degree. C., -60.degree. C., -70.degree. C., or -80.degree. C.

[0672] In some embodiments, the disclosure provides a method of delivering a therapeutic and/or prophylactic (e.g., RNA, such as mRNA) to a cell (e.g., a mammalian cell). This method includes the step of administering to a subject (e.g., a mammal, such as a human) a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (lie) and (ii) a therapeutic and/or prophylactic, in which administering involves contacting the cell with the nanoparticle composition, whereby the therapeutic and/or prophylactic is delivered to the cell.

[0673] In some embodiments, the disclosure provides a method of producing a polypeptide of interest in a cell (e.g., a mammalian cell). The method includes the step of contacting the cell with a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) and (ii) an mRNA encoding the polypeptide of interest, whereby the mRNA is capable of being translated in the cell to produce the polypeptide.

[0674] In some embodiments, the disclosure provides a method of treating a disease or disorder in a mammal (e.g., a human) in need thereof. The method includes the step of administering to the mammal a therapeutically effective amount of a nanoparticle composition including (i) a lipid component including a phospholipid (such as a polyunsaturated lipid), a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) and (ii) a therapeutic and/or prophylactic (e.g., an mRNA). In some embodiments, the disease or disorder is characterized by dysfunctional or aberrant protein or polypeptide activity. For example, the disease or disorder is selected from the group consisting of rare diseases, infectious diseases, cancer and proliferative diseases, genetic diseases (e.g., cystic fibrosis), autoimmune diseases, diabetes, neurodegenerative diseases, cardio- and reno-vascular diseases, and metabolic diseases.

[0675] In some embodiments, the disclosure provides a method of delivering (e.g., specifically delivering) a therapeutic and/or prophylactic to a mammalian organ (e.g., a liver, spleen, lung, or femur). This method includes the step of administering to a subject (e.g., a mammal) a nanoparticle composition including (i) a lipid component including a phospholipid, a PEG lipid, a structural lipid, and a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) and (ii) a therapeutic and/or prophylactic (e.g., an mRNA), in which administering involves contacting the cell with the nanoparticle composition, whereby the therapeutic and/or prophylactic is delivered to the target organ (e.g., a liver, spleen, lung, or femur).

[0676] In some embodiments, the disclosure features a method for the enhanced delivery of a therapeutic and/or prophylactic (e.g., an mRNA) to a target tissue (e.g., a liver, spleen, lung, or femur). This method includes administering to a subject (e.g., a mammal) a nanoparticle composition, the composition including (i) a lipid component including a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe), a phospholipid, a structural lipid, and a PEG lipid; and (ii) a therapeutic and/or prophylactic, the administering including contacting the target tissue with the nanoparticle composition, whereby the therapeutic and/or prophylactic is delivered to the target tissue.

[0677] In some embodiments, the disclosure features a method of lowering immunogenicity comprising introducing the nanoparticle composition of the disclosure into cells, wherein the nanoparticle composition reduces the induction of the cellular immune response of the cells to the nanoparticle composition, as compared to the induction of the cellular immune response in cells induced by a reference composition which comprises a reference lipid instead of a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe). For example, the cellular immune response is an innate immune response, an adaptive immune response, or both.

[0678] The disclosure also includes methods of synthesizing a compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe) and methods of making a nanoparticle composition including a lipid component comprising the compound of Formula (I), (IA), (II), (IIa), (IIb), (IIc), (IId) or (IIe).

Modes of Vaccine Administration

[0679] Respiratory virus RNA (e.g. mRNA) vaccines may be administered by any route which results in a therapeutically effective outcome. These include, but are not limited, to intradermal, intramuscular, and/or subcutaneous administration. The present disclosure provides methods comprising administering RNA (e.g., mRNA) vaccines to a subject in need thereof. The exact amount required will vary from subject to subject, depending on the species, age, and general condition of the subject, the severity of the disease, the particular composition, its mode of administration, its mode of activity, and the like. Respiratory virus RNA (e.g., mRNA) vaccines compositions are typically formulated in dosage unit form for ease of administration and uniformity of dosage. It will be understood, however, that the total daily usage of RNA (e.g., mRNA) vaccine compositions may be decided by the attending physician within the scope of sound medical judgment. The specific therapeutically effective, prophylactically effective, or appropriate imaging dose level for any particular patient will depend upon a variety of factors including the disorder being treated and the severity of the disorder; the activity of the specific compound employed; the specific composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with the specific compound employed; and like factors well known in the medical arts.

[0680] In some embodiments, respiratory virus RNA (e.g. mRNA) vaccines compositions may be administered at dosage levels sufficient to deliver 0.0001 mg/kg to 100 mg/kg, 0.001 mg/kg to 0.05 mg/kg, 0.005 mg/kg to 0.05 mg/kg, 0.001 mg/kg to 0.005 mg/kg, 0.05 mg/kg to 0.5 mg/kg, 0.01 mg/kg to 50 mg/kg, 0.1 mg/kg to 40 mg/kg, 0.5 mg/kg to 30 mg/kg, 0.01 mg/kg to 10 mg/kg, 0.1 mg/kg to 10 mg/kg, or 1 mg/kg to 25 mg/kg, of subject body weight per day, one or more times a day, per week, per month, etc. to obtain the desired therapeutic, diagnostic, prophylactic, or imaging effect (see, e.g., the range of unit doses described in International Publication No WO2013078199, the contents of which are herein incorporated by reference in their entirety). The desired dosage may be delivered three times a day, two times a day, once a day, every other day, every third day, every week, every two weeks, every three weeks, every four weeks, every 2 months, every three months, every 6 months, etc. In some embodiments, the desired dosage may be delivered using multiple administrations (e.g., two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, or more administrations). When multiple administrations are employed, split dosing regimens such as those described herein may be used. In exemplary embodiments, respiratory virus RNA (e.g., mRNA) vaccines compositions may be administered at dosage levels sufficient to deliver 0.0005 mg/kg to 0.01 mg/kg, e.g., about 0.0005 mg/kg to about 0.0075 mg/kg, e.g., about 0.0005 mg/kg, about 0.001 mg/kg, about 0.002 mg/kg, about 0.003 mg/kg, about 0.004 mg/kg or about 0.005 mg/kg.

[0681] In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered once or twice (or more) at dosage levels sufficient to deliver 0.025 mg/kg to 0.250 mg/kg, 0.025 mg/kg to 0.500 mg/kg, 0.025 mg/kg to 0.750 mg/kg, or 0.025 mg/kg to 1.0 mg/kg.

[0682] In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered twice (e.g., Day 0 and Day 7, Day 0 and Day 14, Day 0 and Day 21, Day 0 and Day 28, Day 0 and Day 60, Day 0 and Day 90, Day 0 and Day 120, Day 0 and Day 150, Day 0 and Day 180, Day 0 and 3 months later, Day 0 and 6 months later, Day 0 and 9 months later, Day 0 and 12 months later, Day 0 and 18 months later, Day 0 and 2 years later, Day 0 and 5 years later, or Day 0 and 10 years later) at a total dose of or at dosage levels sufficient to deliver a total dose of 0.0100 mg, 0.025 mg, 0.050 mg, 0.075 mg, 0.100 mg, 0.125 mg, 0.150 mg, 0.175 mg, 0.200 mg, 0.225 mg, 0.250 mg, 0.275 mg, 0.300 mg, 0.325 mg, 0.350 mg, 0.375 mg, 0.400 mg, 0.425 mg, 0.450 mg, 0.475 mg, 0.500 mg, 0.525 mg, 0.550 mg, 0.575 mg, 0.600 mg, 0.625 mg, 0.650 mg, 0.675 mg, 0.700 mg, 0.725 mg, 0.750 mg, 0.775 mg, 0.800 mg, 0.825 mg, 0.850 mg, 0.875 mg, 0.900 mg, 0.925 mg, 0.950 mg, 0.975 mg, or 1.0 mg. Higher and lower dosages and frequency of administration are encompassed by the present disclosure. For example, a respiratory virus RNA (e.g., mRNA) vaccine composition may be administered three or four times.

[0683] In some embodiments, respiratory virus RNA (e.g., mRNA) vaccine compositions may be administered twice (e.g., Day 0 and Day 7, Day 0 and Day 14, Day 0 and Day 21, Day 0 and Day 28, Day 0 and Day 60, Day 0 and Day 90, Day 0 and Day 120, Day 0 and Day 150, Day 0 and Day 180, Day 0 and 3 months later, Day 0 and 6 months later, Day 0 and 9 months later, Day 0 and 12 months later, Day 0 and 18 months later, Day 0 and 2 years later, Day 0 and 5 years later, or Day 0 and 10 years later) at a total dose of or at dosage levels sufficient to deliver a total dose of 0.010 mg, 0.025 mg, 0.100 mg or 0.400 mg.

[0684] In some embodiments, the respiratory virus RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of between 10 .mu.g/kg and 400 .mu.g/kg of the nucleic acid vaccine (in an effective amount to vaccinate the subject). In some embodiments the RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of between 10 .mu.g and 400 .mu.g of the nucleic acid vaccine (in an effective amount to vaccinate the subject). In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as a single dosage of 25-1000 .mu.g (e.g., a single dosage of mRNA encoding hMPV, PIV3, RSV, MeV and/or BetaCoV antigen). In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine is administered to the subject as a single dosage of 25, 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 .mu.g. For example, a respiratory virus RNA (e.g., mRNA) vaccine may be administered to a subject as a single dose of 25-100, 25-500, 50-100, 50-500, 50-1000, 100-500, 100-1000, 250-500, 250-1000, or 500-1000 .mu.g. In some embodiments, a respiratory virus RNA (e.g., mRNA) vaccine for use in a method of vaccinating a subject is administered to the subject as two dosages, the combination of which equals 25-1000 .mu.g of the respiratory virus RNA (e.g., mRNA) vaccine.

[0685] A respiratory virus RNA (e.g. mRNA) vaccine pharmaceutical composition described herein can be formulated into a dosage form described herein, such as an intranasal, intratracheal, or injectable (e.g., intravenous, intraocular, intravitreal, intramuscular, intradermal, intracardiac, intraperitoneal, and subcutaneous).

Respiratory Virus RNA (e.g., mRNA) Vaccine Formulations and Methods of Use

[0686] Some aspects of the present disclosure provide formulations of the respiratory virus RNA (e.g., mRNA) vaccine, wherein the RNA (e.g., mRNA) vaccine is formulated in an effective amount to produce an antigen specific immune response in a subject (e.g., production of antibodies specific to an hMPV, PIV3, RSV, MeV and/or BetaCoV antigenic polypeptide). "An effective amount" is a dose of an RNA (e.g., mRNA) vaccine effective to produce an antigen-specific immune response. Also provided herein are methods of inducing an antigen-specific immune response in a subject.

[0687] In some embodiments, the antigen-specific immune response is characterized by measuring an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide antibody titer produced in a subject administered a respiratory virus RNA (e.g., mRNA) vaccine as provided herein. An antibody titer is a measurement of the amount of antibodies within a subject, for example, antibodies that are specific to a particular antigen (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) or epitope of an antigen. Antibody titer is typically expressed as the inverse of the greatest dilution that provides a positive result. Enzyme-linked immunosorbent assay (ELISA) is a common assay for determining antibody titers, for example.

[0688] In some embodiments, an antibody titer is used to assess whether a subject has had an infection or to determine whether immunizations are required. In some embodiments, an antibody titer is used to determine the strength of an autoimmune response, to determine whether a booster immunization is needed, to determine whether a previous vaccine was effective, and to identify any recent or prior infections. In accordance with the present disclosure, an antibody titer may be used to determine the strength of an immune response induced in a subject by the respiratory virus RNA (e.g., mRNA) vaccine.

[0689] In some embodiments, an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject is increased by at least 1 log relative to a control. For example, anti-antigenic polypeptide antibody titer produced in a subject may be increased by at least 1.5, at least 2, at least 2.5, or at least 3 log relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1, 1.5, 2, 2.5 or 3 log relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased by 1-3 log relative to a control. For example, the anti-antigenic polypeptide antibody titer produced in a subject may be increased by 1-1.5, 1-2, 1-2.5, 1-3, 1.5-2, 1.5-2.5, 1.5-3, 2-2.5, 2-3, or 2.5-3 log relative to a control.

[0690] In some embodiments, the anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject is increased at least 2 times relative to a control. For example, the anti-antigenic polypeptide antibody titer produced in a subject may be increased at least 3 times, at least 4 times, at least 5 times, at least 6 times, at least 7 times, at least 8 times, at least 9 times, or at least 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is increased 2, 3, 4, 5, 6, 7, 8, 9, or 10 times relative to a control. In some embodiments, the anti-antigenic polypeptide antibody titer produced in a subject is increased 2-10 times relative to a control. For example, the anti-antigenic polypeptide antibody titer produced in a subject may be increased 2-10, 2-9, 2-8, 2-7, 2-6, 2-5, 2-4, 2-3, 3-10, 3-9, 3-8, 3-7, 3-6, 3-5, 3-4, 4-10, 4-9, 4-8, 4-7, 4-6, 4-5, 5-10, 5-9, 5-8, 5-7, 5-6, 6-10, 6-9, 6-8, 6-7, 7-10, 7-9, 7-8, 8-10, 8-9, or 9-10 times relative to a control.

[0691] A control, in some embodiments, is the anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has not been administered a respiratory virus RNA (e.g., mRNA) vaccine of the present disclosure. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has been administered a live attenuated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. An attenuated vaccine is a vaccine produced by reducing the virulence of a viable (live). An attenuated virus is altered in a manner that renders it harmless or less virulent relative to live, unmodified virus. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject administered inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject administered a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. Recombinant protein vaccines typically include protein antigens that either have been produced in a heterologous expression system (e.g., bacteria or yeast) or purified from large amounts of the pathogenic organism. In some embodiments, a control is an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject who has been administered an hMPV, PIV3, RSV, MeV and/or BetaCoV virus-like particle (VLP) vaccine. For example, an hMPV VLP vaccine used as a control may be a hMPV VLPs, comprising (or consisting of) viral matrix (M) and fusion (F) proteins, generated by expressing viral proteins in suspension-adapted human embryonic kidney epithelial (293-F) cells (see, e.g., Cox R G et al., J Virol. 2014 June; 88(11): 6368-6379, the contents of which are herein incorporated by reference).

[0692] In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose that is reduced compared to the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. A "standard of care," as provided herein, refers to a medical or psychological treatment guideline and can be general or specific. "Standard of care" specifies appropriate treatment based on scientific evidence and collaboration between medical professionals involved in the treatment of a given condition. It is the diagnostic and treatment process that a physician/clinician should follow for a certain type of patient, illness or clinical circumstance. A "standard of care dose," as provided herein, refers to the dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine, that a physician/clinician or other medical professional would administer to a subject to treat or prevent hMPV, PIV3, RSV, MeV and/or BetaCoV, or a hMPV-, PIV3-, RSV-, MeV- and/or BetaCoV-related condition, while following the standard of care guideline for treating or preventing hMPV, PIV3, RSV, MeV and/or BetaCoV, or a hMPV-, PIV3-, RSV-, MeV- and/or BetaCoV-related condition.

[0693] In some embodiments, the anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a subject administered an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is equivalent to an anti-antigenic polypeptide (e.g., an anti-hMPV, anti-PIV3, anti-RSV, anti-MeV and/or anti-BetaCoV antigenic polypeptide) antibody titer produced in a control subject administered a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine.

[0694] In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to an at least 2-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. For example, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine may be a dose equivalent to an at least 3-fold, at least 4-fold, at least 5-fold, at least 6-fold, at least 7-fold, at least 8-fold, at least 9-fold, or at least 10-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to an at least at least 100-fold, at least 500-fold, or at least 1000-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 20-, 50-, 100-, 250-, 500-, or 1000-fold reduction in a standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, the anti-antigenic polypeptide antibody titer produced in a subject administered an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or protein hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. In some embodiments, an effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2-fold to 1000-fold (e.g., 2-fold to 100-fold, 10-fold to 1000-fold) reduction in the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine, wherein the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine.

[0695] In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose equivalent to a 2 to 1000-, 2 to 900-, 2 to 800-, 2 to 700-, 2 to 600-, 2 to 500-, 2 to 400-, 2 to 300-, 2 to 200-, 2 to 100-, 2 to 90-, 2 to 80-, 2 to 70-, 2 to 60-, 2 to 50-, 2 to 40-, 2 to 30-, 2 to 20-, 2 to 10-, 2 to 9-, 2 to 8-, 2 to 7-, 2 to 6-, 2 to 5-, 2 to 4-, 2 to 3-, 3 to 1000-, 3 to 900-, 3 to 800-, 3 to 700-, 3 to 600-, 3 to 500-, 3 to 400-, 3 to 3 to 00-, 3 to 200-, 3 to 100-, 3 to 90-, 3 to 80-, 3 to 70-, 3 to 60-, 3 to 50-, 3 to 40-, 3 to 30-, 3 to 20-, 3 to 10-, 3 to 9-, 3 to 8-, 3 to 7-, 3 to 6-, 3 to 5-, 3 to 4-, 4 to 1000-, 4 to 900-, 4 to 800-, 4 to 700-, 4 to 600-, 4 to 500-, 4 to 400-, 4 to 4 to 00-, 4 to 200-, 4 to 100-, 4 to 90-, 4 to 80-, 4 to 70-, 4 to 60-, 4 to 50-, 4 to 40-, 4 to 30-, 4 to 20-, 4 to 10-, 4 to 9-, 4 to 8-, 4 to 7-, 4 to 6-, 4 to 5-, 4 to 4-, 5 to 1000-, 5 to 900-, 5 to 800-, 5 to 700-, 5 to 600-, 5 to 500-, 5 to 400-, 5 to 300-, 5 to 200-, 5 to 100-, 5 to 90-, 5 to 80-, 5 to 70-, 5 to 60-, 5 to 50-, 5 to 40-, 5 to 30-, 5 to 20-, 5 to 10-, 5 to 9-, 5 to 8-, 5 to 7-, 5 to 6-, 6 to 1000-, 6 to 900-, 6 to 800-, 6 to 700-, 6 to 600-, 6 to 500-, 6 to 400-, 6 to 300-, 6 to 200-, 6 to 100-, 6 to 90-, 6 to 80-, 6 to 70-, 6 to 60-, 6 to 50-, 6 to 40-, 6 to 30-, 6 to 20-, 6 to 10-, 6 to 9-, 6 to 8-, 6 to 7-, 7 to 1000-, 7 to 900-, 7 to 800-, 7 to 700-, 7 to 600-, 7 to 500-, 7 to 400-, 7 to 300-, 7 to 200-, 7 to 100-, 7 to 90-, 7 to 80-, 7 to 70-, 7 to 60-, 7 to 50-, 7 to 40-, 7 to 30-, 7 to 20-, 7 to 10-, 7 to 9-, 7 to 8-, 8 to 1000-, 8 to 900-, 8 to 800-, 8 to 700-, 8 to 600-, 8 to 500-, 8 to 400-, 8 to 300-, 8 to 200-, 8 to

100-, 8 to 90-, 8 to 80-, 8 to 70-, 8 to 60-, 8 to 50-, 8 to 40-, 8 to 30-, 8 to 20-, 8 to 10-, 8 to 9-, 9 to 1000-, 9 to 900-, 9 to 800-, 9 to 700-, 9 to 600-, 9 to 500-, 9 to 400-, 9 to 300-, 9 to 200-, 9 to 100-, 9 to 90-, 9 to 80-, 9 to 70-, 9 to 60-, 9 to 50-, 9 to 40-, 9 to 30-, 9 to 20-, 9 to 10-, 10 to 1000-, 10 to 900-, 10 to 800-, 10 to 700-, 10 to 600-, 10 to 500-, 10 to 400-, 10 to 300-, 10 to 200-, 10 to 100-, 10 to 90-, 10 to 80-, 10 to 70-, 10 to 60-, 10 to 50-, 10 to 40-, 10 to 30-, 10 to 20-, 20 to 1000-, 20 to 900-, 20 to 800-, 20 to 700-, 20 to 600-, 20 to 500-, 20 to 400-, 20 to 300-, 20 to 200-, 20 to 100-, 20 to 90-, 20 to 80-, 20 to 70-, 20 to 60-, 20 to 50-, 20 to 40-, 20 to 30-, 30 to 1000-, 30 to 900-, 30 to 800-, 30 to 700-, 30 to 600-, 30 to 500-, 30 to 400-, 30 to 300-, 30 to 200-, 30 to 100-, 30 to 90-, 30 to 80-, 30 to 70-, 30 to 60-, 30 to 50-, 30 to 40-, 40 to 1000-, 40 to 900-, 40 to 800-, 40 to 700-, 40 to 600-, 40 to 500-, 40 to 400-, 40 to 300-, 40 to 200-, 40 to 100-, 40 to 90-, 40 to 80-, 40 to 70-, 40 to 60-, 40 to 50-, 50 to 1000-, 50 to 900-, 50 to 800-, 50 to 700-, 50 to 600-, 50 to 500-, 50 to 400-, 50 to 300-, 50 to 200-, 50 to 100-, 50 to 90-, 50 to 80-, 50 to 70-, 50 to 60-, 60 to 1000-, 60 to 900-, 60 to 800-, 60 to 700-, 60 to 600-, 60 to 500-, 60 to 400-, 60 to 300-, 60 to 200-, 60 to 100-, 60 to 90-, 60 to 80-, 60 to 70-, 70 to 1000-, 70 to 900-, 70 to 800-, 70 to 700-, 70 to 600-, 70 to 500-, 70 to 400-, 70 to 300-, 70 to 200-, 70 to 100-, 70 to 90-, 70 to 80-, 80 to 1000-, 80 to 900-, 80 to 800-, 80 to 700-, 80 to 600-, 80 to 500-, 80 to 400-, 80 to 300-, 80 to 200-, 80 to 100-, 80 to 90-, 90 to 1000-, 90 to 900-, 90 to 800-, 90 to 700-, 90 to 600-, 90 to 500-, 90 to 400-, 90 to 300-, 90 to 200-, 90 to 100-, 100 to 1000-, 100 to 900-, 100 to 800-, 100 to 700-, 100 to 600-, 100 to 500-, 100 to 400-, 100 to 300-, 100 to 200-, 200 to 1000-, 200 to 900-, 200 to 800-, 200 to 700-, 200 to 600-, 200 to 500-, 200 to 400-, 200 to 300-, 300 to 1000-, 300 to 900-, 300 to 800-, 300 to 700-, 300 to 600-, 300 to 500-, 300 to 400-, 400 to 1000-, 400 to 900-, 400 to 800-, 400 to 700-, 400 to 600-, 400 to 500-, 500 to 1000-, 500 to 900-, 500 to 800-, 500 to 700-, 500 to 600-, 600 to 1000-, 600 to 900-, 600 to 800-, 600 to 700-, 700 to 1000-, 700 to 900-, 700 to 800-, 800 to 1000-, 800 to 900-, or 900 to 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, the anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine. In some embodiments, the effective amount is a dose equivalent to (or equivalent to an at least) 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, 10-, 20-, 30-, 40-, 50-, 60-, 70-, 80-, 90-, 100-, 110-, 120-, 130-, 140-, 150-, 160-, 170-, 1280-, 190-, 200-, 210-, 220-, 230-, 240-, 250-, 260-, 270-, 280-, 290-, 300-, 310-, 320-, 330-, 340-, 350-, 360-, 370-, 380-, 390-, 400-, 410-, 420-, 430-, 440-, 450-, 4360-, 470-, 480-, 490-, 500-, 510-, 520-, 530-, 540-, 550-, 560-, 5760-, 580-, 590-, 600-, 610-, 620-, 630-, 640-, 650-, 660-, 670-, 680-, 690-, 700-, 710-, 720-, 730-, 740-, 750-, 760-, 770-, 780-, 790-, 800-, 810-, 820-, 830-, 840-, 850-, 860-, 870-, 880-, 890-, 900-, 910-, 920-, 930-, 940-, 950-, 960-, 970-, 980-, 990-, or 1000-fold reduction in the standard of care dose of a recombinant hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine. In some embodiments, an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant or purified hMPV, PIV3, RSV, MeV and/or BetaCoV protein vaccine or a live attenuated or inactivated hMPV, PIV3, RSV, MeV and/or BetaCoV vaccine.

[0696] In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 50-1000 .mu.g. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 50-1000, 50-900, 50-800, 50-700, 50-600, 50-500, 50-400, 50-300, 50-200, 50-100, 50-90, 50-80, 50-70, 50-60, 60-1000, 60-900, 60-800, 60-700, 60-600, 60-500, 60-400, 60-300, 60-200, 60-100, 60-90, 60-80, 60-70, 70-1000, 70-900, 70-800, 70-700, 70-600, 70-500, 70-400, 70-300, 70-200, 70-100, 70-90, 70-80, 80-1000, 80-900, 80-800, 80-700, 80-600, 80-500, 80-400, 80-300, 80-200, 80-100, 80-90, 90-1000, 90-900, 90-800, 90-700, 90-600, 90-500, 90-400, 90-300, 90-200, 90-100, 100-1000, 100-900, 100-800, 100-700, 100-600, 100-500, 100-400, 100-300, 100-200, 200-1000, 200-900, 200-800, 200-700, 200-600, 200-500, 200-400, 200-300, 300-1000, 300-900, 300-800, 300-700, 300-600, 300-500, 300-400, 400-1000, 400-900, 400-800, 400-700, 400-600, 400-500, 500-1000, 500-900, 500-800, 500-700, 500-600, 600-1000, 600-900, 600-900, 600-700, 700-1000, 700-900, 700-800, 800-1000, 800-900, or 900-1000 .mu.g. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 50, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 .mu.g. In some embodiments, the effective amount is a dose of 25-500 .mu.g administered to the subject a total of two times. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a dose of 25-500, 25-400, 25-300, 25-200, 25-100, 25-50, 50-500, 50-400, 50-300, 50-200, 50-100, 100-500, 100-400, 100-300, 100-200, 150-500, 150-

400, 150-300, 150-200, 200-500, 200-400, 200-300, 250-500, 250-400, 250-300, 300-500, 300-400, 350-500, 350-400, 400-500 or 450-500 .mu.g administered to the subject a total of two times. In some embodiments, the effective amount of a respiratory virus RNA (e.g., mRNA) vaccine is a total dose of 25, 50, 100, 150, 200, 250, 300, 350, 400, 450, or 500 .mu.g administered to the subject a total of two times.

Examples of Additional Embodiments of the Disclosure

[0697] Additional embodiments of the present disclosure are encompassed by the following numbered paragraphs:

1. A respiratory virus vaccine, comprising: at least one ribonucleic acid (RNA) polynucleotide having an open reading frame encoding at least one, at least two, at least three, at least four or at least five antigenic polypeptides selected from human Metapneumovirus (hMPV) antigenic polypeptides or immunogenic fragments thereof, human parainfluenza virus type 3 (PIV3) antigenic polypeptides or immunogenic fragments thereof, respiratory syncytial virus (RSV) antigenic polypeptides or immunogenic fragments thereof, measles virus (MeV) antigenic polypeptides or immunogenic fragments thereof, and Betacoronavirus (BetaCoV) antigenic polypeptides or immunogenic fragments thereof. 2. The respiratory virus vaccine of paragraph 1, comprising:

[0698] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and a PIV3 antigenic polypeptide or an immunogenic fragment thereof; or

[0699] at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof.

3. The respiratory virus vaccine of paragraph 2, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13. 4. The respiratory virus vaccine of paragraph 1, comprising:

[0700] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and a RSV antigenic polypeptide or an immunogenic fragment thereof; or

[0701] at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof.

5. The respiratory virus vaccine of paragraph 4, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8. 6. The respiratory virus vaccine of paragraph 1, comprising:

[0702] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and MeV antigenic polypeptide or an immunogenic fragment thereof; or

[0703] at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

7. The respiratory virus vaccine of paragraph 6, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the MeV antigenic

polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 8. The respiratory virus vaccine of paragraph 1, comprising:

[0704] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0705] at least two RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

9. The respiratory virus vaccine of paragraph 8, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 10. The respiratory virus vaccine of paragraph 1, comprising:

[0706] at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and a RSV antigenic polypeptide or an immunogenic fragment thereof; or

[0707] at least two RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof.

11. The respiratory virus vaccine of paragraph 10, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13. 12. The respiratory virus vaccine of paragraph 1, comprising:

[0708] at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

[0709] at least two RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

13. The respiratory virus vaccine of paragraph 12, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 14. The respiratory virus vaccine of paragraph 1, comprising:

[0710] at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and a BetaCoV antigenic

[0711] polypeptide or an immunogenic fragment thereof; or at least two RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

15. The respiratory virus vaccine of paragraph 14, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or

95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 16. The respiratory virus vaccine of paragraph 1, comprising:

[0712] at least one RNA polynucleotide having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

[0713] at least two RNA polynucleotides, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

17. The respiratory virus vaccine of paragraph 16, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 18. The respiratory virus vaccine of paragraph 1, comprising:

[0714] at least one RNA polynucleotide having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0715] at least two RNA polynucleotides, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

19. The respiratory virus vaccine of paragraph 18, wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 20. The respiratory virus vaccine of paragraph 1, comprising:

[0716] at least one RNA polynucleotide having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0717] at least two RNA polynucleotides, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

21. The respiratory virus vaccine of paragraph 20, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 22. The respiratory virus vaccine of paragraph 1, comprising:

[0718] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and a RSV antigenic polypeptide or an immunogenic fragment thereof; or

[0719] at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof.

23. The respiratory virus vaccine of paragraph 22, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95%

identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13. 24. The respiratory virus vaccine of paragraph 1, comprising:

[0720] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

[0721] at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

25. The respiratory virus vaccine of paragraph 24, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 26. The respiratory virus vaccine of paragraph 1, comprising:

[0722] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0723] at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

27. The respiratory virus vaccine of paragraph 26, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13 and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34. 28. The respiratory virus vaccine of paragraph 1, comprising:

[0724] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

[0725] at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

29. The respiratory virus vaccine of paragraph 28, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the MeV antigenic

polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 30. The respiratory virus vaccine of paragraph 1, comprising:

[0726] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0727] at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

31. The respiratory virus vaccine of paragraph 30, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34. 32. The respiratory virus vaccine of paragraph 1, comprising:

[0728] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0729] at least two or three RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

33. The respiratory virus vaccine of paragraph 32, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34. 34. The respiratory virus vaccine of paragraph 1, comprising:

[0730] at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

[0731] at least two or three RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

35. The respiratory virus vaccine of paragraph 34, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 36. The respiratory virus vaccine of paragraph 1, comprising:

[0732] at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0733] at least two or three RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

37. The respiratory virus vaccine of paragraph 36, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34. 38. The respiratory virus vaccine of paragraph 1, comprising:

[0734] at least one RNA polynucleotide having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0735] at least two or three RNA polynucleotides, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

39. The respiratory virus vaccine of paragraph 38, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34. 40. The respiratory virus vaccine of paragraph 1, comprising:

[0736] at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0737] at least two or three RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

41. The respiratory virus vaccine of paragraph 40, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 23-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 23-34. 42. The respiratory virus vaccine of paragraph 1, comprising:

[0738] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a MeV antigenic polypeptide or an immunogenic fragment thereof; or

[0739] at least two, three or four RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof.

43. The respiratory virus vaccine of paragraph 42, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50. 44. The respiratory virus vaccine of paragraph 1, comprising:

[0740] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0741] at least two, three or four RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

45. The respiratory virus vaccine of paragraph 44, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 46. The respiratory virus vaccine of paragraph 1, comprising:

[0742] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0743] at least two, three or four RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

47. The respiratory virus vaccine of paragraph 46, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid

sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 48. The respiratory virus vaccine of paragraph 1, comprising:

[0744] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0745] at least two, three or four RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

49. The respiratory virus vaccine of paragraph 48, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 50. The respiratory virus vaccine of paragraph 1, comprising:

[0746] at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0747] at least two, three or four RNA polynucleotides, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

51. The respiratory virus vaccine of paragraph 50, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 52. The respiratory virus vaccine of paragraph 1, comprising:

[0748] at least one RNA polynucleotide having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, a PIV3 antigenic polypeptide or an immunogenic fragment thereof, a RSV antigenic polypeptide or an immunogenic fragment thereof, a MeV antigenic polypeptide or an immunogenic fragment thereof, and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0749] at least two, three, four or five RNA polynucleotides, one having an open reading frame encoding a hMPV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a RSV antigenic polypeptide or an immunogenic fragment thereof, one having an open reading frame encoding a MeV antigenic polypeptide or an immunogenic fragment thereof, and one having an open reading frame encoding a BetaCoV antigenic polypeptide or an immunogenic fragment thereof.

53. The respiratory virus vaccine of paragraph 52, wherein the hMPV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 5-8 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 5-8, wherein the PIV3 antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 12-13 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 12-13, wherein the MeV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 47-50 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 47-50, and/or wherein the BetaCoV antigenic polypeptide comprises an amino acid sequence identified by any one of SEQ ID NO: 24-34 or an amino acid sequence having at least 90% or 95% identity to an amino acid sequence identified by any one of SEQ ID NO: 24-34. 54. The vaccine of any one of paragraphs 1-53, wherein at least one RNA polynucleotide has less than 80% identity to wild-type mRNA sequence. 55. The vaccine of any one of paragraphs 1-53, wherein at least one RNA polynucleotide has at least 80% identity to wild-type mRNA sequence, but does not include wild-type mRNA sequence. 56. The vaccine of any one of paragraphs 1-55, wherein at least one antigenic polypeptide has membrane fusion activity, attaches to cell receptors, causes fusion of viral and cellular membranes, and/or is responsible for binding of the virus to a cell being infected. 57. The vaccine of any one of paragraphs 1-56, wherein at least one RNA polynucleotide comprises at least one chemical modification. 58. The vaccine of paragraph 57, wherein the chemical modification is selected from pseudouridine, N1-methylpseudouridine, N1-ethylpseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcytosine, 5-methyluridine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine. 59. The vaccine of paragraph 57 or 58, wherein the chemical modification is in the 5-position of the uracil. 60. The vaccine of any one of paragraphs 57-59, wherein the chemical modification is a N1-methylpseudouridine or N1-ethylpseudouridine. 61. The vaccine of any one of paragraphs 57-60, wherein at least 80%, at least 90% or 100% of the uracil in the open reading frame have a chemical modification. 62. The vaccine of any one of paragraphs 1-61, wherein at least one RNA polynucleotide further encodes at least one 5' terminal cap, optionally wherein the 5' terminal cap is 7mG(5')ppp(5')N1mpNp. 63. The vaccine of any one of paragraphs 1-62, wherein at least one antigenic polypeptide or immunogenic fragment thereof is fused to a signal peptide selected from: a HuIgGk signal peptide (METPAQLLFLLLLWLPDTTG; SEQ ID NO: 15); IgE heavy chain epsilon-1 signal peptide (MDWTWILFLVAAATRVHS; SEQ ID NO: 16); Japanese encephalitis PRM signal sequence (MLGSNSGQRVVFTILLLLVAPAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVSLAIVTACAGA; SEQ ID NO:19). 64. The vaccine of paragraph 63, wherein the signal peptide is fused to the N-terminus or the C-terminus of at least one antigenic polypeptide. 65. The vaccine of any one of paragraphs 1-64, wherein the antigenic polypeptide or immunogenic fragment thereof comprises a mutated N-linked glycosylation site. 66. The vaccine of any one of paragraphs 1-65 formulated in a nanoparticle, optionally a a lipid nanoparticle. 67. The vaccine of paragraph 66, wherein the lipid nanoparticle comprises a cationic lipid, a PEG-modified lipid, a sterol and a non-cationic lipid; optionally wherein the lipid nanoparticle carrier comprises a molar ratio of about 20-60% cationic lipid, 0.5-15% PEG-modified lipid, 25-55% sterol, and 25% non-cationic lipid; optionally wherein the cationic lipid is an ionizable cationic lipid and the non-cationic lipid is a neutral lipid, and the sterol is a cholesterol; and optionally wherein the cationic lipid is selected from 2,2-dilinoleyl-4-dimethylaminoethyl-[1,3]-dioxolane (DLin-KC2-DMA), dilinoleyl-methyl-4-dimethylaminobutyrate (DLin-MC3-DMA), and di((Z)-non-2-en-1-yl) 9-((4-(dimethylamino)butanoyl)oxy)heptadecanedioate (L319). Formula (II) 68. The vaccine of paragraph 66 or 67, wherein the nanoparticle (e.g., lipid nanoparticle) comprises a compound of Formula (I) and/or Formula (II),

optionally Compound 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122. 69. The vaccine of any one of paragraphs 1-68 further comprising an adjuvant, optionally a flagellin protein or peptide that optionally comprises an amino acid sequence identified by any one of SEQ ID NO: 54-56. 70. The vaccine of any one of paragraphs 1-69, wherein the open reading frame is codon-optimized. 71. The vaccine of any one of paragraphs 1-70 formulated in an effective amount to produce an antigen-specific immune response. 72. A method of inducing an immune response in a subject, the method comprising administering to the subject the vaccine of any one of paragraphs 1-71 in an amount effective to produce an antigen-specific immune response in the subject. 73. The method of paragraph 72, wherein the subject is administered a single dose of the vaccine, or wherein the subject is administered a first dose and then a booster dose of the vaccine. 74. The method of paragraph 72 or 73, wherein the vaccine is administered to the subject by intradermal injection or intramuscular injection. 75. The method of any one of paragraphs 72-74, wherein an anti-antigenic polypeptide antibody titer produced in the subject is increased by at least 1 log relative to a control, and/or wherein the anti-antigenic polypeptide antibody titer produced in the subject is increased at least 2 times relative to a control. 76. The method of any one of paragraphs 72-75, wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has not been administered a vaccine against the virus, and/or wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a live attenuated vaccine or an inactivated vaccine against the virus, and/or, wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a recombinant protein vaccine or purified protein vaccine against the virus, and/or wherein the control is an anti-antigenic polypeptide antibody titer produced in a subject who has been administered a VLP vaccine against the virus. 77. The method of any one of paragraphs 72-76, wherein the effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a recombinant protein vaccine or a purified protein vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a recombinant protein vaccine or a purified protein vaccine against the virus, respectively; and/or wherein the effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a live attenuated vaccine or an inactivated vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a live attenuated vaccine or an inactivated vaccine against the virus, respectively; and/or wherein the effective amount is a dose equivalent to an at least 2-fold reduction in the standard of care dose of a VLP vaccine against the virus, and wherein an anti-antigenic polypeptide antibody titer produced in the subject is equivalent to an anti-antigenic polypeptide antibody titer produced in a control subject administered the standard of care dose of a VLP vaccine against the virus. 78. The method of any one of paragraphs 72-77, wherein the effective amount is a total dose of 50 .mu.g-1000 .mu.g, optionally wherein the effective amount is a dose of 25 .mu.g, 100 .mu.g, 400 .mu.g, or 500 .mu.g administered to the subject a total of two times. 79. The method of any one of paragraphs 72-78, wherein the efficacy of the vaccine against the virus is greater than 65%; and/or wherein the vaccine immunizes the subject against the virus for up to 2 years or wherein the vaccine immunizes the subject against the virus for more than 2 years. 80. The method of any one of paragraphs 72-79, wherein the subject has an age of about 5 years old or younger or wherein the subject has an age of about 60 years old or older; and/or wherein the subject has a chronic pulmonary disease; and/or the subject has been exposed to the virus, wherein the subject is infected with the virus, or wherein the subject is at risk of infection by the virus; and/or wherein the subject is immunocompromised. 81. The respiratory virus vaccine of any one of paragraphs 1-71, comprising at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide having an open reading frame encoding at least one (e.g., at least two, at least three, at least four, or at least five) antigenic polypeptide selected from hMPV antigenic polypeptides (SEQ ID NO: 5-8), PIV3 antigenic polypeptides (SEQ ID NO: 12-13), RSV antigenic polypeptides, MeV antigenic polypeptides (SEQ ID NO: 47-50) and BetaCoV antigenic polypeptides (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1; (SEQ ID NO: 24-34)), formulated in a cationic lipid nanoparticle

[0750] (a) having a molar ratio of about 20-60% cationic lipid, about 5-25% non-cationic lipid, about 25-55% sterol, and about 0.5-15% PEG-modified lipid, and/or

[0751] (b) comprising a compound of Formula (I) and/or Formula (II),

[0752] wherein the at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide comprises at least one chemical modification.

82. The respiratory virus vaccine of any one of paragraphs 1-71, comprising at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide having an open reading frame encoding at least one (e.g., at least two, at least three, at least four, or at least five) antigenic polypeptide selected from hMPV antigenic polypeptides (SEQ ID NO: 5-8), PIV3 antigenic polypeptides (SEQ ID NO: 12-13), RSV antigenic polypeptides, MeV antigenic polypeptides (SEQ ID NO: 47-50) and BetaCoV antigenic polypeptides (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1; (SEQ ID NO: 24-34)), formulated in a cationic lipid nanoparticle

[0753] (a) having a molar ratio of about 20-60% cationic lipid, about 5-25% non-cationic lipid, about 25-55% sterol, and about 0.5-15% PEG-modified lipid, and/or

[0754] (b) comprising at least one (e.g., at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14) Compound selected from Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112 and 122.

83. The respiratory virus vaccine of paragraphs 81 or 82, wherein the at least one antigenic polypeptide is selected from hMPV antigentic polypeptides (e.g., SEQ ID NO: 5-8). 84. The respiratory virus vaccine of any one of paragraphs 81-83, wherein the at least one antigenic polypeptide is selected from PIV3 antigentic polypeptides (e.g., SEQ ID NO: 12-13). 85. The respiratory virus vaccine of any one of paragraphs 81-84, wherein the at least one antigenic polypeptide is selected from RSV antigentic polypeptides. 86. The respiratory virus vaccine of any one of paragraphs 81-85, wherein the at least one antigenic polypeptide is selected from MeV antigentic polypeptides (e.g., SEQ ID NO: 47-50). 87. The respiratory virus vaccine of any one of paragraphs 81-86, wherein the at least one antigenic polypeptide is selected from BetaCoV antigentic polypeptides (e.g., SEQ ID NO: 24-34). 88. The respiratory virus vaccine of paragraph 87, wherein the BetaCoV antigentic polypeptides are MERS antigentic polypeptides. 89. The respiratory virus vaccine of paragraph 87, wherein the BetaCoV antigentic polypeptides are ***SARS*** antigentic polypeptides. 90. The respiratory virus vaccine of any one of paragraphs 81-89, wherein the at least one (e.g., at least two, at least three, at least four, or at least five) RNA polynucleotide comprises at least one chemical modification (e.g., selected from pseudouridine, N1-methylpseudouridine, N1-ethylpseudouridine, 2-thiouridine, 4'-thiouridine, 5-methylcytosine, 5-methyluridine, 2-thio-1-methyl-1-deaza-pseudouridine, 2-thio-1-methyl-pseudouridine, 2-thio-5-aza-uridine, 2-thio-dihydropseudouridine, 2-thio-dihydrouridine, 2-thio-pseudouridine, 4-methoxy-2-thio-pseudouridine, 4-methoxy-pseudouridine, 4-thio-1-methyl-pseudouridine, 4-thio-pseudouridine, 5-aza-uridine, dihydropseudouridine, 5-methoxyuridine and 2'-O-methyl uridine). 91. A respiratory virus vaccine, comprising:

[0755] at least one messenger ribonucleic acid (mRNA) polynucleotide having a 5' terminal cap, an open reading frame encoding at least one respiratory virus antigenic polypeptide, and a 3' polyA tail.

92. The vaccine of paragraph 91, wherein the at least one mRNA polynucleotide comprises a sequence identified by any one of SEQ ID NO: 57-80. 93. The vaccine of paragraph 91 or 92, wherein the 5' terminal cap is or comprises 7mG(5')ppp(5')N1mpNp. 94. The vaccine of any one of paragraphs 91-93, wherein 100% of the uracil in the open reading frame is modified to include N1-methyl pseudouridine at the 5-position of the uracil. 95. The vaccine of any one of paragraphs 91-94, wherein the vaccine is formulated in a lipid nanoparticle comprising: DLin-MC3-DMA; cholesterol; 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC); and polyethylene glycol (PEG)2000-DMG. 96. The vaccine of paragraph 95, wherein the lipid nanoparticle further comprises trisodium citrate buffer, sucrose and water. 97. A respiratory syncytial virus (RSV) vaccine, comprising:

[0756] at least one messenger ribonucleic acid (mRNA) polynucleotide having a 5' terminal cap 7mG(5')ppp(5')N1mpNp, a sequence identified by any one of SEQ ID NO: 57-80 and a 3' polyA tail, formulated in a lipid nanoparticle comprising DLin-MC3-DMA, cholesterol, 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC), and polyethylene glycol (PEG)2000-DMG, wherein the uracil nucleotides of the sequence identified by any one of SEQ ID NO: 57-80 are modified to include N1-methyl pseudouridine at the 5-position of the uracil nucleotide.

[0757] This disclosure is not limited in its application to the details of construction and the arrangement of components set forth in the following description or illustrated in the drawings. The disclosure is capable of other embodiments and of being practiced or of being carried out in various ways. Also, the phraseology and terminology used herein is for the purpose of description and should not be regarded as limiting. The use of "including," "comprising," or "having," "containing," "involving," and variations thereof herein, is meant to encompass the items listed thereafter and equivalents thereof as well as additional items.

EXAMPLES

Example 1: Manufacture of Polynucleotides

[0758] According to the present disclosure, the manufacture of polynucleotides and/or parts or regions thereof may be accomplished utilizing the methods taught in International Publication WO2014/152027, entitled "Manufacturing Methods for Production of RNA Transcripts," the contents of which is incorporated herein by reference in its entirety.

[0759] Purification methods may include those taught in International Publication WO2014/152030 and International Publication WO2014/152031, each of which is incorporated herein by reference in its entirety.

[0760] Detection and characterization methods of the polynucleotides may be performed as taught in International Publication WO2014/144039, which is incorporated herein by reference in its entirety.

[0761] Characterization of the polynucleotides of the disclosure may be accomplished using polynucleotide mapping, reverse transcriptase sequencing, charge distribution analysis, detection of RNA impurities, or any combination of two or more of the foregoing. "Characterizing" comprises determining the RNA transcript sequence, determining the purity of the RNA transcript, or determining the charge heterogeneity of the RNA transcript, for example. Such methods are taught in, for example, International Publication WO2014/144711 and International Publication WO2014/144767, the content of each of which is incorporated herein by reference in its entirety.

Example 2: Chimeric Polynucleotide Synthesis

[0762] According to the present disclosure, two regions or parts of a chimeric polynucleotide may be joined or ligated using triphosphate chemistry. A first region or part of 100 nucleotides or less is chemically synthesized with a 5' monophosphate and terminal 3'desOH or blocked OH, for example. If the region is longer than 80 nucleotides, it may be synthesized as two strands for ligation.

[0763] If the first region or part is synthesized as a non-positionally modified region or part using in vitro transcription (IVT), conversion the 5'monophosphate with subsequent capping of the 3' terminus may follow.

[0764] Monophosphate protecting groups may be selected from any of those known in the art.

[0765] The second region or part of the chimeric polynucleotide may be synthesized using either chemical synthesis or IVT methods. IVT methods may include an RNA polymerase that can utilize a primer with a modified cap. Alternatively, a cap of up to 130 nucleotides may be chemically synthesized and coupled to the IVT region or part.

[0766] For ligation methods, ligation with DNA T4 ligase, followed by treatment with DNase should readily avoid concatenation.

[0767] The entire chimeric polynucleotide need not be manufactured with a phosphate-sugar backbone. If one of the regions or parts encodes a polypeptide, then such region or part may comprise a phosphate-sugar backbone.

[0768] Ligation is then performed using any known click chemistry, orthoclick chemistry, solulink, or other bioconjugate chemistries known to those in the art.

[0769] Synthetic Route

[0770] The chimeric polynucleotide may be made using a series of starting segments. Such segments include:

[0771] (a) a capped and protected 5' segment comprising a normal 3'OH (SEG. 1)

[0772] (b) a 5' triphosphate segment, which may include the coding region of a polypeptide and a normal 3'OH (SEG. 2)

[0773] (c) a 5' monophosphate segment for the 3' end of the chimeric polynucleotide (e.g., the tail) comprising cordycepin or no 3'OH (SEG. 3)

[0774] After synthesis (chemical or IVT), segment 3 (SEG. 3) may be treated with cordycepin and then with pyrophosphatase to create the 5' monophosphate.

[0775] Segment 2 (SEG. 2) may then be ligated to SEG. 3 using RNA ligase. The ligated polynucleotide is then purified and treated with pyrophosphatase to cleave the diphosphate. The treated SEG. 2-SEG. 3 construct may then be purified and SEG. 1 is ligated to the 5' terminus. A further purification step of the chimeric polynucleotide may be performed.

[0776] Where the chimeric polynucleotide encodes a polypeptide, the ligated or joined segments may be represented as: 5'UTR (SEG. 1), open reading frame or ORF (SEG. 2) and 3'UTR+PolyA (SEG. 3).

[0777] The yields of each step may be as much as 90-95%.

Example 3: PCR for cDNA Production

[0778] PCR procedures for the preparation of cDNA may be performed using 2.times.KAPA HIFI.TM. HotStart ReadyMix by Kapa Biosystems (Woburn, Mass.). This system includes 2.times.KAPA ReadyMix 12.5 .mu.l; Forward Primer (10 .mu.M) 0.75 .mu.l; Reverse Primer (10 .mu.M) 0.75 .mu.l; Template cDNA 100 ng; and dH.sub.20 diluted to 25.0 .mu.l. The reaction conditions may be at 95.degree. C. for 5 min. The reaction may be performed for 25 cycles of 98.degree. C. for 20 sec, then 58.degree. C. for 15 sec, then 72.degree. C. for 45 sec, then 72.degree. C. for 5 min, then 4.degree. C. to termination.

[0779] The reaction may be cleaned up using Invitrogen's PURELINK.TM. PCR Micro Kit (Carlsbad, Calif.) per manufacturer's instructions (up to 5 .mu.g). Larger reactions may require a cleanup using a product with a larger capacity. Following the cleanup, the cDNA may be quantified using the NANODROP.TM. and analyzed by agarose gel electrophoresis to confirm that the cDNA is the expected size. The cDNA may then be submitted for sequencing analysis before proceeding to the in vitro transcription reaction.

Example 4: In Vitro Transcription (IVT)

[0780] The in vitro transcription reaction generates RNA polynucleotides. Such polynucleotides may comprise a region or part of the polynucleotides of the disclosure, including chemically modified RNA (e.g., mRNA) polynucleotides. The chemically modified RNA polynucleotides can be uniformly modified polynucleotides. The in vitro transcription reaction utilizes a custom mix of nucleotide triphosphates (NTPs). The NTPs may comprise chemically modified NTPs, or a mix of natural and chemically modified NTPs, or natural NTPs.

[0781] A typical in vitro transcription reaction includes the following:

TABLE-US-00001 1) Template cDNA 1.0 .mu.g 2) 10x transcription buffer 2.0 .mu.l (400 mM Tris-HCl pH 8.0, 190 mM MgCl.sub.2, 50 mM DTT, 10 mM Spermidine) 3) Custom NTPs (25 mM each) 0.2 .mu.l 4) RNase Inhibitor 20 U 5) T7 RNA polymerase 3000 U 6) dH.sub.20 up to 20.0 .mu.l. and 7) Incubation at 37.degree. C. for 3 hr-5 hrs.

[0782] The crude IVT mix may be stored at 4.degree. C. overnight for cleanup the next day. 1 U of RNase-free DNase may then be used to digest the original template. After 15 minutes of incubation at 37.degree. C., the mRNA may be purified using Ambion's MEGACLEAR.TM. Kit (Austin, Tex.) following the manufacturer's instructions. This kit can purify up to 500 .mu.g of RNA. Following the cleanup, the RNA polynucleotide may be quantified using the NanoDrop and analyzed by agarose gel electrophoresis to confirm the RNA polynucleotide is the proper size and that no degradation of the RNA has occurred.

Example 5: Enzymatic Capping

[0783] Capping of a RNA polynucleotide is performed as follows where the mixture includes: IVT RNA 60 .mu.g-180 .mu.g and dH.sub.20 up to 72 .mu.l. The mixture is incubated at 65.degree. C. for 5 minutes to denature RNA, and then is transferred immediately to ice.

[0784] The protocol then involves the mixing of 10.times. Capping Buffer (0.5 M Tris-HCl (pH 8.0), 60 mM KCl, 12.5 mM MgCl.sub.2) (10.0 .mu.l); 20 mM GTP (5.0 .mu.l); 20 mM S-Adenosyl Methionine (2.5 .mu.l); RNase Inhibitor (100 U); 2'-O-Methyltransferase (400U); Vaccinia capping enzyme (Guanylyl transferase) (40 U); dH.sub.20 (Up to 28 .mu.l); and incubation at 37.degree. C. for 30 minutes for 60 .mu.g RNA or up to 2 hours for 180 .mu.g of RNA.

[0785] The RNA polynucleotide may then be purified using Ambion's MEGACLEAR.TM. Kit (Austin, Tex.) following the manufacturer's instructions. Following the cleanup, the RNA may be quantified using the NANODROP.TM. (ThermoFisher, Waltham, Mass.) and analyzed by agarose gel electrophoresis to confirm the RNA polynucleotide is the proper size and that no degradation of the RNA has occurred. The RNA polynucleotide product may also be sequenced by running a reverse-transcription-PCR to generate the cDNA for sequencing.

Example 6: PolyA Tailing Reaction

[0786] Without a poly-T in the cDNA, a poly-A tailing reaction must be performed before cleaning the final product. This is done by mixing capped IVT RNA (100 .mu.l); RNase Inhibitor (20 U); 10.times. Tailing Buffer (0.5 M Tris-HCl (pH 8.0), 2.5 M NaCl, 100 mM MgCl.sub.2) (12.0 .mu.l); 20 mM ATP (6.0 .mu.l); Poly-A Polymerase (20 U); dH.sub.20 up to 123.5 .mu.l and incubation at 37.degree. C. for 30 min. If the poly-A tail is already in the transcript, then the tailing reaction may be skipped and proceed directly to cleanup with Ambion's MEGACLEAR.TM. kit (Austin, Tex.) (up to 500 .mu.g). Poly-A Polymerase may be a recombinant enzyme expressed in yeast.

[0787] It should be understood that the processivity or integrity of the polyA tailing reaction may not always result in an exact size polyA tail. Hence, polyA tails of approximately between 40-200 nucleotides, e.g., about 40, 50, 60, 70, 80, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 150-165, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164 or 165 are within the scope of the present disclosure.

Example 7. Natural 5' Caps and 5' Cap Analogues

[0788] 5'-capping of polynucleotides may be completed concomitantly during the in vitro-transcription reaction using the following chemical RNA cap analogs to generate the 5'-guanosine cap structure according to manufacturer protocols: 3'-O-Me-m7G(5')ppp(5') G [the ARCA cap]; G(5')ppp(5')A; G(5')ppp(5')G; m7G(5')ppp(5')A; m7G(5')ppp(5')G (New England BioLabs, Ipswich, Mass.). 5'-capping of modified RNA may be completed post-transcriptionally using a Vaccinia Virus Capping Enzyme to generate the "Cap 0" structure: m7G(5')ppp(5')G (New England BioLabs, Ipswich, Mass.). Cap 1 structure may be generated using both Vaccinia Virus Capping Enzyme and a 2'-O methyl-transferase to generate: m7G(5')ppp(5')G-2'-O-methyl. Cap 2 structure may be generated from the Cap 1 structure followed by the 2'-O-methylation of the 5'-antepenultimate nucleotide using a 2'-O methyl-transferase. Cap 3 structure may be generated from the Cap 2 structure followed by the 2'-O-methylation of the 5'-preantepenultimate nucleotide using a 2'-O methyl-transferase. Enzymes are preferably derived from a recombinant source.

[0789] When transfected into mammalian cells, the modified mRNAs have a stability of between 12-18 hours or more than 18 hours, e.g., 24, 36, 48, 60, 72 or greater than 72 hours.

Example 8: Capping Assays

Protein Expression Assay

[0790] Polynucleotides (e.g., mRNA) encoding a polypeptide, containing any of the caps taught herein, can be transfected into cells at equal concentrations. The amount of protein secreted into the culture medium can be assayed by ELISA at 6, 12, 24 and/or 36 hours post-transfection. Synthetic polynucleotides that secrete higher levels of protein into the medium correspond to a synthetic polynucleotide with a higher translationally-competent cap structure.

Purity Analysis Synthesis

[0791] RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be compared for purity using denaturing Agarose-Urea gel electrophoresis or HPLC analysis. RNA polynucleotides with a single, consolidated band by electrophoresis correspond to the higher purity product compared to polynucleotides with multiple bands or streaking bands. Chemically modified RNA polynucleotides with a single HPLC peak also correspond to a higher purity product. The capping reaction with a higher efficiency provides a more pure polynucleotide population.

Cytokine Analysis

[0792] RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be transfected into cells at multiple concentrations. The amount of pro-inflammatory cytokines, such as TNF-alpha and IFN-beta, secreted into the culture medium can be assayed by ELISA at 6, 12, 24 and/or 36 hours post-transfection. RNA polynucleotides resulting in the secretion of higher levels of pro-inflammatory cytokines into the medium correspond to a polynucleotides containing an immune-activating cap structure.

Capping Reaction Efficiency

[0793] RNA (e.g., mRNA) polynucleotides encoding a polypeptide, containing any of the caps taught herein can be analyzed for capping reaction efficiency by LC-MS after nuclease treatment. Nuclease treatment of capped polynucleotides yield a mixture of free nucleotides and the capped 5'-5-triphosphate cap structure detectable by LC-MS. The amount of capped product on the LC-MS spectra can be expressed as a percent of total polynucleotide from the reaction and correspond to capping reaction efficiency. The cap structure with a higher capping reaction efficiency has a higher amount of capped product by LC-MS.

Example 9: Agarose Gel Electrophoresis of Modified RNA or RT PCR Products

[0794] Individual RNA polynucleotides (200-400 ng in a 20 .mu.l volume) or reverse transcribed PCR products (200-400 ng) may be loaded into a well on a non-denaturing 1.2% Agarose E-Gel (Invitrogen, Carlsbad, Calif.) and run for 12-15 minutes, according to the manufacturer protocol.

Example 10: Nanodrop Modified RNA Quantification and UV Spectral Data

[0795] Chemically modified RNA polynucleotides in TE buffer (1 .mu.l) are used for Nanodrop UV absorbance readings to quantitate the yield of each polynucleotide from an chemical synthesis or in vitro transcription reaction.

Example 11: Formulation of Modified mRNA Using Lipidoids

[0796] RNA (e.g., mRNA) polynucleotides may be formulated for in vitro experiments by mixing the polynucleotides with the lipidoid at a set ratio prior to addition to cells. In vivo formulation may require the addition of extra ingredients to facilitate circulation throughout the body. To test the ability of these lipidoids to form particles suitable for in vivo work, a standard formulation process used for siRNA-lipidoid formulations may be used as a starting point. After formation of the particle, polynucleotide is added and allowed to integrate with the complex. The encapsulation efficiency is determined using a standard dye exclusion assays.

Example 12: Immunogenicity Study

[0797] The instant study is designed to test the immunogenicity in mice of candidate hMPV vaccines comprising a mRNA polynucleotide encoding Fusion (F) glycoprotein, major surface glycoprotein G, or a combination thereof, obtained from hMPV.

[0798] Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Candidate vaccines are chemically modified or unmodified. A total of four immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each immunization until weeks 33-51. Serum antibody titers against Fusion (F) glycoprotein or major surface glycoprotein (G) protein are determined by ELISA. Sera collected from each mouse during weeks 10-16 are pooled, and total IgG purified. Purified antibodies are used for immunoelectron microscopy, antibody-affinity testing, and in vitro protection assays.

Example 13: hMPV Rodent Challenge

[0799] The instant study is designed to test the efficacy in cotton rats of candidate hMPV vaccines against a lethal challenge using an hMPV vaccine comprising mRNA encoding Fusion (F) glycoprotein, major surface glycoprotein G, or a combination of both antigens obtained from hMPV. Cotton rats are challenged with a lethal dose of the hMPV.

[0800] Animals are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) at week 0 and week 3 with candidate hMPV vaccines with and without adjuvant. Candidate vaccines are chemically modified or unmodified. The animals are then challenged with a lethal dose of hMPV on week 7 via IV, IM or ID. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

[0801] In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %) or DLin-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

Example 14: Immunogenicity of hMPV mRNA Vaccine in BALB/c Mice

[0802] The instant study was designed to test the immunogenicity in BALB/c mice of hMPV vaccines comprising an mRNA polynucleotide encoding the hMPV Fusion (F) glycoprotein. The mRNA polynucleotide encodes the full-length fusion protein and comprises the wild-type nucleotide sequence obtained from the hMPV A2a strain. Mice were divided into 3 groups (n=8 for each group) and immunized intramuscularly (IM) with PBS, a 10 .mu.g dose of mRNA vaccines encoding hMPV fusion protein, or a 2 .mu.g dose of mRNA vaccines encoding hMPV fusion protein. A total of two immunizations were given at 3-week intervals (i.e., at weeks 0, and 3 weeks), and sera were collected after each immunization according to the schedule described in Table 1. Serum antibody titers against hMPV fusion glycoprotein were determined by ELISA and antibodies were detected in the sera collected on day 14 onward. Both vaccine doses tested induced comparable levels of immune response in mice (FIGS. 2A-2C).

[0803] Additionally, mice sera were used for IgG isotyping (FIGS. 3A-3C). Both hMPV fusion protein-specific IgG1 and IgG2a were detected in mice sera. hMPV fusion protein mRNA vaccine also induced Th1 and Th2 cytokine responses, with a Th1 bias.

[0804] Sera from mice immunized with either 10 .mu.g or 2 .mu.g doses of the hMPV fusion protein mRNA vaccine contain neutralizing antibodies. The ability of these antibodies to neutralize hMPV B2 strain was also tested. The antibody-containing sera successfully neutralized the hMPV B2 virus (FIG. 4).

Example 15: T-Cell Stimulation

[0805] The instant study was designed to test T-cell stimulation in the splenocytes of mice immunized with mRNA vaccines encoding hMPV fusion protein, as described herein. Immunization of BALB/c mice was performed as described in Example 14. The splenocytes for each group were pooled and split into two parts. One part of splenocytes from each group of mice was stimulated with hMPV-free media, Concanavalin A or a hMPV fusion protein peptide pool comprising 15-mers (15 amino acids long); while the other part of splenocytes from each group of mice was stimulated with hMPV-free media, Concanavalin A or inactivated hMPV virus. Secreted mouse cytokines were measured using the Meso Scale Discovery (MSD) assay.

[0806] Cytokines specific to Th1 or Th2 responses were measured. For Th1 response, IFN-.gamma., IL2 and IL12 were detected from splenocytes stimulated with the hMPV fusion protein peptide pool at a level comparable to that of Concanavalin A (FIGS. 5A-5C). For a Th2 response, the hMPV fusion protein peptide pool induced the secretion of detectable IL10, TNF-.alpha., IL4 and IL, but not IL5, while Concanavalin A stimulated the secretion of all the above-mentioned Th2 cytokines (FIGS. 6A-6E) at a much higher level.

[0807] In contrast, inactivated hMPV virus only induced the secretion of IL2 in the Th1 response comparable to that of Concanavalin A (FIGS. 7A-7C). For the Th2 response, the inactivated hMPV virus induced the secretion of detectable IL10, TNF-.alpha., IL4 and IL6, but not IL5, while Concanavalin A stimulated the secretion of all the above-mentioned Th2 cytokines (FIGS. 8A-8E) at a much higher level.

Example 16: hMPV Rodent Challenge in Cotton Rats Immunized with mRNA Vaccine Encoding hMPV Fusion Protein

[0808] The instant study was designed to test the efficacy in cotton rats of hMPV vaccines against a lethal challenge. mRNA vaccines encoding hMPV fusion protein were used. The mRNA polynucleotide encodes a full-length fusion protein and comprises the wild-type nucleotide sequence obtained from the hMPV A2a strain.

[0809] Cotton rats were immunized intramuscularly (IM) at week 0 and week 3 with the mRNA vaccines encoding hMPV fusion protein with either 2 .mu.g or 10 .mu.g doses for each immunization. The animals were then challenged with a lethal dose of hMPV in week 7 post initial immunization via IV, IM or ID. The endpoint was day 13 post infection, death or euthanasia. Viral titers in the noses and lungs of the cotton rats were measured. The results (FIGS. 9A and 9B) show that a 10 .mu.g dose of mRNA vaccine protected the cotton mice 100% in the lung and drastically reduced the viral titer in the nose after challenge (.about.2 log reduction). Moreover, a 2 .mu.g dose of mRNA vaccine showed a 1 log reduction in lung viral titer in the cotton mice challenged.

[0810] Further, the histopathology of the lungs of the cotton mice immunized and challenged showed no pathology associated with vaccine-enhanced disease (FIG. 10).

Example 17. Immunogenicity Study

[0811] The instant study is designed to test the immunogenicity in mice of candidate PIV3 vaccines comprising a mRNA polynucleotide encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3.

[0812] Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Candidate vaccines are chemically modified or unmodified. A total of four immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each immunization until weeks 33-51. Serum antibody titers against hemagglutinin-neuraminidase or fusion protein (F or F0) are determined by ELISA. Sera collected from each mouse during weeks 10-16 are, optionally, pooled, and total IgGs are purified. Purified antibodies are used for immunoelectron microscopy, antibody-affinity testing, and in vitro protection assays.

Example 18: PIV3 Rodent Challenge

[0813] The instant study is designed to test the efficacy in cotton rats of candidate PIV3 vaccines against a lethal challenge using a PIV3 vaccine comprising mRNA encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3. Cotton rats are challenged with a lethal dose of the PIV3.

[0814] Animals are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) at week 0 and week 3 with candidate PIV3 vaccines with and without adjuvant. Candidate vaccines are chemically modified or unmodified. The animals are then challenged with a lethal dose of PIV3 on week 7 via IV, IM or ID. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

[0815] In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %) or DLin-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

Example 19: hMPV/PIV Cotton Rat Challenge

[0816] The instant study was designed to test the efficacy in cotton rats of candidate hMPV mRNA vaccines, PIV3 mRNA vaccines, or hMPV/PIV combination mRNA vaccines against a lethal challenge using PIV3 strain or hMPV/A2 strain. The study design is shown in Table 9.

[0817] Cotton rats of 10-12 weeks old were divided into 12 groups (n=5), and each group was vaccinated with mRNA vaccines indicated in Table 9. The PIV3 vaccine comprises mRNA encoding hemagglutinin-neuraminidase or fusion protein (F or F0) obtained from PIV3. The hMPV mRNA vaccine encodes the full-length hMPV fusion protein. The hMPV/PIV combination mRNA vaccine is a mixture of the PIV3 vaccine and hMPV vaccine at a 1:1 ratio.

[0818] Cotton rats were immunized intramuscularly (IM) at week 0 and week 3 with candidate vaccines with the doses indicated in Table 9. Cotton rats immunized with hMPV mRNA vaccines or hMPV/PIV combination mRNA vaccines were challenged with a lethal dose of hMPV/A2 strain on week 7 via IM. Cotton rats immunized with PIV mRNA vaccines or hMPV/PIV combination mRNA vaccines were challenged with a lethal dose of PIV3 strain on week 7 via IM.

[0819] The endpoint was day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis were euthanized. Body temperature and weight were assessed and recorded daily.

[0820] Lung and nose hMPV/A2 (FIG. 12) or PIV3 (FIG. 13) viral titers were assessed. Lung histopathology of the immunized and challenged cotton rat immunized and challenged were assessed to determine pathology associated with vaccine enhance disease. Neutralization antibody titers in the serum of immunized cotton rats on day 0 and 42 post immunization were assessed (FIG. 11).

[0821] hMPV/A2 (FIG. 14) or PIV3 (FIG. 15) neutralizing antibody titers in the serum samples of the immunized cotton rat 42 days post immunization were measured. All mRNA vaccines tested induced strong neutralizing antibodies cotton rats. Lung histopathology of the immunized cotton rats were also evaluated (FIG. 16). Low occurrence of alevolitis and interstitial pneumonia was observed, indicating no antibody-dependent enhancement (ADE) of hMPV or PIV associated diseases.

Example 20: Betacoronavirus Immunogenicity Study

[0822] The instant study is designed to test the immunogenicity in rabbits of candidate Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1 or a combination thereof) vaccines comprising a mRNA polynucleotide encoding the spike (S) protein, the S1 subunit (S1) of the spike protein, or the S2 subunit (S2) of the spike protein obtained from a Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

[0823] Rabbits are vaccinated on week 0 and 3 via intravenous (IV), intramuscular (IM), or intradermal (ID) routes. One group remains unvaccinated and one is administered inactivated Betacoronavirus. Serum is collected from each rabbit on weeks 1, 3 (pre-dose) and 5. Individual bleeds are tested for anti-S, anti-S1 or anti-S2 activity via a virus neutralization assay from all three time points, and pooled samples from week 5 only are tested by Western blot using inactivated Betacoronavirus (e.g., inactivated MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

[0824] In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %) or DLin-MC3-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

Example 21: Betacoronavirus Challenge

[0825] The instant study is designed to test the efficacy in rabbits of candidate Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-HKU1 or a combination thereof) vaccines against a lethal challenge using a Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-HKU1 or a combination thereof) vaccine comprising mRNA encoding the spike (S) protein, the S1 subunit (S1) of the spike protein, or the S2 subunit (S2) of the spike protein obtained from Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1). Rabbits are challenged with a lethal dose (10.times.LD90; .about.100 plaque-forming units; PFU) of Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1).

[0826] The animals used are 6-8 week old female rabbits in groups of 10. Rabbits are vaccinated on weeks 0 and 3 via an IM, ID or IV route of administration. Candidate vaccines are chemically modified or unmodified. Rabbit serum is tested for microneutralization (see Example 14). Rabbits are then challenged with .about.1 LD90 of Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1) on week 7 via an IN, IM, ID or IV route of administration. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

Example 22: Microneutralization Assay

[0827] Nine serial 2-fold dilutions (1:50-1:12,800) of rabbit serum are made in 50 .mu.l virus growth medium (VGM) with trypsin in 96 well microtiter plates. Fifty microliters of virus containing .about.50 pfu of Betacoronavirus (e.g., MERS-CoV, ***SARS***-CoV, HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-NL, HCoV-NH or HCoV-HKU1) is added to the serum dilutions and allowed to incubate for 60 minutes at room temperature (RT). Positive control wells of virus without sera and negative control wells without virus or sera are included in triplicate on each plate. While the serum-virus mixtures incubate, a single cell suspension of Madin-Darby Canine-Kidney cells are prepared by trypsinizing (Gibco 0.5% bovine pancrease trypsin in EDTA) a confluent monolayer and suspended cells are transferred to a 50 ml centrifuge tube, topped with sterile PBS and gently mixed. The cells are then pelleted at 200 g for 5 minutes, supernatant aspirated and cells resuspended in PBS. This procedure is repeated once and the cells are resuspended at a concentration of 3.times.10.sup.5/ml in VGM with porcine trypsin. Then, 100 .mu.l of cells are added to the serum-virus mixtures and the plates incubated at 35.degree. C. in CO.sub.2 for 5 days. The plates are fixed with 80% acetone in phosphate buffered saline (PBS) for 15 minutes at RT, air dried and then blocked for 30 minutes containing PBS with 0.5% gelatin and 2% FCS. An antibody to the S proteins, 51 protein or S2 protein is diluted in PBS with 0.5% gelatin/2% FCS/0.5% Tween 20 and incubated at RT for 2 hours. Wells are washed and horseradish peroxidase-conjugated goat anti-mouse IgG added, followed by another 2 hour incubation. After washing, 0-phenylenediamine dihydrochloride is added and the neutralization titer is defined as the titer of serum that reduced color development by 50% compared to the positive control wells.

Example 23: MERS CoV Vaccine Immunogenicity Study in Mice

[0828] The instant study was designed to test the immunogenicity in mice of candidate MERS-CoV vaccines comprising a mRNA polynucleotide encoding the full-length Spike (S) protein, or the S2 subunit (S2) of the Spike protein obtained from MERS-CoV.

[0829] Mice were vaccinated with a 10 .mu.g dose of MERS-CoV mRNA vaccine encoding either the full-length MERS-CoV Spike (S) protein, or the S2 subunit (S2) of the Spike protein on days 0 and 21. Sera were collected from each mice on days 0, 21, 42, and 56. Individual bleeds were tested for anti-S, anti-S2 activity via a virus neutralization assay from all four time points.

[0830] As shown in FIG. 17, the MERS-CoV vaccine encoding the full-length S protein induced strong immune response after the boost dose on day 21. Further, full-length S protein vaccine generated much higher neutralizing antibody titers as compared to S2 alone (FIG. 18).

Example 24: MERS CoV Vaccine Immunogenicity Study in New Zealand White Rabbits

[0831] The instant study was designed to test the immunogenicity of candidate MERS-CoV mRNA vaccines encoding the full-length Spike (S) protein. The New Zealand white rabbits used in this study weighed about 4-5 kg. The rabbits were divided into three groups (Group 1a, Group 1b, and Group 2, n=8). Rabbits in Group 1a were immunized intramuscularly (IM) with one 20 .mu.g dose of the MERS-CoV mRNA vaccine encoding the full-length Spike protein on day 0. Rabbits in Group 1b were immunized intramuscularly (IM) with one 20 .mu.g dose of the MERS-CoV mRNA vaccine encoding the full-length Spike protein on day 0, and again on day 21 (booster dose). Group 2 received placebo (PBS). The immunized rabbits were then challenged and samples were collected 4 days after challenge. The viral loads in the lungs, bronchoalveolar lavage (Bal), nose, and throat of the rabbits were determined, e.g., via quantitative PCR. Replicating virus in the lung tissues of the rabbits were also detected. Lung histopathology were evaluated and the neutralizing antibody titers in serum samples of the rabbits were determined.

[0832] Two 20 .mu.g doses of MERS-CoV mRNA vaccine resulted in a 3 log reduction of viral load in the nose and led to complete protection in the throat of the New Zealand white rabbits (FIG. 19A). Two 20 .mu.g doses of MERS-CoV mRNA vaccine also resulted in a 4 log reduction of viral load in the BAL of the New Zealand white rabbits (FIG. 19B). One 20 .mu.g dose of MERS-CoV mRNA vaccine resulted in a 2 log reduction of viral load, while two 20 .mu.g doses of MERS-CoV mRNA vaccine resulted in an over 4 log reduction of viral load in the lungs of the New Zealand white rabbits (FIG. 19C).

[0833] Quantitative PCR results show that two 20 .mu.g doses of MERS-CoV mRNA vaccine reduced over 99% (2 log) of viruses in the lungs of New Zealand white rabbits (FIG. 20A). No replicating virus were detected in the lungs (FIG. 20B).

[0834] Further, as shown in FIG. 21, two 20 .mu.g doses of MERS-CoV mRNA vaccine induced significant amount of neutralizing antibodies against MERS-CoV (EC.sub.50 between 500-1000). The MERS-CoV mRNA vaccine induced antibody titer is 3-5 fold better than any other vaccines tested in the same model.

Example 25: Immunogenicity Study

[0835] The instant study is designed to test the immunogenicity in mice of candidate MeV vaccines comprising a mRNA polynucleotide encoding MeV hemagglutinin (HA) protein, MeV Fusion (F) protein or a combination of both.

[0836] Mice are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) with candidate vaccines. Up to three immunizations are given at 3-week intervals (i.e., at weeks 0, 3, 6, and 9), and sera are collected after each immunization until weeks 33-51. Serum antibody titers against MeV HA protein or MeV F protein are determined by ELISA.

Example 26: MeV Rodent Challenge

[0837] The instant study is designed to test the efficacy in transgenic mice of candidate MeV vaccines against a lethal challenge using a MeV vaccine comprising mRNA encoding MeV HA protein or MeV F protein. The transgenic mice express human receptor CD46 or signaling lymphocyte activation molecule (SLAM) (also referred to as CD150). Humans are the only natural host for MeV infection, thus transgenic lines are required for this study. CD46 is a complement regulatory protein that protects host tissue from complement deposition by binding to complement components C3b and C4b. Its expression on murine fibroblast and lymphoid cell lines renders these otherwise refractory cells permissive for MeV infection, and the expression of CD46 on primate cells parallels the clinical tropism of MeV infection in humans and nonhuman primates (Rall G F et al. PNAS USA 1997; 94(9):4659-63). SLAM is a type 1 membrane glycoprotein belonging to the immunoglobulin superfamily. It is expressed on the surface of activated lymphocytes, macrophages, and dendritic cells and is thought to play an important role in lymphocyte signaling. SLAM is a receptor for both wild-type and vaccine MeV strains (Sellin C I et al. J Virol. 2006; 80(13):6420-29).

[0838] CD46 or SLAM/CD150 transgenic mice are challenged with a lethal dose of the MeV. Animals are immunized intravenously (IV), intramuscularly (IM), or intradermally (ID) at week 0 and week 3 with candidate MeV vaccines with and without adjuvant. The animals are then challenged with a lethal dose of MeV on week 7 via IV, IM or ID. Endpoint is day 13 post infection, death or euthanasia. Animals displaying severe illness as determined by >30% weight loss, extreme lethargy or paralysis are euthanized. Body temperature and weight are assessed and recorded daily.

[0839] In experiments where a lipid nanoparticle (LNP) formulation is used, the formulation may include a cationic lipid, non-cationic lipid, PEG lipid and structural lipid in the ratios 50:10:1.5:38.5. The cationic lipid is DLin-KC2-DMA (50 mol %), the non-cationic lipid is DSPC (10 mol %), the PEG lipid is PEG-DOMG (1.5 mol %) and the structural lipid is cholesterol (38.5 mol %), for example.

TABLE-US-00002 TABLE 1 hMPV Immunogenicity studies bleeding schedule Animal groups Day (n = 8) vaccine -2 0 7 14 21 28 35 56 Placebo Group 1 PBS Pre- Prime Bleeds Bleeds Bleeds/ Bleeds Bleeds Harvest Spleens/ (n = 8) (IM) Bleed Boost Terminal Bleeds 10 .mu.g Group 2 10 .mu.g Dose (n = 8) (IM) 2 .mu.g Group 3 2 .mu.g Dose (n = 8) (IM) Total n = 24

[0840] Each of the sequences described herein encompasses a chemically modified sequence or an unmodified sequence which includes no nucleotide modifications.

TABLE-US-00003 TABLE 2 SEQ ID Description Sequence NO: hMPV Nucleic Acid Sequences gi|122891979|gb| ATGAGCTGGAAGGTGGTGATTATCTTCAGCCTGCTGATTA 1 EF051124.1| Human CACCTCAACACGGCCTGAAGGAGAGCTACCTGGAAGAGA metapneumo virus GCTGCTCCACCATCACCGAGGGCTACCTGAGCGTGCTGC isolate TN/92-4 GGACCGGCTGGTACACCAACGTGTTCACCCTGGAGGTGG fusion protein gene, GCGACGTGGAGAACCTGACCTGCAGCGACGGCCCTAGCC complete genome

TGATCAAGACCGAGCTGGACCTGACCAAGAGCGCTCTGA
GAGAGCTGAAGACCGTGTCCGCCGACCAGCTGGCCAGAG
AGGAACAGATCGAGAACCCTCGGCAGAGCAGATTCGTGC
TGGGCGCCATCGCTCTGGGAGTCGCCGCTGCCGCTGCAG
TGACAGCTGGAGTGGCCATTGCTAAGACCATCAGACTGG
AAAGCGAGGTGACAGCCATCAACAATGCCCTGAAGAAG
ACCAACGAGGCCGTGAGCACCCTGGGCAATGGAGTGAGA
GTGCTGGCCACAGCCGTGCGGGAGCTGAAGGACTTCGTG
AGCAAGAACCTGACCAGAGCCATCAACAAGAACAAGTG
CGACATCGATGACCTGAAGATGGCCGTGAGCTTCTCCCA
GTTCAACAGACGGTTCCTGAACGTGGTGAGACAGTTCTC
CGACAACGCTGGAATCACACCTGCCATTAGCCTGGACCT
GATGACCGACGCCGAGCTGGCTAGAGCCGTGCCCAACAT
GCCCACCAGCGCTGGCCAGATCAAGCTGATGCTGGAGAA
CAGAGCCATGGTGCGGAGAAAGGGCTTCGGCATCCTGAT
TGGGGTGTATGGAAGCTCCGTGATCTACATGGTGCAGCT
GCCCATCTTCGGCGTGATCGACACACCCTGCTGGATCGTG
AAGGCCGCTCCTAGCTGCTCCGAGAAGAAAGGAAACTAT
GCCTGTCTGCTGAGAGAGGACCAGGGCTGGTACTGCCAG
AACGCCGGAAGCACAGTGTACTATCCCAACGAGAAGGAC
TGCGAGACCAGAGGCGACCACGTGTTCTGCGACACCGCT
GCCGGAATCAACGTGGCCGAGCAGAGCAAGGAGTGCAA
CATCAACATCAGCACAACCAACTACCCCTGCAAGGTGAG
CACCGGACGGCACCCCATCAGCATGGTGGCTCTGAGCCC
TCTGGGCGCTCTGGTGGCCTGCTATAAGGGCGTGTCCTGT
AGCATCGGCAGCAATCGGGTGGGCATCATCAAGCAGCTG
AACAAGGGATGCTCCTACATCACCAACCAGGACGCCGAC
ACCGTGACCATCGACAACACCGTGTACCAGCTGAGCAAG
GTGGAGGGCGAGCAGCACGTGATCAAGGGCAGACCCGT
GAGCTCCAGCTTCGACCCCATCAAGTTCCCTGAGGACCA
GTTCAACGTGGCCCTGGACCAGGTGTTTGAGAACATCGA
GAACAGCCAGGCCCTGGTGGACCAGAGCAACAGAATCCT
GTCCAGCGCTGAGAAGGGCAACACCGGCTTCATCATTGT
GATCATTCTGATCGCCGTGCTGGGCAGCTCCATGATCCTG
GTGAGCATCTTCATCATTATCAAGAAGACCAAGAAACCC
ACCGGAGCCCCTCCTGAGCTGAGCGGCGTGACCAACAAT GGCTTCATTCCCCACAACTGA
gb|AY525843.1|: ATGTCTTGGAAAGTGATGATCATCATTTCGTTACTCATAA 2 3065-4684 Human
CACCCCAGCACGGGCTAAAGGAGAGTTATTTGGAAGAAT metapneumo virus
CATGTAGTACTATAACTGAGGGATACCTCAGTGTTTTAAG isolate NL/1/99,
AACAGGCTGGTACACTAATGTCTTCACATTAGAAGTTGGT complete genome
GATGTTGAAAATCTTACATGTACTGATGGACCTAGCTTAA
TCAAAACAGAACTTGATCTAACAAAAAGTGCTTTAAGGG
AACTCAAAACAGTCTCTGCTGATCAGTTGGCGAGAGAGG
AGCAAATTGAAAATCCCAGACAATCAAGATTTGTCTTAG
GTGCGATAGCTCTCGGAGTTGCTACAGCAGCAGCAGTCA
CAGCAGGCATTGCAATAGCCAAAACCATAAGGCTTGAGA
GTGAGGTGAATGCAATTAAAGGTGCTCTCAAACAAACTA
ATGAAGCAGTATCCACATTAGGGAATGGTGTGCGGGTCC
TAGCCACTGCAGTGAGAGAGCTAAAAGAATTTGTGAGCA
AAAACCTGACTAGTGCAATCAACAGGAACAAATGTGACA
TTGCTGATCTGAAGATGGCTGTCAGCTTCAGTCAATTCAA
CAGAAGATTTCTAAATGTTGTGCGGCAGTTTTCAGACAAT
GCAGGGATAACACCAGCAATATCATTGGACCTGATGACT
GATGCTGAGTTGGCCAGAGCTGTATCATACATGCCAACA

TCTGCAGGGCAGATAAAACTGATGTTGGAGAACCGCGCA
ATGGTAAGGAGAAAAGGATTTGGAATCCTGATAGGGGTC
TACGGAAGCTCTGTGATTTACATGGTTCAATTGCCGATCT
TTGGTGTCATAGATACACCTTGTTGGATCATCAAGGCAGC
TCCCTCTTGCTCAGAAAAAAACGGGAATTATGCTTGCCTC
CTAAGAGAGGATCAAGGGTGGTATTGTAAAAATGCAGGA
TCTACTGTTTACTACCCAAATGAAAAAGACTGCGAAACA
AGAGGTGATCATGTTTTTTGTGACACAGCAGCAGGGATC
AATGTTGCTGAGCAATCAAGAGAATGCAACATCAACATA
TCTACTACCAACTACCCATGCAAAGTCAGCACAGGAAGA
CACCCTATAAGCATGGTTGCACTATCACCTCTCGGTGCTT
TGGTGGCTTGCTATAAAGGGGTAAGCTGCTCGATTGGCA GCAATTGGGT
TGGAATCATCAAACAATTACCCAAAGGCTGCTCATACAT
AACCAACCAGGATGCAGACACTGTAACAATTGACAATAC
CGTGTATCAACTAAGCAAAGTTGAAGGTGAACAGCATGT
AATAAAAGGGAGACCAGTTTCAAGCAGTTTTGATCCAAT
CAAGTTTCCTGAGGATCAGTTCAATGTTGCGCTTGATCAA
GTCTTCGAAAGCATTGAGAACAGTCAGGCACTAGTGGAC
CAGTCAAACAAAATTCTAAACAGTGCAGAAAAAGGAAA
CACTGGTTTCATTATCGTAGTAATTTTGGTTGCTGTTCTTG
GTCTAACCATGATTTCAGTGAGCATCATCATCATAATCAA
GAAAACAAGGAAGCCCACAGGAGCACCTCCAGAGCTGA
ATGGTGTCACCAACGGCGGTTTCATACCACATAGTTA gb|KJ627414.1|:
ATGTCTTGGAAAGTGATGATTATCATTTCGTTACTCATAA 3 3015-4634 Human
CACCTCAGCATGGACTAAAAGAAAGTTATTTAGAAGAAT metapneumo virus
CATGTAGTACTATAACTGAAGGATATCTCAGTGTTTTAAG strain hMPV/Homo
AACAGGTTGGTACACCAATGTCTTTACATTAGAAGTTGGT sapiens/PER/
GATGTTGAAAATCTTACATGTACTGATGGACCTAGCTTAA CFI0497/2010/B,
TCAAAACAGAACTTGACCTAACCAAAAGTGCTTTAAGAG complete genome
AACTCAAAACAGTTTCTGCTGATCAGTTAGCGAGAGAAG
AACAAATTGAAAATCCCAGACAATCAAGGTTTGTCCTAG
GTGCAATAGCTCTTGGAGTTGCCACAGCAGCAGCAGTCA
CAGCAGGCATTGCAATAGCCAAAACTATAAGGCTTGAGA
GTGAAGTGAATGCAATCAAAGGTGCTCTCAAAACAACCA
ATGAGGCAGTATCAACACTAGGAAATGGAGTGCGGGTCC
TAGCCACTGCAGTAAGAGAGCTGAAAGAATTTGTGAGCA
AAAACCTGACTAGTGCGATCAACAAGAACAAGTGTGACA
TTGCTGATTTGAAGATGGCTGTCAGCTTCAGTCAGTTCAA
CAGAAGATTCCTAAATGTTGTGCGGCAGTTTTCAGACAAT
GCAGGGATAACACCAGCAATATCATTGGACCTGATGAAT
GATGCTGAGCTGGCCAGAGCTGTATCATACATGCCAACA
TCTGCAGGACAGATAAAACTAATGTTAGAGAACCGTGCA
ATGGTGAGGAGAAAAGGATTTGGAATCTTGATAGGGGTC
TACGGAAGCTCTGTGATTTACATGGTCCAGCTGCCGATCT
TTGGTGTCATAAATACACCTTGTTGGATAATCAAGGCAGC
TCCCTCTTGTTCAGAAAAAGATGGAAATTATGCTTGCCTC
CTAAGAGAGGATCAAGGGTGGTATTGTAAAAATGCAGGA
TCCACTGTTTACTACCCAAATGAAAAAGACTGCGAAACA
AGAGGTGATCATGTTTTTTGTGACACAGCAGCAGGGATC
AATGTTGCTGAGCAATCAAGAGAATGCAACATCAACATA
TCTACCACCAACTACCCATGCAAAGTCAGCACAGGAAGA
CACCCTATCAGCATGGTTGCACTATCACCTCTCGGTGCTT
TGGTAGCTTGCTACAAAGGGGTTAGCTGCTCGACTGGCA
GTAATCAGGTTGGAATAATCAAACAACTACCTAAAGGCT

GCTCATACATAACTAACCAGGACGCAGACACTGTAACAA
TTGACAACACTGTGTATCAACTAAGCAAAGTTGAGGGTG
AACAGCATGTAATAAAAGGGAGACCAGTTTCAAGCAGTT
TTGATCCAATCAGGTTTCCTGAGGATCAGTTCAATGTTGC
GCTTGATCAAGTCTTTGAAAGCATTGAAAACAGTCAAGC
ACTAGTGGACCAGTCAAACAAAATTCTGAACAGTGCAGA AAAAGGAAACACTGGT
TTCATTATTGTAATAATTTTGATTGCTGTTCTTGGGTTAAC
CATGATTTCAGTGAGCATCATCATCATAATCAAAAAAAC
AAGGAAGCCCACAGGGGCACCTCCGGAGCTGAATGGTGT
TACCAACGGCGGTTTCATACCGCATAGTTAG gb|KJ723483.1|:
ATGGAGTTGCCAATCCTCAAAACAAATGCAATTACCACA 4 5586-7310 Human
ATCCTTGCTGCAGTCACACTCTGTTTCGCTTCCAGTCAAA respiratory
ACATCACTGAAGAATTTTATCAATCAACATGCAGTGCAG syncytial virus
TTAGCAAAGGCTATCTTAGTGCTCTAAGAACTGGTTGGTA strain RSV A/Homo
TACTAGTGTTATAACTATAGAATTAAGTAATATCAAGGA sapiens/USA/84I-
AAATAAGTGTAATGGAACAGATGCTAAGGTAAAATTGAT 215A-01/1984,
AAAACAAGAATTAGATAAATATAAAAATGCTGTAACAGA complete genome
ATTGCAGTTGCTCATGCAAAGCACACCAGCAGCCAACAA
TCGAGCCAGAAGAGAACTACCAAGGTTTATGAATTATAC
ACTCAATAATACCAAAAATACCAATGTAACATTAAGCAA
GAAAAGGAAAAGAAGATTTCTTGGCTTTTTGTTAGGTGTT
GGATCTGCAATCGCCAGTGGCATTGCTGTATCTAAGGTCC
TGCACCTAGAAGGGGAAGTGAACAAAATCAAAAGTGCTC
TACTATCCACAAACAAGGCTGTAGTCAGCTTATCAAATG
GAGTTAGTGTCTTAACCAGCAAAGTGTTAGACCTCAAAA
ACTATATAGATAAACAGTTGTTACCTATTGTGAACAAGC
AAAGCTGCAGCATATCAAACATTGAAACTGTGATAGAGT
TCCAACAAAAGAACAACAGACTACTAGAGATTACCAGGG
AATTTAGTGTTAATGCAGGTGTAACTACACCTGTAAGCAC
TTATATGTTAACTAATAGTGAATTATTATCATTAATCAAT
GATATGCCTATAACAAATGATCAGAAAAAGTTAATGTCC
AACAATGTTCAAATAGTTAGACAGCAAAGTTACTCTATC
ATGTCCATAATAAAGGAGGAAGTCTTAGCATATGTAGTA
CAATTACCACTATATGGTGTAATAGATACACCCTGTTGGA
AACTGCACACATCCCCTCTATGTACAACCAACACAAAGG
AAGGGTCCAACATCTGCTTAACAAGAACCGACAGAGGAT
GGTATTGTGACAATGCAGGATCAGTATCTTTCTTCCCACA
AGCTGAAACATGTAAAGTTCAATCGAATCGGGTATTTTGT
GACACAATGAACAGTTTAACATTACCAAGTGAAGTAAAT
CTCTGCAACATTGACATATTCAACCCCAAATATGATTGCA
AAATTATGACTTCAAAAACAGATGTAAGCAGCTCCGTTA
TCACATCTCTAGGAGCCATTGTGTCATGCTATGGCAAAAC
TAAATGTACAGCATCCAATAAAAATCGTGGGATCATAAA
GACATTTTCTAACGGGTGTGATTATGTATCAAATAAGGG
GGTGGATACTGTGTCTGTAGGTAATACATTATATTATGTA
AATAAGCAAGAAGGCAAAAGTCTCTATGTAAAAGGTGAA
CCAATAATAAATTTCTATGACCCATTAGTGTTCCCCTCTG
ATGAATTTGATGCATCAATATCTCAAGTCAATGAGAAGA
TTAACCAGAGCCTAGCATTTATTCGTAAATCCGATGAATT
ATTACATAATGTAAATGCTGGTAAATCCACCACAAATAT
CATGATAACTACTATAATTATAGTGATTATAGTAATATTG
TTATCATTAATTGCAGTTGGACTGCTCCTATACTGCAAGG
CCAGAAGCACACCAGTCACACTAAGTAAGGATCAACTGA
GTGGTATAAATAATATTGCATTTAGTAACTGA hMPV mRNA Sequences gi|122891979|gb|

AUGAGCUGGAAGGUGGUGAUUAUCUUCAGCCUGCUGAU 57 EF051124.11 Human
UACACCUCAACACGGCCUGAAGGAGAGCUACCUGGAAG metapneumo virus
AGAGCUGCUCCACCAUCACCGAGGGCUACCUGAGCGUG isolate TN/92-4
CUGCGGACCGGCUGGUACACCAACGUGUUCACCCUGGA fusion protein gene,
GGUGGGCGACGUGGAGAACCUGACCUGCAGCGACGGCC complete genome
CUAGCCUGAUCAAGACCGAGCUGGACCUGACCAAGAGC
GCUCUGAGAGAGCUGAAGACCGUGUCCGCCGACCAGCU
GGCCAGAGAGGAACAGAUCGAGAACCCUCGGCAGAGCA
GAUUCGUGCUGGGCGCCAUCGCUCUGGGAGUCGCCGCU
GCCGCUGCAGUGACAGCUGGAGUGGCCAUUGCUAAGAC
CAUCAGACUGGAAAGCGAGGUGACAGCCAUCAACAAUG
CCCUGAAGAAGACCAACGAGGCCGUGAGCACCCUGGGC
AAUGGAGUGAGAGUGCUGGCCACAGCCGUGCGGGAGCU
GAAGGACUUCGUGAGCAAGAACCUGACCAGAGCCAUCA
ACAAGAACAAGUGCGACAUCGAUGACCUGAAGAUGGCC
GUGAGCUUCUCCCAGUUCAACAGACGGUUCCUGAACGU
GGUGAGACAGUUCUCCGACAACGCUGGAAUCACACCUG
CCAUUAGCCUGGACCUGAUGACCGACGCCGAGCUGGCU
AGAGCCGUGCCCAACAUGCCCACCAGCGCUGGCCAGAU
CAAGCUGAUGCUGGAGAACAGAGCCAUGGUGCGGAGAA
AGGGCUUCGGCAUCCUGAUUGGGGUGUAUGGAAGCUCC
GUGAUCUACAUGGUGCAGCUGCCCAUCUUCGGCGUGAU
CGACACACCCUGCUGGAUCGUGAAGGCCGCUCCUAGCU
GCUCCGAGAAGAAAGGAAACUAUGCCUGUCUGCUGAGA
GAGGACCAGGGCUGGUACUGCCAGAACGCCGGAAGCAC
AGUGUACUAUCCCAACGAGAAGGACUGCGAGACCAGAG
GCGACCACGUGUUCUGCGACACCGCUGCCGGAAUCAAC
GUGGCCGAGCAGAGCAAGGAGUGCAACAUCAACAUCAG
CACAACCAACUACCCCUGCAAGGUGAGCACCGGACGGC
ACCCCAUCAGCAUGGUGGCUCUGAGCCCUCUGGGCGCU
CUGGUGGCCUGCUAUAAGGGCGUGUCCUGUAGCAUCGG
CAGCAAUCGGGUGGGCAUCAUCAAGCAGCUGAACAAGG
GAUGCUCCUACAUCACCAACCAGGACGCCGACACCGUG
ACCAUCGACAACACCGUGUACCAGCUGAGCAAGGUGGA
GGGCGAGCAGCACGUGAUCAAGGGCAGACCCGUGAGCU
CCAGCUUCGACCCCAUCAAGUUCCCUGAGGACCAGUUC
AACGUGGCCCUGGACCAGGUGUUUGAGAACAUCGAGAA
CAGCCAGGCCCUGGUGGACCAGAGCAACAGAAUCCUGU
CCAGCGCUGAGAAGGGCAACACCGGCUUCAUCAUUGUG
AUCAUUCUGAUCGCCGUGCUGGGCAGCUCCAUGAUCCU
GGUGAGCAUCUUCAUCAUUAUCAAGAAGACCAAGAAAC
CCACCGGAGCCCCUCCUGAGCUGAGCGGCGUGACCAAC AAUGGCUUCAUUCCCCACAACUGA
gb|AY525843.1|: AUGUCUUGGAAAGUGAUGAUCAUCAUUUCGUUACUCAU 58 3065-4684 Human
AACACCCCAGCACGGGCUAAAGGAGAGUUAUUUGGAAG metapneumo virus
AAUCAUGUAGUACUAUAACUGAGGGAUACCUCAGUGUU isolate NL/1/99,
UUAAGAACAGGCUGGUACACUAAUGUCUUCACAUUAGA complete genome
AGUUGGUGAUGUUGAAAAUCUUACAUGUACUGAUGGA
CCUAGCUUAAUCAAAACAGAACUUGAUCUAACAAAAAG
UGCUUUAAGGGAACUCAAAACAGUCUCUGCUGAUCAGU
UGGCGAGAGAGGAGCAAAUUGAAAAUCCCAGACAAUCA
AGAUUUGUCUUAGGUGCGAUAGCUCUCGGAGUUGCUAC
AGCAGCAGCAGUCACAGCAGGCAUUGCAAUAGCCAAAA
CCAUAAGGCUUGAGAGUGAGGUGAAUGCAAUUAAAGG
UGCUCUCAAACAAACUAAUGAAGCAGUAUCCACAUUAG

GGAAUGGUGUGCGGGUCCUAGCCACUGCAGUGAGAGAG
CUAAAAGAAUUUGUGAGCAAAAACCUGACUAGUGCAAU
CAACAGGAACAAAUGUGACAUUGCUGAUCUGAAGAUGG
CUGUCAGCUUCAGUCAAUUCAACAGAAGAUUUCUAAAU
GUUGUGCGGCAGUUUUCAGACAAUGCAGGGAUAACACC
AGCAAUAUCAUUGGACCUGAUGACUGAUGCUGAGUUGG
CCAGAGCUGUAUCAUACAUGCCAACAUCUGCAGGGCAG
AUAAAACUGAUGUUGGAGAACCGCGCAAUGGUAAGGAG
AAAAGGAUUUGGAAUCCUGAUAGGGGUCUACGGAAGCU
CUGUGAUUUACAUGGUUCAAUUGCCGAUCUUUGGUGUC
AUAGAUACACCUUGUUGGAUCAUCAAGGCAGCUCCCUC

UUGCUCAGAAAAAAACGGGAAUUAUGCUUGCCUCCUAA
GAGAGGAUCAAGGGUGGUAUUGUAAAAAUGCAGGAUC
UACUGUUUACUACCCAAAUGAAAAAGACUGCGAAACAA
GAGGUGAUCAUGUUUUUUGUGACACAGCAGCAGGGAUC
AAUGUUGCUGAGCAAUCAAGAGAAUGCAACAUCAACAU
AUCUACUACCAACUACCCAUGCAAAGUCAGCACAGGAA
GACACCCUAUAAGCAUGGUUGCACUAUCACCUCUCGGU
GCUUUGGUGGCUUGCUAUAAAGGGGUAAGCUGCUCGAU UGGCAGCAAUUGGGU
UGGAAUCAUCAAACAAUUACCCAAAGGCUGCUCAUACA
UAACCAACCAGGAUGCAGACACUGUAACAAUUGACAAU
ACCGUGUAUCAACUAAGCAAAGUUGAAGGUGAACAGCA
UGUAAUAAAAGGGAGACCAGUUUCAAGCAGUUUUGAUC
CAAUCAAGUUUCCUGAGGAUCAGUUCAAUGUUGCGCUU
GAUCAAGUCUUCGAAAGCAUUGAGAACAGUCAGGCACU
AGUGGACCAGUCAAACAAAAUUCUAAACAGUGCAGAAA
AAGGAAACACUGGUUUCAUUAUCGUAGUAAUUUUGGU
UGCUGUUCUUGGUCUAACCAUGAUUUCAGUGAGCAUCA
UCAUCAUAAUCAAGAAAACAAGGAAGCCCACAGGAGCA
CCUCCAGAGCUGAAUGGUGUCACCAACGGCGGUUUCAU ACCACAUAGUUAG gb|KJ627414.1|:
AUGUCUUGGAAAGUGAUGAUUAUCAUUUCGUUACUCAU 59 3015-4634 Human
AACACCUCAGCAUGGACUAAAAGAAAGUUAUUUAGAAG metapneumo virus
AAUCAUGUAGUACUAUAACUGAAGGAUAUCUCAGUGUU strain hMPV/Homo
UUAAGAACAGGUUGGUACACCAAUGUCUUUACAUUAGA sapiens/PER/
AGUUGGUGAUGUUGAAAAUCUUACAUGUACUGAUGGA CFI0497/2010/B,
CCUAGCUUAAUCAAAACAGAACUUGACCUAACCAAAAG complete genome
UGCUUUAAGAGAACUCAAAACAGUUUCUGCUGAUCAGU
UAGCGAGAGAAGAACAAAUUGAAAAUCCCAGACAAUCA
AGGUUUGUCCUAGGUGCAAUAGCUCUUGGAGUUGCCAC
AGCAGCAGCAGUCACAGCAGGCAUUGCAAUAGCCAAAA
CUAUAAGGCUUGAGAGUGAAGUGAAUGCAAUCAAAGG
UGCUCUCAAAACAACCAAUGAGGCAGUAUCAACACUAG
GAAAUGGAGUGCGGGUCCUAGCCACUGCAGUAAGAGAG
CUGAAAGAAUUUGUGAGCAAAAACCUGACUAGUGCGAU
CAACAAGAACAAGUGUGACAUUGCUGAUUUGAAGAUGG
CUGUCAGCUUCAGUCAGUUCAACAGAAGAUUCCUAAAU
GUUGUGCGGCAGUUUUCAGACAAUGCAGGGAUAACACC
AGCAAUAUCAUUGGACCUGAUGAAUGAUGCUGAGCUGG
CCAGAGCUGUAUCAUACAUGCCAACAUCUGCAGGACAG
AUAAAACUAAUGUUAGAGAACCGUGCAAUGGUGAGGA
GAAAAGGAUUUGGAAUCUUGAUAGGGGUCUACGGAAG
CUCUGUGAUUUACAUGGUCCAGCUGCCGAUCUUUGGUG
UCAUAAAUACACCUUGUUGGAUAAUCAAGGCAGCUCCC

UCUUGUUCAGAAAAAGAUGGAAAUUAUGCUUGCCUCCU
AAGAGAGGAUCAAGGGUGGUAUUGUAAAAAUGCAGGA
UCCACUGUUUACUACCCAAAUGAAAAAGACUGCGAAAC
AAGAGGUGAUCAUGUUUUUUGUGACACAGCAGCAGGGA
UCAAUGUUGCUGAGCAAUCAAGAGAAUGCAACAUCAAC
AUAUCUACCACCAACUACCCAUGCAAAGUCAGCACAGG
AAGACACCCUAUCAGCAUGGUUGCACUAUCACCUCUCG
GUGCUUUGGUAGCUUGCUACAAAGGGGUUAGCUGCUCG
ACUGGCAGUAAUCAGGUUGGAAUAAUCAAACAACUACC
UAAAGGCUGCUCAUACAUAACUAACCAGGACGCAGACA
CUGUAACAAUUGACAACACUGUGUAUCAACUAAGCAAA
GUUGAGGGUGAACAGCAUGUAAUAAAAGGGAGACCAG
UUUCAAGCAGUUUUGAUCCAAUCAGGUUUCCUGAGGAU
CAGUUCAAUGUUGCGCUUGAUCAAGUCUUUGAAAGCAU
UGAAAACAGUCAAGCACUAGUGGACCAGUCAAACAAAA
UUCUGAACAGUGCAGAAAAAGGAAACACUGGU
UUCAUUAUUGUAAUAAUUUUGAUUGCUGUUCUUGGGU
UAACCAUGAUUUCAGUGAGCAUCAUCAUCAUAAUCAAA
AAAACAAGGAAGCCCACAGGGGCACCUCCGGAGCUGAA
UGGUGUUACCAACGGCGGUUUCAUACCGCAUAGUUAG gb|KJ723483.1|:
AUGGAGUUGCCAAUCCUCAAAACAAAUGCAAUUACCAC 60 5586-7310 Human
AAUCCUUGCUGCAGUCACACUCUGUUUCGCUUCCAGUC respiratory
AAAACAUCACUGAAGAAUUUUAUCAAUCAACAUGCAGU syncytial virus
GCAGUUAGCAAAGGCUAUCUUAGUGCUCUAAGAACUGG strain RSVA/Homo
UUGGUAUACUAGUGUUAUAACUAUAGAAUUAAGUAAU sapiens/USA/84I-
AUCAAGGAAAAUAAGUGUAAUGGAACAGAUGCUAAGG 215A-01/1984,
UAAAAUUGAUAAAACAAGAAUUAGAUAAAUAUAAAAA complete genome
UGCUGUAACAGAAUUGCAGUUGCUCAUGCAAAGCACAC
CAGCAGCCAACAAUCGAGCCAGAAGAGAACUACCAAGG
UUUAUGAAUUAUACACUCAAUAAUACCAAAAAUACCAA
UGUAACAUUAAGCAAGAAAAGGAAAAGAAGAUUUCUU
GGCUUUUUGUUAGGUGUUGGAUCUGCAAUCGCCAGUGG
CAUUGCUGUAUCUAAGGUCCUGCACCUAGAAGGGGAAG
UGAACAAAAUCAAAAGUGCUCUACUAUCCACAAACAAG
GCUGUAGUCAGCUUAUCAAAUGGAGUUAGUGUCUUAAC
CAGCAAAGUGUUAGACCUCAAAAACUAUAUAGAUAAAC
AGUUGUUACCUAUUGUGAACAAGCAAAGCUGCAGCAUA
UCAAACAUUGAAACUGUGAUAGAGUUCCAACAAAAGAA
CAACAGACUACUAGAGAUUACCAGGGAAUUUAGUGUUA
AUGCAGGUGUAACUACACCUGUAAGCACUUAUAUGUUA
ACUAAUAGUGAAUUAUUAUCAUUAAUCAAUGAUAUGCC
UAUAACAAAUGAUCAGAAAAAGUUAAUGUCCAACAAUG
UUCAAAUAGUUAGACAGCAAAGUUACUCUAUCAUGUCC
AUAAUAAAGGAGGAAGUCUUAGCAUAUGUAGUACAAU
UACCACUAUAUGGUGUAAUAGAUACACCCUGUUGGAAA
CUGCACACAUCCCCUCUAUGUACAACCAACACAAAGGA
AGGGUCCAACAUCUGCUUAACAAGAACCGACAGAGGAU
GGUAUUGUGACAAUGCAGGAUCAGUAUCUUUCUUCCCA
CAAGCUGAAACAUGUAAAGUUCAAUCGAAUCGGGUAUU
UUGUGACACAAUGAACAGUUUAACAUUACCAAGUGAAG
UAAAUCUCUGCAACAUUGACAUAUUCAACCCCAAAUAU
GAUUGCAAAAUUAUGACUUCAAAAACAGAUGUAAGCAG
CUCCGUUAUCACAUCUCUAGGAGCCAUUGUGUCAUGCU
AUGGCAAAACUAAAUGUACAGCAUCCAAUAAAAAUCGU

GGGAUCAUAAAGACAUUUUCUAACGGGUGUGAUUAUG
UAUCAAAUAAGGGGGUGGAUACUGUGUCUGUAGGUAA
UACAUUAUAUUAUGUAAAUAAGCAAGAAGGCAAAAGU
CUCUAUGUAAAAGGUGAACCAAUAAUAAAUUUCUAUGA
CCCAUUAGUGUUCCCCUCUGAUGAAUUUGAUGCAUCAA
UAUCUCAAGUCAAUGAGAAGAUUAACCAGAGCCUAGCA
UUUAUUCGUAAAUCCGAUGAAUUAUUACAUAAUGUAA
AUGCUGGUAAAUCCACCACAAAUAUCAUGAUAACUACU
AUAAUUAUAGUGAUUAUAGUAAUAUUGUUAUCAUUAA
UUGCAGUUGGACUGCUCCUAUACUGCAAGGCCAGAAGC
ACACCAGUCACACUAAGUAAGGAUCAACUGAGUGGUAU AAAUAAUAUUGCAUUUAGUAACUGA

TABLE-US-00004 TABLE 3 hMPV Amino Acid Sequences SEQ ID Description Sequence NO:
gi|122891979|gb| MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGW 5 EF051124.1| Human
YTNVFTLEVGDVENLTCSDGPSLIKTELDLTKSALRELKTVS metapneumo virus
ADQLAREEQIENPRQSRFVLGAIALGVAAAAAVTAGVAIAK isolate TN/92-4
TIRLESEVTAINNALKKTNEAVSTLGNGVRVLATAVRELKD fusion protein gene,
FVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS complete cds
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRA
MVRRKGFGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPS
CSEKKGNYACLLREDQGWYCQNAGSTVYYPNEKDCETRG
DHVFCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISM
VALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD
ADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQF
NVALDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAV
LGSSMILVSIFIIIKKTKKPTGAPPELSGVTNNGFIPHN gb|AY525843.1|:
MSWKVMIIISLLITPQHGLKESYLEESCSTITEGYLSVLRTGW 6 3065-4684 Human
YTNVFTLEVGDVENLTCTDGPSLIKTELDLTKSALRELKTVS metapneumo virus
ADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGIAIAKT isolate NL/1/99,
IRLESEVNAIKGALKQTNEAVSTLGNGVRVLATAVRELKEF complete cds
VSKNLTSAINRNKCDIADLKMAVSFSQFNRRFLNVVRQFSD
NAGITPAISLDLMTDAELARAVSYMPTSAGQIKLMLENRAM
VRRKGFGILIGVYGSSVIYMVQLPIFGVIDTPCWIIKAAPSCS
EKNGNYACLLREDQGWYCKNAGSTVYYPNEKDCETRGDH
VFCDTAAGINVAEQSRECNINISTTNYPCKVSTGRHPISMVA
LSPLGALVACYKGVSCSIGSNWVGIIKQLPKGCSYITNQDAD
TVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFNV
ALDQVFESIENSQALVDQSNKILNSAEKGNTGFIIVVILVAVL
GLTMISVSIIIIIKKTRKPTGAPPELNGVTNGGFIPHS gb|KJ627414.1|:
MSWKVMIIISLLITPQHGLKESYLEESCSTITEGYLSVLRTGW 7 3015-4634 Human
YTNVFTLEVGDVENLTCTDGPSLIKTELDLTKSALRELKTVS metapneumo virus
ADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGIAIAKT strain hMPV/Homo
IRLESEVNAIKGALKTTNEAVSTLGNGVRVLATAVRELKEF sapiens/PER/CFI04
VSKNLTSAINKNKCDIADLKMAVSFSQFNRRFLNVVRQFSD 97/2010/B,
NAGITPAISLDLMNDAELARAVSYMPTSAGQIKLMLENRAM complete cds
VRRKGFGILIGVYGSSVIYMVQLPIFGVINTPCWIIKAAPSCS
EKDGNYACLLREDQGWYCKNAGSTVYYPNEKDCETRGDH
VFCDTAAGINVAEQSRECNINISTTNYPCKVSTGRHPISMVA
LSPLGALVACYKGVSCSTGSNQVGIIKQLPKGCSYITNQDAD
TVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIRFPEDQFNV
ALDQVFESIENSQALVDQSNKILNSAEKGNTGFIIVIILIAVLG
LTMISVSIIIIIKKTRKPTGAPPELNGVTNGGFIPHS gb|KJ723483.1|:
MELPILKTNAITTILAAVTLCFASSQNITEEFYQSTCSAVSKG 8 5586-7310 Human
YLSALRTGWYTSVITIELSNIKENKCNGTDAKVKLIKQELDK respiratory

YKNAVTELQLLMQSTPAANNRARRELPRFMNYTLNNTKNT syncytial virus NVTLSKKRKRRFLGFLLGVGSAIASGIAVSKVLHLEGEVNKI strain RSVA/Homo KSALLSTNKAVVSLSNGVSVLTSKVLDLKNYIDKQLLPIVN sapiens/USA/84I-KQSCSISNIETVIEFQQKNNRLLEITREFSVNAGVTTPVSTYM 215A-01/1984, LTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMSIIKE complete cds EVLAYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTR TDRGWYCDNAGS VSFFPQAETCKVQSNRVFCDTMNSLTLP SEVNLCNIDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGK TKCTASNKNRGIIKTFSNGCDYVSNKGVDTVSVGNTLYYVN KQEGKSLYVKGEPIINFYDPLVFPSDEFDASISQVNEKINQSL AFIRKSDELLHNVNAGKSTTNIMITTIIIVIIVILLSLIAVGLLL YCKARSTPVTLSKDQLSGINNIAFSN

TABLE-US-00005 TABLE 4 hMPV NCBI Accession Numbers (Amino Acid Sequences) Virus GenBank Accession F [Human metapneumovirus] [Human metapneumovirus] AEK26895.1 fusion glycoprotein [Human metapneumovirus] ACJ53565.1 fusion glycoprotein [Human metapneumovirus] ACJ53566.1 fusion glycoprotein [Human metapneumovirus] ACJ53569.1 fusion protein [Human metapneumovirus] AEZ52347.1 fusion glycoprotein [Human metapneumovirus] ACJ53574.1 fusion glycoprotein [Human metapneumovirus] AHV79473.1 fusion glycoprotein [Human metapneumovirus] ACJ53570.1 fusion glycoprotein [Human metapneumovirus] ACJ53567.1 fusion protein [Human metapneumovirus] AAS22125.1 fusion glycoprotein [Human metapneumovirus] AHV79795.1 fusion glycoprotein [Human metapneumovirus] AHV79455.1 fusion glycoprotein [Human metapneumovirus] ACJ53568.1 fusion protein [Human metapneumovirus] AAS22109.1 fusion glycoprotein [Human metapneumovirus] AGU68417.1 fusion glycoprotein [Human metapneumovirus] AGJ74228.1 fusion glycoprotein [Human metapneumovirus] ACJ53575.1 fusion protein [Human metapneumovirus] AAU25820.1 fusion glycoprotein [Human metapneumovirus] AGU68377.1 fusion glycoprotein [Human metapneumovirus] AGU68371.1 fusion glycoprotein [Human metapneumovirus] AGJ74087.1 fusion glycoprotein [Human metapneumovirus] ACJ53560.1 fusion glycoprotein [Human metapneumovirus] AHV79858.1 fusion glycoprotein [Human metapneumovirus] ACJ53577.1 fusion protein [Human metapneumovirus] AAS22085.1 fusion protein [Human metapneumovirus] AEZ52348.1 fusion glycoprotein [Human metapneumovirus] AGJ74044.1 fusion glycoprotein [Human metapneumovirus] ACJ53563.1 fusion glycoprotein precursor [Human metapneumovirus] YP_012608.1 fusion glycoprotein [Human metapneumovirus] AGJ74053.1 fusion protein [Human metapneumovirus] BAM37562.1 fusion glycoprotein [Human metapneumovirus] ACJ53561.1 fusion glycoprotein [Human metapneumovirus] AGU68387.1 fusion [Human metapneumovirus] AGL74060.1 fusion glycoprotein precursor [Human metapneumovirus] AAV88364.1 fusion protein [Human metapneumovirus] AAN52910.1 fusion protein [Human metapneumovirus] AAN52915.1 fusion protein [Human metapneumovirus] BAM37564.1 fusion glycoprotein precursor [Human metapneumovirus] BAH59618.1 fusion protein [Human metapneumovirus] AAQ90144.1 fusion glycoprotein [Human metapneumovirus] AHV79446.1 fusion protein [Human metapneumovirus] AEL87260.1 fusion glycoprotein [Human metapneumovirus] AHV79867.1 fusion protein [Human metapneumovirus] ABQ66027.2 fusion glycoprotein [Human metapneumovirus] ACJ53621.1 fusion protein [Human metapneumovirus] AAN52911.1 fusion glycoprotein [Human metapneumovirus] AHV79536.1 fusion glycoprotein [Human metapneumovirus] AGU68411.1 fusion protein [Human metapneumovirus] AEZ52346.1 fusion protein [Human metapneumovirus] AAN52913.1 fusion protein [Human metapneumovirus] AAN52908.1 fusion glycoprotein [Human metapneumovirus] ACJ53553.1 fusion glycoprotein [Human metapneumovirus] AIY25727.1 fusion protein [Human metapneumovirus] ABM67072.1 fusion protein [Human metapneumovirus] AEZ52361.1 fusion protein [Human metapneumovirus] AAS22093.1 fusion glycoprotein [Human metapneumovirus] AGH27049.1 fusion protein [Human metapneumovirus] AAK62968.2 fusion glycoprotein [Human metapneumovirus] ACJ53556.1 fusion glycoprotein [Human metapneumovirus] ACJ53620.1 fusion protein [Human metapneumovirus] ABQ58820.1 F [Human metapneumovirus] [Human metapneumovirus] AEK26886.1 fusion glycoprotein [Human metapneumovirus] ACJ53619.1 fusion glycoprotein [Human metapneumovirus] ACJ53555.1 fusion [Human metapneumovirus] AGL74057.1 fusion protein [Human metapneumovirus] ABD27850.1 fusion protein [Human metapneumovirus] AEZ52349.1 fusion protein [Human metapneumovirus] ABD27848.1 fusion protein [Human metapneumovirus] ABD27846.1 fusion protein [Human metapneumovirus] ABQ66021.1 fusion protein [Human metapneumovirus] AFM57710.1 fusion protein [Human metapneumovirus] AFM57709.1 fusion protein [Human metapneumovirus] ABH05968.1 fusion protein [Human metapneumovirus] AEZ52350.1 fusion protein [Human metapneumovirus] AFM57712.1 fusion protein [Human metapneumovirus] AEZ52364.1 fusion protein [Human metapneumovirus] AAN52912.1 fusion protein [Human metapneumovirus] AEZ52363.1 fusion [Human metapneumovirus] AGL74059.1 fusion glycoprotein [Human metapneumovirus] ACJ53583.1 fusion protein [Human metapneumovirus] AEZ52356.1 fusion protein [Human metapneumovirus] AEZ52353.1 fusion glycoprotein [Human metapneumovirus] ACJ53581.1 fusion glycoprotein [Human metapneumovirus] ACJ53578.1 fusion protein [Human metapneumovirus] AAS22117.1 fusion protein [Human metapneumovirus] BAN75965.1 fusion protein [Human metapneumovirus] AGF92105.1 fusion protein [Human metapneumovirus] AAS22077.1 fusion protein [Human metapneumovirus] AAN52909.1 fusion glycoprotein [Human metapneumovirus] ACJ53586.1 fusion protein [Human metapneumovirus] AAQ90145.1 fusion glycoprotein [Human metapneumovirus] AGT75042.1 fusion [Human metapneumovirus] AGL74058.1 fusion protein [Human metapneumovirus] AEL87263.1 fusion glycoprotein [Human metapneumovirus] AGH27057.1 fusion glycoprotein [Human metapneumovirus] AHV79491.1 F [Human metapneumovirus] [Human metapneumovirus] AEK26906.1 fusion glycoprotein [Human metapneumovirus] ACJ53580.1 fusion protein [Human metapneumovirus] AEZ52354.1 fusion protein [Human metapneumovirus] AAN52914.1 G [Human metapneumovirus] [Human metapneumovirus] AEK26901.1 glycoprotein [Human metapneumovirus] AFI56738.1 glycoprotein [Human metapneumovirus] AFI56739.1 glycoprotein [Human metapneumovirus] AFI56745.1 G protein [Human metapneumovirus] AAQ62718.1 G protein [Human metapneumovirus] AAQ62719.1 attachment glycoprotein G [Human metapneumovirus] AGH27104.1 G protein [Human metapneumovirus] AAQ62729.1 G protein [Human metapneumovirus] AAQ62728.1 glycoprotein [Human metapneumovirus] AFI56753.1 glycoprotein [Human metapneumovirus] AFI56746.1 glycoprotein [Human metapneumovirus] AFI56750.1 glycoprotein [Human metapneumovirus] AFI56747.1 G protein [Human metapneumovirus] AAQ62721.1 glycoprotein [Human metapneumovirus] AAT46573.1 glycoprotein [Human metapneumovirus] AFI56748.1 glycoprotein [Human metapneumovirus] AFI56736.1 glycoprotein [Human metapneumovirus] AFI56749.1 attachment glycoprotein G [Human metapneumovirus] AGH27131.1 attachment glycoprotein G [Human metapneumovirus] AHV79558.1 glycoprotein [Human metapneumovirus] AFI56740.1 glycoprotein [Human metapneumovirus] AFI56741.1 glycoprotein [Human metapneumovirus] AFI56744.1 attachment glycoprotein G [Human metapneumovirus] AHV79790.1 attachment glycoprotein G [Human metapneumovirus] AGH27122.1 attachment glycoprotein G [Human metapneumovirus] AHV79763.1 attachment glycoprotein G [Human metapneumovirus] AGZ48849.1 glycoprotein [Human metapneumovirus] AFI56743.1 attachment glycoprotein G [Human metapneumovirus] AHV79450.1 glycoprotein [Human metapneumovirus] AFI56751.1 attachment glycoprotein [Human metapneumovirus] AAS48482.1 attachment glycoprotein G [Human metapneumovirus] AHV79889.1 attachment surface glycoprotein [Human metapneumovirus] AGW43050.1 glycoprotein [Human metapneumovirus] AFI56754.1 attachment glycoprotein G [Human metapneumovirus] AHV79601.1 glycoprotein [Human metapneumovirus] AFI56752.1 attachment glycoprotein G [Human metapneumovirus] AHV79871.1 G protein [Human metapneumovirus] AEZ68099.1 attachment glycoprotein G [Human metapneumovirus] AHV79817.1 attachment glycoprotein G [Human metapneumovirus] AHV79943.1 attachment glycoprotein G [Human metapneumovirus] BAN75968.1 attachment surface glycoprotein [Human metapneumovirus] AGW43045.1 attachment glycoprotein G [Human metapneumovirus] AHV79628.1 attachment glycoprotein [Human metapneumovirus] AFK49783.1 G protein [Human metapneumovirus] AAQ62723.1 attachment glycoprotein [Human metapneumovirus] ABD27839.1 attachment surface glycoprotein [Human metapneumovirus] AGW43046.1 G protein [Human metapneumovirus] AAQ62717.1 glycoprotein [Human metapneumovirus] AFI56742.1 attachment protein [Human metapneumovirus] ABQ44522.1 glycoprotein [Human metapneumovirus] AFI56735.1 attachment surface glycoprotein [Human metapneumovirus] AGW43065.1 G protein [Human metapneumovirus] AAQ62724.1 attachment surface glycoprotein [Human metapneumovirus] AGW43075.1 attachment surface glycoprotein [Human metapneumovirus] AGW43062.1 glycoprotein [Human metapneumovirus] AAT46579.1 attachment surface glycoprotein [Human metapneumovirus] AGW43064.1 attachment surface glycoprotein [Human metapneumovirus] AGW43054.1 attachment surface glycoprotein [Human metapneumovirus] AGW43042.1 attachment surface glycoprotein [Human metapneumovirus] AGW43078.1 attachment surface glycoprotein [Human metapneumovirus] AGW43067.1 G protein [Human metapneumovirus] AAQ62722.1 attachment surface glycoprotein [Human metapneumovirus] AGW43063.1 glycoprotein [Human metapneumovirus] AAT46571.1 glycoprotein [Human metapneumovirus] AAT46578.1 attachment glycoprotein G [Human metapneumovirus] AGJ74232.1 glycoprotein [Human metapneumovirus] AAT46580.1 glycoprotein [Human metapneumovirus] AAT46574.1 attachment surface glycoprotein [Human metapneumovirus] AGW43061.1

attachment glycoprotein [Human metapneumovirus] AFK49791.1 attachment surface glycoprotein [Human metapneumovirus] AGW43047.1 glycoprotein [Human metapneumovirus] ABC26386.1 attachment glycoprotein [Human metapneumovirus] AAS48466.1 attachment surface glycoprotein [Human metapneumovirus] AGW43048.1 attachment glycoprotein G [Human metapneumovirus] AGH27140.1 attachment surface glycoprotein [Human metapneumovirus] AGW43049.1 attachment glycoprotein G [Human metapneumovirus] AGJ74082.1 attachment glycoprotein G [Human metapneumovirus] AHV79442.1 attachment glycoprotein G [Human metapneumovirus] AGJ74091.1 attachment glycoprotein G [Human metapneumovirus] AHV79477.1 attachment surface glycoprotein [Human metapneumovirus] AGW43056.1 attachment protein [Human metapneumovirus] ABQ44523.1 attachment glycoprotein G [Human metapneumovirus] BAH59622.1 attachment surface glycoprotein [Human metapneumovirus] AGW43070.1 glycoprotein [Human metapneumovirus] AAT46585.1 attachment glycoprotein G [Human metapneumovirus] AGU68409.1 attachment glycoprotein G [Human metapneumovirus] AGJ74223.1 attachment glycoprotein [Human metapneumovirus] AAS22129.1 attachment glycoprotein G [Human metapneumovirus] AGJ74048.1 G protein [Human metapneumovirus] AAQ62725.1 glycoprotein [Human metapneumovirus] ABC26384.1 attachment protein [Human metapneumovirus] ABQ44525.1 attachment glycoprotein G [Human metapneumovirus] YP_012612.1 attachment surface glycoprotein [Human metapneumovirus] AGW43071.1 attachment glycoprotein G [Human metapneumovirus] AGJ74162.1 attachment glycoprotein G [Human metapneumovirus] AGH27095.1 attachment glycoprotein G [Human metapneumovirus] AHV79531.1 G protein [Human metapneumovirus] AAQ62726.1 attachment glycoprotein [Human metapneumovirus] AAS48465.1 attachment surface glycoprotein [Human metapneumovirus] AGW43058.1 P [Human metapneumovirus] [Human metapneumovirus] AEK26894.1 phosphoprotein [Human metapneumovirus] AHV79631.1 phosphoprotein [Human metapneumovirus] AHV79901.1 phosphoprotein [Human metapneumovirus] AHV79570.1 phosphoprotein [Human metapneumovirus] AGJ74076.1 phosphoprotein [Human metapneumovirus] AAS22123.1 phosphoprotein [Human metapneumovirus] ABB16895.1 phosphoprotein [Human metapneumovirus] AHV79579.1 phosphoprotein [Human metapneumovirus] AGJ74244.1 phosphoprotein [Human metapneumovirus] AHV79856.1 phosphoprotein [Human metapneumovirus] ACJ70113.1 phosphoprotein [Human metapneumovirus] AGZ48843.1 phosphoprotein [Human metapneumovirus] AHV79498.1 phosphoprotein [Human metapneumovirus] AHV79480.1 phosphoprotein [Human metapneumovirus] ABQ43382.1 phosphoprotein [Human metapneumovirus] AAS22107.1 phosphoprotein [Human metapneumovirus] ABB16898.1 phosphoprotein [Human metapneumovirus] AGH27134.1 phosphoprotein [Human metapneumovirus] ABB16899.1 phosphoprotein [Human metapneumovirus] AGH27098.1 phosphoprotein [Human metapneumovirus] AAN52866.1 phosphoprotein [Human metapneumovirus] AAS22083.1 phosphoprotein [Human metapneumovirus] YP_012606.1 phosphoprotein [Human metapneumovirus] AHV79973.1 phosphoprotein [Human metapneumovirus] AHV79462.1 phosphoprotein [Human metapneumovirus] AGJ74042.1 phosphoprotein [Human metapneumovirus] AAV88362.1 P [Human metapneumovirus] [Human metapneumovirus] AIL23591.1 phosphoprotein [Human metapneumovirus] AHV79453.1 phosphoprotein [Human metapneumovirus] AGJ74261.1 phosphoprotein [Human metapneumovirus] AGH27116.1 phosphoprotein [Human metapneumovirus] ABB16444.1 phosphoprotein [Human metapneumovirus] ABB16445.1 phosphoprotein [Human metapneumovirus] AHV79507.1 phosphoprotein [Human metapneumovirus] BAH59616.1 phosphoprotein [Human metapneumovirus] ABB16443.1 phosphoprotein [Human metapneumovirus] ABQ43388.1 phosphoprotein [Human metapneumovirus] ABQ43389.1 phosphoprotein [Human metapneumovirus] ABQ43395.1 phosphoprotein [Human metapneumovirus] ABQ43385.1 phosphoprotein [Human metapneumovirus] AAP84042.1 phosphoprotein [Human metapneumovirus] AAN52868.1 phosphoprotein [Human metapneumovirus] AAP84041.1 phosphoprotein [Human metapneumovirus] AGH27080.1 phosphoprotein [Human metapneumovirus] ABQ43387.1

phosphoprotein [Human metapneumovirus] AAS22099.1 phosphoprotein [Human metapneumovirus] ABB16896.1 phosphoprotein [Human metapneumovirus] AGJ74094.1 phosphoprotein [Human metapneumovirus] AEZ68089.1 phosphoprotein [Human metapneumovirus] ABK97002.1 phosphoprotein [Human metapneumovirus] AAP13486.1 phosphoprotein [Human metapneumovirus] AHV79444.1 phosphoprotein [Human metapneumovirus] AHV79865.1 phosphoprotein [Human metapneumovirus] AGJ74226.1 phosphoprotein [Human metapneumovirus] ABQ43383.1 phosphoprotein [Human metapneumovirus] AAN52863.1 phosphoprotein [Human metapneumovirus] AHV79775.1 phosphoprotein

[Human metapneumovirus] AEZ68094.1 phosphoprotein [Human metapneumovirus] AHV79883.1 phosphoprotein [Human metapneumovirus] AEZ68092.1 phosphoprotein [Human metapneumovirus] ABQ43390.1 phosphoprotein [Human metapneumovirus] ABQ43386.1 phosphoprotein [Human metapneumovirus] ABQ43391.1 phosphoprotein [Human metapneumovirus] ACS16062.1 phosphoprotein [Human metapneumovirus] AEZ68090.1 phosphoprotein [Human metapneumovirus] AAK62967.1 phosphoprotein [Human metapneumovirus] AEZ68093.1 phosphoprotein [Human metapneumovirus] AEZ68088.1 phosphoprotein [Human metapneumovirus] ABQ43392.1 phosphoprotein [Human metapneumovirus] ABQ43393.1 phosphoprotein [Human metapneumovirus] ABQ43384.1 phosphoprotein [Human metapneumovirus] ABQ43394.1 phosphoprotein [Human metapneumovirus] ABK96999.1 phosphoprotein [Human metapneumovirus] AHV79489.1 phosphoprotein [Human metapneumovirus] AGJ74235.1 phosphoprotein [Human metapneumovirus] AAS22075.1 phosphoprotein [Human metapneumovirus] AAS22115.1 phosphoprotein [Human metapneumovirus] AII17601.1 phosphoprotein [Human metapneumovirus] ABK97000.1 phosphoprotein [Human metapneumovirus] AHV79561.1 phosphoprotein [Human metapneumovirus] AGT75040.1 phosphoprotein [Human metapneumovirus] AAN52864.1 phosphoprotein [Human metapneumovirus] ABK97001.1 phosphoprotein [Human metapneumovirus] AGT74979.1 phosphoprotein [Human metapneumovirus] AHV79955.1 phosphoprotein [Human metapneumovirus] AGH27055.1 phosphoprotein [Human metapneumovirus] AAV88361.1 phosphoprotein [Human metapneumovirus] ABQ43397.1 phosphoprotein [Human metapneumovirus] AGJ74173.1 P [Human metapneumovirus] [Human metapneumovirus] AEK26904.1 phosphoprotein [Human metapneumovirus] ACJ70104.1 phosphoprotein [Human metapneumovirus] ABK97003.1 phosphoprotein [Human metapneumovirus] AGT74955.1 phosphoprotein [Human metapneumovirus] AAN52856.1 phosphoprotein [Human metapneumovirus] AAN52862.1 phosphoprotein [Human metapneumovirus] AGJ74138.1 phosphoprotein [Human metapneumovirus] AHV79613.1 phosphoprotein [Human metapneumovirus] AGJ74060.1 phosphoprotein [Human metapneumovirus] AAQ67684.1 phosphoprotein [Human metapneumovirus] AEA02278.1 N [Human metapneumovirus] [Human metapneumovirus] AEK26899.1 nucleoprotein [Human metapneumovirus] ACS16061.1 nucleoprotein [Human metapneumovirus] AAS88425.1 nucleoprotein [Human metapneumovirus] YP_012605.1 nucleoprotein [Human metapneumovirus] AHV79882.1 nucleoprotein [Human metapneumovirus] AHV79774.1 nucleocapsid protein [Human metapneumovirus] AAN52886.1 nucleoprotein [Human metapneumovirus] AAS22082.1 nucleoprotein [Human metapneumovirus] AHV79864.1 nucleoprotein [Human metapneumovirus] AHV79828.1 nucleoprotein [Human metapneumovirus] AGJ74084.1 nucleocapsid protein [Human metapneumovirus] AAN52888.1 N [Human metapneumovirus] [Human metapneumovirus] AIL23590.1 nucleoprotein [Human metapneumovirus] AAK62966.1 nucleoprotein [Human metapneumovirus] AHV79972.1 nucleoprotein [Human metapneumovirus] AHV79470.1 nucleoprotein [Human metapneumovirus] AHV79452.1 nucleoprotein [Human metapneumovirus] AGJ74243.1 nucleoprotein [Human metapneumovirus] AHV79533.1 nucleoprotein [Human metapneumovirus] AGJ74181.1 nucleoprotein [Human metapneumovirus] AHV79497.1 nucleoprotein [Human metapneumovirus] AHV79702.1 nucleoprotein [Human metapneumovirus] AHV79648.1 nucleoprotein [Human metapneumovirus] AHV79435.1 putative nucleoprotein [Human metapneumovirus] AGJ74260.1 nucleocapsid protein [Human metapneumovirus] AAN52887.1 nucleoprotein [Human metapneumovirus] AGU68386.1 nucleocapsid protein [Human metapneumovirus] AAN52899.1 nucleoprotein [Human metapneumovirus] AAR17673.1 nucleocapsid protein [Human metapneumovirus] AAN52898.1 nucleoprotein [Human metapneumovirus] AEA02277.1 nucleoprotein [Human metapneumovirus] AHV79612.1 nucleoprotein [Human metapneumovirus] AGU68416.1 nucleoprotein [Human metapneumovirus] AGU68408.1 nucleoprotein [Human metapneumovirus] AGU68370.1 nucleoprotein [Human metapneumovirus] AAQ67683.1 nucleoprotein [Human metapneumovirus] AGJ74137.1 nucleoprotein [Human metapneumovirus] AGU68344.1 nucleocapsid protein [Human metapneumovirus] ABK96997.1 nucleoprotein [Human metapneumovirus] AGU68413.1 nucleocapsid protein [Human metapneumovirus] AAN52891.1 nucleoprotein [Human metapneumovirus] AGU68360.1 nucleoprotein [Human metapneumovirus] AGU68353.1 nucleocapsid protein [Human metapneumovirus] ABK96996.1 nucleoprotein [Human metapneumovirus] AAR17666.1 N [Human metapneumovirus] [Human metapneumovirus] AEK26903.1 nucleoprotein [Human metapneumovirus] AGT75039.1 nucleoprotein [Human metapneumovirus] AGU68410.1 nucleoprotein [Human metapneumovirus] AAS22074.1 nucleoprotein [Human metapneumovirus] AHV79560.1 nucleoprotein [Human metapneumovirus] AGT74978.1 nucleoprotein [Human metapneumovirus] AGJ74128.1 nucleoprotein [Human metapneumovirus] AAR17663.1 nucleoprotein [Human metapneumovirus] AAR17662.1 nucleoprotein [Human metapneumovirus] AAR17664.1 nucleoprotein [Human metapneumovirus]

AAR17657.1 nucleoprotein [Human metapneumovirus] AAR17659.1 nucleoprotein [Human metapneumovirus] AAR17661.1 nucleoprotein [Human metapneumovirus] AGU68352.1 nucleoprotein [Human metapneumovirus] AGU68373.1 nucleoprotein [Human metapneumovirus] AGU68376.1 nucleoprotein [Human metapneumovirus] AGU68342.1 nucleoprotein [Human metapneumovirus] AGU68365.1 nucleoprotein [Human metapneumovirus] AGU68363.1 nucleoprotein [Human metapneumovirus] AGU68398.1 nucleoprotein [Human metapneumovirus] AGU68348.1 nucleoprotein [Human metapneumovirus] AGU68354.1 nucleoprotein [Human metapneumovirus] AGU68391.1 nucleoprotein [Human metapneumovirus] AGU68389.1 nucleoprotein [Human metapneumovirus] AGU68399.1 nucleoprotein [Human metapneumovirus] AGU68337.1 nucleoprotein [Human metapneumovirus] AAR17660.1 nucleoprotein [Human metapneumovirus] AAR17667.1 nucleoprotein [Human metapneumovirus] AGU68402.1 nucleoprotein [Avian metapneumovirus type C] CDN30025.1 nucleoprotein [Avian metapneumovirus] AGZ87947.1 Nucleoprotein [Avian metapneumovirus type C] CAL25113.1 nucleocapsid protein [Avian metapneumovirus] ABO42286.1 nucleocapsid protein [Avian metapneumovirus] AAK38430.1 nucleocapsid protein [Avian metapneumovirus] AAK54155.1 nucleocapsid protein [Avian metapneumovirus] AAK38426.1 nucleocapsid protein [Avian metapneumovirus] AAK38425.1 nucleocapsid protein [Avian metapneumovirus] AAK38424.1 nucleocapsid protein [Avian metapneumovirus] AAF05909.1 nucleocapsid protein [Avian metapneumovirus] AAK38435.1 nucleocapsid protein [Avian metapneumovirus] AAK38428.1 nucleoprotein [Human metapneumovirus] AAR17669.1 nucleocapsid protein [Avian metapneumovirus] AAK38429.1 nucleocapsid protein [Avian metapneumovirus] AAK38427.1 nucleocapsid protein [Avian metapneumovirus] AAK38423.1 nucleocapsid protein [Avian metapneumovirus] AAK38434.1 nucleoprotein [Human metapneumovirus] AGU68338.1 nucleoprotein [Avian metapneumovirus] YP_443837.1 nucleoprotein [Human metapneumovirus] AGU68384.1 nucleocapsid protein [Avian metapneumovirus] AAK38431.1 nucleoprotein [Human metapneumovirus] AGU68405.1 nucleoprotein [Human metapneumovirus] AGU68382.1 nucleoprotein [Human metapneumovirus] AGU68395.1 nucleocapsid [Human metapneumovirus] AAL35389.3 nucleoprotein [Human metapneumovirus] AEZ68064.1

TABLE-US-00006 TABLE 5 SEQ ID Description Sequence NO: PIV3 Nucleic Acid Sequences
>gb|KJ672601.1|: ATGCCAATTTCAATACTGTTAATTATTACAACCATGATC 9 4990-6609 Human
ATGGCATCACACTGCCAAATAGACATCACAAAACTACA parainfluenza virus
GCATGTAGGTGTATTGGTCAACAGTCCCAAAGGGATGA 3 strain
AGATATCACAAAACTTCGAAACAAGATATCTAATCCTGA HPIV3/Homo sapiens/
GTCTCATACCAAAAATAGAAGATTCTAACTCTTGTGGTG PER/FLA4815/2008
ACCAACAGATCAAGCAATACAAGAGGTTATTGGATAGA [fusion
CTGATCATTCCTTTATATGATGGACTAAGATTACAGAAG glycoprotein F0]
GATGTGATAGTGACTAATCAAGAATCCAATGAAAACAC
TGATCCCAGAACAGAACGATTCTTTGGAGGGGTAATTGG
AACTATTGCTCTAGGAGTAGCAACCTCAGCACAAATTAC
AGCAGCAGTTGCTCTGGTTGAAGCCAAGCAGGCAAGAT
CAGACATTGAAAAACTCAAGGAAGCAATCAGGGACACA
AATAAAGCAGTGCAGTCAGTTCAGAGCTCTGTAGGAAA
TTTGATAGTAGCAATTAAATCAGTCCAGGATTATGTCAA
CAAAGAAATCGTGCCATCGATTGCGAGACTAGGTTGTG
AAGCAGCAGGACTTCAGTTAGGGATTGCATTAACACAG
CATTACTCAGAATTAACAAATATATTTGGTGATAACATA
GGATCGTTACAAGAAAAAGGAATAAAATTACAAGGTAT
AGCATCATTATACCGTACAAATATCACAGAAATATTCAC
AACATCAACAGTTGACAAATATGATATTTATGATCTATT
ATTTACAGAATCAATAAAGGTGAGAGTTATAGATGTTGA
TTTGAATGATTACTCAATAACCCTCCAAGTCAGACTCCC
TTTATTGACCAGACTGCTGAACACTCAAATCTACAAAGT
AGATTCCATATCATACAATATCCAAAATAGAGAATGGTA
TATCCCTCTTCCCAGCCATATCATGACGAAAGGGGCATT
TCTAGGTGGAGCAGATGTCAAAGAATGCATAGAAGCAT
TCAGCAGTTATATATGCCCTTCTGATCCAGGATTTGTACT
AAACCATGAAATGGAGAGCTGTCTATCAGGAAACATAT

CCCAATGTCCAAGAACCACAGTCACATCAGACATAGTTC
CTAGGTATGCATTTGTCAATGGAGGAGTGGTTGCGAATT
GTATAACAACTACATGTACATGCAATGGTATCGGTAATA
GAATCAACCAACCACCTGATCAAGGAGTCAAAATTATA
ACACATAAAGAATGTAATACAATAGGTATCAACGGAAT
GCTATTCAACACAAACAAAGAAGGAACTCTTGCATTCTA
CACACCAGACGACATAACATTAAACAATTCTGTTGCACT
TGATCCGATTGACATATCAATCGAGCTCAACAAGGCCAA
ATCAGATCTTGAGGAATCAAAAGAATGGATAAGAAGGT
CAAATCAAAAGCTAGATTCTATTGGAAGTTGGCATCAAT
CTAGCACTACAATCATAGTTATTTTGATAATGATGATTA
TATTGTTTATAATTAATATAACAATAATTACAATTGCAA
TTAAGTATTACAGAATTCAAAAGAGAAATCGAGTGGAT
CAAAATGATAAGCCGTATGTATTAACAAACAAG gi|612507167|gb|
ATGGAATACTGGAAGCACACCAACCACGGAAAGGATGC 10 AHX22430.1|
TGGTAATGAGCTGGAGACATCCACAGCCACTCATGGCA hemagglutinin-
ACAAGCTCACCAACAAGATAACATATATATTGTGGACG neuraminidase
ATAACCCTGGTGTTATTATCAATAGTCTTCATCATAGTG [Human
CTAACTAATTCCATCAAAAGTGAAAAGGCCCGCGAATC parainfluenza virus
ATTGCTACAAGACATAAATAATGAGTTTATGGAAGTTAC 3]
AGAAAAGATCCAAGTGGCATCGGATAATACTAATGATC
TAATACAGTCAGGAGTGAATACAAGGCTTCTTACAATTC
AGAGTCATGTCCAGAATTATATACCAATATCATTGACAC
AACAAATATCGGATCTTAGGAAATTCATTAGTGAAATTA
CAATTAGAAATGATAATCAAGAAGTGCCACCACAAAGA
ATAACACATGATGTGGGTATAAAACCTTTAAATCCAGAT
GATTTCTGGAGATGCACGTCTGGTCTTCCATCTTTGATG
AAAACTCCAAAAATAAGATTAATGCCGGGACCAGGATT
ATTAGCTATGCCAACGACTGTTGATGGCTGTGTCAGAAC
CCCGTCCTTAGTGATAAATGATCTGATTTATGCTTACAC
CTCAAATCTAATTACTCGAGGTTGCCAGGATATAGGGAA
ATCATATCAAGTATTACAGATAGGGATAATAACTGTAAA
CTCAGACTTGGTACCTGACTTAAATCCTAGGATCTCTCA
TACCTTCAACATAAATGACAATAGAAAGTCATGTTCTCT
AGCACTCCTAAATACAGATGTATATCAACTGTGTTCAAC
CCCAAAAGTTGATGAAAGATCAGATTATGCATCATCAG
GCATAGAAGATATTGTACTTGATATTGTCAATTATGATG
GCTCAATCTCGACAACAAGATTTAAGAATAATAATATAA
GTTTTGATCAACCATATGCGGCATTATACCCATCTGTTG
GACCAGGGATATACTACAAAGGCAAAATAATATTTCTC
GGGTATGGAGGTCTTGAACATCCAATAAATGAGAATGC
AATCTGCAACACAACTGGGTGTCCTGGGAAAACACAGA
GAGACTGTAATCAAGCATCTCATAGTCCATGGTTTTCAG
ATAGAAGGATGGTCAACTCTATAATTGTTGTTGACAAGG
GCTTGAACTCAGTTCCAAAATTGAAGGTATGGACGATAT
CTATGAGACAAAATTACTGGGGGTCAGAAGGAAGATTA
CTTCTACTAGGTAACAAGATCTACATATACACAAGATCT
ACAAGTTGGCACAGCAAGTTACAATTAGGAATAATTGA
CATTACTGACTACAGTGATATAAGGATAAAATGGACAT
GGCATAATGTGCTATCAAGACCAGGAAACAATGAATGT
CCATGGGGACATTCATGTCCGGATGGATGTATAACGGG
AGTATATACCGATGCATATCCACTCAATCCCACAGGAAG
CATTGTATCATCTGTCATATTGGACTCACAAAAATCGAG
AGTCAACCCAGTCATAACTTACTCAACAGCAACCGAAA

GGGTAAACGAGCTGGCTATCCGAAACAAAACACTCTCA
GCTGGGTACACAACAACAAGCTGCATTACACACTATAA
CAAAGGGTATTGTTTTCATATAGTAGAAATAAATCATAA
AAGCTTAAACACATTTCAACCCATGTTGTTCAAAACAGA GATTCCAAAAAGCTGCAGT
HPIV3_HN_Codon ATGGAATACTGGAAGCACACCAACCACGGCAAGGACGC 11 Optimized
CGGCAACGAGCTGGAAACCAGCACAGCCACACACGGCA
ACAAGCTGACCAACAAGATCACCTACATCCTGTGGACC
ATCACCCTGGTGCTGCTGAGCATCGTGTTCATCATCGTG
CTGACCAATAGCATCAAGAGCGAGAAGGCCAGAGAGAG
CCTGCTGCAGGACATCAACAACGAGTTCATGGAAGTGA
CCGAGAAGATCCAGGTGGCCAGCGACAACACCAACGAC
CTGATCCAGAGCGGCGTGAACACCCGGCTGCTGACCATC
CAGAGCCACGTGCAGAACTACATCCCCATCAGCCTGACC
CAGCAGATCAGCGACCTGCGGAAGTTCATCAGCGAGAT
CACCATCCGGAACGACAACCAGGAAGTGCCCCCCCAGA
GAATCACCCACGACGTGGGCATCAAGCCCCTGAACCCC
GACGATTTCTGGCGGTGTACAAGCGGCCTGCCCAGCCTG
ATGAAGACCCCCAAGATCCGGCTGATGCCTGGCCCTGG
ACTGCTGGCCATGCCTACCACAGTGGATGGCTGTGTGCG
GACCCCCAGCCTCGTGATCAACGATCTGATCTACGCCTA
CACCAGCAACCTGATCACCCGGGGCTGCCAGGATATCG
GCAAGAGCTACCAGGTGCTGCAGATCGGCATCATCACC
GTGAACTCCGACCTGGTGCCCGACCTGAACCCTCGGATC
AGCCACACCTTCAACATCAACGACAACAGAAAGAGCTG
CAGCCTGGCTCTGCTGAACACCGACGTGTACCAGCTGTG
CAGCACCCCCAAGGTGGACGAGAGAAGCGACTACGCCA
GCAGCGGCATCGAGGATATCGTGCTGGACATCGTGAAC
TACGACGGCAGCATCAGCACCACCCGGTTCAAGAACAA
CAACATCAGCTTCGACCAGCCCTACGCCGCCCTGTACCC
TTCTGTGGGCCCTGGCATCTACTACAAGGGCAAGATCAT
CTTCCTGGGCTACGGCGGCCTGGAACACCCCATCAACGA
GAACGCCATCTGCAACACCACCGGCTGCCCTGGCAAGA
CCCAGAGAGACTGCAATCAGGCCAGCCACAGCCCCTGG
TTCAGCGACCGCAGAATGGTCAACTCTATCATCGTGGTG
GACAAGGGCCTGAACAGCGTGCCCAAGCTGAAAGTGTG
GACAATCAGCATGCGCCAGAACTACTGGGGCAGCGAGG
GCAGACTTCTGCTGCTGGGAAACAAGATCTACATCTACA
CCCGGTCCACCAGCTGGCACAGCAAACTGCAGCTGGGA
ATCATCGACATCACCGACTACAGCGACATCCGGATCAA
GTGGACCTGGCACAACGTGCTGAGCAGACCCGGCAACA
ATGAGTGCCCTTGGGGCCACAGCTGCCCCGATGGATGTA
TCACCGGCGTGTACACCGACGCCTACCCCCTGAATCCTA
CCGGCTCCATCGTGTCCAGCGTGATCCTGGACAGCCAGA
AAAGCAGAGTGAACCCCGTGATCACATACAGCACCGCC
ACCGAGAGAGTGAACGAACTGGCCATCAGAAACAAGAC
CCTGAGCGCCGGCTACACCACCACAAGCTGCATCACAC
ACTACAACAAGGGCTACTGCTTCCACATCGTGGAAATCA
ACCACAAGTCCCTGAACACCTTCCAGCCCATGCTGTTCA AGACCGAGATCCCCAAGAGCTGCTCC
HPIV3_F_Codon ATGCCCATCAGCATCCTGCTGATCATCACCACAATGATC 12 Optimized
ATGGCCAGCCACTGCCAGATCGACATCACCAAGCTGCA
GCACGTGGGCGTGCTCGTGAACAGCCCCAAGGGCATGA
AGATCAGCCAGAACTTCGAGACACGCTACCTGATCCTGA
GCCTGATCCCCAAGATCGAGGACAGCAACAGCTGCGGC
GACCAGCAGATCAAGCAGTACAAGCGGCTGCTGGACAG

ACTGATCATCCCCCTGTACGACGGCCTGCGGCTGCAGAA
AGACGTGATCGTGACCAACCAGGAAAGCAACGAGAACA
CCGACCCCCGGACCGAGAGATTCTTCGGCGGCGTGATCG
GCACAATCGCCCTGGGAGTGGCCACAAGCGCCCAGATT
ACAGCCGCTGTGGCCCTGGTGGAAGCCAAGCAGGCCAG
AAGCGACATCGAGAAGCTGAAAGAGGCCATCCGGGACA
CCAACAAGGCCGTGCAGAGCGTGCAGTCCAGCGTGGGC
AATCTGATCGTGGCCATCAAGTCCGTGCAGGACTACGTG
AACAAAGAAATCGTGCCCTCTATCGCCCGGCTGGGCTGT
GAAGCTGCCGGACTGCAGCTGGGCATTGCCCTGACACA
GCACTACAGCGAGCTGACCAACATCTTCGGCGACAACA
TCGGCAGCCTGCAGGAAAAGGGCATTAAGCTGCAGGGA
ATCGCCAGCCTGTACCGCACCAACATCACCGAGATCTTC
ACCACCAGCACCGTGGATAAGTACGACATCTACGACCT
GCTGTTCACCGAGAGCATCAAAGTGCGCGTGATCGACGT
GGACCTGAACGACTACAGCATCACCCTGCAAGTGCGGC
TGCCCCTGCTGACCAGACTGCTGAACACCCAGATCTACA
AGGTGGACAGCATCTCCTACAACATCCAGAACCGCGAG
TGGTACATCCCTCTGCCCAGCCACATTATGACCAAGGGC
GCCTTTCTGGGCGGAGCCGACGTGAAAGAGTGCATCGA
GGCCTTCAGCAGCTACATCTGCCCCAGCGACCCTGGCTT
CGTGCTGAACCACGAGATGGAAAGCTGCCTGAGCGGCA
ACATCAGCCAGTGCCCCAGAACCACCGTGACCTCCGAC
ATCGTGCCCAGATACGCCTTCGTGAATGGCGGCGTGGTG
GCCAACTGCATCACCACCACCTGTACCTGCAACGGCATC
GGCAACCGGATCAACCAGCCTCCCGATCAGGGCGTGAA
GATTATCACCCACAAAGAGTGTAACACCATCGGCATCA
ACGGCATGCTGTTCAATACCAACAAAGAGGGCACCCTG
GCCTTCTACACCCCCGACGATATCACCCTGAACAACTCC
GTGGCTCTGGACCCCATCGACATCTCCATCGAGCTGAAC
AAGGCCAAGAGCGACCTGGAAGAGTCCAAAGAGTGGAT
CCGGCGGAGCAACCAGAAGCTGGACTCTATCGGCAGCT
GGCACCAGAGCAGCACCACCATCATCGTGATCCTGATTA
TGATGATTATCCTGTTCATCATCAACATTACCATCATCAC
TATCGCCATTAAGTACTACCGGATCCAGAAACGGAACC
GGGTGGACCAGAATGACAAGCCCTACGTGCTGACAAAC AAG PIV3 mRNA Sequences
>gb|KJ672601.1|: AUGCCAAUUUCAAUACUGUUAAUUAUUACAACCAUGA 61 4990-6609 Human
UCAUGGCAUCACACUGCCAAAUAGACAUCACAAAACU parainfluenza virus
ACAGCAUGUAGGUGUAUUGGUCAACAGUCCCAAAGGG 3 strain
AUGAAGAUAUCACAAAACUUCGAAACAAGAUAUCUAA HPIV3/Homo sapiens/
UCCUGAGUCUCAUACCAAAAAUAGAAGAUUCUAACUC PER/FLA4815/
UUGUGGUGACCAACAGAUCAAGCAAUACAAGAGGUUA 2008 [fusion
UUGGAUAGACUGAUCAUUCCUUUAUAUGAUGGACUAA glycoprotein F0]
GAUUACAGAAGGAUGUGAUAGUGACUAAUCAAGAAUC
CAAUGAAAACACUGAUCCCAGAACAGAACGAUUCUUU
GGAGGGGUAAUUGGAACUAUUGCUCUAGGAGUAGCAA
CCUCAGCACAAAUUACAGCAGCAGUUGCUCUGGUUGA
AGCCAAGCAGGCAAGAUCAGACAUUGAAAAACUCAAG
GAAGCAAUCAGGGACACAAAUAAAGCAGUGCAGUCAG
UUCAGAGCUCUGUAGGAAAUUUGAUAGUAGCAAUUAA
AUCAGUCCAGGAUUAUGUCAACAAAGAAAUCGUGCCA
UCGAUUGCGAGACUAGGUUGUGAAGCAGCAGGACUUC
AGUUAGGGAUUGCAUUAACACAGCAUUACUCAGAAUU
AACAAAUAUAUUUGGUGAUAACAUAGGAUCGUUACAA

GAAAAAGGAAUAAAAUUACAAGGUAUAGCAUCAUUAU
ACCGUACAAAUAUCACAGAAAUAUUCACAACAUCAAC
AGUUGACAAAUAUGAUAUUUAUGAUCUAUUAUUUACA
GAAUCAAUAAAGGUGAGAGUUAUAGAUGUUGAUUUGA
AUGAUUACUCAAUAACCCUCCAAGUCAGACUCCCUUU
AUUGACCAGACUGCUGAACACUCAAAUCUACAAAGUA
GAUUCCAUAUCAUACAAUAUCCAAAAUAGAGAAUGGU
AUAUCCCUCUUCCCAGCCAUAUCAUGACGAAAGGGGC
AUUUCUAGGUGGAGCAGAUGUCAAAGAAUGCAUAGAA
GCAUUCAGCAGUUAUAUAUGCCCUUCUGAUCCAGGAU
UUGUACUAAACCAUGAAAUGGAGAGCUGUCUAUCAGG
AAACAUAUCCCAAUGUCCAAGAACCACAGUCACAUCA
GACAUAGUUCCUAGGUAUGCAUUUGUCAAUGGAGGAG
UGGUUGCGAAUUGUAUAACAACUACAUGUACAUGCAA
UGGUAUCGGUAAUAGAAUCAACCAACCACCUGAUCAA
GGAGUCAAAAUUAUAACACAUAAAGAAUGUAAUACAA
UAGGUAUCAACGGAAUGCUAUUCAACACAAACAAAGA
AGGAACUCUUGCAUUCUACACACCAGACGACAUAACA
UUAAACAAUUCUGUUGCACUUGAUCCGAUUGACAUAU
CAAUCGAGCUCAACAAGGCCAAAUCAGAUCUUGAGGA
AUCAAAAGAAUGGAUAAGAAGGUCAAAUCAAAAGCUA
GAUUCUAUUGGAAGUUGGCAUCAAUCUAGCACUACAA
UCAUAGUUAUUUUGAUAAUGAUGAUUAUAUUGUUUAU
AAUUAAUAUAACAAUAAUUACAAUUGCAAUUAAGUAU
UACAGAAUUCAAAAGAGAAAUCGAGUGGAUCAAAAUG
AUAAGCCGUAUGUAUUAACAAACAAG gi|612507167|gb|
AUGGAAUACUGGAAGCACACCAACCACGGAAAGGAUG 62 AHX22430.1|
CUGGUAAUGAGCUGGAGACAUCCACAGCCACUCAUGG hemagglutinin-
CAACAAGCUCACCAACAAGAUAACAUAUAUAUUGUGG neuraminidase
ACGAUAACCCUGGUGUUAUUAUCAAUAGUCUUCAUCA [Human
UAGUGCUAACUAAUUCCAUCAAAAGUGAAAAGGCCCG parainfluenza virus
CGAAUCAUUGCUACAAGACAUAAAUAAUGAGUUUAUG 3]
GAAGUUACAGAAAAGAUCCAAGUGGCAUCGGAUAAUA
CUAAUGAUCUAAUACAGUCAGGAGUGAAUACAAGGCU
UCUUACAAUUCAGAGUCAUGUCCAGAAUUAUAUACCA
AUAUCAUUGACACAACAAAUAUCGGAUCUUAGGAAAU
UCAUUAGUGAAAUUACAAUUAGAAAUGAUAAUCAAGA
AGUGCCACCACAAAGAAUAACACAUGAUGUGGGUAUA
AAACCUUUAAAUCCAGAUGAUUUCUGGAGAUGCACGU
CUGGUCUUCCAUCUUUGAUGAAAACUCCAAAAAUAAG
AUUAAUGCCGGGACCAGGAUUAUUAGCUAUGCCAACG
ACUGUUGAUGGCUGUGUCAGAACCCCGUCCUUAGUGA
UAAAUGAUCUGAUUUAUGCUUACACCUCAAAUCUAAU

UACUCGAGGUUGCCAGGAUAUAGGGAAAUCAUAUCAA
GUAUUACAGAUAGGGAUAAUAACUGUAAACUCAGACU
UGGUACCUGACUUAAAUCCUAGGAUCUCUCAUACCUU
CAACAUAAAUGACAAUAGAAAGUCAUGUUCUCUAGCA
CUCCUAAAUACAGAUGUAUAUCAACUGUGUUCAACCC
CAAAAGUUGAUGAAAGAUCAGAUUAUGCAUCAUCAGG
CAUAGAAGAUAUUGUACUUGAUAUUGUCAAUUAUGAU
GGCUCAAUCUCGACAACAAGAUUUAAGAAUAAUAAUA
UAAGUUUUGAUCAACCAUAUGCGGCAUUAUACCCAUC
UGUUGGACCAGGGAUAUACUACAAAGGCAAAAUAAUA

UUUCUCGGGUAUGGAGGUCUUGAACAUCCAAUAAAUG
AGAAUGCAAUCUGCAACACAACUGGGUGUCCUGGGAA
AACACAGAGAGACUGUAAUCAAGCAUCUCAUAGUCCA
UGGUUUUCAGAUAGAAGGAUGGUCAACUCUAUAAUUG
UUGUUGACAAGGGCUUGAACUCAGUUCCAAAAUUGAA
GGUAUGGACGAUAUCUAUGAGACAAAAUUACUGGGGG
UCAGAAGGAAGAUUACUUCUACUAGGUAACAAGAUCU
ACAUAUACACAAGAUCUACAAGUUGGCACAGCAAGUU
ACAAUUAGGAAUAAUUGACAUUACUGACUACAGUGAU
AUAAGGAUAAAAUGGACAUGGCAUAAUGUGCUAUCAA
GACCAGGAAACAAUGAAUGUCCAUGGGGACAUUCAUG
UCCGGAUGGAUGUAUAACGGGAGUAUAUACCGAUGCA
UAUCCACUCAAUCCCACAGGAAGCAUUGUAUCAUCUG
UCAUAUUGGACUCACAAAAAUCGAGAGUCAACCCAGU
CAUAACUUACUCAACAGCAACCGAAAGGGUAAACGAG
CUGGCUAUCCGAAACAAAACACUCUCAGCUGGGUACA
CAACAACAAGCUGCAUUACACACUAUAACAAAGGGUA
UUGUUUUCAUAUAGUAGAAAUAAAUCAUAAAAGCUUA
AACACAUUUCAACCCAUGUUGUUCAAAACAGAGAUUC CAAAAAGCUGCAGU HPIV3_HN_Codon
AUGGAAUACUGGAAGCACACCAACCACGGCAAGGACG 63 Optimized
CCGGCAACGAGCUGGAAACCAGCACAGCCACACACGGC
AACAAGCUGACCAACAAGAUCACCUACAUCCUGUGGA
CCAUCACCCUGGUGCUGCUGAGCAUCGUGUUCAUCAUC
GUGCUGACCAAUAGCAUCAAGAGCGAGAAGGCCAGAG
AGAGCCUGCUGCAGGACAUCAACAACGAGUUCAUGGA
AGUGACCGAGAAGAUCCAGGUGGCCAGCGACAACACC
AACGACCUGAUCCAGAGCGGCGUGAACACCCGGCUGCU
GACCAUCCAGAGCCACGUGCAGAACUACAUCCCCAUCA
GCCUGACCCAGCAGAUCAGCGACCUGCGGAAGUUCAUC
AGCGAGAUCACCAUCCGGAACGACAACCAGGAAGUGC
CCCCCCAGAGAAUCACCCACGACGUGGGCAUCAAGCCC
CUGAACCCCGACGAUUUCUGGCGGUGUACAAGCGGCC
UGCCCAGCCUGAUGAAGACCCCCAAGAUCCGGCUGAUG
CCUGGCCCUGGACUGCUGGCCAUGCCUACCACAGUGGA
UGGCUGUGUGCGGACCCCCAGCCUCGUGAUCAACGAUC
UGAUCUACGCCUACACCAGCAACCUGAUCACCCGGGGC
UGCCAGGAUAUCGGCAAGAGCUACCAGGUGCUGCAGA
UCGGCAUCAUCACCGUGAACUCCGACCUGGUGCCCGAC
CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA
CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACACC
GACGUGUACCAGCUGUGCAGCACCCCCAAGGUGGACG
AGAGAAGCGACUACGCCAGCAGCGGCAUCGAGGAUAU
CGUGCUGGACAUCGUGAACUACGACGGCAGCAUCAGC
ACCACCCGGUUCAAGAACAACAACAUCAGCUUCGACCA
GCCCUACGCCGCCCUGUACCCUUCUGUGGGCCCUGGCA
UCUACUACAAGGGCAAGAUCAUCUUCCUGGGCUACGG
CGGCCUGGAACACCCCAUCAACGAGAACGCCAUCUGCA
ACACCACCGGCUGCCCUGGCAAGACCCAGAGAGACUGC
AAUCAGGCCAGCCACAGCCCCUGGUUCAGCGACCGCAG
AAUGGUCAACUCUAUCAUCGUGGUGGACAAGGGCCUG
AACAGCGUGCCCAAGCUGAAAGUGUGGACAAUCAGCA
UGCGCCAGAACUACUGGGGCAGCGAGGGCAGACUUCU
GCUGCUGGGAAACAAGAUCUACAUCUACACCCGGUCC
ACCAGCUGGCACAGCAAACUGCAGCUGGGAAUCAUCG

ACAUCACCGACUACAGCGACAUCCGGAUCAAGUGGACC
UGGCACAACGUGCUGAGCAGACCCGGCAACAAUGAGU
GCCCUUGGGGCCACAGCUGCCCCGAUGGAUGUAUCACC
GGCGUGUACACCGACGCCUACCCCCUGAAUCCUACCGG
CUCCAUCGUGUCCAGCGUGAUCCUGGACAGCCAGAAA
AGCAGAGUGAACCCCGUGAUCACAUACAGCACCGCCAC
CGAGAGAGUGAACGAACUGGCCAUCAGAAACAAGACC
CUGAGCGCCGGCUACACCACCACAAGCUGCAUCACACA
CUACAACAAGGGCUACUGCUUCCACAUCGUGGAAAUC
AACCACAAGUCCCUGAACACCUUCCAGCCCAUGCUGUU
CAAGACCGAGAUCCCCAAGAGCUGCUCC HPIV3_F_Codon
AUGCCCAUCAGCAUCCUGCUGAUCAUCACCACAAUGAU 64 Optimized mRNA
CAUGGCCAGCCACUGCCAGAUCGACAUCACCAAGCUGC sequence
AGCACGUGGGCGUGCUCGUGAACAGCCCCAAGGGCAU
GAAGAUCAGCCAGAACUUCGAGACACGCUACCUGAUC
CUGAGCCUGAUCCCCAAGAUCGAGGACAGCAACAGCU
GCGGCGACCAGCAGAUCAAGCAGUACAAGCGGCUGCU
GGACAGACUGAUCAUCCCCCUGUACGACGGCCUGCGGC
UGCAGAAAGACGUGAUCGUGACCAACCAGGAAAGCAA
CGAGAACACCGACCCCCGGACCGAGAGAUUCUUCGGCG
GCGUGAUCGGCACAAUCGCCCUGGGAGUGGCCACAAG
CGCCCAGAUUACAGCCGCUGUGGCCCUGGUGGAAGCCA
AGCAGGCCAGAAGCGACAUCGAGAAGCUGAAAGAGGC
CAUCCGGGACACCAACAAGGCCGUGCAGAGCGUGCAG
UCCAGCGUGGGCAAUCUGAUCGUGGCCAUCAAGUCCG
UGCAGGACUACGUGAACAAAGAAAUCGUGCCCUCUAU
CGCCCGGCUGGGCUGUGAAGCUGCCGGACUGCAGCUG
GGCAUUGCCCUGACACAGCACUACAGCGAGCUGACCAA
CAUCUUCGGCGACAACAUCGGCAGCCUGCAGGAAAAG
GGCAUUAAGCUGCAGGGAAUCGCCAGCCUGUACCGCA
CCAACAUCACCGAGAUCUUCACCACCAGCACCGUGGAU
AAGUACGACAUCUACGACCUGCUGUUCACCGAGAGCA
UCAAAGUGCGCGUGAUCGACGUGGACCUGAACGACUA
CAGCAUCACCCUGCAAGUGCGGCUGCCCCUGCUGACCA
GACUGCUGAACACCCAGAUCUACAAGGUGGACAGCAU
CUCCUACAACAUCCAGAACCGCGAGUGGUACAUCCCUC
UGCCCAGCCACAUUAUGACCAAGGGCGCCUUUCUGGGC
GGAGCCGACGUGAAAGAGUGCAUCGAGGCCUUCAGCA
GCUACAUCUGCCCCAGCGACCCUGGCUUCGUGCUGAAC
CACGAGAUGGAAAGCUGCCUGAGCGGCAACAUCAGCC
AGUGCCCCAGAACCACCGUGACCUCCGACAUCGUGCCC
AGAUACGCCUUCGUGAAUGGCGGCGUGGUGGCCAACU
GCAUCACCACCACCUGUACCUGCAACGGCAUCGGCAAC
CGGAUCAACCAGCCUCCCGAUCAGGGCGUGAAGAUUA
UCACCCACAAAGAGUGUAACACCAUCGGCAUCAACGGC
AUGCUGUUCAAUACCAACAAAGAGGGCACCCUGGCCU
UCUACACCCCCGACGAUAUCACCCUGAACAACUCCGUG
GCUCUGGACCCCAUCGACAUCUCCAUCGAGCUGAACAA
GGCCAAGAGCGACCUGGAAGAGUCCAAAGAGUGGAUC
CGGCGGAGCAACCAGAAGCUGGACUCUAUCGGCAGCU
GGCACCAGAGCAGCACCACCAUCAUCGUGAUCCUGAUU
AUGAUGAUUAUCCUGUUCAUCAUCAACAUUACCAUCA
UCACUAUCGCCAUUAAGUACUACCGGAUCCAGAAACG
GAACCGGGUGGACCAGAAUGACAAGCCCUACGUGCUG ACAAACAAG

TABLE-US-00007 TABLE 6 PIV3 Amino Acid Sequences SEQ ID Description Sequence NO: >gi|612507166|gb| MPISILLIITTMIMASHCQIDITKLQHVGVLVNSPKGMKISQ 13 AHX22429.1| NFETRYLILSLIPKIEDSNSCGDQQIKQYKRLLDRLIIPLYDG fusion LRLQKDVIVTNQESNENTDPRTERFFGGVIGTIALGVATSA glycoprotein QITAAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSVG F0 [Human NLIVAIKSVQDYVNKEIVPSIARLGCEAAGLQLGIALTQHYS parainfluenza ELTNIFGDNIGSLQEKGIKLQGIASLYRTNITEIFTTSTVDKY virus 3] DIYDLLFTESIKVRVIDVDLNDYSITLQVRLPLLTRLLNTQIY KVDSISYNIQNREWYIPLPSHIMTKGAFLGGADVKECIEAFS SYICPSDPGFVLNHEMESCLSGNISQCPRTTVTSDIVPRYAF VNGGVVANCITTTCTCNGIGNRINQPPDQGVKIITHKECNTI GINGMLFNTNKEGTLAFYTPDDITLNNSVALDPIDISIELNK AKSDLEESKEWIRRSNQKLDSIGSWHQSSTTIIVILIMMIILFI INITIITIAIKYYRIQKRNRVDQNDKPYVLTNK gi|612507167|gb| MEYWKHTNHGKDAGNELETSTATHGNKLTNKITYILWTIT 14 AHX22430.1| LVLLSIVFIIVLTNSIKSEKARESLLQDINNEFMEVTEKIQVA hemagglutinin-SDNTNDLIQSGVNTRLLTIQSHVQNYIPISLTQQISDLRKFIS neuraminidase EITIRNDNQEVPPQRITHDVGIKPLNPDDFWRCTSGLPSLMK [Human TPKIRLMPGPGLLAMPTTVDGCVRTPSLVINDLIYAYTSNLI parainfluenza TRGCQDIGKSYQVLQIGIITVNSDLVPDLNPRISHTFNINDN virus 3] RKSCSLALLNTDVYQLCSTPKVDERSDYASSGIEDIVLDIV NYDGSISTTRFKNNNISFDQPYAALYPSVGPGIYYKGKIIFL GYGGLEHPINENAICNTTGCPGKTQRDCNQASHSPWFSDR RMVNSIIVVDKGLNSVPKLKVWTISMRQNYWGSEGRLLLL GNKIYIYTRSTSWHSKLQLGIIDITDYSDIRIKWTWHNVLSR PGNNECPWGHSCPDGCITGVYTDAYPLNPTGSIVSSVILDS QKSRVNPVITYSTATERVNELAIRNKTLSAGYTTTSCITHY NKGYCFHIVEINHKSLNTFQPMLFKTEIPKSCS

TABLE-US-00008 TABLE 7 PIV3 NCBI Accession Numbers (Nucleic Acid and Amino Acid Sequences) Description GenBank Accession Fusion glycoprotein F0 [Human parainfluenza virus 3] KJ672601.1|: HPIV3/Homo sapiens/PER/FLA4815/2008 4990-6609 AHX22429 (Fusion protein) hemagglutinin-neuraminidase [Human parainfluenza virus 3] KJ672601.1|: HPIV3/Homo sapiens/PER/FLA4815/2008 6724-8442 AHX22430 (HN protein) Recombinant PIV3/PIV1 virus fusion glycoprotein (F) AF016281 and hemagglutinin (HN) genes, complete cds; and RNA AAC23947 dependent RNA polymerase (L) gene, partial cds. (hemagglutinin) Recombinant PIV3/PIV1 virus fusion glycoprotein (F) AF016281 and hemagglutinin (HN) genes, complete cds; and RNA AAC23947 dependent RNA polymerase (L) gene, partial cds. (fusion protein) hemagglutinin-neuraminidase [Human parainfluenza virus 3] BAO32044.1 hemagglutinin-neuraminidase [Human parainfluenza virus 3] BAO32051.1 C protein [Human parainfluenza virus 3] NP_599251.1 C protein [Human parainfluenza virus 3] ABZ85670.1 C protein [Human parainfluenza virus 3] AGT75164.1 C protein [Human parainfluenza virus 3] AAB48686.1 C protein [Human parainfluenza virus 3] AHX22115.1 C protein [Human parainfluenza virus 3] AGW51066.1 C protein [Human parainfluenza virus 3] AGW51162.1 C protein [Human parainfluenza virus 3] AGT75252.1 C protein [Human parainfluenza virus 3] AGT75188.1 C protein [Human parainfluenza virus 3] AGW51218.1 C protein [Human parainfluenza virus 3] AGW51074.1 C protein [Human parainfluenza virus 3] AGT75323.1 C protein [Human parainfluenza virus 3] AGT75307.1 C protein [Human parainfluenza virus 3] AHX22131.1 C protein [Human parainfluenza virus 3] AGW51243.1 C protein [Human parainfluenza virus 3] AGT75180.1 C protein [Human parainfluenza virus 3] AGT75212.1 C protein [Human parainfluenza virus 3] AGW51186.1 C protein [Human parainfluenza virus 3] AHX22075.1 C protein [Human parainfluenza virus 3] AHX22163.1 C protein [Human parainfluenza virus 3] AGT75196.1 C protein [Human parainfluenza virus 3] AHX22491.1 C protein [Human parainfluenza virus 3] AHX22139.1 C protein [Human parainfluenza virus 3] AGW51138.1 C protein [Human parainfluenza virus 3] AGW51114.1 C protein [Human parainfluenza virus 3] AGT75220.1 C protein [Human parainfluenza virus 3] AHX22251.1 RecName: Full = Protein C; AltName: Full = VP18 protein P06165.1 C protein [Human parainfluenza virus 3]

AHX22187.1 C protein [Human parainfluenza virus 3] AGT75228.1 C protein [Human parainfluenza virus 3] AHX22179.1 C protein [Human parainfluenza virus 3] AHX22427.1 C protein [Human parainfluenza virus 3] AGW51210.1 nonstructural protein C [Human parainfluenza virus 3] BAA00922.1 C protein [Human parainfluenza virus 3] AHX22315.1 C protein [Human parainfluenza virus 3] AGW51259.1 C protein [Human parainfluenza virus 3] AHX22435.1 C protein [Human parainfluenza virus 3] AHX22123.1 C protein [Human parainfluenza virus 3] AHX22299.1 C protein [Human parainfluenza virus 3] AGW51267.1 unnamed protein product [Human parainfluenza virus 3] CAA28430.1 C protein [Human parainfluenza virus 3] AGW51178.1 C protein [Human parainfluenza virus 3] AHX22411.1 RecName: Full = Protein C P06164.1 phosphoprotein [Human parainfluenza virus 3] NP_067149.1 phosphoprotein [Human parainfluenza virus 3] AAB48685.1 phosphoprotein [Human parainfluenza virus 3] AHX22498.1 phosphoprotein [Human parainfluenza virus 3] AHX22490.1 phosphoprotein [Human parainfluenza virus 3] AGT75259.1 phosphoprotein [Human parainfluenza virus 3] AGW51137.1 phosphoprotein [Human parainfluenza virus 3] AGW51145.1 phosphoprotein [Human parainfluenza virus 3] AGT75298.1 phosphoprotein [Human parainfluenza virus 3] AGW51113.1 phosphoprotein [Human parainfluenza virus 3] AGT75203.1 phosphoprotein [Human parainfluenza virus 3] AGT75163.1 phosphoprotein [Human parainfluenza virus 3] AHX22506.1 phosphoprotein [Human parainfluenza virus 3] AGW51129.1 phosphoprotein [Human parainfluenza virus 3] AHX22194.1 phosphoprotein [Human parainfluenza virus 3] AGT75211.1 phosphoprotein [Human parainfluenza virus 3] AHX22258.1 phosphoprotein [Human parainfluenza virus 3] AGW51121.1 phosphoprotein [Human parainfluenza virus 3] AGT75282.1 phosphoprotein [Human parainfluenza virus 3] AHX22146.1 phosphoprotein [Human parainfluenza virus 3] AHX22138.1 phosphoprotein [Human parainfluenza virus 3] AHX22322.1 phosphoprotein [Human parainfluenza virus 3] AHX22370.1 phosphoprotein [Human parainfluenza virus 3] AHX22098.1 phosphoprotein [Human parainfluenza virus 3] AHX22130.1 phosphoprotein [Human parainfluenza virus 3] AHX22418.1 phosphoprotein [Human parainfluenza virus 3] AHX22114.1 phosphoprotein [Human parainfluenza virus 3] AHX22410.1 phosphoprotein [Human parainfluenza virus 3] AGT75306.1 phosphoprotein [Human parainfluenza virus 3] AHX22170.1 phosphoprotein [Human parainfluenza virus 3] AHX22266.1 phosphoprotein [Human parainfluenza virus 3] AHX22090.1 phosphoprotein [Human parainfluenza virus 3] AGT75195.1 phosphoprotein [Human parainfluenza virus 3] AHX22226.1 phosphoprotein [Human parainfluenza virus 3] AHX22178.1 phosphoprotein [Human parainfluenza virus 3] AHX22122.1 phosphoprotein [Human parainfluenza virus 3] AHX22186.1 phosphoprotein [Human parainfluenza virus 3] AHX22066.1 phosphoprotein [Human parainfluenza virus 3] AHX22522.1 phosphoprotein [Human parainfluenza virus 3] AGW51225.1 phosphoprotein [Human parainfluenza virus 3] BAN29032.1 phosphoprotein [Human parainfluenza virus 3] ABZ85669.1 phosphoprotein [Human parainfluenza virus 3] AHX22426.1 phosphoprotein [Human parainfluenza virus 3] AHX22058.1 phosphoprotein [Simian Agent 10] ADR00400.1 phosphoprotein [Human parainfluenza virus 3] AHX22250.1 phosphoprotein [Human parainfluenza virus 3] AHX22434.1 phosphoprotein [Human parainfluenza virus 3] AHX22298.1 phosphoprotein [Human parainfluenza virus 3] AHX22442.1 phosphoprotein [Human parainfluenza virus 3] AHX22074.1 phosphoprotein [Human parainfluenza virus 3] AGW51153.1 phosphoprotein [Human parainfluenza virus 3] AGW51241.1 phosphoprotein [Human parainfluenza virus 3] AHX22210.1 phosphoprotein [Human parainfluenza virus 3] AGW51105.1 phosphoprotein [Human parainfluenza virus 3] AGT75251.1 phosphoprotein [Human parainfluenza virus 3] AHX22362.1 phosphoprotein [Human parainfluenza virus 3] AHX22474.1 phosphoprotein [Human parainfluenza virus 3] AGW51217.1 phosphoprotein [Human parainfluenza virus 3] AIG60038.1 phosphoprotein [Human parainfluenza virus 3] AHX22378.1 phosphoprotein [Human parainfluenza virus 3] AGW51057.1 phosphoprotein [Human parainfluenza virus 3] AGT75187.1 phosphoprotein [Human parainfluenza virus 3] AGW51233.1 phosphoprotein [Human parainfluenza virus 3] AHX22482.1 phosphoprotein [Human parainfluenza virus 3] AGW51161.1 phosphoprotein [Human parainfluenza virus 3] AHX22306.1 phosphoprotein [Human parainfluenza virus 3] AHX22162.1 phosphoprotein [Human parainfluenza virus 3] ACJ70087.1 phosphoprotein [Human parainfluenza virus 3] AHX22466.1 phosphoprotein [Human parainfluenza virus 3] AHX22346.1 phosphoprotein [Human parainfluenza virus 3] AGW51089.1 phosphoprotein [Human parainfluenza virus 3] AGW51073.1 phosphoprotein [Human parainfluenza virus 3] AGW51185.1 phosphoprotein [Human parainfluenza virus 3] AGW51065.1 phosphoprotein [Human parainfluenza virus 3] ABY47603.1 phosphoprotein [Human parainfluenza virus 3] AGW51049.1 phosphoprotein [Human parainfluenza virus 3] AHX22330.1 phosphoprotein [Human parainfluenza virus 3] AGW51250.1 phosphoprotein [Human parainfluenza virus 3]

AGT75227.1 phosphoprotein [Human parainfluenza virus 3] AGW51282.1 phosphoprotein [Human parainfluenza virus 3] AGW51209.1 phosphoprotein [Human parainfluenza virus 3] AGW51193.1 phosphoprotein [Human parainfluenza virus 3] AGT75322.1 phosphoprotein [Human parainfluenza virus 3] AGT75219.1 phosphoprotein [Human parainfluenza virus 3] AGW51258.1 phosphoprotein [Human parainfluenza virus 3] AGW51041.1 phosphoprotein [Human parainfluenza virus 3] ACD99698.1 phosphoprotein [Human parainfluenza virus 3] AGW51266.1 phosphoprotein [Human parainfluenza virus 3] AGT75179.1 phosphoprotein [Human parainfluenza virus 3] AHX22282.1 phosphoprotein [Human parainfluenza virus 3] AGW51169.1 phosphoprotein [Human parainfluenza virus 3] AGW51274.1 phosphoprotein [Human parainfluenza virus 3] AGW51201.1 phosphoprotein [Human parainfluenza virus 3] AGW51177.1 RecName: Full = Phosphoprotein; Short = Protein P P06162.1 P protein [Human parainfluenza virus 3] AAA66818.1 phosphoprotein [Human parainfluenza virus 3] AAA46866.1 phosphoprotein [Human parainfluenza virus 3] BAA00031.1 polymerase-associated nucleocapsid phosphoprotein RRNZP5 (version 2) - parainfluenza virus type 3 [Human parainfluenza virus 3] phosphoprotein [Human parainfluenza virus 3] AGT75171.1 phosphoprotein [Human parainfluenza virus 3] BAA00921.1 D protein [Human parainfluenza virus 3] NP_599250.1 D protein [Human parainfluenza virus 3] AHX22377.1 D protein [Human parainfluenza virus 3] AHX22121.1 D protein [Human parainfluenza virus 3] AGT75297.1 D protein [Human parainfluenza virus 3] AGW51136.1 D protein [Human parainfluenza virus 3] AGW51242.1 D protein [Human parainfluenza virus 3] AGW51112.1 D protein [Human parainfluenza virus 3] AHX22497.1 D protein [Human parainfluenza virus 3] AHX22145.1 D protein [Human parainfluenza virus 3] AGT75202.1 D protein [Human parainfluenza virus 3] AHX22385.1 D protein [Human parainfluenza virus 3] AGW51216.1 D protein [Human parainfluenza virus 3] AGT75281.1 D protein [Human parainfluenza virus 3] AGT75194.1 D protein [Human parainfluenza virus 3] AHX22521.1 D protein [Human parainfluenza virus 3] AGW51120.1 D protein [Human parainfluenza virus 3] AGT75313.1 D protein [Human parainfluenza virus 3] AHX22249.1 D protein [Human parainfluenza virus 3] AHX22097.1 D protein [Human parainfluenza virus 3] AGW51144.1 D protein [Human parainfluenza virus 3] AHX22089.1 D protein [Human parainfluenza virus 3] AHX22225.1 D protein [Human parainfluenza virus 3] AHX22137.1 D protein [Human parainfluenza virus 3] AHX22065.1 D protein [Human parainfluenza virus 3] AGW51224.1 D protein [Human parainfluenza virus 3] AGT75210.1 D protein [Human parainfluenza virus 3] AHX22393.1 D protein [Human parainfluenza virus 3] AGT75258.1 D protein [Human parainfluenza virus 3] AHX22345.1 D protein [Human parainfluenza virus 3] AGT75250.1 D protein [Human parainfluenza virus 3] AHX22113.1 D protein [Human parainfluenza virus 3] AGW51232.1 D protein [Human parainfluenza virus 3] AHX22057.1 D protein [Human parainfluenza virus 3] AHX22209.1 D protein [Human parainfluenza virus 3] AGW51056.1 D protein [Human parainfluenza virus 3] AHX22161.1 D protein [Simian Agent 10] ADR00402.1 D protein [Human parainfluenza virus 3] AHX22361.1 D protein [Human parainfluenza virus 3] AGW51281.1 D protein [Human parainfluenza virus 3] AGW51184.1 D protein [Human parainfluenza virus 3] AGW51160.1 D protein [Human parainfluenza virus 3] AHX22465.1 D protein [Human parainfluenza virus 3] AHX22329.1 D protein [Human parainfluenza virus 3] AGW51064.1 D protein [Human parainfluenza virus 3] AGW51040.1 D protein [Human parainfluenza virus 3] AGT75226.1 D protein [Human parainfluenza virus 3] AHX22425.1 D protein [Human parainfluenza virus 3] AHX22305.1 D protein [Human parainfluenza virus 3] AGW51249.1 D protein [Human parainfluenza virus 3] AHX22481.1 D protein [Human parainfluenza virus 3] AHX22281.1 D protein [Human parainfluenza virus 3] AGW51048.1 D protein [Human parainfluenza virus 3] AHX22297.1 D protein [Human parainfluenza virus 3] AGW51088.1 D protein [Human parainfluenza virus 3] AGT75305.1 D protein [Human parainfluenza virus 3] AHX22185.1 D protein [Human parainfluenza virus 3] AGW51104.1 D protein [Human parainfluenza virus 3] AHX22081.1 D protein [Human parainfluenza virus 3] AGW51192.1 D protein [Human parainfluenza virus 3] AHX22489.1 D protein [Human parainfluenza virus 3] AHX22441.1 D protein [Human parainfluenza virus 3] AHX22409.1 D protein [Human parainfluenza virus 3] AHX22369.1 D protein [Human parainfluenza virus 3] AHX22321.1 D protein [Human parainfluenza virus 3] AHX22073.1 D protein [Human parainfluenza virus 3] AGW51152.1 D protein [Human parainfluenza virus 3] AGW51072.1 D protein [Human parainfluenza virus 3] AGT75321.1 D protein [Human parainfluenza virus 3] AHX22257.1 D protein [Human parainfluenza virus 3] AHX22129.1 D protein [Human parainfluenza virus 3] AHX22417.1 D protein [Human parainfluenza virus 3] AGT75218.1 D protein [Human parainfluenza virus 3] AHX22265.1 D protein [Human parainfluenza virus 3] AGT75178.1 D protein [Human parainfluenza virus 3] AHX22433.1 D protein [Human parainfluenza virus 3] AGW51273.1 D protein [Human parainfluenza virus 3] AGW51208.1 D protein [Human parainfluenza virus 3] AGT75170.1 D protein [Human parainfluenza virus 3] AGT75162.1 D protein [Human parainfluenza virus 3] AGW51257.1 D protein [Human parainfluenza virus 3]

AGW51200.1 D protein [Human parainfluenza virus 3] AGW51176.1 D protein [Human parainfluenza virus 3] AGT75186.1

D protein [Human parainfluenza virus 3] AGW51265.1 D protein [Human parainfluenza virus 3] AGW51168.1

TABLE-US-00009 TABLE 8 Signal Peptides SEQ Description Sequence ID NO: HuIgG.sub.k signal METPAQLLFLLL 15 peptide LWLPDTTG IgE heavy chain MDWTWILFLVAA 16 epsilon -1 signal ATRVHS peptide Japanese MLGSNSGQRVVF 17 encephalitis PRM TILLLLVAPAYS signal sequence VSVg protein MKCLLYLAFLFI 18 signal sequence GVNCA Japanese MWLVSLAIVTAC 19 encephalitis JEV AGA signal sequence

TABLE-US-00010 TABLE 9 hMPV/PIV Cotton Rat Challenge Study Design Group n Test Article [conc]/.mu.g Route Challenge 1 5 Placebo n/a IM hMPV/A2 2 5 hMPV vaccine mRNA 30 IM hMPV/A2 3 5 hMPV vaccine mRNA 15 IM hMPV/A2 4 5 hMPV vaccine mRNA 10 IM hMPV/A2 5 5 hMPV/PIV3 vaccine 30 IM hMPV/A2 mRNA (15/15) 6 5 FI-hMPV n/a IM hMPV/A2 7 5 Placebo n/a IM PIV3 8 5 PIV3 vaccine mRNA 30 IM PIV3 9 5 PIV3 vaccine mRNA 15 IM PIV3 10 5 PIV3 vaccine mRNA 10 IM PIV3 11 5 hMPV/PIV3 vaccine 30 IM PIV3 mRNA (15/15) 12 5 FI-PIV3 n/a IM PIV3 60

TABLE-US-00011 TABLE 10 SEQ ID Strain Nucleic Acid Sequence NO: Betacoronavirus Nucleic Acid Sequence gb|KJ156934.1|: ATGATACACTCAGTGTTTCTACTGATGTTCTTGTTAACACC 20 21405-25466
Middle TACAGAAAGTTACGTTGATGTAGGGCCAGATTCTGTTAAG East respiratory
TCTGCTTGTATTGAGGTTGATATACAACAGACCTTCTTTGA syndrome
TAAAACTTGGCCTAGGCCAATTGATGTTTCTAAGGCTGAC coronavirus
GGTATTATATACCCTCAAGGCCGTACATATTCTAACATAA isolate
CTATCACTTATCAAGGTCTTTTTCCCTATCAGGGAGACCAT Riyadh_14_2013,
GGTGATATGTATGTTTACTCTGCAGGACATGCTACAGGCA spike protein
CAACTCCACAAAAGTTGTTTGTAGCTAACTATTCTCAGGA (nucleotide)
CGTCAAACAGTTTGCTAATGGGTTTGTCGTCCGTATAGGA
GCAGCTGCCAATTCCACTGGCACTGTTATTATTAGCCCATC
TACCAGCGCTACTATACGAAAAATTTACCCTGCTTTTATGC
TGGGTTCTTCAGTTGGTAATTTCTCAGATGGTAAAATGGG
CCGCTTCTTCAATCATACTCTAGTTCTTTTGCCCGATGGAT
GTGGCACTTTACTTAGAGCTTTTTATTGTATTCTAGAGCCT
CGCTCTGGAAATCATTGTCCTGCTGGCAATTCCTATACTTC
TTTTGCCACTTATCACACTCCTGCAACAGATTGTTCTGATG
GCAATTACAATCGTAATGCCAGTCTGAACTCTTTTAAGGA
GTATTTTAATTTACGTAACTGCACCTTTATGTACACTTATA
ACATTACCGAAGATGAGATTTTAGAGTGGTTTGGCATTAC
ACAAACTGCTCAAGGTGTTCACCTCTTCTCATCTCGGTATG
TTGATTTGTACGGCGGCAATATGTTTCAATTTGCCACCTTG
CCTGTTTATGATACTATTAAGTATTATTCTATCATTCCTCA
CAGTATTCGTTCTATCCAAAGTGATAGAAAAGCTTGGGCT
GCCTTCTACGTATATAAACTTCAACCGTTAACTTTCCTGTT
GGATTTTTCTGTTGATGGTTATATACGCAGAGCTATAGACT
GTGGTTTTAATGATTTGTCACAACTCCACTGCTCATATGAA
TCCTTCGATGTTGAATCTGGAGTTTATTCAGTTTCGTCTTT
CGAAGCAAAACCTTCTGGCTCAGTTGTGGAACAGGCTGAA
GGTGTTGAATGTGATTTTTCACCTCTTCTGTCTGGCACACC
TCCTCAGGTTTATAATTTCAAGCGTTTGGTTTTTACCAATT
GCAATTATAATCTTACCAAATTGCTTTCACTTTTTTCTGTG
AATGATTTTACTTGTAGTCAAATATCTCCAGCAGCAATTGC
TAGCAACTGTTATTCTTCACTGATTTTGGATTATTTTTCAT
ACCCACTTAGTATGAAATCCGATCTCAGTGTTAGTTCTGCT
GGTCCAATATCCCAGTTTAATTATAAACAGTCCTTTTCTAA

TCCCACATGTTTGATCTTAGCGACTGTTCCTCATAACCTTA
CTACTATTACTAAGCCTCTTAAGTACAGCTATATTAACAA
GTGCTCTCGTCTTCTTTCTGATGATCGTACTGAAGTACCTC
AGTTAGTGAACGCTAATCAATACTCACCCTGTGTATCCATT
GTCCCATCCACTGTGTGGGAAGACGGTGATTATTATAGGA
AACAACTATCTCCACTTGAAGGTGGTGGCTGGCTTGTTGC
TAGTGGCTCAACTGTTGCCATGACTGAGCAATTACAGATG
GGCTTTGGTATTACAGTTCAATATGGTACAGACACCAATA
GTGTTTGCCCCAAGCTTGAATTTGCTAATGACACAAAAAT
TGCCTCTCAATTAGGCAATTGCGTGGAATATTCCCTCTATG
GTGTTTCGGGCCGTGGTGTTTTTCAGAATTGCACAGCTGTA
GGTGTTCGACAGCAGCGCTTTGTTTATGATGCGTACCAGA
ATTTAGTTGGCTATTATTCTGATGATGGCAACTACTACTGT
CTGCGTGCTTGTGTTAGTGTTCCTGTTTCTGTCATCTATGA
TAAAGAAACTAAAACCCACGCTACTCTATTTGGTAGTGTT
GCATGTGAACACATTTCTTCTACCATGTCTCAATACTCCCG
TTCTACGCGATCAATGCTTAAACGGCGAGATTCTACATAT
GGCCCCCTTCAGACACCTGTTGGTTGTGTCCTAGGACTTGT
TAATTCCTCTTTGTTCGTAGAGGACTGCAAGTTGCCTCTCG
GTCAATCTCTCTGTGCTCTTCCTGACACACCTAGTACTCTC
ACACCTCGCAGTGTGCGCTCTGTGCCAGGTGAAATGCGCT
TGGCATCCATTGCTTTTAATCATCCCATTCAGGTTGATCAA
CTTAATAGTAGTTATTTAAATTAAGTATACCCACTAATTT
TTCCTTTGGTGTGACTCAGGAGTACATTCAGACAACCATTC
AGAAAGTTACTGTTGATTGTAAACAGTACGTTTGCAATGG
TTTCCAGAAGTGTGAGCAATTACTGCGCGAGTATGGCCAG
TTTTGTTCCAAAATAAACCAGGCTCTCCATGGTGCCAATTT
ACGCCAGGATGATTCTGTACGTAATTTGTTTGCGAGCGTG
AAAAGCTCTCAATCATCTCCTATCATACCAGGTTTTGGAG
GTGACTTTAATTTGACACTTCTAGAACCTGTTTCTATATCT
ACTGGCAGTCGTAGTGCACGTAGTGCTATTGAGGATTTGC
TATTTGACAAAGTCACTATAGCTGATCCTGGTTATATGCA
AGGTTACGATGATTGTATGCAGCAAGGTCCAGCATCAGCT
CGTGATCTTATTTGTGCTCAATATGTGGCTGGTTATAAAGT
ATTACCTCCTCTTATGGATGTTAATATGGAAGCCGCGTATA
CTTCATCTTTGCTTGGCAGCATAGCAGGTGTTGGCTGGACT
GCTGGCTTATCCTCCTTTGCTGCTATTCCATTTGCACAGAG
TATYTTTTATAGGTTAAACGGTGTTGGCATTACTCAACAG
GTTCTTTCAGAGAACCAAAAGCTTATTGCCAATAAGTTTA
ATCAGGCTCTGGGAGCTATGCAAACAGGCTTCACTACAAC
TAATGAAGCTTTTCGGAAGGTTCAGGATGCTGTGAACAAC
AATGCACAGGCTCTATCCAAATTAGCTAGCGAGCTATCTA
ATACTTTTGGTGCTATTTCCGCCTCTATTGGAGACATCATA
CAACGTCTTGATGTTCTCGAACAGGACGCCCAAATAGACA
GACTTATTAATGGCCGTTTGACAACACTAAATGCTTTTGTT
GCACAGCAGCTTGTTCGTTCCGAATCAGCTGCTCTTTCCGC
TCAATTGGCTAAAGATAAAGTCAATGAGTGTGTCAAGGCA
CAATCCAAGCGTTCTGGATTTTGCGGTCAAGGCACACATA
TAGTGTCCTTTGTTGTAAATGCCCCTAATGGCCTTTACTTT
ATGCATGTTGGTTATTACCCTAGCAACCACATTGAGGTTGT
TTCTGCTTATGGTCTTTGCGATGCAGCTAACCCTACTAATT
GTATAGCCCCTGTTAATGGCTACTTTATTAAAACTAATAAC
ACTAGGATTGTTGATGAGTGGTCATATACTGGCTCGTCCTT
CTATGCACCTGAGCCCATCACCTCTCTTAATACTAAGTATG

TTGCACCACAGGTGACATACCAAAACATTTCTACTAACCT
CCCTCCTCCTCTTCTCGGCAATTCCACCGGGATTGACTTCC
AAGATGAGTTGGATGAGTTTTTCAAAAATGTTAGCACCAG
TATACCTAATTTTGGTTCTCTAACACAGATTAATACTACAT
TACTCGATCTTACCTACGAGATGTTGTCTCTTCAACAAGTT
GTTAAAGCCCTTAATGAGTCTTACATAGACCTTAAAGAGC
TTGGCAATTATACTTATTACAACAAATGGCCGTGGTACAT
TTGGCTTGGTTTCATTGCTGGGCTTGTTGCCTTAGCTCTAT
GCGTCTTCTTCATACTGTGCTGCACTGGTTGTGGCACAAAC
TGTATGGGAAAACTTAAGTGTAATCGTTGTTGTGATAGAT
ACGAGGAATACGACCTCGAGCCGCATAAGGTTCATGTTCA CTAA MERS S FL
ATGATACACTCAGTGTTTCTACTGATGTTCTTGTTAACACC 21 SPIKE
TACAGAAAGTTACGTTGATGTAGGGCCAGATTCTGTTAAG 2cEMC/2012
TCTGCTTGTATTGAGGTTGATATACAACAGACTTTCTTTGA (XBaI change
TAAAACTTGGCCTAGGCCAATTGATGTTTCTAAGGCTGAC (T to G))
GGTATTATATACCCTCAAGGCCGTACATATTCTAACATAA (nucleotide)
CTATCACTTATCAAGGTCTTTTTCCCTATCAGGGAGACCAT
GGTGATATGTATGTTTACTCTGCAGGACATGCTACAGGCA
CAACTCCACAAAAGTTGTTTGTAGCTAACTATTCTCAGGA
CGTCAAACAGTTTGCTAATGGGTTTGTCGTCCGTATAGGA
GCAGCTGCCAATTCCACTGGCACTGTTATTATTAGCCCATC
TACCAGCGCTACTATACGAAAAATTTACCCTGCTTTTATGC
TGGGTTCTTCAGTTGGTAATTTCTCAGATGGTAAAATGGG
CCGCTTCTTCAATCATACTCTAGTTCTTTTGCCCGATGGAT
GTGGCACTTTACTTAGAGCTTTTTATTGTATTCTGGAGCCT
CGCTCTGGAAATCATTGTCCTGCTGGCAATTCCTATACTTC
TTTTGCCACTTATCACACTCCTGCAACAGATTGTTCTGATG
GCAATTACAATCGTAATGCCAGTCTGAACTCTTTTAAGGA
GTATTTTAATTTACGTAACTGCACCTTTATGTACACTTATA
ACATTACCGAAGATGAGATTTTAGAGTGGTTTGGCATTAC
ACAAACTGCTCAAGGTGTTCACCTCTTCTCATCTCGGTATG
TTGATTTGTACGGCGGCAATATGTTTCAATTTGCCACCTTG
CCTGTTTATGATACTATTAAGTATTATTCTATCATTCCTCA
CAGTATTCGTTCTATCCAAAGTGATAGAAAAGCTTGGGCT
GCCTTCTACGTATATAAACTTCAACCGTTAACTTTCCTGTT
GGATTTTTCTGTTGATGGTTATATACGCAGAGCTATAGACT
GTGGTTTTAATGATTTGTCACAACTCCACTGCTCATATGAA
TCCTTCGATGTTGAATCTGGAGTTTATTCAGTTTCGTCTTT
CGAAGCAAAACCTTCTGGCTCAGTTGTGGAACAGGCTGAA
GGTGTTGAATGTGATTTTTCACCTCTTCTGTCTGGCACACC
TCCTCAGGTTTATAATTTCAAGCGTTTGGTTTTTACCAATT
GCAATTATAATCTTACCAAATTGCTTTCACTTTTTTCTGTG
AATGATTTTACTTGTAGTCAAATATCTCCAGCAGCAATTGC
TAGCAACTGTTATTCTTCACTGATTTTGGATTACTTTTCAT
ACCCACTTAGTATGAAATCCGATCTCAGTGTTAGTTCTGCT
GGTCCAATATCCCAGTTTAATTATAAACAGTCCTTTTCTAA
TCCCACATGTTTGATTTTAGCGACTGTTCCTCATAACCTTA
CTACTATTACTAAGCCTCTTAAGTACAGCTATATTAACAA
GTGCTCTCGTCTTCTTTCTGATGATCGTACTGAAGTACCTC
AGTTAGTGAACGCTAATCAATACTCACCCTGTGTATCCATT
GTCCCATCCACTGTGTGGGAAGACGGTGATTATTATAGGA
AACAACTATCTCCACTTGAAGGTGGTGGCTGGCTTGTTGC
TAGTGGCTCAACTGTTGCCATGACTGAGCAATTACAGATG
GGCTTTGGTATTACAGTTCAATATGGTACAGACACCAATA

GTGTTTGCCCCAAGCTTGAATTTGCTAATGACACAAAAAT
TGCCTCTCAATTAGGCAATTGCGTGGAATATTCCCTCTATG
GTGTTTCGGGCCGTGGTGTTTTTCAGAATTGCACAGCTGTA
GGTGTTCGACAGCAGCGCTTTGTTTATGATGCGTACCAGA
ATTTAGTTGGCTATTATTCTGATGATGGCAACTACTACTGT
TTGCGTGCTTGTGTTAGTGTTCCTGTTTCTGTCATCTATGAT
AAAGAAACTAAAACCCACGCTACTCTATTTGGTAGTGTTG
CATGTGAACACATTTCTTCTACCATGTCTCAATACTCCCGT
TCTACGCGATCAATGCTTAAACGGCGAGATTCTACATATG
GCCCCCTTCAGACACCTGTTGGTTGTGTCCTAGGACTTGTT
AATTCCTCTTTGTTCGTAGAGGACTGCAAGTTGCCTCTTGG
TCAATCTCTCTGTGCTCTTCCTGACACACCTAGTACTCTCA
CACCTCGCAGTGTGCGCTCTGTTCCAGGTGAAATGCGCTT
GGCATCCATTGCTTTTAATCATCCTATTCAGGTTGATCAAC
TTAATAGTAGTTATTTAAATTAAGTATACCCACTAATTTT
TCCTTTGGTGTGACTCAGGAGTACATTCAGACAACCATTC
AGAAAGTTACTGTTGATTGTAAACAGTACGTTTGCAATGG
TTTCCAGAAGTGTGAGCAATTACTGCGCGAGTATGGCCAG
TTTTGTTCCAAAATAAACCAGGCTCTCCATGGTGCCAATTT
ACGCCAGGATGATTCTGTACGTAATTTGTTTGCGAGCGTG
AAAAGCTCTCAATCATCTCCTATCATACCAGGTTTTGGAG
GTGACTTTAATTTGACACTTCTGGAACCTGTTTCTATATCT
ACTGGCAGTCGTAGTGCACGTAGTGCTATTGAGGATTTGC
TATTTGACAAAGTCACTATAGCTGATCCTGGTTATATGCA
AGGTTACGATGATTGCATGCAGCAAGGTCCAGCATCAGCT
CGTGATCTTATTTGTGCTCAATATGTGGCTGGTTACAAAGT
ATTACCTCCTCTTATGGATGTTAATATGGAAGCCGCGTATA
CTTCATCTTTGCTTGGCAGCATAGCAGGTGTTGGCTGGACT
GCTGGCTTATCCTCCTTTGCTGCTATTCCATTTGCACAGAG
TATCTTTTATAGGTTAAACGGTGTTGGCATTACTCAACAGG
TTCTTTCAGAGAACCAAAAGCTTATTGCCAATAAGTTTAA
TCAGGCTCTGGGAGCTATGCAAACAGGCTTCACTACAACT
AATGAAGCTTTTCAGAAGGTTCAGGATGCTGTGAACAACA
ATGCACAGGCTCTATCCAAATTAGCTAGCGAGCTATCTAA
TACTTTTGGTGCTATTTCCGCCTCTATTGGAGACATCATAC
AACGTCTTGATGTTCTCGAACAGGACGCCCAAATAGACAG
ACTTATTAATGGCCGTTTGACAACACTAAATGCTTTTGTTG
CACAGCAGCTTGTTCGTTCCGAATCAGCTGCTCTTTCCGCT
CAATTGGCTAAAGATAAAGTCAATGAGTGTGTCAAGGCAC
AATCCAAGCGTTCTGGATTTTGCGGTCAAGGCACACATAT
AGTGTCCTTTGTTGTAAATGCCCCTAATGGCCTTTACTTCA
TGCATGTTGGTTATTACCCTAGCAACCACATTGAGGTTGTT
TCTGCTTATGGTCTTTGCGATGCAGCTAACCCTACTAATTG
TATAGCCCCTGTTAATGGCTACTTTATTAAAACTAATAACA
CTAGGATTGTTGATGAGTGGTCATATACTGGCTCGTCCTTC
TATGCACCTGAGCCCATTACCTCCCTTAATACTAAGTATGT
TGCACCACAGGTGACATACCAAAACATTTCTACTAACCTC
CCTCCTCCTCTTCTCGGCAATTCCACCGGGATTGACTTCCA
AGATGAGTTGGATGAGTTTTTCAAAAATGTTAGCACCAGT
ATACCTAATTTTGGTTCCCTAACACAGATTAATACTACATT
ACTCGATCTTACCTACGAGATGTTGTCTCTTCAACAAGTTG
TTAAAGCCCTTAATGAGTCTTACATAGACCTTAAAGAGCT
TGGCAATTATACTTATTACAACAAATGGCCGTGGTACATT
TGGCTTGGTTTCATTGCTGGGCTTGTTGCCTTAGCTCTATG

CGTCTTCTTCATACTGTGCTGCACTGGTTGTGGCACAAACT
GTATGGGAAAACTTAAGTGTAATCGTTGTTGTGATAGATA
CGAGGAATACGACCTCGAGCCGCATAAGGTTCATGTTCAC TAA Novel_MERS_S2_
ATGATCCACTCCGTGTTCCTCCTCATGTTCCTGTTGACCCC 22 subunit_trimeric
CACTGAGTCAGACTGCAAGCTCCCGCTGGGACAGTCCCTG vaccine
TGTGCGCTGCCTGACACTCCTAGCACTCTGACCCCACGCTC (nucleotide)
CGTGCGGTCGGTGCCTGGCGAAATGCGGCTGGCCTCCATC
GCCTTCAATCACCCAATCCAAGTGGATCAGCTGAATAGCT
CGTATTTCAAGCTGTCCATCCCCACGAACTTCTCGTTCGGG
GTCACCCAGGAGTACATCCAGACCACAATTCAGAAGGTCA
CCGTCGATTGCAAGCAATACGTGTGCAACGGCTTCCAGAA
GTGCGAGCAGCTGCTGAGAGAATACGGGCAGTTTTGCAGC
AAGATCAACCAGGCGCTGCATGGAGCTAACTTGCGCCAGG
ACGACTCCGTGCGCAACCTCTTTGCCTCTGTGAAGTCATCC
CAGTCCTCCCCAATCATCCCGGGATTCGGAGGGGACTTCA
ACCTGACCCTCCTGGAGCCCGTGTCGATCAGCACCGGTAG
CAGATCGGCGCGCTCAGCCATTGAAGATCTTCTGTTCGAC
AAGGTCACCATCGCCGATCCGGGCTACATGCAGGGATACG
ACGACTGTATGCAGCAGGGACCAGCCTCCGCGAGGGACCT
CATCTGCGCGCAATACGTGGCCGGGTACAAAGTGCTGCCT
CCTCTGATGGATGTGAACATGGAGGCCGCTTATACTTCGT
CCCTGCTCGGCTCTATCGCCGGCGTGGGGTGGACCGCCGG
CCTGTCCTCCTTCGCCGCTATCCCCTTTGCACAATCCATTT
TCTACCGGCTCAACGGCGTGGGCATTACTCAACAAGTCCT
GTCGGAGAACCAGAAGTTGATCGCAAACAAGTTCAATCA
GGCCCTGGGGGCCATGCAGACTGGATTCACTACGACTAAC
GAAGCGTTCCAGAAGGTCCAGGACGCTGTGAACAACAAC
GCCCAGGCGCTCTCAAAGCTGGCCTCCGAACTCAGCAACA
CCTTCGGAGCCATCAGCGCATCGATCGGTGACATAATTCA
GCGGCTGGACGTGCTGGAGCAGGACGCCCAGATCGACCG
CCTCATCAACGGACGGCTGACCACCTTGAATGCCTTCGTG
GCACAACAGCTGGTCCGGAGCGAATCAGCGGCACTTTCCG
CCCAACTCGCCAAGGACAAAGTCAACGAATGCGTGAAGG
CCCAGTCCAAGAGGTCCGGTTTCTGCGGTCAAGGAACCCA
TATTGTGTCCTTCGTCGTGAACGCGCCCAACGGTCTGTACT
TTATGCACGTCGGCTACTACCCGAGCAATCATATCGAAGT
GGTGTCCGCCTACGGCCTGTGCGATGCCGCTAACCCCACT
AACTGTATTGCCCCTGTGAACGGATATTTTATTAAGACCA
ACAACACCCGCATTGTGGACGAATGGTCATACACCGGTTC
GTCCTTCTACGCGCCCGAGCCCATCACTTCACTGAACACC
AAATACGTGGCTCCGCAAGTGACCTACCAGAACATCTCCA
CCAATTTGCCGCCGCCGCTGCTCGGAAACAGCACCGGAAT

TGATTTCCAAGATGAACTGGACGAATTCTTCAAGAACGTG
TCCACTTCCATTCCCAACTTCGGAAGCCTGACACAGATCA
ACACCACCCTTCTCGACCTGACCTACGAGATGCTGAGCCT
TCAACAAGTGGTCAAGGCCCTGAACGAGAGCTACATCGAC
CTGAAGGAGCTGGGCAACTATACCTACTACAACAAGTGGC
CGGACAAGATTGAGGAGATTCTGTCGAAAATCTACCACAT
TGAAAACGAGATCGCCAGAATCAAGAAGCTTATCGGCGA AGCC MERS_S0_Full-
ATGGAAACCCCTGCCCAGCTGCTGTTCCTGCTGCTGCTGTG 23 length Spike
GCTGCCTGATACCACCGGCAGCTATGTGGACGTGGGCCCC protein
GATAGCGTGAAGTCCGCCTGTATCGAAGTGGACATCCAGC (nucleotide,
AGACCTTTTTCGACAAGACCTGGCCCAGACCCATCGACGT codon

GTCCAAGGCCGACGGCATCATCTATCCACAAGGCCGGACC optimized)
TACAGCAACATCACCATTACCTACCAGGGCCTGTTCCCAT
ATCAAGGCGACCACGGCGATATGTACGTGTACTCTGCCGG
CCACGCCACCGGCACCACACCCCAGAAACTGTTCGTGGCC
AACTACAGCCAGGACGTGAAGCAGTTCGCCAACGGCTTCG
TCGTGCGGATTGGCGCCGCTGCCAATAGCACCGGCACAGT
GATCATCAGCCCCAGCACCAGCGCCACCATCCGGAAGATC
TACCCCGCCTTCATGCTGGGCAGCTCCGTGGGCAATTTCA
GCGACGGCAAGATGGGCCGGTTCTTCAACCACACCCTGGT
GCTGCTGCCCGATGGCTGTGGCACACTGCTGAGAGCCTTC
TACTGCATCCTGGAACCCAGAAGCGGCAACCACTGCCCTG
CCGGCAATAGCTACACCAGCTTCGCCACCTACCACACACC
CGCCACCGATTGCTCCGACGGCAACTACAACCGGAACGCC
AGCCTGAACAGCTTCAAAGAGTACTTCAACCTGCGGAACT
GCACCTTCATGTACACCTACAATATCACCGAGGACGAGAT
CCTGGAATGGTTCGGCATCACCCAGACCGCCCAGGGCGTG
CACCTGTTCAGCAGCAGATACGTGGACCTGTACGGCGGCA
ACATGTTCCAGTTTGCCACCCTGCCCGTGTACGACACCATC
AAGTACTACAGCATCATCCCCCACAGCATCCGGTCCATCC
AGAGCGACAGAAAAGCCTGGGCCGCCTTCTACGTGTACAA
GCTGCAGCCCCTGACCTTCCTGCTGGACTTCAGCGTGGAC
GGCTACATCAGACGGGCCATCGACTGCGGCTTCAACGACC
TGAGCCAGCTGCACTGCTCCTACGAGAGCTTCGACGTGGA
AAGCGGCGTGTACAGCGTGTCCAGCTTCGAGGCCAAGCCT
AGCGGCAGCGTGGTGGAACAGGCTGAGGGCGTGGAATGC
GACTTCAGCCCTCTGCTGAGCGGCACCCCTCCCCAGGTGT
ACAACTTCAAGCGGCTGGTGTTCACCAACTGCAATTACAA
CCTGACCAAGCTGCTGAGCCTGTTCTCCGTGAACGACTTC
ACCTGTAGCCAGATCAGCCCTGCCGCCATTGCCAGCAACT
GCTACAGCAGCCTGATCCTGGACTACTTCAGCTACCCCCT
GAGCATGAAGTCCGATCTGAGCGTGTCCTCCGCCGGACCC
ATCAGCCAGTTCAACTACAAGCAGAGCTTCAGCAACCCTA
CCTGCCTGATTCTGGCCACCGTGCCCCACAATCTGACCAC
CATCACCAAGCCCCTGAAGTACAGCTACATCAACAAGTGC
AGCAGACTGCTGTCCGACGACCGGACCGAAGTGCCCCAGC
TCGTGAACGCCAACCAGTACAGCCCCTGCGTGTCCATCGT
GCCCAGCACCGTGTGGGAGGACGGCGACTACTACAGAAA
GCAGCTGAGCCCCCTGGAAGGCGGCGGATGGCTGGTGGCT
TCTGGAAGCACAGTGGCCATGACCGAGCAGCTGCAGATG
GGCTTTGGCATCACCGTGCAGTACGGCACCGACACCAACA
GCGTGTGCCCCAAGCTGGAATTCGCCAATGACACCAAGAT
CGCCAGCCAGCTGGGAAACTGCGTGGAATACTCCCTGTAT
GGCGTGTCCGGACGGGGCGTGTTCCAGAATTGCACAGCAG
TGGGAGTGCGGCAGCAGAGATTCGTGTACGATGCCTACCA
GAACCTCGTGGGCTACTACAGCGACGACGGCAATTACTAC
TGCCTGCGGGCCTGTGTGTCCGTGCCCGTGTCCGTGATCTA
CGACAAAGAGACAAAGACCCACGCCACACTGTTCGGCTCC
GTGGCCTGCGAGCACATCAGCTCCACCATGAGCCAGTACT
CCCGCTCCACCCGGTCCATGCTGAAGCGGAGAGATAGCAC
CTACGGCCCCCTGCAGACACCTGTGGGATGTGTGCTGGGC
CTCGTGAACAGCTCCCTGTTTGTGGAAGATTGCAAGCTGC
CCCTGGGCCAGAGCCTGTGTGCCCTGCCAGATACCCCTAG
CACCCTGACCCCTAGAAGCGTGCGCTCTGTGCCCGGCGAA
ATGCGGCTGGCCTCTATCGCCTTCAATCACCCCATCCAGGT

GGACCAGCTGAACTCCAGCTACTTCAAGCTGAGCATCCCC
ACCAACTTCAGCTTCGGCGTGACCCAGGAGTACATCCAGA
CCACAATCCAGAAAGTGACCGTGGACTGCAAGCAGTACGT
GTGCAACGGCTTTCAGAAGTGCGAACAGCTGCTGCGCGAG
TACGGCCAGTTCTGCAGCAAGATCAACCAGGCCCTGCACG
GCGCCAACCTGAGACAGGATGACAGCGTGCGGAACCTGTT
CGCCAGCGTGAAAAGCAGCCAGTCCAGCCCCATCATCCCT
GGCTTCGGCGGCGACTTTAACCTGACCCTGCTGGAACCTG
TGTCCATCAGCACCGGCTCCAGAAGCGCCAGATCCGCCAT
CGAGGACCTGCTGTTCGACAAAGTGACCATTGCCGACCCC
GGCTACATGCAGGGCTACGACGATTGCATGCAGCAGGGCC
CAGCCAGCGCCAGGGATCTGATCTGTGCCCAGTATGTGGC
CGGCTACAAGGTGCTGCCCCCCCTGATGGACGTGAACATG
GAAGCCGCCTACACCTCCAGCCTGCTGGGCTCTATTGCTG
GCGTGGGATGGACAGCCGGCCTGTCTAGCTTTGCCGCCAT
CCCTTTCGCCCAGAGCATCTTCTACCGGCTGAACGGCGTG
GGCATCACACAACAGGTGCTGAGCGAGAACCAGAAGCTG
ATCGCCAACAAGTTTAACCAGGCACTGGGCGCCATGCAGA
CCGGCTTCACCACCACCAACGAGGCCTTCAGAAAGGTGCA
GGACGCCGTGAACAACAACGCCCAGGCTCTGAGCAAGCT
GGCCTCCGAGCTGAGCAATACCTTCGGCGCCATCAGCGCC
TCCATCGGCGACATCATCCAGCGGCTGGACGTGCTGGAAC
AGGACGCCCAGATCGACCGGCTGATCAACGGCAGACTGA
CCACCCTGAACGCCTTCGTGGCACAGCAGCTCGTGCGGAG
CGAATCTGCCGCTCTGTCTGCTCAGCTGGCCAAGGACAAA
GTGAACGAGTGCGTGAAGGCCCAGTCCAAGCGGAGCGGC
TTTTGTGGCCAGGGCACCCACATCGTGTCCTTCGTCGTGAA
TGCCCCCAACGGCCTGTACTTTATGCACGTGGGCTATTACC
CCAGCAACCACATCGAGGTGGTGTCCGCCTATGGCCTGTG
CGACGCCGCCAATCCTACCAACTGTATCGCCCCCGTGAAC
GGCTACTTCATCAAGACCAACAACACCCGGATCGTGGACG
AGTGGTCCTACACAGGCAGCAGCTTCTACGCCCCCGAGCC
CATCACCTCCCTGAACACCAAATACGTGGCCCCCCAAGTG
ACATACCAGAACATCTCCACCAACCTGCCCCCTCCACTGC
TGGGAAATTCCACCGGCATCGACTTCCAGGACGAGCTGGA
CGAGTTCTTCAAGAACGTGTCCACCTCCATCCCCAACTTCG
GCAGCCTGACCCAGATCAACACCACTCTGCTGGACCTGAC
CTACGAGATGCTGTCCCTGCAACAGGTCGTGAAAGCCCTG
AACGAGAGCTACATCGACCTGAAAGAGCTGGGGAACTAC
ACCTACTACAACAAGTGGCCTTGGTACATTTGGCTGGGCT
TTATCGCCGGCCTGGTGGCCCTGGCCCTGTGCGTGTTCTTC
ATCCTGTGCTGCACCGGCTGCGGCACCAATTGCATGGGCA
AGCTGAAATGCAACCGGTGCTGCGACAGATACGAGGAAT
ACGACCTGGAACCTCACAAAGTGCATGTGCAC Betacoronavirus mRNA Sequences gb|KJ156934.1|:
AUGAUACACUCAGUGUUUCUACUGAUGUUCUUGUUAAC 65 21405-25466
ACCUACAGAAAGUUACGUUGAUGUAGGGCCAGAUUCUG Middle East
UUAAGUCUGCUUGUAUUGAGGUUGAUAUACAACAGACC respiratory
UUCUUUGAUAAAACUUGGCCUAGGCCAAUUGAUGUUUC syndrome
UAAGGCUGACGGUAUUAUAUACCCUCAAGGCCGUACAU coronavirus
AUUCUAACAUAACUAUCACUUAUCAAGGUCUUUUUCCCU isolate
AUCAGGGAGACCAUGGUGAUAUGUAUGUUUACUCUGCA Riyadh_14_2013,
GGACAUGCUACAGGCACAACUCCACAAAAGUUGUUUGU spike protein
AGCUAACUAUUCUCAGGACGUCAAACAGUUUGCUAAUG (nucleotide)
GGUUUGUCGUCCGUAUAGGAGCAGCUGCCAAUUCCACUG

GCACUGUUAUUAUUAGCCCAUCUACCAGCGCUACUAUAC
GAAAAAUUUACCCUGCUUUUAUGCUGGGUUCUUCAGUU
GGUAAUUUCUCAGAUGGUAAAAUGGGCCGCUUCUUCAA
UCAUACUCUAGUUCUUUUGCCCGAUGGAUGUGGCACUU
UACUUAGAGCUUUUUAUUGUAUUCUAGAGCCUCGCUCU
GGAAAUCAUUGUCCUGCUGGCAAUUCCUAUACUUCUUU
UGCCACUUAUCACACUCCUGCAACAGAUUGUUCUGAUGG
CAAUUACAAUCGUAAUGCCAGUCUGAACUCUUUUAAGG
AGUAUUUUAAUUUACGUAACUGCACCUUUAUGUACACU
UAUAACAUUACCGAAGAUGAGAUUUUAGAGUGGUUUGG
CAUUACACAAACUGCUCAAGGUGUUCACCUCUUCUCAUC
UCGGUAUGUUGAUUUGUACGGCGGCAAUAUGUUUCAAU
UUGCCACCUUGCCUGUUUAUGAUACUAUUAAGUAUUAU
UCUAUCAUUCCUCACAGUAUUCGUUCUAUCCAAAGUGAU
AGAAAAGCUUGGGCUGCCUUCUACGUAUAUAAACUUCA
ACCGUUAACUUUCCUGUUGGAUUUUUCUGUUGAUGGUU
AUAUACGCAGAGCUAUAGACUGUGGUUUUAAUGAUUUG
UCACAACUCCACUGCUCAUAUGAAUCCUUCGAUGUUGAA
UCUGGAGUUUAUUCAGUUUCGUCUUUCGAAGCAAAACC
UUCUGGCUCAGUUGUGGAACAGGCUGAAGGUGUUGAAU
GUGAUUUUUCACCUCUUCUGUCUGGCACACCUCCUCAGG
UUUAUAAUUUCAAGCGUUUGGUUUUUACCAAUUGCAAU
UAUAAUCUUACCAAAUUGCUUUCACUUUUUUCUGUGAA
UGAUUUUACUUGUAGUCAAAUAUCUCCAGCAGCAAUUG
CUAGCAACUGUUAUUCUUCACUGAUUUUGGAUUAUUUU
UCAUACCCACUUAGUAUGAAAUCCGAUCUCAGUGUUAG
UUCUGCUGGUCCAAUAUCCCAGUUUAAUUAUAAACAGU
CCUUUUCUAAUCCCACAUGUUUGAUCUUAGCGACUGUUC
CUCAUAACCUUACUACUAUUACUAAGCCUCUUAAGUACA
GCUAUAUUAACAAGUGCUCUCGUCUUCUUUCUGAUGAU
CGUACUGAAGUACCUCAGUUAGUGAACGCUAAUCAAUA
CUCACCCUGUGUAUCCAUUGUCCCAUCCACUGUGUGGGA
AGACGGUGAUUAUUAUAGGAAACAACUAUCUCCACUUG
AAGGUGGUGGCUGGCUUGUUGCUAGUGGCUCAACUGUU
GCCAUGACUGAGCAAUUACAGAUGGGCUUUGGUAUUAC
AGUUCAAUAUGGUACAGACACCAAUAGUGUUUGCCCCA
AGCUUGAAUUUGCUAAUGACACAAAAAUUGCCUCUCAA
UUAGGCAAUUGCGUGGAAUAUUCCCUCUAUGGUGUUUC
GGGCCGUGGUGUUUUUCAGAAUUGCACAGCUGUAGGUG
UUCGACAGCAGCGCUUUGUUUAUGAUGCGUACCAGAAU
UUAGUUGGCUAUUAUUCUGAUGAUGGCAACUACUACUG
UCUGCGUGCUUGUGUUAGUGUUCCUGUUUCUGUCAUCU
AUGAUAAAGAAACUAAAACCCACGCUACUCUAUUUGGU
AGUGUUGCAUGUGAACACAUUUCUUCUACCAUGUCUCA
AUACUCCCGUUCUACGCGAUCAAUGCUUAAACGGCGAGA
UUCUACAUAUGGCCCCCUUCAGACACCUGUUGGUUGUGU
CCUAGGACUUGUUAAUUCCUCUUUGUUCGUAGAGGACU
GCAAGUUGCCUCUCGGUCAAUCUCUCUGUGCUCUUCCUG
ACACACCUAGUACUCUCACACCUCGCAGUGUGCGCUCUG
UGCCAGGUGAAAUGCGCUUGGCAUCCAUUGCUUUUAAU
CAUCCCAUUCAGGUUGAUCAACUUAAUAGUAGUUAUUU
UAAAUUAAGUAUACCCACUAAUUUUUCCUUUGGUGUGA
CUCAGGAGUACAUUCAGACAACCAUUCAGAAAGUUACU
GUUGAUUGUAAACAGUACGUUUGCAAUGGUUUCCAGAA

GUGUGAGCAAUUACUGCGCGAGUAUGGCCAGUUUUGUU
CCAAAAUAAACCAGGCUCUCCAUGGUGCCAAUUUACGCC
AGGAUGAUUCUGUACGUAAUUUGUUUGCGAGCGUGAAA
AGCUCUCAAUCAUCUCCUAUCAUACCAGGUUUUGGAGGU
GACUUUAAUUUGACACUUCUAGAACCUGUUUCUAUAUC
UACUGGCAGUCGUAGUGCACGUAGUGCUAUUGAGGAUU
UGCUAUUUGACAAAGUCACUAUAGCUGAUCCUGGUUAU
AUGCAAGGUUACGAUGAUUGUAUGCAGCAAGGUCCAGC
AUCAGCUCGUGAUCUUAUUUGUGCUCAAUAUGUGGCUG
GUUAUAAAGUAUUACCUCCUCUUAUGGAUGUUAAUAUG
GAAGCCGCGUAUACUUCAUCUUUGCUUGGCAGCAUAGCA
GGUGUUGGCUGGACUGCUGGCUUAUCCUCCUUUGCUGCU
AUUCCAUUUGCACAGAGUAUYUUUUAUAGGUUAAACGG
UGUUGGCAUUACUCAACAGGUUCUUUCAGAGAACCAAA
AGCUUAUUGCCAAUAAGUUUAAUCAGGCUCUGGGAGCU
AUGCAAACAGGCUUCACUACAACUAAUGAAGCUUUUCG
GAAGGUUCAGGAUGCUGUGAACAACAAUGCACAGGCUC
UAUCCAAAUUAGCUAGCGAGCUAUCUAAUACUUUUGGU
GCUAUUUCCGCCUCUAUUGGAGACAUCAUACAACGUCUU
GAUGUUCUCGAACAGGACGCCCAAAUAGACAGACUUAU
UAAUGGCCGUUUGACAACACUAAAUGCUUUUGUUGCAC
AGCAGCUUGUUCGUUCCGAAUCAGCUGCUCUUUCCGCUC
AAUUGGCUAAAGAUAAAGUCAAUGAGUGUGUCAAGGCA
CAAUCCAAGCGUUCUGGAUUUUGCGGUCAAGGCACACAU
AUAGUGUCCUUUGUUGUAAAUGCCCCUAAUGGCCUUUA
CUUUAUGCAUGUUGGUUAUUACCCUAGCAACCACAUUG
AGGUUGUUUCUGCUUAUGGUCUUUGCGAUGCAGCUAAC
CCUACUAAUUGUAUAGCCCCUGUUAAUGGCUACUUUAU
UAAAACUAAUAACACUAGGAUUGUUGAUGAGUGGUCAU
AUACUGGCUCGUCCUUCUAUGCACCUGAGCCCAUCACCU
CUCUUAAUACUAAGUAUGUUGCACCACAGGUGACAUACC
AAAACAUUUCUACUAACCUCCCUCCUCCUCUUCUCGGCA
AUUCCACCGGGAUUGACUUCCAAGAUGAGUUGGAUGAG
UUUUUCAAAAAUGUUAGCACCAGUAUACCUAAUUUUGG
UUCUCUAACACAGAUUAAUACUACAUUACUCGAUCUUAC
CUACGAGAUGUUGUCUCUUCAACAAGUUGUUAAAGCCC
UUAAUGAGUCUUACAUAGACCUUAAAGAGCUUGGCAAU
UAUACUUAUUACAACAAAUGGCCGUGGUACAUUUGGCU
UGGUUUCAUUGCUGGGCUUGUUGCCUUAGCUCUAUGCG
UCUUCUUCAUACUGUGCUGCACUGGUUGUGGCACAAACU
GUAUGGGAAAACUUAAGUGUAAUCGUUGUUGUGAUAGA
UACGAGGAAUACGACCUCGAGCCGCAUAAGGUUCAUGU UCACUAA MERS S FL
AUGAUACACUCAGUGUUUCUACUGAUGUUCUUGUUAAC 66 SPIKE
ACCUACAGAAAGUUACGUUGAUGUAGGGCCAGAUUCUG 2cEMC/2012
UUAAGUCUGCUUGUAUUGAGGUUGAUAUACAACAGACU (XBaI change
UUCUUUGAUAAAACUUGGCCUAGGCCAAUUGAUGUUUC (U to G))
UAAGGCUGACGGUAUUAUAUACCCUCAAGGCCGUACAU (nucleotide)
AUUCUAACAUAACUAUCACUUAUCAAGGUCUUUUUCCCU
AUCAGGGAGACCAUGGUGAUAUGUAUGUUUACUCUGCA
GGACAUGCUACAGGCACAACUCCACAAAAGUUGUUUGU
AGCUAACUAUUCUCAGGACGUCAAACAGUUUGCUAAUG
GGUUUGUCGUCCGUAUAGGAGCAGCUGCCAAUUCCACUG
GCACUGUUAUUAUUAGCCCAUCUACCAGCGCUACUAUAC
GAAAAUUUACCCUGCUUUUAUGCUGGGUUCUUCAGUU

GGUAAUUUCUCAGAUGGUAAAAUGGGCCGCUUCUUCAA
UCAUACUCUAGUUCUUUUGCCCGAUGGAUGUGGCACUU
UACUUAGAGCUUUUUAUUGUAUUCUGGAGCCUCGCUCU
GGAAAUCAUUGUCCUGCUGGCAAUUCCUAUACUUCUUU
UGCCACUUAUCACACUCCUGCAACAGAUUGUUCUGAUGG
CAAUUACAAUCGUAAUGCCAGUCUGAACUCUUUUAAGG
AGUAUUUUAAUUUACGUAACUGCACCUUUAUGUACACU
UAUAACAUUACCGAAGAUGAGAUUUUAGAGUGGUUUGG
CAUUACACAAACUGCUCAAGGUGUUCACCUCUUCUCAUC
UCGGUAUGUUGAUUUGUACGGCGGCAAUAUGUUUCAAU
UUGCCACCUUGCCUGUUUAUGAUACUAUUAAGUAUUAU
UCUAUCAUUCCUCACAGUAUUCGUUCUAUCCAAAGUGAU
AGAAAAGCUUGGGCUGCCUUCUACGUAUAUAAACUUCA
ACCGUUAACUUUCCUGUUGGAUUUUUCUGUUGAUGGUU
AUAUACGCAGAGCUAUAGACUGUGGUUUUAAUGAUUUG
UCACAACUCCACUGCUCAUAUGAAUCCUUCGAUGUUGAA
UCUGGAGUUUAUUCAGUUUCGUCUUUCGAAGCAAAACC
UUCUGGCUCAGUUGUGGAACAGGCUGAAGGUGUUGAAU

GUGAUUUUUCACCUCUUCUGUCUGGCACACCUCCUCAGG
UUUAUAAUUUCAAGCGUUUGGUUUUUACCAAUUGCAAU
UAUAAUCUUACCAAAUUGCUUUCACUUUUUUCUGUGAA
UGAUUUUACUUGUAGUCAAAUAUCUCCAGCAGCAAUUG
CUAGCAACUGUUAUUCUUCACUGAUUUUGGAUUACUUU
UCAUACCCACUUAGUAUGAAAUCCGAUCUCAGUGUUAG
UUCUGCUGGUCCAAUAUCCCAGUUUAAUUAUAAACAGU
CCUUUUCUAAUCCCACAUGUUUGAUUUUAGCGACUGUUC
CUCAUAACCUUACUACUAUUACUAAGCCUCUUAAGUACA
GCUAUAUUAACAAGUGCUCUCGUCUUCUUUCUGAUGAU
CGUACUGAAGUACCUCAGUUAGUGAACGCUAAUCAAUA
CUCACCCUGUGUAUCCAUUGUCCCAUCCACUGUGUGGGA
AGACGGUGAUUAUUAUAGGAAACAACUAUCUCCACUUG
AAGGUGGUGGCUGGCUUGUUGCUAGUGGCUCAACUGUU
GCCAUGACUGAGCAAUUACAGAUGGGCUUUGGUAUUAC
AGUUCAAUAUGGUACAGACACCAAUAGUGUUUGCCCCA
AGCUUGAAUUUGCUAAUGACACAAAAAUUGCCUCUCAA
UUAGGCAAUUGCGUGGAAUAUUCCCUCUAUGGUGUUUC
GGGCCGUGGUGUUUUUCAGAAUUGCACAGCUGUAGGUG
UUCGACAGCAGCGCUUUGUUUAUGAUGCGUACCAGAAU
UUAGUUGGCUAUUAUUCUGAUGAUGGCAACUACUACUG
UUUGCGUGCUUGUGUUAGUGUUCCUGUUUCUGUCAUCU
AUGAUAAAGAAACUAAAACCCACGCUACUCUAUUUGGU
AGUGUUGCAUGUGAACACAUUUCUUCUACCAUGUCUCA
AUACUCCCGUUCUACGCGAUCAAUGCUUAAACGGCGAGA
UUCUACAUAUGGCCCCCUUCAGACACCUGUUGGUUGUGU
CCUAGGACUUGUUAAUUCCUCUUUGUUCGUAGAGGACU
GCAAGUUGCCUCUUGGUCAAUCUCUCUGUGCUCUUCCUG
ACACACCUAGUACUCUCACACCUCGCAGUGUGCGCUCUG
UUCCAGGUGAAAUGCGCUUGGCAUCCAUUGCUUUUAAU
CAUCCUAUUCAGGUUGAUCAACUUAAUAGUAGUUAUUU
UAAAUUAAGUAUACCCACUAAUUUUUCCUUUGGUGUGA
CUCAGGAGUACAUUCAGACAACCAUUCAGAAAGUUACU
GUUGAUUGUAAACAGUACGUUUGCAAUGGUUUCCAGAA
GUGUGAGCAAUUACUGCGCGAGUAUGGCCAGUUUUGUU

CCAAAAUAAACCAGGCUCUCCAUGGUGCCAAUUUACGCC
AGGAUGAUUCUGUACGUAAUUUGUUUGCGAGCGUGAAA
AGCUCUCAAUCAUCUCCUAUCAUACCAGGUUUUGGAGGU
GACUUUAAUUUGACACUUCUGGAACCUGUUUCUAUAUC
UACUGGCAGUCGUAGUGCACGUAGUGCUAUUGAGGAUU
UGCUAUUUGACAAAGUCACUAUAGCUGAUCCUGGUUAU
AUGCAAGGUUACGAUGAUUGCAUGCAGCAAGGUCCAGC
AUCAGCUCGUGAUCUUAUUUGUGCUCAAUAUGUGGCUG
GUUACAAAGUAUUACCUCCUCUUAUGGAUGUUAAUAUG
GAAGCCGCGUAUACUUCAUCUUUGCUUGGCAGCAUAGCA
GGUGUUGGCUGGACUGCUGGCUUAUCCUCCUUUGCUGCU
AUUCCAUUUGCACAGAGUAUCUUUUAUAGGUUAAACGG
UGUUGGCAUUACUCAACAGGUUCUUUCAGAGAACCAAA
AGCUUAUUGCCAAUAAGUUUAAUCAGGCUCUGGGAGCU
AUGCAAACAGGCUUCACUACAACUAAUGAAGCUUUUCA
GAAGGUUCAGGAUGCUGUGAACAACAAUGCACAGGCUC
UAUCCAAAUUAGCUAGCGAGCUAUCUAAUACUUUUGGU
GCUAUUUCCGCCUCUAUUGGAGACAUCAUACAACGUCUU
GAUGUUCUCGAACAGGACGCCCAAAUAGACAGACUUAU
UAAUGGCCGUUUGACAACACUAAAUGCUUUUGUUGCAC
AGCAGCUUGUUCGUUCCGAAUCAGCUGCUCUUUCCGCUC
AAUUGGCUAAAGAUAAAGUCAAUGAGUGUGUCAAGGCA
CAAUCCAAGCGUUCUGGAUUUUGCGGUCAAGGCACACAU
AUAGUGUCCUUUGUUGUAAAUGCCCCUAAUGGCCUUUA
CUUCAUGCAUGUUGGUUAUUACCCUAGCAACCACAUUGA
GGUUGUUUCUGCUUAUGGUCUUUGCGAUGCAGCUAACC
CUACUAAUUGUAUAGCCCCUGUUAAUGGCUACUUUAUU
AAAACUAAUAACACUAGGAUUGUUGAUGAGUGGUCAUA
UACUGGCUCGUCCUUCUAUGCACCUGAGCCCAUUACCUC
CCUUAAUACUAAGUAUGUUGCACCACAGGUGACAUACCA
AAACAUUUCUACUAACCUCCCUCCUCCUCUUCUCGGCAA
UUCCACCGGGAUUGACUUCCAAGAUGAGUUGGAUGAGU
UUUUCAAAAAUGUUAGCACCAGUAUACCUAAUUUUGGU
UCCCUAACACAGAUUAAUACUACAUUACUCGAUCUUACC
UACGAGAUGUUGUCUCUUCAACAAGUUGUUAAAGCCCU
UAAUGAGUCUUACAUAGACCUUAAAGAGCUUGGCAAUU
AUACUUAUUACAACAAAUGGCCGUGGUACAUUUGGCUU
GGUUUCAUUGCUGGGCUUGUUGCCUUAGCUCUAUGCGU
CUUCUUCAUACUGUGCUGCACUGGUUGUGGCACAAACUG
UAUGGGAAAACUUAAGUGUAAUCGUUGUUGUGAUAGAU
ACGAGGAAUACGACCUCGAGCCGCAUAAGGUUCAUGUUC ACUAA Novel_MERS_S2_
AUGAUCCACUCCGUGUUCCUCCUCAUGUUCCUGUUGACC 67 subunit_trimeric
CCCACUGAGUCAGACUGCAAGCUCCCGCUGGGACAGUCC vaccine
CUGUGUGCGCUGCCUGACACUCCUAGCACUCUGACCCCA (nucleotide)
CGCUCCGUGCGGUCGGUGCCUGGCGAAAUGCGGCUGGCC
UCCAUCGCCUUCAAUCACCCAAUCCAAGUGGAUCAGCUG
AAUAGCUCGUAUUUCAAGCUGUCCAUCCCCACGAACUUC
UCGUUCGGGGUCACCCAGGAGUACAUCCAGACCACAAUU
CAGAAGGUCACCGUCGAUUGCAAGCAAUACGUGUGCAAC
GGCUUCCAGAAGUGCGAGCAGCUGCUGAGAGAAUACGG
GCAGUUUUGCAGCAAGAUCAACCAGGCGCUGCAUGGAGC
UAACUUGCGCCAGGACGACUCCGUGCGCAACCUCUUUGC
CUCUGUGAAGUCAUCCCAGUCCUCCCCAAUCAUCCCGGG
AUUCGGAGGGGACUUCAACCUGACCCUCCUGGAGCCCGU

GUCGAUCAGCACCGGUAGCAGAUCGGCGCGCUCAGCCAU
UGAAGAUCUUCUGUUCGACAAGGUCACCAUCGCCGAUCC
GGGCUACAUGCAGGGAUACGACGACUGUAUGCAGCAGG
GACCAGCCUCCGCGAGGGACCUCAUCUGCGCGCAAUACG
UGGCCGGGUACAAAGUGCUGCCUCCUCUGAUGGAUGUG
AACAUGGAGGCCGCUUAUACUUCGUCCCUGCUCGGCUCU
AUCGCCGGCGUGGGGUGGACCGCCGGCCUGUCCUCCUUC
GCCGCUAUCCCCUUUGCACAAUCCAUUUUCUACCGGCUC
AACGGCGUGGGCAUUACUCAACAAGUCCUGUCGGAGAAC
CAGAAGUUGAUCGCAAACAAGUUCAAUCAGGCCCUGGG
GGCCAUGCAGACUGGAUUCACUACGACUAACGAAGCGUU
CCAGAAGGUCCAGGACGCUGUGAACAACAACGCCCAGGC
GCUCUCAAAGCUGGCCUCCGAACUCAGCAACACCUUCGG
AGCCAUCAGCGCAUCGAUCGGUGACAUAAUUCAGCGGCU
GGACGUGCUGGAGCAGGACGCCCAGAUCGACCGCCUCAU
CAACGGACGGCUGACCACCUUGAAUGCCUUCGUGGCACA
ACAGCUGGUCCGGAGCGAAUCAGCGGCACUUUCCGCCCA
ACUCGCCAAGGACAAAGUCAACGAAUGCGUGAAGGCCCA
GUCCAAGAGGUCCGGUUUCUGCGGUCAAGGAACCCAUAU
UGUGUCCUUCGUCGUGAACGCGCCCAACGGUCUGUACUU
UAUGCACGUCGGCUACUACCCGAGCAAUCAUAUCGAAGU
GGUGUCCGCCUACGGCCUGUGCGAUGCCGCUAACCCCAC
UAACUGUAUUGCCCCUGUGAACGGAUAUUUUAUUAAGA
CCAACAACACCCGCAUUGUGGACGAAUGGUCAUACACCG
GUUCGUCCUUCUACGCGCCCGAGCCCAUCACUUCACUGA
ACACCAAAUACGUGGCUCCGCAAGUGACCUACCAGAACA
UCUCCACCAAUUUGCCGCCGCCGCUGCUCGGAAACAGCA
CCGGAAUUGAUUUCCAAGAUGAACUGGACGAAUUCUUC
AAGAACGUGUCCACUUCCAUUCCCAACUUCGGAAGCCUG
ACACAGAUCAACACCACCCUUCUCGACCUGACCUACGAG
AUGCUGAGCCUUCAACAAGUGGUCAAGGCCCUGAACGAG
AGCUACAUCGACCUGAAGGAGCUGGGCAACUAUACCUAC
UACAACAAGUGGCCGGACAAGAUUGAGGAGAUUCUGUC
GAAAAUCUACCACAUUGAAAACGAGAUCGCCAGAAUCA AGAAGCUUAUCGGCGAAGCC
MERS_S0_Full- AUGGAAACCCCUGCCCAGCUGCUGUUCCUGCUGCUGCUG 68 length Spike
UGGCUGCCUGAUACCACCGGCAGCUAUGUGGACGUGGGC protein
CCCGAUAGCGUGAAGUCCGCCUGUAUCGAAGUGGACAUC (nucleotide,
CAGCAGACCUUUUUCGACAAGACCUGGCCCAGACCCAUC codon
GACGUGUCCAAGGCCGACGGCAUCAUCUAUCCACAAGGC optimized)
CGGACCUACAGCAACAUCACCAUUACCUACCAGGGCCUG
UUCCCAUAUCAAGGCGACCACGGCGAUAUGUACGUGUAC
UCUGCCGGCCACGCCACCGGCACCACACCCCAGAAACUG
UUCGUGGCCAACUACAGCCAGGACGUGAAGCAGUUCGCC
AACGGCUUCGUCGUGCGGAUUGGCGCCGCUGCCAAUAGC
ACCGGCACAGUGAUCAUCAGCCCCAGCACCAGCGCCACC
AUCCGGAAGAUCUACCCCGCCUUCAUGCUGGGCAGCUCC
GUGGGCAAUUUCAGCGACGGCAAGAUGGGCCGGUUCUU
CAACCACACCCUGGUGCUGCUGCCCGAUGGCUGUGGCAC
ACUGCUGAGAGCCUUCUACUGCAUCCUGGAACCCAGAAG
CGGCAACCACUGCCCUGCCGGCAAUAGCUACACCAGCUU
CGCCACCUACCACACACCCGCCACCGAUUGCUCCGACGG
CAACUACAACCGGAACGCCAGCCUGAACAGCUUCAAAGA
GUACUUCAACCUGCGGAACUGCACCUUCAUGUACACCUA
CAAUAUCACCGAGGACGAGAUCCUGGAAUGGUUCGGCA

UCACCCAGACCGCCCAGGGCGUGCACCUGUUCAGCAGCA
GAUACGUGGACCUGUACGGCGGCAACAUGUUCCAGUUU
GCCACCCUGCCCGUGUACGACACCAUCAAGUACUACAGC
AUCAUCCCCCACAGCAUCCGGUCCAUCCAGAGCGACAGA
AAAGCCUGGGCCGCCUUCUACGUGUACAAGCUGCAGCCC
CUGACCUUCCUGCUGGACUUCAGCGUGGACGGCUACAUC
AGACGGGCCAUCGACUGCGGCUUCAACGACCUGAGCCAG
CUGCACUGCUCCUACGAGAGCUUCGACGUGGAAAGCGGC
GUGUACAGCGUGUCCAGCUUCGAGGCCAAGCCUAGCGGC
AGCGUGGUGGAACAGGCUGAGGGCGUGGAAUGCGACUU
CAGCCCUCUGCUGAGCGGCACCCCUCCCCAGGUGUACAA
CUUCAAGCGGCUGGUGUUCACCAACUGCAAUUACAACCU
GACCAAGCUGCUGAGCCUGUUCUCCGUGAACGACUUCAC
CUGUAGCCAGAUCAGCCCUGCCGCCAUUGCCAGCAACUG
CUACAGCAGCCUGAUCCUGGACUACUUCAGCUACCCCCU
GAGCAUGAAGUCCGAUCUGAGCGUGUCCUCCGCCGGACC
CAUCAGCCAGUUCAACUACAAGCAGAGCUUCAGCAACCC
UACCUGCCUGAUUCUGGCCACCGUGCCCCACAAUCUGAC
CACCAUCACCAAGCCCCUGAAGUACAGCUACAUCAACAA
GUGCAGCAGACUGCUGUCCGACGACCGGACCGAAGUGCC
CCAGCUCGUGAACGCCAACCAGUACAGCCCCUGCGUGUC
CAUCGUGCCCAGCACCGUGUGGGAGGACGGCGACUACUA
CAGAAAGCAGCUGAGCCCCCUGGAAGGCGGCGGAUGGCU
GGUGGCUUCUGGAAGCACAGUGGCCAUGACCGAGCAGCU
GCAGAUGGGCUUUGGCAUCACCGUGCAGUACGGCACCGA
CACCAACAGCGUGUGCCCCAAGCUGGAAUUCGCCAAUGA
CACCAAGAUCGCCAGCCAGCUGGGAAACUGCGUGGAAUA
CUCCCUGUAUGGCGUGUCCGGACGGGGCGUGUUCCAGAA
UUGCACAGCAGUGGGAGUGCGGCAGCAGAGAUUCGUGU
ACGAUGCCUACCAGAACCUCGUGGGCUACUACAGCGACG
ACGGCAAUUACUACUGCCUGCGGGCCUGUGUGUCCGUGC
CCGUGUCCGUGAUCUACGACAAAGAGACAAAGACCCACG
CCACACUGUUCGGCUCCGUGGCCUGCGAGCACAUCAGCU
CCACCAUGAGCCAGUACUCCCGCUCCACCCGGUCCAUGC
UGAAGCGGAGAGAUAGCACCUACGGCCCCCUGCAGACAC
CUGUGGGAUGUGUGCUGGGCCUCGUGAACAGCUCCCUGU
UUGUGGAAGAUUGCAAGCUGCCCCUGGGCCAGAGCCUGU
GUGCCCUGCCAGAUACCCCUAGCACCCUGACCCCUAGAA
GCGUGCGCUCUGUGCCCGGCGAAAUGCGGCUGGCCUCUA
UCGCCUUCAAUCACCCCAUCCAGGUGGACCAGCUGAACU
CCAGCUACUUCAAGCUGAGCAUCCCCACCAACUUCAGCU
UCGGCGUGACCCAGGAGUACAUCCAGACCACAAUCCAGA
AAGUGACCGUGGACUGCAAGCAGUACGUGUGCAACGGC
UUUCAGAAGUGCGAACAGCUGCUGCGCGAGUACGGCCAG
UUCUGCAGCAAGAUCAACCAGGCCCUGCACGGCGCCAAC
CUGAGACAGGAUGACAGCGUGCGGAACCUGUUCGCCAGC
GUGAAAAGCAGCCAGUCCAGCCCCAUCAUCCCUGGCUUC
GGCGGCGACUUUAACCUGACCCUGCUGGAACCUGUGUCC
AUCAGCACCGGCUCCAGAAGCGCCAGAUCCGCCAUCGAG
GACCUGCUGUUCGACAAAGUGACCAUUGCCGACCCCGGC
UACAUGCAGGGCUACGACGAUUGCAUGCAGCAGGGCCCA
GCCAGCGCCAGGGAUCUGAUCUGUGCCCAGUAUGUGGCC
GGCUACAAGGUGCUGCCCCCCCUGAUGGACGUGAACAUG
GAAGCCGCCUACACCUCCAGCCUGCUGGGCUCUAUUGCU

GGCGUGGGAUGGACAGCCGGCCUGUCUAGCUUUGCCGCC
AUCCCUUUCGCCCAGAGCAUCUUCUACCGGCUGAACGGC
GUGGGCAUCACACAACAGGUGCUGAGCGAGAACCAGAA
GCUGAUCGCCAACAAGUUUAACCAGGCACUGGGCGCCAU
GCAGACCGGCUUCACCACCACCAACGAGGCCUUCAGAAA
GGUGCAGGACGCCGUGAACAACAACGCCCAGGCUCUGAG
CAAGCUGGCCUCCGAGCUGAGCAAUACCUUCGGCGCCAU
CAGCGCCUCCAUCGGCGACAUCAUCCAGCGGCUGGACGU
GCUGGAACAGGACGCCCAGAUCGACCGGCUGAUCAACGG
CAGACUGACCACCCUGAACGCCUUCGUGGCACAGCAGCU
CGUGCGGAGCGAAUCUGCCGCUCUGUCUGCUCAGCUGGC
CAAGGACAAAGUGAACGAGUGCGUGAAGGCCCAGUCCA
AGCGGAGCGGCUUUUGUGGCCAGGGCACCCACAUCGUGU
CCUUCGUCGUGAAUGCCCCCAACGGCCUGUACUUUAUGC
ACGUGGGCUAUUACCCCAGCAACCACAUCGAGGUGGUGU
CCGCCUAUGGCCUGUGCGACGCCGCCAAUCCUACCAACU
GUAUCGCCCCCGUGAACGGCUACUUCAUCAAGACCAACA
ACACCCGGAUCGUGGACGAGUGGUCCUACACAGGCAGCA
GCUUCUACGCCCCCGAGCCCAUCACCUCCCUGAACACCA
AAUACGUGGCCCCCCAAGUGACAUACCAGAACAUCUCCA
CCAACCUGCCCCCUCCACUGCUGGGAAAUUCCACCGGCA
UCGACUUCCAGGACGAGCUGGACGAGUUCUUCAAGAACG
UGUCCACCUCCAUCCCCAACUUCGGCAGCCUGACCCAGA
UCAACACCACUCUGCUGGACCUGACCUACGAGAUGCUGU
CCCUGCAACAGGUCGUGAAAGCCCUGAACGAGAGCUACA
UCGACCUGAAAGAGCUGGGGAACUACACCUACUACAACA
AGUGGCCUUGGUACAUUUGGCUGGGCUUUAUCGCCGGCC
UGGUGGCCCUGGCCCUGUGCGUGUUCUUCAUCCUGUGCU
GCACCGGCUGCGGCACCAAUUGCAUGGGCAAGCUGAAAU
GCAACCGGUGCUGCGACAGAUACGAGGAAUACGACCUGG AACCUCACAAAGUGCAUGUGCAC

TABLE-US-00012 TABLE 11 Betacoronavirus Amino Acid Sequences SEQ ID Strain Amino Acid Sequence NO: gb|KJ156934.1|: MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDK 24 21405-25466 TWPRPIDVSKADGIIYPQGRTYSNITITYQGLFPYQGDHGDM Middle East YVYSAGHATGTTpQKLFVANYSQDVKQFANGFVVRIGAAANS respiratory TGTVIISPSTSATIRKIYPAFMLGSSVGNFSDGKMGRFFNHT syndrome LVLLPDGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTP coronavirus ATDCSDGNYNRNASLNSFKEYFNLRNCTFMYTYNITEDEILE isolate WFGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYS Riyadh_14_2013, IIPHSIRSIQSDRKAWAAFYVYKLQPLTFLLDFSVDGYIRRA spike protein IDCGFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQA (amino acid)
EGVECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSV
NDFtCSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAG
PISQFNYKQSFSNPTCLILATVPHNLTTITKPLKYSYINKCS
RLLSDDRTEVPQLVNANQYSPCVSIVPSTVWEDGDYYRKQLS
PLEGGGWLVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKL
EFANDTKIASQLGNCVEYSLYGVSGRGVFQNCTAVGVRQQRF
VYDAYQNLVGYYSDDGNYYCLRACVSVPVSVIYDKETKTHAT
LFGSVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCV
LGLVNSSLFVEDCKLPLGQSLCALPDTPSTLTPRSVRSVPGE
MRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTT
IQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINqALHGANL
RQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSISTG
SRSARSAIEDLLFDKVTIADPGYMQGYDDCMQQGPASARDLI

CAQYVAGYKVLPPLMDVNMEAAYTSSLLGSIAGVGWTAGLSS
FAAIPFAQSIFYRLNGVGITQQVLSENQKLIANKFNQALGAM
QTGFTTTNEAFrKVQDAVNNNAQALSKLASELSNTFGAISAS
IGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESA
ALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVVNAPNGL
YFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNGYFIKTN
NTRIVDEWSYTGSSFYAPEPITSLNTKYVAPQVTYQNISTNL
PPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTLL
DLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWPWYIWLG
FIAGLVALALCVFFILCCTGCGTNCMGKLKCNRCCDRYEEYD LEPHKVHVH MERS S FL
MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDK 25 SPIKE
TWPRPIDVSKADGIIYPQGRTYSNITITYQGLFPYQGDHGDM 2cEMC/2012
YVYSAGHATGTTPQKLFVANYSQDVKQFANGFVVRIGAAANS (XBaI change
TGTVIISPSTSATIRKIYPAFMLGSSVGNFSDGKMGRFFNHT (T to G))
LVLLPDGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTP (amino acid)
ATDCSDGNYNRNASLNSFKEYFNLRNCTFMYTYNITEDEILE
WFGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYS
IIPHSIRSIQSDRKAWAAFYVYKLQPLTFLLDFSVDGYIRRA
IDCGFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQA
EGVECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSV
NDFTCSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAG
PISQFNYKQSFSNPTCLILATVPHNLTTITKPLKYSYINKCS
RLLSDDRTEVPQLVNANQYSPCVSIVPSTVWEDGDYYRKQLS
PLEGGGWLVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKL
EFANDTKIASQLGNCVEYSLYGVSGRGVFQNCTAVGVRQQRF
VYDAYQNLVGYYSDDGNYYCLRACVSVPVSVIYDKETKTHAT
LFGSVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCV
LGLVNSSLFVEDCKLPLGQSLCALPDTPSTLTPRSVRSVPGE
MRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTT
IQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINQALHGANL
RQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSISTG
SRSARSAIEDLLFDKVTIADPGYMQGYDDCMQQGPASARDLI
CAQYVAGYKVLPPLMDVNMEAAYTSSLLGSIAGVGWTAGLSS
FAAIPFAQSIFYRLNGVGITQQVLSENQKLIANKFNQALGAM
QTGFTTTNEAFQKVQDAVNNNAQALSKLASELSNTFGAISAS
IGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESA
ALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVVNAPNGL
YFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNGYFIKTN
NTRIVDEWSYTGSSFYAPEPITSLNTKYVAPQVTYQNISTNL
PPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTLL
DLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWPWYIWLG
FIAGLVALALCVFFILCCTGCGTNCMGKLKCNRCCDRYEEYD LEPHKVHVH Novel_MERS_S2_
MIHSVFLLMFLLTPTESDCKLPLGQSLCALPDTPSTLTPRSV 26 subunit_trimeric
RSVPGEMRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQ vaccine (amino
EYIQTTIQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINQA acid)
LHGANLRQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEP
VSISTGSRSARSAIEDLLFDKVTIADPGYMQGYDDCMQQGPA
SARDLICAQYVAGYKVLPPLMDVNMEAAYTSSLLGSIAGVGW
TAGLSSFAAIPFAQSIFYRLNGVGITQQVLSENQKLIANKFN
QALGAMQTGFTTTNEAFQKVQDAVNNNAQALSKLASELSNTF
GAISASIGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQL
VRSESAALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVV
NAPNGLYFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNG
YFIKTNNTRIVDEWSYTGSSFYAPEPITSLNTKYVAPQVTYQ

NISTNLPPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQ
INTTLLDLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWP DKIEEILSKIYHIENEIARIKKLIGEA
Isolate A1- MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDK 27 Hasa_1_2013
TWPRPIDVSKADGIIYPQGRTYSNITITYQGLFPYQGDHGDM (NCBI accession
YVYSAGHATGTTPQKLFVANYSQDVKQFANGFVVRIGAAANS #AGN70962)
TGTVIISPSTSATIRKIYPAFMLGSSVGNFSDGKMGRFFNHT
LVLLPDGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTP
ATDCSDGNYNRNASLNSFKEYFNLRNCTFMYTYNITEDEILE
WFGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYS
IIPHSIRSIQSDRKAWAAFYVYKLQPLTFLLDFSVDGYIRRA
IDCGFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQA
EGVECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSV
NDFTCSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAG
PISQFNYKQSFSNPTCLILATVPHNLTTITKPLKYSYINKCS
RLLSDDRTEVPQLVNANQYSPCVSIVPSTVWEDGDYYRKQLS
PLEGGGWLVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKL
EFANDTKIASQLGNCVEYSLYGVSGRGVFQNCTAVGVRQQRF
VYDAYQNLVGYYSDDGNYYCLRACVSVPVSVIYDKETKTHAT
LFGSVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCV
LGLVNSSLFVEDCKLPLGQSLCALPDTPSTLTPRSVRSVPGE
MRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTT
IQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINQALHGANL
RQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSISTG
SRSARSAIEDLLFDKVTIADPGYMQGYDDCMQQGPASARDLI
CAQYVAGYKVLPPLMDVNMEAAYTSSLLGSIAGVGWTAGLSS
FAAIPFAQSIFYRLNGVGITQQVLSENQKLIANKFNQALGAM
QTGFTTTNEAFRKVQDAVNNNAQALSKLASELSNTFGAISAS
IGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESA
ALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVVNAPNGL
YFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNGYFIKTN
NTRIVDEWSYTGSSFYAPEPITSLNTKYVAPHVTYQNISTNL
PPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTLL
DLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWPWYIWLG
FIAGLVALALCVFFILCCTGCGTNCMGKLKCNRCCDRYEEYD LEPHKVHVH Middle East
MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDK 28 respiratory
TWPRPIDVSKADGIIYPQGRTYSNITITYQGLFPYQGDHGDM syndrome
YVYSAGHATGTTPQKLFVANYSQDVKQFANGFVVRIGAAANS coronavirus S
TGTVIISPSTSATIRKIYPAFMLGSSVGNFSDGKMGRFFNHT protein
LVLLPDGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTP UniProtKB-
ATDCSDGNYNRNASLNSFKEYFNLRNCTFMYTYNITEDEILE R9UQ53
WFGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYS
IIPHSIRSIQSDRKAWAAFYVYKLQPLTFLLDFSVDGYIRRA
IDCGFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQA
EGVECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSV
NDFTCSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAG
PISQFNYKQSFSNPTCLILATVPHNLTTITKPLKYSYINKCS
RLLSDDRTEVPQLVNANQYSPCVSIVPSTVWEDGDYYRKQLS
PLEGGGWLVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKL
EFANDTKIASQLGNCVEYSLYGVSGRGVFQNCTAVGVRQQRF
VYDAYQNLVGYYSDDGNYYCLRACVSVPVSVIYDKETKTHAT
LFGSVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCV
LGLVNSSLFVEDCKLPLGQSLCALPDTPSTLTPRSVRSVPGE
MRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTT
IQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINQALHGANL

RQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSISTG
SRSARSAIEDLLFDKVTIADPGYMQGYDDCMQQGPASARDLI
CAQYVAGYKVLPPLMDVNMEAAYTSSLLGSIAGVGWTAGLSS
FAAIPFAQSIFYRLNGVGITQQVLSENQKLIANKFNQALGAM
QTGFTTTNEAFRKVQDAVNNNAQALSKLASELSNTFGAISAS
IGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESA
ALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVVNAPNGL
YFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNGYFIKTN
NTRIVDEWSYTGSSFYAPEPITSLNTKYVAPHVTYQNISTNL
PPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTLL
DLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWPWYIWLG
FIAGLVALALCVFFILCCTGCGTNCMGKLKCNRCCDRYEEYD LEPHKVHVH Human ***SARS***
MFIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYY 29 coronavirus
PDEIFRSDTLYLTQDLFLPFYSNVTGFHTINHTFGNPVIPFK (***SARS***-CoV)
DGIYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTNVVIR (Severe acute
ACNFELCDNPFFAVSKPMGTQTHTMIFDNAFNCTFEYISDAF respiratory
SLDVSEKSGNFKHLREFVFKNKDGFLYVYKGYQPIDVVRDLP syndrome
SGFNTLKPIFKLPLGINITNFRAILTAFSPAQDIWGTSAAAY coronavirus)
FVGYLKPTTFMLKYDENGTITDAVDCSQNPLAELKCSVKSFE Spike
IDKGIYQTSNFRVVPSGDVVRFPNITNLCPFGEVFNATKFPS glycoprotein
VYAWERKKISNCVADYSVLYNSTFFSTFKCYGVSATKLNDLC UniProtKB-
FSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCV P59594
LAWNTRNIDATSTGNYNYKYRYLRHGKLRPFERDISNVPFSP
DGKPCTPPALNCYWPLNDYGFYTTTGIGYQPYRVVVLSFELL
NAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTPSSKRFQ
PFQQFGRDVSDFTDSVRDPKTSEILDISPCSFGGVSVITPGT
NASSEVAVLYQDVNCTDVSTAIHADQLTPAWRIYSTGNNVFQ
TQAGCLIGAEHVDTSYECDIPIGAGICASYHTVSLLRSTSQK
SIVAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMA
KTSVDCNMYICGDSTECANLLLQYGSFCTQLNRALSGIAAEQ
DRNTREVFAQVKQMYKTPTLKYFGGFNFSQILPDPLKPTKRS
FIEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNGL
TVLPPLLTDDMIAAYTAALVSGTATAGWTFGAGAALQIPFAM
QMAYRFNGIGVTQNVLYENQKQIANQFNKAISQIQESLTTTS
TALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRL
DKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAA
TKMSECVLGQSKRVDFCGKGYHLMSFPQAAPHGVVFLHVTYV
PSQERNFTTAPAICHEGKAYFPREGVFVFNGTSWFITQRNFF
SPQIITTDNTFVSGNCDVVIGIINNTVYDPLQPELDSFKEEL
DKYFKNHTSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLN
ESLIDLQELGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCC
MTSCCSCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT Human
MFLILLISLPTAFAVIGDLKCTSDNINDKDTGPPPISTDTVD 30 coronavirus OC43
VTNGLGTYYVLDRVYLNTTLFLNGYYPTSGSTYRNMALKGSV (HCoV-OC43)
LLSRLWFKPPFLSDFINGIFAKVKNTKVIKDRVMYSEFPAIT Spike
IGSTFVNTSYSVVVQPRTINSTQDGDNKLQGLLEVSVCQYNM glycoprotein
CEYPQTICHPNLGNHRKELWHLDTGVVSCLYKRNFTYDVNAD UniProtKB-
YLYFHFYQEGGTFYAYFTDTGVVTKFLFNVYLGMALSHYYVM P36334
PLTCNSKLTLEYWVTPLTSRQYLLAFNQDGIIFNAEDCMSDF
MSEIKCKTQSIAPPTGVYELNGYTVQPIADVYRRKPNLPNCN
IEAWLNDKSVPSPLNWERKTFSNCNFNMSSLMSFIQADSFTC
NNIDAAKIYGMCFSSITIDKFAIPNGRKVDLQLGNLGYLQSF
NYRIDTTATSCQLYYNLPAANVSVSRFNPSTWNKRFGFIEDS
VFKPRPAGVLTNHDVVYAQHCFKAPKNFCPCKLNGSCVGSGP

GKNNGIGTCPAGTNYLTCDNLCTPDPITFTGTYKCPQTKSLV
GIGEHCSGLAVKSDYCGGNSCTCRPQAFLGWSADSCLQGDKC
NIFANFILHDVNSGLTCSTDLQKANTDIILGVCVNYDLYGIL
GQGIFVEVNATYYNSWQNLLYDSNGNLYGFRDYIINRTFMIR
SCYSGRVSAAFHANSSEPALLFRNIKCNYVFNNSLTRQLQPI
NYFDSYLGCVVNAYNSTAISVQTCDLTVGSGYCVDYSKNRRS
RGAITTGYRFTNFEPFTVNSVNDSLEPVGGLYEIQIPSEFTI
GNMVEFIQTSSPKVTIDCAAFVCGDYAACKSQLVEYGSFCDN
INAILTEVNELLDTTQLQVANSLMNGVTLSTKLKDGVNFNVD
DINFSPVLGCLGSECSKASSRSAIEDLLFDKVKLSDVGFVEA
YNNCTGGAEIRDLICVQSYKGIKVLPPLLSENQISGYTLAAT
SASLFPPWTAAAGVPFYLNVQYRINGLGVTMDVLSQNQKLIA
NAFNNALYAIQEGFDATNSALVKIQAVVNANAEALNNLLQQL
SNRFGAISASLQEILSRLDALEAEAQIDRLINGRLTALNAYV
SQQLSDSTLVKFSAAQAMEKVNECVKSQSSRINFCGNGNHII
SLVQNAPYGLYFIHFSYVPTKYVTARVSPGLCIAGDRGIAPK
SGYFVNVNNTWMYTGSGYYYPEPITENNVVVMSTCAVNYTKA
PYVMLNTSIPNLPDFKEELDQWFKNQTSVAPDLSLDYINVTF
LDLQVEMNRLQEAIKVLNQSYINLKDIGTYEYYVKWPWYVWL
LICLAGVAMLVLLFFICCCTGCGTSCFKKCGGCCDDYTGYQE LVIKTSHDD Human
MFLIIFILPTTLAVIGDFNCTNSFINDYNKTIPRISEDVVDV 31 coronavirus
SLGLGTYYVLNRVYLNTTLLFTGYFPKSGANFRDLALKGSIY HKU1 (isolate
LSTLWYKPPFLSDFNNGIFSKVKNTKLYVNNTLYSEFSTIVI N5) (HCoV-
GSVFVNTSYTIVVQPHNGILEITACQYTMCEYPHTVCKSKGS HKU1) Spike
IRNESWHIDSSEPLCLFKKNFTYNVSADWLYFHFYQERGVFY glycoprotein
AYYADVGMPTTFLFSLYLGTILSHYYVMPLTCNAISSNTDNE UniProtKB-
TLEYWVTPLSRRQYLLNFDEHGVITNAVDCSSSFLSEIQCKT Q0ZME7
QSFAPNTGVYDLSGFTVKPVATVYRRIPNLPDCDIDNWLNNV
SVPSPLNWERRIFSNCNFNLSTLLRLVHVDSFSCNNLDKSKI
FGSCFNSITVDKFAIPNRRRDDLQLGSSGFLQSSNYKIDISS
SSCQLYYSLPLVNVTINNFNPSSWNRRYGFGSFNLSSYDVVY
SDHCFSVNSDFCPCADPSVVNSCAKSKPPSAICPAGTKYRHC
DLDTTLYVKNWCRCSCLPDPISTYSPNTCPQKKVVVGIGEHC
PGLGINEEKCGTQLNHSSCFCSPDAFLGWSFDSCISNNRCNI
FSNFIFNGINSGTTCSNDLLYSNTEISTGVCVNYDLYGITGQ
GIFKEVSAAYYNNWQNLLYDSNGNIIGFKDFLTNKTYTILPC
YSGRVSAAFYQNSSSPALLYRNLKCSYVLNNISFISQPFYFD
SYLGCVLNAVNLTSYSVSSCDLRMGSGFCIDYALPSSRRKRR
GISSPYRFVTFEPFNVSFVNDSVETVGGLFEIQIPTNFTIAG
HEEFIQTSSPKVTIDCSAFVCSNYAACHDLLSEYGTFCDNIN
SILNEVNDLLDITQLQVANALMQGVTLSSNLNTNLHSDVDNI
DFKSLLGCLGSQCGSSSRSLLEDLLFNKVKLSDVGFVEAYNN
CTGGSEIRDLLCVQSFNGIKVLPPILSETQISGYTTAATVAA
MFPPWSAAAGVPFSLNVQYRINGLGVTMDVLNKNQKLIANAF
NKALLSIQNGFTATNSALAKIQSVVNANAQALNSLLQQLFNK
FGAISSSLQEILSRLDNLEAQVQIDRLINGRLTALNAYVSQQ
LSDITLIKAGASRAIEKVNECVKSQSPRINFCGNGNHILSLV

QNAPYGLLFIHFSYKPTSFKTVLVSPGLCLSGDRGIAPKQGY
FIKQNDSWMFTGSSYYYPEPISDKNVVFMNSCSVNFTKAPFI
YLNNSIPNLSDFEAELSLWFKNHTSIAPNLTFNSHINATFLD
LYYEMNVIQESIKSLNSSFINLKEIGTYEMYVKWPWYIWLLI
VILFIIFLMILFFICCCTGCGSACFSKCHNCCDEYGGHNDFV IKASHDD Novel_***SARS***_S2
MFIFLLFLTLTSGSDLDRALSGIAAEQDRNTREVFAQVKQMY 32

KTPTLKYFGGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADA
GFMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAY
TAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNV
LYENQKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNAQ
ALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITG
RLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVD
FCGKGYHLMSFPQAAPHGVVFLHVTYVPSQERNFTTAPAICH
EGKAYFPREGVFVFNGTSWFITQRNFFSPQIITTDNTFVSGN
CDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLG
DISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQY
IKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACSCG SCCKFDEDDSEPVLKGVKLHYT
Novel_MERS_S2 MIHSVFLLMFLLTPTESDCKLPLGQSLCALPDTPSTLTPRSV 33
RSVPGEMRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQ
EYIQTTIQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINQA
LHGANLRQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEP
VSISTGSRSARSAIEDLLFDKVTIADPGYMQGYDDCMQQGPA
SARDLICAQYVAGYKVLPPLMDVNMEAAYTSSLLGSIAGVGW
TAGLSSFAAIPFAQSIFYRLNGVGITQQVLSENQKLIANKFN
QALGAMQTGFTTTNEAFQKVQDAVNNNAQALSKLASELSNTF
GAISASIGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQL
VRSESAALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVV
NAPNGLYFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNG
YFIKTNNTRIVDEWSYTGSSFYAPEPITSLNTKYVAPQVTYQ
NISTNLPPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQ
INTTLLDLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWP Novel_Trimeric_
MFIFLLFLTLTSGSDLDRALSGIAAEQDRNTREVFAQVKQMY 34 ***SARS***_S2
KTPTLKYFGGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADA
GFMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAY
TAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNV
LYENQKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNAQ
ALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITG
RLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRVD
FCGKGYHLMSFPQAAPHGVVFLHVTYVPSQERNFTTAPAICH
EGKAYFPREGVFVFNGTSWFITQRNFFSPQIITTDNTFVSGN
CDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLG
DISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQY
IKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCLKGACSCG SCCKFDEDDSEPVLKGVKLHYT

TABLE-US-00013 TABLE 12 Full-length Spike Glycoprotein Amino Acid Sequences (Homo sapiens strains) GenBank Accession Country Collection Date Release Date Virus Name AFY13307 United 2012 Sep. 11 2012 Dec. 5 Betacoronavirus England 1, Kingdom complete genome AFS88936 2012 Jun. 13 2012 Sep. 27 Human betacoronavirus 2c EMC/2012, complete genome AGG22542 United 2012 Sep. 19 2013 Feb. 27 Human betacoronavirus 2c England- Kingdom Qatar/2012, complete genome AHY21469 Jordan 2012 2014 May 4 Human betacoronavirus 2c Jordan- N3/2012 isolate MG167, complete genome AGH58717 Jordan 2012 April 2013 Mar. 25 Human betacoronavirus 2c Jordan- N3/2012, complete genome AGV08444 Saudi 2013 May 7 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_12_2013, complete genome AGV08546 Saudi 2013 May 11 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_15_2013, complete genome AGV08535 Saudi 2013 May 12 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_16_2013, complete genome AGV08558 Saudi 2013 May 15 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_17_2013, complete genome AGV08573 Saudi 2013 May 23 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_18_2013, complete genome AGV08480 Saudi 2013 May 23 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_19_2013, complete genome AGN70962 Saudi 2013 May 9 2013 Jun. 10 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_1_2013, complete genome AGV08492 Saudi 2013 May 30 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_21_2013, complete genome AHI48517 Saudi 2013 May 2 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_25_2013, complete genome AGN70951 Saudi 2013 Apr. 21 2013 Jun. 10 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_2_2013, complete genome AGN70973 Saudi 2013 Apr. 22 2013 Jun. 10 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_3_2013, complete genome AGN70929 Saudi 2013 May 1 2013 Jun. 10 Middle East respiratory syndrome Arabia coronavirus isolate Al- Hasa_4_2013, complete genome AGV08408 Saudi 2012 Jun. 19 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Bisha_1_2012, complete genome AGV08467 Saudi 2013 May 13 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Buraidah_1_2013, complete genome AID50418 United 2013 Feb. 10 2014 Jun. 18 Middle East respiratory syndrome Kingdom coronavirus isolate England/2/2013, complete genome AJD81451 United 2013 Feb. 10 2015 Jan. 18 Middle East respiratory syndrome Kingdom coronavirus isolate England/3/2013, complete genome AJD81440 United 2013 Feb. 13 2015 Jan. 18 Middle East respiratory syndrome Kingdom coronavirus isolate England/4/2013, complete genome AHB33326 France 2013 May 7 2013 Dec. 7 Middle East respiratory syndrome coronavirus isolate FRA/UAE, complete genome AIZ48760 USA 2014 June 2014 Dec. 14 Middle East respiratory syndrome coronavirus isolate Florida/USA- 2_Saudi Arabia_2014, complete genome AGV08455 Saudi 2013 Jun. 4 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Hafr-Al- Batin_1_2013, complete genome AHI48561 Saudi 2013 Aug. 5 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Hafr-Al- Batin_2_2013, complete genome AHI48539 Saudi 2013 Aug. 28 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Hafr-Al- Batin_6_2013, complete genome AIZ74417 France 2013 Apr. 26 2015 Mar. 10 Middle East respiratory syndrome coronavirus isolate Hu-France (UAE) - FRA1_1627- 2013_BAL_Sanger, complete genome AIZ74433 France 2013 May 7 2015 Mar. 10 Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_IS_HTS, complete genome AIZ74439 France 2013 May 7 2015 Mar. 10 Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_InSpu_Sanger, complete genome AIZ74450 France 2013 May 7 2015 Mar. 10 Middle East respiratory syndrome coronavirus isolate Hu-France - FRA2_130569-2013_Isolate_Sanger, complete genome AKK52602 Saudi 2015 Feb. 10 2015 Jun. 8 Middle East respiratory syndrome Arabia coronavirus isolate Hu/Riyadh_KSA_2959_2015, complete genome AKK52612 Saudi 2015 Mar. 1 2015 Jun. 8 Middle East respiratory syndrome Arabia coronavirus isolate Hu/Riyadh_KSA_4050_2015, complete genome AHN10812 Saudi 2013 Nov. 6 2014 Mar. 24 Middle East respiratory syndrome Arabia coronavirus isolate Jeddah_1_2013, complete genome AID55071 Saudi 2014 Apr. 21 2014 Nov. 12 Middle East respiratory syndrome Arabia coronavirus isolate Jeddah_C10306/KSA/2014-04-20, complete genome AID55066 Saudi 2014 2014 Nov. 12 Middle East respiratory syndrome Arabia coronavirus isolate Jeddah_C7149/KSA/2014-04-05, complete genome AID55067 Saudi 2014 2014 Nov. 12 Middle East respiratory syndrome Arabia coronavirus isolate Jeddah_C7569/KSA/2014-04-03, complete genome AID55068 Saudi 2014 Apr. 7 2014 Nov. 12 Middle East respiratory syndrome Arabia coronavirus isolate Jeddah_C7770/KSA/2014-04-07, complete genome AID55069 Saudi 2014 Apr. 12 2014 Nov. 12 Middle East respiratory syndrome Arabia coronavirus isolate Jeddah_C8826/KSA/2014-04-12, complete genome AID55070 Saudi 2014 Apr. 14 2014 Nov. 12 Middle East respiratory syndrome Arabia coronavirus isolate Jeddah_C9055/KSA/2014-04-14, complete genome AHE78108 Saudi 2013 Nov. 5 2014 May 1 Middle East respiratory syndrome Arabia coronavirus isolate MERS-CoV- Jeddah-human-1, complete genome AKL59401 South 2015 May 20 2015 Jun. 9 Middle East respiratory syndrome Korea coronavirus isolate MERS- CoV/KOR/KNIH/002_05_2015, complete genome ALD51904 Thailand 2015 Jun. 17 2015 Jul. 7 Middle East respiratory syndrome coronavirus isolate MERS-CoV/THA/CU/17_06_2015, complete genome AID55072 Saudi 2014 Apr. 15 2014 Nov. 12 Middle East respiratory syndrome Arabia coronavirus isolate Makkah_C9355/KSA/Makkah/2014- 04-15, complete genome AHC74088 Qatar 2013 Oct. 13 2013 Dec. 23 Middle East respiratory syndrome coronavirus isolate Qatar3, complete genome AHC74098 Qatar 2013 Oct. 17 2013 Dec. 23 Middle East respiratory syndrome coronavirus isolate Qatar4, complete genome AHI48572 Saudi 2013 Aug. 15 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Riyadh_14_2013, complete genome AGV08379 Saudi 2012 Oct. 23 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Riyadh_1_2012, complete genome AID55073 Saudi 2014 Apr. 22 2014 Nov. 12 Middle East respiratory syndrome Arabia coronavirus isolate Riyadh_2014KSA_683/KSA/2014, complete genome AGV08584 Saudi 2012 Oct. 30 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Riyadh_2_2012, complete genome AGV08390 Saudi 2013 Feb. 5 2013 Sep. 17 Middle East respiratory syndrome Arabia coronavirus isolate Riyadh_3_2013, complete genome

AHI48605 Saudi 2013 Mar. 1 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Riyadh_4_2013, complete genome AHI48583 Saudi 2013 Jul. 2 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Riyadh_5_2013, complete genome AHI48528 Saudi 2013 Jul. 17 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Riyadh_9_2013, complete genome AHI48594 Saudi 2013 Jun. 12 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Taif_1_2013, complete genome AHI48550 Saudi 2013 Jun. 12 2014 Feb. 6 Middle East respiratory syndrome Arabia coronavirus isolate Wadi-Ad- Dawasir_1_2013, complete genome AIY60558 United 2014 Mar. 7 2014 Dec. 6 Middle East respiratory syndrome Arab coronavirus strain Abu Emirates Dhabi/Gayathi_UAE_2_2014, complete genome AIY60538 United 2014 Apr. 10 2014 Dec. 6 Middle East respiratory syndrome Arab coronavirus strain Abu Emirates Dhabi_UAE_16_2014, complete genome AIY60528 United 2014 Apr. 10 2014 Dec. 6 Middle East respiratory syndrome Arab coronavirus strain Abu Emirates Dhabi_UAE_18_2014, complete genome AIY60588 United 2014 Apr. 13 2014 Dec. 6 Middle East respiratory syndrome Arab coronavirus strain Abu Emirates Dhabi_UAE_26_2014, complete genome AIY60548 United 2014 Apr. 19 2014 Dec. 6 Middle East respiratory syndrome Arab coronavirus strain Abu Emirates Dhabi_UAE_30_2014, complete genome AIY60568 United 2014 Apr. 17 2014 Dec. 6 Middle East respiratory syndrome Arab coronavirus strain Abu Emirates Dhabi_UAE_33_2014, complete genome AIY60518 United 2014 Apr. 7 2014 Dec. 6 Middle East respiratory syndrome Arab coronavirus strain Abu Emirates Dhabi_UAE_8_2014, complete genome AIY60578 United 2013 Nov. 15 2014 Dec. 6 Middle East respiratory syndrome Arab coronavirus strain Abu Emirates Dhabi_UAE_9_2013, complete genome AKJ80137 China 2015 May 27 2015 Jun. 5 Middle East respiratory syndrome coronavirus strain ChinaGD01, complete genome AHZ64057 USA 2014 May 10 2014 May 14 Middle East respiratory syndrome coronavirus strain Florida/USA- 2_Saudi Arabia_2014, complete genome AKM76229 Oman 2013 Oct. 28 2015 Jun. 23 Middle East respiratory syndrome coronavirus strain Hu/Oman_2285_2013, complete genome AKM76239 Oman 2013 Dec. 28 2015 Jun. 23 Middle East respiratory syndrome coronavirus strain Hu/Oman_2874_2013, complete genome AKI29284 Saudi 2015 Jan. 6 2015 May 27 Middle East respiratory syndrome Arabia coronavirus strain Hu/Riyadh-KSA- 2049/2015, complete genome AKI29265 Saudi 2015 Jan. 21 2015 May 27 Middle East respiratory syndrome Arabia coronavirus strain Hu/Riyadh-KSA- 2343/2015, complete genome AKI29255 Saudi 2015 Jan. 21 2015 May 27 Middle East respiratory syndrome Arabia coronavirus strain Hu/Riyadh-KSA-

2345/2015, complete genome AKI29275 Saudi 2015 Jan. 26 2015 May 27 Middle East respiratory syndrome Arabia coronavirus strain Hu/Riyadh-KSA- 2466/2015, complete genome AKK52582 Saudi 2015 Feb. 10 2015 Jun. 8 Middle East respiratory syndrome Arabia coronavirus strain Hu/Riyadh_KSA_2959_2015, complete genome AKK52592 Saudi 2015 Mar. 1 2015 Jun. 8 Middle East respiratory syndrome Arabia coronavirus strain Hu/Riyadh_KSA_4050_2015, complete genome AHZ58501 USA 2014 Apr. 30 2014 May 13 Middle East respiratory syndrome coronavirus strain Indiana/USA- 1_Saudi Arabia_2014, complete genome AGN52936 United 2013 2013 Jun. 10 Middle East respiratory syndrome Arab coronavirus, complete genome Emirates

TABLE-US-00014 TABLE 13 SEQ ID Description Sequence NO: MeV Nucleic Acid Sequences
GC_F_MEASLES_B3.1 TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT 35 Sequence, NT (5'
CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA UTR, ORF, 3'
GAAATATAAGAGCCACCATGGGTCTCAAGGTGAACGTC UTR)
TCTGCCGTATTCATGGCAGTACTGTTAACTCTCCAAACA Sequence Length:
CCCGCCGGTCAAATTCATTGGGGCAATCTCTCTAAGAT 1864
AGGGGTAGTAGGAATAGGAAGTGCAAGCTACAAAGTT
ATGACTCGTTCCAGCCATCAATCATTAGTCATAAAATT
AATGCCCAATATAACTCTCCTCAATAACTGCACGAGGG
TAGAGATTGCAGAATACAGGAGACTACTAAGAACAGTT
TTGGAACCAATTAGGGATGCACTTAATGCAATGACCCA
GAACATAAGGCCGGTTCAGAGCGTAGCTTCAAGTAGGA
GACACAAGAGATTTGCGGGAGTAGTCCTGGCAGGTGCG
GCCCTAGGTGTTGCCACAGCTGCTCAGATAACAGCCGG
CATTGCACTTCACCGGTCCATGCTGAACTCTCAGGCCAT
CGACAATCTGAGAGCGAGCCTGGAAACTACTAATCAGG
CAATTGAGGCAATCAGACAAGCAGGGCAGGAGATGAT

ATTGGCTGTTCAGGGTGTCCAAGACTACATCAATAATG
AGCTGATACCGTCTATGAACCAGCTATCTTGTGATCTA
ATCGGTCAGAAGCTCGGGCTCAAATTGCTTAGATACTA
TACAGAAATCCTGTCATTATTTGGCCCCAGCCTACGGG
ACCCCATATCTGCGGAGATATCTATCCAGGCTTTGAGTT
ATGCACTTGGAGGAGATATCAATAAGGTGTTAGAAAAG
CTCGGATACAGTGGAGGCGATTTACTAGGCATCTTAGA
GAGCAGAGGAATAAAGGCTCGGATAACTCACGTCGAC
ACAGAGTCCTACTTCATAGTCCTCAGTATAGCCTATCCG
ACGCTGTCCGAGATTAAGGGGGTGATTGTCCACCGGCT
AGAGGGGGTCTCGTACAACATAGGCTCTCAAGAGTGGT
ATACCACTGTGCCCAAGTATGTTGCAACCCAAGGGTAC
CTTATCTCGAATTTTGATGAGTCATCATGTACTTTCATG
CCAGAGGGGACTGTGTGCAGCCAAAATGCCTTGTACCC
GATGAGTCCTCTGCTCCAAGAATGCCTCCGGGGGTCCA
CCAAGTCCTGTGCTCGTACACTCGTATCCGGGTCTTTTG
GGAACCGGTTCATTTTATCACAAGGGAACCTAATAGCC
AATTGTGCATCAATTCTTTGTAAGTGTTACACAACAGGT
ACGATTATTAATCAAGACCCTGACAAGATCCTAACATA
CATTGCTGCCGATCGCTGCCCGGTAGTCGAGGTGAACG
GCGTGACCATCCAAGTCGGGAGCAGGAGGTATCCAGA
CGCTGTGTACTTGCACAGAATTGACCTCGGTCCTCCCAT
ATCATTGGAGAGGTTGGACGTAGGGACAAATCTGGGG
AATGCAATTGCCAAATTGGAGGATGCCAAGGAATTGTT
GGAATCATCGGACCAGATATTGAGAAGTATGAAAGGTT
TATCGAGCACTAGCATAGTCTACATCCTGATTGCAGTG
TGTCTTGGAGGGTTGATAGGGATCCCCACTTTAATATGT
TGCTGCAGGGGGCGTTGTAACAAAAAGGGAGAACAAG
TTGGTATGTCAAGACCAGGCCTAAAGCCTGACCTTACA
GGAACATCAAAATCCTATGTAAGATCGCTTTGATGATA
ATAGGCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTT
GGGCCTCCCCCCAGCCCCTCCTCCCCTTCCTGCACCCGT
ACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC GC_F_MEASLES_B3.1
ATGGGTCTCAAGGTGAACGTCTCTGCCGTATTCATGGC 36 ORF Sequence, NT
AGTACTGTTAACTCTCCAAACACCCGCCGGTCAAATTC
ATTGGGGCAATCTCTCTAAGATAGGGGTAGTAGGAATA
GGAAGTGCAAGCTACAAAGTTATGACTCGTTCCAGCCA
TCAATCATTAGTCATAAAATTAATGCCCAATATAACTCT
CCTCAATAACTGCACGAGGGTAGAGATTGCAGAATACA
GGAGACTACTAAGAACAGTTTTGGAACCAATTAGGGAT
GCACTTAATGCAATGACCCAGAACATAAGGCCGGTTCA
GAGCGTAGCTTCAAGTAGGAGACACAAGAGATTTGCG
GGAGTAGTCCTGGCAGGTGCGGCCCTAGGTGTTGCCAC
AGCTGCTCAGATAACAGCCGGCATTGCACTTCACCGGT
CCATGCTGAACTCTCAGGCCATCGACAATCTGAGAGCG
AGCCTGGAAACTACTAATCAGGCAATTGAGGCAATCAG
ACAAGCAGGGCAGGAGATGATATTGGCTGTTCAGGGTG
TCCAAGACTACATCAATAATGAGCTGATACCGTCTATG
AACCAGCTATCTTGTGATCTAATCGGTCAGAAGCTCGG
GCTCAAATTGCTTAGATACTATACAGAAATCCTGTCATT
ATTTGGCCCCAGCCTACGGGACCCCATATCTGCGGAGA
TATCTATCCAGGCTTTGAGTTATGCACTTGGAGGAGAT
ATCAATAAGGTGTTAGAAAAGCTCGGATACAGTGGAG
GCGATTTACTAGGCATCTTAGAGAGCAGAGGAATAAAG

GCTCGGATAACTCACGTCGACACAGAGTCCTACTTCAT
AGTCCTCAGTATAGCCTATCCGACGCTGTCCGAGATTA
AGGGGGTGATTGTCCACCGGCTAGAGGGGGTCTCGTAC
AACATAGGCTCTCAAGAGTGGTATACCACTGTGCCCAA
GTATGTTGCAACCCAAGGGTACCTTATCTCGAATTTTGA
TGAGTCATCATGTACTTTCATGCCAGAGGGGACTGTGT
GCAGCCAAAATGCCTTGTACCCGATGAGTCCTCTGCTC
CAAGAATGCCTCCGGGGGTCCACCAAGTCCTGTGCTCG
TACACTCGTATCCGGGTCTTTTGGGAACCGGTTCATTTT
ATCACAAGGGAACCTAATAGCCAATTGTGCATCAATTC
TTTGTAAGTGTTACACAACAGGTACGATTATTAATCAA
GACCCTGACAAGATCCTAACATACATTGCTGCCGATCG
CTGCCCGGTAGTCGAGGTGAACGGCGTGACCATCCAAG
TCGGGAGCAGGAGGTATCCAGACGCTGTGTACTTGCAC
AGAATTGACCTCGGTCCTCCCATATCATTGGAGAGGTT
GGACGTAGGGACAAATCTGGGGAATGCAATTGCCAAA
TTGGAGGATGCCAAGGAATTGTTGGAATCATCGGACCA
GATATTGAGAAGTATGAAAGGTTTATCGAGCACTAGCA
TAGTCTACATCCTGATTGCAGTGTGTCTTGGAGGGTTGA
TAGGGATCCCCACTTTAATATGTTGCTGCAGGGGGCGT
TGTAACAAAAAGGGAGAACAAGTTGGTATGTCAAGAC
CAGGCCTAAAGCCTGACCTTACAGGAACATCAAAATCC TATGTAAGATCGCTTTGA
GC_F_MEASLES_B3.1 G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT 37 mRNA Sequence
ATAAGAGCCACCATGGGTCTCAAGGTGAACGTCTCTGC (assumes T100 tail)
CGTATTCATGGCAGTACTGTTAACTCTCCAAACACCCG mRNA Sequence
CCGGTCAAATTCATTGGGGCAATCTCTCTAAGATAGGG Length: 1925
GTAGTAGGAATAGGAAGTGCAAGCTACAAAGTTATGA
CTCGTTCCAGCCATCAATCATTAGTCATAAAATTAATGC
CCAATATAACTCTCCTCAATAACTGCACGAGGGTAGAG
ATTGCAGAATACAGGAGACTACTAAGAACAGTTTTGGA
ACCAATTAGGGATGCACTTAATGCAATGACCCAGAACA
TAAGGCCGGTTCAGAGCGTAGCTTCAAGTAGGAGACAC
AAGAGATTTGCGGGAGTAGTCCTGGCAGGTGCGGCCCT
AGGTGTTGCCACAGCTGCTCAGATAACAGCCGGCATTG
CACTTCACCGGTCCATGCTGAACTCTCAGGCCATCGAC
AATCTGAGAGCGAGCCTGGAAACTACTAATCAGGCAAT
TGAGGCAATCAGACAAGCAGGGCAGGAGATGATATTG
GCTGTTCAGGGTGTCCAAGACTACATCAATAATGAGCT
GATACCGTCTATGAACCAGCTATCTTGTGATCTAATCG
GTCAGAAGCTCGGGCTCAAATTGCTTAGATACTATACA
GAAATCCTGTCATTATTTGGCCCCAGCCTACGGGACCC
CATATCTGCGGAGATATCTATCCAGGCTTTGAGTTATGC
ACTTGGAGGAGATATCAATAAGGTGTTAGAAAAGCTCG
GATACAGTGGAGGCGATTTACTAGGCATCTTAGAGAGC
AGAGGAATAAAGGCTCGGATAACTCACGTCGACACAG
AGTCCTACTTCATAGTCCTCAGTATAGCCTATCCGACGC
TGTCCGAGATTAAGGGGGTGATTGTCCACCGGCTAGAG
GGGGTCTCGTACAACATAGGCTCTCAAGAGTGGTATAC
CACTGTGCCCAAGTATGTTGCAACCCAAGGGTACCTTA
TCTCGAATTTTGATGAGTCATCATGTACTTTCATGCCAG
AGGGGACTGTGTGCAGCCAAAATGCCTTGTACCCGATG
AGTCCTCTGCTCCAAGAATGCCTCCGGGGGTCCACCAA
GTCCTGTGCTCGTACACTCGTATCCGGGTCTTTTGGGAA
CCGGTTCATTTTATCACAAGGGAACCTAATAGCCAATT

GTGCATCAATTCTTTGTAAGTGTTACACAACAGGTACG
ATTATTAATCAAGACCCTGACAAGATCCTAACATACAT
TGCTGCCGATCGCTGCCCGGTAGTCGAGGTGAACGGCG
TGACCATCCAAGTCGGGAGCAGGAGGTATCCAGACGCT
GTGTACTTGCACAGAATTGACCTCGGTCCTCCCATATCA
TTGGAGAGGTTGGACGTAGGGACAAATCTGGGGAATG
CAATTGCCAAATTGGAGGATGCCAAGGAATTGTTGGAA
TCATCGGACCAGATATTGAGAAGTATGAAAGGTTTATC
GAGCACTAGCATAGTCTACATCCTGATTGCAGTGTGTC
TTGGAGGGTTGATAGGGATCCCCACTTTAATATGTTGCT
GCAGGGGGCGTTGTAACAAAAAGGGAGAACAAGTTGG
TATGTCAAGACCAGGCCTAAAGCCTGACCTTACAGGAA
CATCAAAATCCTATGTAAGATCGCTTTGATGATAATAG
GCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTTGGGC
CTCCCCCCAGCCCCTCCTCCCCTTCCTGCACCCGTACCC
CCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGCAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAATCTAG GC_F_MEASLES_D8
TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT 38 Sequence, NT (5'
CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA UTR, ORF, 3'
GAAATATAAGAGCCACCATGGGTCTCAAGGTGAACGTC UTR)
TCTGTCATATTCATGGCAGTACTGTTAACTCTTCAAACA Sequence Length:
CCCACCGGTCAAATCCATTGGGGCAATCTCTCTAAGAT 1864
AGGGGTGGTAGGGGTAGGAAGTGCAAGCTACAAAGTT
ATGACTCGTTCCAGCCATCAATCATTAGTCATAAAGTT
AATGCCCAATATAACTCTCCTCAACAATTGCACGAGGG
TAGGGATTGCAGAATACAGGAGACTACTGAGAACAGTT
CTGGAACCAATTAGAGATGCACTTAATGCAATGACCCA
GAATATAAGACCGGTTCAGAGTGTAGCTTCAAGTAGGA
GACACAAGAGATTTGCGGGAGTTGTCCTGGCAGGTGCG
GCCCTAGGCGTTGCCACAGCTGCTCAAATAACAGCCGG
TATTGCACTTCACCAGTCCATGCTGAACTCTCAAGCCAT
CGACAATCTGAGAGCGAGCCTAGAAACTACTAATCAGG
CAATTGAGGCAATCAGACAAGCAGGGCAGGAGATGAT
ATTGGCTGTTCAGGGTGTCCAAGACTACATCAATAATG
AGCTGATACCGTCTATGAATCAACTATCTTGTGATTTAA
TCGGCCAGAAGCTAGGGCTCAAATTGCTCAGATACTAT
ACAGAAATCCTGTCATTATTTGGCCCCAGCTTACGGGA
CCCCATATCTGCGGAGATATCTATCCAGGCTTTGAGCT
ATGCGCTTGGAGGAGATATCAATAAGGTGTTGGAAAAG
CTCGGATACAGTGGAGGTGATCTACTGGGCATCTTAGA
GAGCAGAGGAATAAAGGCCCGGATAACTCACGTCGAC
ACAGAGTCCTACTTCATTGTACTCAGTATAGCCTATCCG
ACGCTATCCGAGATTAAGGGGGTGATTGTCCACCGGCT
AGAGGGGGTCTCGTACAACATAGGCTCTCAAGAGTGGT
ATACCACTGTGCCCAAGTATGTTGCAACCCAAGGGTAC
CTTATCTCGAATTTTGATGAGTCATCATGCACTTTCATG
CCAGAGGGGACTGTGTGCAGCCAGAATGCCTTGTACCC
GATGAGTCCTCTGCTCCAAGAATGCCTCCGGGGGTCCA
CTAAGTCCTGTGCTCGTACACTCGTATCCGGGTCTTTCG
GGAACCGGTTCATTTTATCACAGGGGAACCTAATAGCC
AATTGTGCATCAATCCTTTGCAAGTGTTACACAACAGG
AACAATCATTAATCAAGACCCTGACAAGATCCTAACAT

ACATTGCTGCCGATCACTGCCCGGTGGTCGAGGTGAAT
GGCGTGACCATCCAAGTCGGGAGCAGGAGGTATCCGG
ACGCTGTGTACTTGCACAGGATTGACCTCGGTCCTCCC
ATATCTTTGGAGAGGTTGGACGTAGGGACAAATCTGGG
GAATGCAATTGCTAAGTTGGAGGATGCCAAGGAATTGT
TGGAGTCATCGGACCAGATATTGAGGAGTATGAAAGGT
TTATCGAGCACTAGTATAGTTTACATCCTGATTGCAGTG
TGTCTTGGAGGATTGATAGGGATCCCCGCTTTAATATGT
TGCTGCAGGGGGCGTTGTAACAAGAAGGGAGAACAAG
TTGGTATGTCAAGACCAGGCCTAAAGCCTGATCTTACA
GGAACATCAAAATCCTATGTAAGGTCACTCTGATGATA
ATAGGCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTT
GGGCCTCCCCCCAGCCCCTCCTCCCCTTCCTGCACCCGT
ACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC GC_F_MEASLES_D8
ATGGGTCTCAAGGTGAACGTCTCTGTCATATTCATGGC 39 ORF Sequence, NT
AGTACTGTTAACTCTTCAAACACCCACCGGTCAAATCC
ATTGGGGCAATCTCTCTAAGATAGGGGTGGTAGGGGTA
GGAAGTGCAAGCTACAAAGTTATGACTCGTTCCAGCCA
TCAATCATTAGTCATAAAGTTAATGCCCAATATAACTCT
CCTCAACAATTGCACGAGGGTAGGGATTGCAGAATACA
GGAGACTACTGAGAACAGTTCTGGAACCAATTAGAGAT
GCACTTAATGCAATGACCCAGAATATAAGACCGGTTCA
GAGTGTAGCTTCAAGTAGGAGACACAAGAGATTTGCGG
GAGTTGTCCTGGCAGGTGCGGCCCTAGGCGTTGCCACA
GCTGCTCAAATAACAGCCGGTATTGCACTTCACCAGTC
CATGCTGAACTCTCAAGCCATCGACAATCTGAGAGCGA
GCCTAGAAACTACTAATCAGGCAATTGAGGCAATCAGA
CAAGCAGGGCAGGAGATGATATTGGCTGTTCAGGGTGT
CCAAGACTACATCAATAATGAGCTGATACCGTCTATGA
ATCAACTATCTTGTGATTTAATCGGCCAGAAGCTAGGG
CTCAAATTGCTCAGATACTATACAGAAATCCTGTCATT
ATTTGGCCCCAGCTTACGGGACCCCATATCTGCGGAGA
TATCTATCCAGGCTTTGAGCTATGCGCTTGGAGGAGAT
ATCAATAAGGTGTTGGAAAAGCTCGGATACAGTGGAG
GTGATCTACTGGGCATCTTAGAGAGCAGAGGAATAAAG
GCCCGGATAACTCACGTCGACACAGAGTCCTACTTCAT
TGTACTCAGTATAGCCTATCCGACGCTATCCGAGATTA
AGGGGGTGATTGTCCACCGGCTAGAGGGGGTCTCGTAC
AACATAGGCTCTCAAGAGTGGTATACCACTGTGCCCAA
GTATGTTGCAACCCAAGGGTACCTTATCTCGAATTTTGA
TGAGTCATCATGCACTTTCATGCCAGAGGGGACTGTGT
GCAGCCAGAATGCCTTGTACCCGATGAGTCCTCTGCTC
CAAGAATGCCTCCGGGGGTCCACTAAGTCCTGTGCTCG
TACACTCGTATCCGGGTCTTTCGGGAACCGGTTCATTTT
ATCACAGGGGAACCTAATAGCCAATTGTGCATCAATCC
TTTGCAAGTGTTACACAACAGGAACAATCATTAATCAA
GACCCTGACAAGATCCTAACATACATTGCTGCCGATCA
CTGCCCGGTGGTCGAGGTGAATGGCGTGACCATCCAAG
TCGGGAGCAGGAGGTATCCGGACGCTGTGTACTTGCAC
AGGATTGACCTCGGTCCTCCCATATCTTTGGAGAGGTT
GGACGTAGGGACAAATCTGGGGAATGCAATTGCTAAGT
TGGAGGATGCCAAGGAATTGTTGGAGTCATCGGACCAG
ATATTGAGGAGTATGAAAGGTTTATCGAGCACTAGTAT
AGTTTACATCCTGATTGCAGTGTGTCTTGGAGGATTGAT

AGGGATCCCCGCTTTAATATGTTGCTGCAGGGGGCGTT
GTAACAAGAAGGGAGAACAAGTTGGTATGTCAAGACC
AGGCCTAAAGCCTGATCTTACAGGAACATCAAAATCCT ATGTAAGGTCACTCTGA
GC_F_MEASLES_D8 G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT 40

mRNA Sequence ATAAGAGCCACCATGGGTCTCAAGGTGAACGTCTCTGT (assumes T100 tail)
CATATTCATGGCAGTACTGTTAACTCTTCAAACACCCAC Sequence Length:
CGGTCAAATCCATTGGGGCAATCTCTCTAAGATAGGGG 1925
TGGTAGGGGTAGGAAGTGCAAGCTACAAAGTTATGACT
CGTTCCAGCCATCAATCATTAGTCATAAAGTTAATGCC
CAATATAACTCTCCTCAACAATTGCACGAGGGTAGGGA
TTGCAGAATACAGGAGACTACTGAGAACAGTTCTGGAA
CCAATTAGAGATGCACTTAATGCAATGACCCAGAATAT
AAGACCGGTTCAGAGTGTAGCTTCAAGTAGGAGACACA
AGAGATTTGCGGGAGTTGTCCTGGCAGGTGCGGCCCTA
GGCGTTGCCACAGCTGCTCAAATAACAGCCGGTATTGC
ACTTCACCAGTCCATGCTGAACTCTCAAGCCATCGACA
ATCTGAGAGCGAGCCTAGAAACTACTAATCAGGCAATT
GAGGCAATCAGACAAGCAGGGCAGGAGATGATATTGG
CTGTTCAGGGTGTCCAAGACTACATCAATAATGAGCTG
ATACCGTCTATGAATCAACTATCTTGTGATTTAATCGGC
CAGAAGCTAGGGCTCAAATTGCTCAGATACTATACAGA
AATCCTGTCATTATTTGGCCCCAGCTTACGGGACCCCAT
ATCTGCGGAGATATCTATCCAGGCTTTGAGCTATGCGC
TTGGAGGAGATATCAATAAGGTGTTGGAAAAGCTCGGA
TACAGTGGAGGTGATCTACTGGGCATCTTAGAGAGCAG
AGGAATAAAGGCCCGGATAACTCACGTCGACACAGAG
TCCTACTTCATTGTACTCAGTATAGCCTATCCGACGCTA
TCCGAGATTAAGGGGGTGATTGTCCACCGGCTAGAGGG
GGTCTCGTACAACATAGGCTCTCAAGAGTGGTATACCA
CTGTGCCCAAGTATGTTGCAACCCAAGGGTACCTTATC
TCGAATTTTGATGAGTCATCATGCACTTTCATGCCAGAG
GGGACTGTGTGCAGCCAGAATGCCTTGTACCCGATGAG
TCCTCTGCTCCAAGAATGCCTCCGGGGGTCCACTAAGT
CCTGTGCTCGTACACTCGTATCCGGGTCTTTCGGGAACC
GGTTCATTTTATCACAGGGGAACCTAATAGCCAATTGT
GCATCAATCCTTTGCAAGTGTTACACAACAGGAACAAT
CATTAATCAAGACCCTGACAAGATCCTAACATACATTG
CTGCCGATCACTGCCCGGTGGTCGAGGTGAATGGCGTG
ACCATCCAAGTCGGGAGCAGGAGGTATCCGGACGCTGT
GTACTTGCACAGGATTGACCTCGGTCCTCCCATATCTTT
GGAGAGGTTGGACGTAGGGACAAATCTGGGGAATGCA
ATTGCTAAGTTGGAGGATGCCAAGGAATTGTTGGAGTC
ATCGGACCAGATATTGAGGAGTATGAAAGGTTTATCGA
GCACTAGTATAGTTTACATCCTGATTGCAGTGTGTCTTG
GAGGATTGATAGGGATCCCCGCTTTAATATGTTGCTGC
AGGGGGCGTTGTAACAAGAAGGGAGAACAAGTTGGTA
TGTCAAGACCAGGCCTAAAGCCTGATCTTACAGGAACA
TCAAAATCCTATGTAAGGTCACTCTGATGATAATAGGC
TGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTTGGGCCTC
CCCCCAGCCCCTCCTCCCCTTCCTGCACCCGTACCCCCG
TGGTCTTTGAATAAAGTCTGAGTGGGCGGCAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAAAATCTAG

GC_H_MEASLES_B3 TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT 41 Sequence, NT (5'
CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA UTR, ORF, 3'
GAAATATAAGAGCCACCATGTCACCGCAACGAGACCG UTR)
GATAAATGCCTTCTACAAAGATAACCCTTATCCCAAGG Sequence Length:
GAAGTAGGATAGTTATTAACAGAGAACATCTTATGATT 2065
GACAGACCCTATGTTCTGCTGGCTGTTCTGTTCGTCATG
TTTCTGAGCTTGATCGGATTGCTGGCAATTGCAGGCATT
AGACTTCATCGGGCAGCCATCTACACCGCGGAGATCCA
TAAAAGCCTCAGTACCAATCTGGATGTGACTAACTCCA
TCGAGCATCAGGTCAAGGACGTGCTGACACCACTCTTT
AAAATCATCGGGGATGAAGTGGGCCTGAGAACACCTC
AGAGATTCACTGACCTAGTGAAATTCATCTCGGACAAG
ATTAAATTCCTTAATCCGGATAGGGAGTACGACTTCAG
AGATCTCACTTGGTGCATCAACCCGCCAGAGAGGATCA
AACTAGATTATGATCAATACTGTGCAGATGTGGCTGCT
GAAGAGCTCATGAATGCATTGGTGAACTCAACTCTACT
GGAGACCAGAACAACCACTCAGTTCCTAGCTGTCTCAA
AGGGAAACTGCTCAGGGCCCACTACAATCAGAGGTCA
ATTCTCAAACATGTCGCTGTCCTTGTTGGACTTGTACTT
AGGTCGAGGTTACAATGTGTCATCTATAGTCACTATGA
CATCCCAGGGAATGTATGGGGGAACCTACCTAGTTGAA
AAGCCTAATCTGAACAGCAAAGGGTCAGAGTTGTCACA
ACTGAGCATGTACCGAGTGTTTGAAGTAGGTGTGATCA
GAAACCCGGGTTTGGGGGCTCCGGTGTTCCATATGACA
AACTATTTTGAGCAACCAGTCAGTAATGGTCTCGGCAA
CTGTATGGTGGCTTTGGGGGAGCTCAAACTCGCAGCCC
TTTGTCACGGGGACGATTCTATCATAATTCCCTATCAGG
GATCAGGGAAAGGTGTCAGCTTCCAGCTCGTCAAGCTG
GGTGTCTGGAAATCCCCAACCGACATGCAATCCTGGGT
CCCCTTATCAACGGATGATCCAGTGGTAGACAGGCTTT
ACCTCTCATCTCACAGAGGTGTCATCGCTGACAATCAA
GCAAAATGGGCTGTCCCGACAACACGAACAGATGACA
AGTTGCGAATGGAGACATGCTTCCAGCAGGCGTGTAAA
GGTAAAATCCAAGCACTCTGCGAGAATCCCGAGTGGGT
ACCATTGAAGGATAACAGGATTCCTTCATACGGGGTCC
TGTCTGTTGATCTGAGTCTGACGGTTGAGCTTAAAATCA
AAATTGCTTCGGGATTCGGGCCATTGATCACACACGGC
TCAGGGATGGACCTATACAAATCCAACTGCAACAATGT
GTATTGGCTGACTATTCCGCCAATGAGAAATCTAGCCT
TAGGCGTAATCAACACATTGGAGTGGATACCGAGATTC
AAGGTTAGTCCCAACCTCTTCACTGTCCCAATTAAGGA
AGCAGGCGAAGACTGCCATGCCCCAACATACCTACCTG
CGGAGGTGGACGGTGATGTCAAACTCAGTTCCAACCTG
GTGATTCTACCTGGTCAAGATCTCCAATATGTTTTGGCA
ACCTACGATACCTCCAGGGTTGAGCATGCTGTGGTTTA
TTACGTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTA
TCCTTTTAGGTTGCCTATAAAGGGGGTCCCAATCGAAC
TACAAGTGGAATGCTTCACATGGGATCAAAAACTCTGG
TGCCGTCACTTCTGTGTGCTTGCGGACTCAGAATCCGGT
GGACTTATCACTCACTCTGGGATGGTGGGCATGGGAGT
CAGCTGCACAGCTACCCGGGAAGATGGAACCAATCGC
AGATAATGATAATAGGCTGGAGCCTCGGTGGCCAAGCT
TCTTGCCCCTTGGGCCTCCCCCCAGCCCCTCCTCCCCTT
CCTGCACCCGTACCCCCGTGGTCTTTGAATAAAGTCTG AGTGGGCGGC GC_H_MEASLES_B3

ATGTCACCGCAACGAGACCGGATAAATGCCTTCTACAA 42 ORF Sequence, NT
AGATAACCCTTATCCCAAGGGAAGTAGGATAGTTATTA
ACAGAGAACATCTTATGATTGACAGACCCTATGTTCTG
CTGGCTGTTCTGTTCGTCATGTTTCTGAGCTTGATCGGA
TTGCTGGCAATTGCAGGCATTAGACTTCATCGGGCAGC
CATCTACACCGCGGAGATCCATAAAAGCCTCAGTACCA
ATCTGGATGTGACTAACTCCATCGAGCATCAGGTCAAG
GACGTGCTGACACCACTCTTTAAAATCATCGGGGATGA
AGTGGGCCTGAGAACACCTCAGAGATTCACTGACCTAG
TGAAATTCATCTCGGACAAGATTAAATTCCTTAATCCG
GATAGGGAGTACGACTTCAGAGATCTCACTTGGTGCAT
CAACCCGCCAGAGAGGATCAAACTAGATTATGATCAAT
ACTGTGCAGATGTGGCTGCTGAAGAGCTCATGAATGCA
TTGGTGAACTCAACTCTACTGGAGACCAGAACAACCAC
TCAGTTCCTAGCTGTCTCAAAGGGAAACTGCTCAGGGC
CCACTACAATCAGAGGTCAATTCTCAAACATGTCGCTG
TCCTTGTTGGACTTGTACTTAGGTCGAGGTTACAATGTG
TCATCTATAGTCACTATGACATCCCAGGGAATGTATGG
GGGAACCTACCTAGTTGAAAAGCCTAATCTGAACAGCA
AAGGGTCAGAGTTGTCACAACTGAGCATGTACCGAGTG
TTTGAAGTAGGTGTGATCAGAAACCCGGGTTTGGGGGC
TCCGGTGTTCCATATGACAAACTATTTTGAGCAACCAG
TCAGTAATGGTCTCGGCAACTGTATGGTGGCTTTGGGG
GAGCTCAAACTCGCAGCCCTTTGTCACGGGGACGATTC
TATCATAATTCCCTATCAGGGATCAGGGAAAGGTGTCA
GCTTCCAGCTCGTCAAGCTGGGTGTCTGGAAATCCCCA
ACCGACATGCAATCCTGGGTCCCCTTATCAACGGATGA
TCCAGTGGTAGACAGGCTTTACCTCTCATCTCACAGAG
GTGTCATCGCTGACAATCAAGCAAAATGGGCTGTCCCG
ACAACACGAACAGATGACAAGTTGCGAATGGAGACAT
GCTTCCAGCAGGCGTGTAAAGGTAAAATCCAAGCACTC
TGCGAGAATCCCGAGTGGGTACCATTGAAGGATAACAG
GATTCCTTCATACGGGGTCCTGTCTGTTGATCTGAGTCT
GACGGTTGAGCTTAAAATCAAAATTGCTTCGGGATTCG
GGCCATTGATCACACACGGCTCAGGGATGGACCTATAC
AAATCCAACTGCAACAATGTGTATTGGCTGACTATTCC
GCCAATGAGAAATCTAGCCTTAGGCGTAATCAACACAT
TGGAGTGGATACCGAGATTCAAGGTTAGTCCCAACCTC
TTCACTGTCCCAATTAAGGAAGCAGGCGAAGACTGCCA
TGCCCCAACATACCTACCTGCGGAGGTGGACGGTGATG
TCAAACTCAGTTCCAACCTGGTGATTCTACCTGGTCAA
GATCTCCAATATGTTTTGGCAACCTACGATACCTCCAG
GGTTGAGCATGCTGTGGTTTATTACGTTTACAGCCCAA
GCCGCTCATTTTCTTACTTTTATCCTTTTAGGTTGCCTAT
AAAGGGGGTCCCAATCGAACTACAAGTGGAATGCTTCA
CATGGGATCAAAAACTCTGGTGCCGTCACTTCTGTGTG
CTTGCGGACTCAGAATCCGGTGGACTTATCACTCACTCT
GGGATGGTGGGCATGGGAGTCAGCTGCACAGCTACCCG GGAAGATGGAACCAATCGCAGATAA
GC_H_MEASLES_B3 G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT 43 mRNA Sequence
ATAAGAGCCACCATGTCACCGCAACGAGACCGGATAA (assumes T100 tail)
ATGCCTTCTACAAAGATAACCCTTATCCCAAGGGAAGT Sequence Length:
AGGATAGTTATTAACAGAGAACATCTTATGATTGACAG 2126
ACCCTATGTTCTGCTGGCTGTTCTGTTCGTCATGTTTCT
GAGCTTGATCGGATTGCTGGCAATTGCAGGCATTAGAC

TTCATCGGGCAGCCATCTACACCGCGGAGATCCATAAA
AGCCTCAGTACCAATCTGGATGTGACTAACTCCATCGA
GCATCAGGTCAAGGACGTGCTGACACCACTCTTTAAAA
TCATCGGGGATGAAGTGGGCCTGAGAACACCTCAGAG
ATTCACTGACCTAGTGAAATTCATCTCGGACAAGATTA
AATTCCTTAATCCGGATAGGGAGTACGACTTCAGAGAT
CTCACTTGGTGCATCAACCCGCCAGAGAGGATCAAACT
AGATTATGATCAATACTGTGCAGATGTGGCTGCTGAAG
AGCTCATGAATGCATTGGTGAACTCAACTCTACTGGAG
ACCAGAACAACCACTCAGTTCCTAGCTGTCTCAAAGGG
AAACTGCTCAGGGCCCACTACAATCAGAGGTCAATTCT
CAAACATGTCGCTGTCCTTGTTGGACTTGTACTTAGGTC
GAGGTTACAATGTGTCATCTATAGTCACTATGACATCC
CAGGGAATGTATGGGGGAACCTACCTAGTTGAAAAGCC
TAATCTGAACAGCAAAGGGTCAGAGTTGTCACAACTGA
GCATGTACCGAGTGTTTGAAGTAGGTGTGATCAGAAAC
CCGGGTTTGGGGGCTCCGGTGTTCCATATGACAAACTA
TTTTGAGCAACCAGTCAGTAATGGTCTCGGCAACTGTA
TGGTGGCTTTGGGGGAGCTCAAACTCGCAGCCCTTTGT
CACGGGGACGATTCTATCATAATTCCCTATCAGGGATC
AGGGAAAGGTGTCAGCTTCCAGCTCGTCAAGCTGGGTG
TCTGGAAATCCCCAACCGACATGCAATCCTGGGTCCCC
TTATCAACGGATGATCCAGTGGTAGACAGGCTTTACCT
CTCATCTCACAGAGGTGTCATCGCTGACAATCAAGCAA
AATGGGCTGTCCCGACAACACGAACAGATGACAAGTTG
CGAATGGAGACATGCTTCCAGCAGGCGTGTAAAGGTAA
AATCCAAGCACTCTGCGAGAATCCCGAGTGGGTACCAT
TGAAGGATAACAGGATTCCTTCATACGGGGTCCTGTCT
GTTGATCTGAGTCTGACGGTTGAGCTTAAAATCAAAAT
TGCTTCGGGATTCGGGCCATTGATCACACACGGCTCAG
GGATGGACCTATACAAATCCAACTGCAACAATGTGTAT
TGGCTGACTATTCCGCCAATGAGAAATCTAGCCTTAGG
CGTAATCAACACATTGGAGTGGATACCGAGATTCAAGG
TTAGTCCCAACCTCTTCACTGTCCCAATTAAGGAAGCA
GGCGAAGACTGCCATGCCCCAACATACCTACCTGCGGA
GGTGGACGGTGATGTCAAACTCAGTTCCAACCTGGTGA
TTCTACCTGGTCAAGATCTCCAATATGTTTTGGCAACCT
ACGATACCTCCAGGGTTGAGCATGCTGTGGTTTATTAC
GTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTATCCT
TTTAGGTTGCCTATAAAGGGGGTCCCAATCGAACTACA
AGTGGAATGCTTCACATGGGATCAAAAACTCTGGTGCC
GTCACTTCTGTGTGCTTGCGGACTCAGAATCCGGTGGA
CTTATCACTCACTCTGGGATGGTGGGCATGGGAGTCAG
CTGCACAGCTACCCGGGAAGATGGAACCAATCGCAGAT
AATGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTCTT
GCCCCTTGGGCCTCCCCCCAGCCCCTCCTCCCCTTCCTG
CACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGTG
GGCGGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAATC TAG GC_H_MEASLES_D8
TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT 44 Sequence, NT (5'
CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA UTR, ORF, 3'
GAAATATAAGAGCCACCATGTCACCACAACGAGACCG UTR)
GATAAATGCCTTCTACAAAGACAACCCCCATCCTAAGG Sequence Length:

GAAGTAGGATAGTTATTAACAGAGAACATCTTATGATT 2065
GATAGACCTTATGTTTTGCTGGCTGTTCTATTCGTCATG
TTTCTGAGCTTGATCGGGTTGCTAGCCATTGCAGGCATT
AGACTTCATCGGGCAGCCATCTACACCGCAGAGATCCA
TAAAAGCCTCAGCACCAATCTGGATGTAACTAACTCAA
TCGAGCATCAGGTTAAGGACGTGCTGACACCACTCTTC
AAGATCATCGGTGATGAAGTGGGCTTGAGGACACCTCA
GAGATTCACTGACCTAGTGAAGTTCATCTCTGACAAGA
TTAAATTCCTTAATCCGGACAGGGAATACGACTTCAGA
GATCTCACTTGGTGTATCAACCCGCCAGAGAGAATCAA
ATTGGATTATGATCAATACTGTGCAGATGTGGCTGCTG
AAGAACTCATGAATGCATTGGTGAACTCAACTCTACTG
GAGACCAGGGCAACCAATCAGTTCCTAGCTGTCTCAAA
GGGAAACTGCTCAGGGCCCACTACAATCAGAGGCCAAT
TCTCAAACATGTCGCTGTCCCTGTTGGACTTGTATTTAA
GTCGAGGTTACAATGTGTCATCTATAGTCACTATGACA
TCCCAGGGAATGTACGGGGGAACTTACCTAGTGGAAAA
GCCTAATCTGAGCAGCAAAGGGTCAGAGTTGTCACAAC
TGAGCATGCACCGAGTGTTTGAAGTAGGTGTTATCAGA
AATCCGGGTTTGGGGGCTCCGGTATTCCATATGACAAA
CTATCTTGAGCAACCAGTCAGTAATGATTTCAGCAACT
GCATGGTGGCTTTGGGGGAGCTCAAGTTCGCAGCCCTC
TGTCACAGGGAAGATTCTATCACAATTCCCTATCAGGG
ATCAGGGAAAGGTGTCAGCTTCCAGCTTGTCAAGCTAG
GTGTCTGGAAATCCCCAACCGACATGCAATCCTGGGTC
CCCCTATCAACGGATGATCCAGTGATAGACAGGCTTTA
CCTCTCATCTCACAGAGGCGTTATCGCTGACAATCAAG
CAAAATGGGCTGTCCCGACAACACGGACAGATGACAA
GTTGCGAATGGAGACATGCTTCCAGCAGGCGTGTAAGG
GTAAAATCCAAGCACTTTGCGAGAATCCCGAGTGGACA
CCATTGAAGGATAACAGGATTCCTTCATACGGGGTCTT
GTCTGTTGATCTGAGTCTGACAGTTGAGCTTAAAATCA

AAATTGTTTCAGGATTCGGGCCATTGATCACACACGGT
TCAGGGATGGACCTATACAAATCCAACCACAACAATAT
GTATTGGCTGACTATCCCGCCAATGAAGAACCTGGCCT
TAGGTGTAATCAACACATTGGAGTGGATACCGAGATTC
AAGGTTAGTCCCAACCTCTTCACTGTTCCAATTAAGGA
AGCAGGCGAGGACTGCCATGCCCCAACATACCTACCTG
CGGAGGTGGATGGTGATGTCAAACTCAGTTCCAATCTG
GTGATTCTACCTGGTCAAGATCTCCAATATGTTCTGGCA
ACCTACGATACTTCCAGAGTTGAACATGCTGTAGTTTAT
TACGTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTAT
CCTTTTAGGTTGCCTGTAAGGGGGGTCCCCATTGAATTA
CAAGTGGAATGCTTCACATGGGACCAAAAACTCTGGTG
CCGTCACTTCTGTGTGCTTGCGGACTCAGAATCTGGTGG
ACATATCACTCACTCTGGGATGGTGGGCATGGGAGTCA
GCTGCACAGCCACTCGGGAAGATGGAACCAGCCGCAG
ATAGTGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTC
TTGCCCCTTGGGCCTCCCCCCAGCCCCTCCTCCCCTTCC
TGCACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAG TGGGCGGC GC_H_MEASLES_D8
ATGTCACCACAACGAGACCGGATAAATGCCTTCTACAA 45 ORF Sequence, NT
AGACAACCCCCATCCTAAGGGAAGTAGGATAGTTATTA
ACAGAGAACATCTTATGATTGATAGACCTTATGTTTTGC

TGGCTGTTCTATTCGTCATGTTTCTGAGCTTGATCGGGT
TGCTAGCCATTGCAGGCATTAGACTTCATCGGGCAGCC
ATCTACACCGCAGAGATCCATAAAAGCCTCAGCACCAA
TCTGGATGTAACTAACTCAATCGAGCATCAGGTTAAGG
ACGTGCTGACACCACTCTTCAAGATCATCGGTGATGAA
GTGGGCTTGAGGACACCTCAGAGATTCACTGACCTAGT
GAAGTTCATCTCTGACAAGATTAAATTCCTTAATCCGG
ACAGGGAATACGACTTCAGAGATCTCACTTGGTGTATC
AACCCGCCAGAGAGAATCAAATTGGATTATGATCAATA
CTGTGCAGATGTGGCTGCTGAAGAACTCATGAATGCAT
TGGTGAACTCAACTCTACTGGAGACCAGGGCAACCAAT
CAGTTCCTAGCTGTCTCAAAGGGAAACTGCTCAGGGCC
CACTACAATCAGAGGCCAATTCTCAAACATGTCGCTGT
CCCTGTTGGACTTGTATTTAAGTCGAGGTTACAATGTGT
CATCTATAGTCACTATGACATCCCAGGGAATGTACGGG
GGAACTTACCTAGTGGAAAAGCCTAATCTGAGCAGCAA
AGGGTCAGAGTTGTCACAACTGAGCATGCACCGAGTGT
TTGAAGTAGGTGTTATCAGAAATCCGGGTTTGGGGGCT
CCGGTATTCCATATGACAAACTATCTTGAGCAACCAGT
CAGTAATGATTTCAGCAACTGCATGGTGGCTTTGGGGG
AGCTCAAGTTCGCAGCCCTCTGTCACAGGGAAGATTCT
ATCACAATTCCCTATCAGGGATCAGGGAAAGGTGTCAG
CTTCCAGCTTGTCAAGCTAGGTGTCTGGAAATCCCCAA
CCGACATGCAATCCTGGGTCCCCCTATCAACGGATGAT
CCAGTGATAGACAGGCTTTACCTCTCATCTCACAGAGG
CGTTATCGCTGACAATCAAGCAAAATGGGCTGTCCCGA
CAACACGGACAGATGACAAGTTGCGAATGGAGACATG
CTTCCAGCAGGCGTGTAAGGGTAAAATCCAAGCACTTT
GCGAGAATCCCGAGTGGACACCATTGAAGGATAACAG
GATTCCTTCATACGGGGTCTTGTCTGTTGATCTGAGTCT
GACAGTTGAGCTTAAAATCAAAATTGTTTCAGGATTCG
GGCCATTGATCACACACGGTTCAGGGATGGACCTATAC
AAATCCAACCACAACAATATGTATTGGCTGACTATCCC
GCCAATGAAGAACCTGGCCTTAGGTGTAATCAACACAT
TGGAGTGGATACCGAGATTCAAGGTTAGTCCCAACCTC
TTCACTGTTCCAATTAAGGAAGCAGGCGAGGACTGCCA
TGCCCCAACATACCTACCTGCGGAGGTGGATGGTGATG
TCAAACTCAGTTCCAATCTGGTGATTCTACCTGGTCAAG
ATCTCCAATATGTTCTGGCAACCTACGATACTTCCAGA
GTTGAACATGCTGTAGTTTATTACGTTTACAGCCCAAGC
CGCTCATTTTCTTACTTTTATCCTTTTAGGTTGCCTGTAA
GGGGGGTCCCCATTGAATTACAAGTGGAATGCTTCACA
TGGGACCAAAAACTCTGGTGCCGTCACTTCTGTGTGCTT
GCGGACTCAGAATCTGGTGGACATATCACTCACTCTGG
GATGGTGGGCATGGGAGTCAGCTGCACAGCCACTCGGG AAGATGGAACCAGCCGCAGATAG
GC_H_MEASLES_D8 G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT 46 mRNA Sequence
ATAAGAGCCACCATGTCACCACAACGAGACCGGATAA (assumes T100 tail)
ATGCCTTCTACAAAGACAACCCCCATCCTAAGGGAAGT Sequence Length:
AGGATAGTTATTAACAGAGAACATCTTATGATTGATAG 2126
ACCTTATGTTTTGCTGGCTGTTCTATTCGTCATGTTTCTG
AGCTTGATCGGGTTGCTAGCCATTGCAGGCATTAGACT
TCATCGGGCAGCCATCTACACCGCAGAGATCCATAAAA
GCCTCAGCACCAATCTGGATGTAACTAACTCAATCGAG
CATCAGGTTAAGGACGTGCTGACACCACTCTTCAAGAT

CATCGGTGATGAAGTGGGCTTGAGGACACCTCAGAGAT
TCACTGACCTAGTGAAGTTCATCTCTGACAAGATTAAA
TTCCTTAATCCGGACAGGGAATACGACTTCAGAGATCT
CACTTGGTGTATCAACCCGCCAGAGAGAATCAAATTGG
ATTATGATCAATACTGTGCAGATGTGGCTGCTGAAGAA
CTCATGAATGCATTGGTGAACTCAACTCTACTGGAGAC
CAGGGCAACCAATCAGTTCCTAGCTGTCTCAAAGGGAA
ACTGCTCAGGGCCCACTACAATCAGAGGCCAATTCTCA
AACATGTCGCTGTCCCTGTTGGACTTGTATTTAAGTCGA
GGTTACAATGTGTCATCTATAGTCACTATGACATCCCA
GGGAATGTACGGGGGAACTTACCTAGTGGAAAAGCCT
AATCTGAGCAGCAAAGGGTCAGAGTTGTCACAACTGAG
CATGCACCGAGTGTTTGAAGTAGGTGTTATCAGAAATC
CGGGTTTGGGGGCTCCGGTATTCCATATGACAAACTAT
CTTGAGCAACCAGTCAGTAATGATTTCAGCAACTGCAT
GGTGGCTTTGGGGGAGCTCAAGTTCGCAGCCCTCTGTC
ACAGGGAAGATTCTATCACAATTCCCTATCAGGGATCA
GGGAAAGGTGTCAGCTTCCAGCTTGTCAAGCTAGGTGT
CTGGAAATCCCCAACCGACATGCAATCCTGGGTCCCCC
TATCAACGGATGATCCAGTGATAGACAGGCTTTACCTC
TCATCTCACAGAGGCGTTATCGCTGACAATCAAGCAAA
ATGGGCTGTCCCGACAACACGGACAGATGACAAGTTGC
GAATGGAGACATGCTTCCAGCAGGCGTGTAAGGGTAA
AATCCAAGCACTTTGCGAGAATCCCGAGTGGACACCAT
TGAAGGATAACAGGATTCCTTCATACGGGGTCTTGTCT
GTTGATCTGAGTCTGACAGTTGAGCTTAAAATCAAAAT
TGTTTCAGGATTCGGGCCATTGATCACACACGGTTCAG
GGATGGACCTATACAAATCCAACCACAACAATATGTAT
TGGCTGACTATCCCGCCAATGAAGAACCTGGCCTTAGG
TGTAATCAACACATTGGAGTGGATACCGAGATTCAAGG
TTAGTCCCAACCTCTTCACTGTTCCAATTAAGGAAGCA
GGCGAGGACTGCCATGCCCCAACATACCTACCTGCGGA
GGTGGATGGTGATGTCAAACTCAGTTCCAATCTGGTGA
TTCTACCTGGTCAAGATCTCCAATATGTTCTGGCAACCT
ACGATACTTCCAGAGTTGAACATGCTGTAGTTTATTAC
GTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTATCCT
TTTAGGTTGCCTGTAAGGGGGGTCCCCATTGAATTACA
AGTGGAATGCTTCACATGGGACCAAAAACTCTGGTGCC
GTCACTTCTGTGTGCTTGCGGACTCAGAATCTGGTGGA
CATATCACTCACTCTGGGATGGTGGGCATGGGAGTCAG
CTGCACAGCCACTCGGGAAGATGGAACCAGCCGCAGA
TAGTGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTCT
TGCCCCTTGGGCCTCCCCCCAGCCCCTCCTCCCCTTCCT
GCACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGT
GGGCGGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAT CTAG MeV mRNA Sequences
GC_F_MEASLES_B3.1 UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC 69 Sequence, NT (5'
UCACUAUAGGGAAAUAAGAGAGAAAAGAAGAGUAAG UTR, ORF, 3'
AAGAAAUAUAAGAGCCACCAUGGGUCUCAAGGUGAA UTR)
CGUCUCUGCCGUAUUCAUGGCAGUACUGUUAACUCUC Sequence Length:
CAAACACCCGCCGGUCAAAUUCAUUGGGGCAAUCUCU 1864
CUAAGAUAGGGGUAGUAGGAAUAGGAAGUGCAAGCU
ACAAAGUUAUGACUCGUUCCAGCCAUCAAUCAUUAGU

CAUAAAAUUAAUGCCCAAUAUAACUCUCCUCAAUAAC
UGCACGAGGGUAGAGAUUGCAGAAUACAGGAGACUA
CUAAGAACAGUUUUGGAACCAAUUAGGGAUGCACUU
AAUGCAAUGACCCAGAACAUAAGGCCGGUUCAGAGCG
UAGCUUCAAGUAGGAGACACAAGAGAUUUGCGGGAG
UAGUCCUGGCAGGUGCGGCCCUAGGUGUUGCCACAGC
UGCUCAGAUAACAGCCGGCAUUGCACUUCACCGGUCC
AUGCUGAACUCUCAGGCCAUCGACAAUCUGAGAGCGA
GCCUGGAAACUACUAAUCAGGCAAUUGAGGCAAUCAG
ACAAGCAGGGCAGGAGAUGAUAUUGGCUGUUCAGGG
UGUCCAAGACUACAUCAAUAAUGAGCUGAUACCGUCU
AUGAACCAGCUAUCUUGUGAUCUAAUCGGUCAGAAGC
UCGGGCUCAAAUUGCUUAGAUACUAUACAGAAAUCCU
GUCAUUAUUUGGCCCCAGCCUACGGGACCCCAUAUCU
GCGGAGAUAUCUAUCCAGGCUUUGAGUUAUGCACUU
GGAGGAGAUAUCAAUAAGGUGUUAGAAAAGCUCGGA
UACAGUGGAGGCGAUUUACUAGGCAUCUUAGAGAGC
AGAGGAAUAAAGGCUCGGAUAACUCACGUCGACACAG
AGUCCUACUUCAUAGUCCUCAGUAUAGCCUAUCCGAC
GCUGUCCGAGAUUAAGGGGGUGAUUGUCCACCGGCUA
GAGGGGGUCUCGUACAACAUAGGCUCUCAAGAGUGG
UAUACCACUGUGCCCAAGUAUGUUGCAACCCAAGGGU
ACCUUAUCUCGAAUUUUGAUGAGUCAUCAUGUACUU
UCAUGCCAGAGGGGACUGUGUGCAGCCAAAAUGCCUU
GUACCCGAUGAGUCCUCUGCUCCAAGAAUGCCUCCGG
GGGUCCACCAAGUCCUGUGCUCGUACACUCGUAUCCG
GGUCUUUUGGGAACCGGUUCAUUUUAUCACAAGGGA
ACCUAAUAGCCAAUUGUGCAUCAAUUCUUUGUAAGU
GUUACACAACAGGUACGAUUAUUAAUCAAGACCCUGA
CAAGAUCCUAACAUACAUUGCUGCCGAUCGCUGCCCG
GUAGUCGAGGUGAACGGCGUGACCAUCCAAGUCGGGA
GCAGGAGGUAUCCAGACGCUGUGUACUUGCACAGAAU
UGACCUCGGUCCUCCCAUAUCAUUGGAGAGGUUGGAC
GUAGGGACAAAUCUGGGGAAUGCAAUUGCCAAAUUG
GAGGAUGCCAAGGAAUUGUUGGAAUCAUCGGACCAG
AUAUUGAGAAGUAUGAAAGGUUUAUCGAGCACUAGC
AUAGUCUACAUCCUGAUUGCAGUGUGUCUUGGAGGG
UUGAUAGGGAUCCCCACUUUAAUAUGUUGCUGCAGG
GGGCGUUGUAACAAAAAGGGAGAACAAGUUGGUAUG
UCAAGACCAGGCCUAAAGCCUGACCUUACAGGAACAU
CAAAAUCCUAUGUAAGAUCGCUUUGAUGAUAAUAGG
CUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCUUGGGC
CUCCCCCCAGCCCCUCCUCCCCUUCCUGCACCCGUACC
CCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGGC GC_F_MEASLES_B3.1
AUGGGUCUCAAGGUGAACGUCUCUGCCGUAUUCAUGG 70 ORF Sequence, NT
CAGUACUGUUAACUCUCCAAACACCCGCCGGUCAAAU
UCAUUGGGGCAAUCUCUCUAAGAUAGGGGUAGUAGG
AAUAGGAAGUGCAAGCUACAAAGUUAUGACUCGUUC
CAGCCAUCAAUCAUUAGUCAUAAAAUUAAUGCCCAAU
AUAACUCUCCUCAAUAACUGCACGAGGGUAGAGAUUG
CAGAAUACAGGAGACUACUAAGAACAGUUUUGGAAC
CAAUUAGGGAUGCACUUAAUGCAAUGACCCAGAACAU
AAGGCCGGUUCAGAGCGUAGCUUCAAGUAGGAGACAC
AAGAGAUUUGCGGGAGUAGUCCUGGCAGGUGCGGCCC

UAGGUGUUGCCACAGCUGCUCAGAUAACAGCCGGCAU
UGCACUUCACCGGUCCAUGCUGAACUCUCAGGCCAUC
GACAAUCUGAGAGCGAGCCUGGAAACUACUAAUCAGG
CAAUUGAGGCAAUCAGACAAGCAGGGCAGGAGAUGA
UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA
AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA
UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA
UACUAUACAGAAAUCCUGUCAUUAUUGGCCCCAGCC
UACGGGACCCCAUAUCUGCGGAGAUAUCUAUCCAGGC
UUUGAGUUAUGCACUUGGAGGAGAUAUCAAUAAGGU
GUUAGAAAAGCUCGGAUACAGUGGAGGCGAUUUACU
AGGCAUCUUAGAGAGCAGAGGAAUAAAGGCUCGGAU
AACUCACGUCGACACAGAGUCCUACUUCAUAGUCCUC
AGUAUAGCCUAUCCGACGCUGUCCGAGAUUAAGGGGG
UGAUUGUCCACCGGCUAGAGGGGGUCUCGUACAACAU
AGGCUCUCAAGAGUGGUAUACCACUGUGCCCAAGUAU
GUUGCAACCCAAGGGUACCUUAUCUCGAAUUUUGAUG
AGUCAUCAUGUACUUUCAUGCCAGAGGGGACUGUGU
GCAGCCAAAAUGCCUUGUACCCGAUGAGUCCUCUGCU
CCAAGAAUGCCUCCGGGGGUCCACCAAGUCCUGUGCU
CGUACACUCGUAUCCGGGUCUUUUGGGAACCGGUUCA
UUUUAUCACAAGGGAACCUAAUAGCCAAUUGUGCAUC
AAUUCUUUGUAAGUGUUACACAACAGGUACGAUUAU
UAAUCAAGACCCUGACAAGAUCCUAACAUACAUUGCU
GCCGAUCGCUGCCCGGUAGUCGAGGUGAACGGCGUGA
CCAUCCAAGUCGGGAGCAGGAGGUAUCCAGACGCUGU
GUACUUGCACAGAAUUGACCUCGGUCCUCCCAUAUCA
UUGGAGAGGUUGGACGUAGGGACAAAUCUGGGGAAU
GCAAUUGCCAAAUUGGAGGAUGCCAAGGAAUUGUUG
GAAUCAUCGGACCAGAUAUUGAGAAGUAUGAAAGGU
UUAUCGAGCACUAGCAUAGUCUACAUCCUGAUUGCAG
UGUGUCUUGGAGGGUUGAUAGGGAUCCCCACUUUAA
UAUGUUGCUGCAGGGGGCGUUGUAACAAAAAGGGAG
AACAAGUUGGUAUGUCAAGACCAGGCCUAAAGCCUGA
CCUUACAGGAACAUCAAAAUCCUAUGUAAGAUCGCUU UGA GC_F_MEASLES_B3.1
G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA 71 mRNA Sequence
UAUAAGAGCCACCAUGGGUCUCAAGGUGAACGUCUCU (assumes T100 tail)
GCCGUAUUCAUGGCAGUACUGUUAACUCUCCAAACAC mRNA Sequence
CCGCCGGUCAAAUUCAUUGGGGCAAUCUCUCUAAGAU Length: 1925
AGGGGUAGUAGGAAUAGGAAGUGCAAGCUACAAAGU
UAUGACUCGUUCCAGCCAUCAAUCAUUAGUCAUAAAA
UUAAUGCCCAAUAUAACUCUCCUCAAUAACUGCACGA
GGGUAGAGAUUGCAGAAUACAGGAGACUACUAAGAA
CAGUUUUGGAACCAAUUAGGGAUGCACUUAAUGCAA
UGACCCAGAACAUAAGGCCGGUUCAGAGCGUAGCUUC
AAGUAGGAGACACAAGAGAUUUGCGGGAGUAGUCCU
GGCAGGUGCGGCCCUAGGUGUUGCCACAGCUGCUCAG
AUAACAGCCGGCAUUGCACUUCACCGGUCCAUGCUGA
ACUCUCAGGCCAUCGACAAUCUGAGAGCGAGCCUGGA
AACUACUAAUCAGGCAAUUGAGGCAAUCAGACAAGCA
GGGCAGGAGAUGAUAUUGGCUGUUCAGGGUGUCCAA
GACUACAUCAAUAAUGAGCUGAUACCGUCUAUGAACC
AGCUAUCUUGUGAUCUAAUCGGUCAGAAGCUCGGGCU
CAAAUUGCUUAGAUACUAUACAGAAAUCCUGUCAUU

AUUUGGCCCCAGCCUACGGGACCCCAUAUCUGCGGAG
AUAUCUAUCCAGGCUUUGAGUUAUGCACUUGGAGGA
GAUAUCAAUAAGGUGUUAGAAAAGCUCGGAUACAGU
GGAGGCGAUUUACUAGGCAUCUUAGAGAGCAGAGGA

AUAAAGGCUCGGAUAACUCACGUCGACACAGAGUCCU
ACUUCAUAGUCCUCAGUAUAGCCUAUCCGACGCUGUC
CGAGAUUAAGGGGGUGAUUGUCCACCGGCUAGAGGG
GGUCUCGUACAACAUAGGCUCUCAAGAGUGGUAUACC
ACUGUGCCCAAGUAUGUUGCAACCCAAGGGUACCUUA
UCUCGAAUUUUGAUGAGUCAUCAUGUACUUUCAUGCC
AGAGGGGACUGUGUGCAGCCAAAAUGCCUUGUACCCG
AUGAGUCCUCUGCUCCAAGAAUGCCUCCGGGGGUCCA
CCAAGUCCUGUGCUCGUACACUCGUAUCCGGGUCUUU
UGGGAACCGGUUCAUUUUAUCACAAGGGAACCUAAU
AGCCAAUUGUGCAUCAAUUCUUUGUAAGUGUUACAC
AACAGGUACGAUUAUUAAUCAAGACCCUGACAAGAUC
CUAACAUACAUUGCUGCCGAUCGCUGCCCGGUAGUCG
AGGUGAACGGCGUGACCAUCCAAGUCGGGAGCAGGAG
GUAUCCAGACGCUGUGUACUUGCACAGAAUUGACCUC
GGUCCUCCCAUAUCAUUGGAGAGGUUGGACGUAGGG
ACAAAUCUGGGGAAUGCAAUUGCCAAAUUGGAGGAU
GCCAAGGAAUUGUUGGAAUCAUCGGACCAGAUAUUG
AGAAGUAUGAAAGGUUUAUCGAGCACUAGCAUAGUC
UACAUCCUGAUUGCAGUGUGUCUUGGAGGGUUGAUA
GGGAUCCCCACUUUAAUAUGUUGCUGCAGGGGGCGUU
GUAACAAAAAGGGAGAACAAGUUGGUAUGUCAAGAC
CAGGCCUAAAGCCUGACCUUACAGGAACAUCAAAAUC
CUAUGUAAGAUCGCUUUGAUGAUAAUAGGCUGGAGC
CUCGGUGGCCAAGCUUCUUGCCCCUUGGGCCUCCCCC
CAGCCCCUCCUCCCCUUCCUGCACCCGUACCCCCGUGG
UCUUUGAAUAAAGUCUGAGUGGGCGGCAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAAUCUAG
GC_F_MEASLES_D8 UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC 72 Sequence, NT (5'
UCACUAUAGGGAAAUAAGAGAGAAAAGAAGAGUAAG UTR, ORF, 3'
AAGAAAUAUAAGAGCCACCAUGGGUCUCAAGGUGAA UTR)
CGUCUCUGUCAUAUUCAUGGCAGUACUGUUAACUCUU Sequence Length:
CAAACACCCACCGGUCAAAUCCAUUGGGGCAAUCUCU 1864
CUAAGAUAGGGGUGGUAGGGGUAGGAAGUGCAAGCU
ACAAAGUUAUGACUCGUUCCAGCCAUCAAUCAUUAGU
CAUAAAGUUAAUGCCCAAUAUAACUCUCCUCAACAAU
UGCACGAGGGUAGGGAUUGCAGAAUACAGGAGACUA
CUGAGAACAGUUCUGGAACCAAUUAGAGAUGCACUU
AAUGCAAUGACCCAGAAUAUAAGACCGGUUCAGAGU
GUAGCUUCAAGUAGGAGACACAAGAGAUUUGCGGGA
GUUGUCCUGGCAGGUGCGGCCCUAGGCGUUGCCACAG
CUGCUCAAAUAACAGCCGGUAUUGCACUUCACCAGUC
CAUGCUGAACUCUCAAGCCAUCGACAAUCUGAGAGCG
AGCCUAGAAACUACUAAUCAGGCAAUUGAGGCAAUCA
GACAAGCAGGGCAGGAGAUGAUAUUGGCUGUUCAGG
GUGUCCAAGACUACAUCAAUAAUGAGCUGAUACCGUC
UAUGAAUCAACUAUCUUGUGAUUUAAUCGGCCAGAA
GCUAGGGCUCAAAUUGCUCAGAUACUAUACAGAAAUC

CUGUCAUUAUUUGGCCCCAGCUUACGGGACCCCAUAU
CUGCGGAGAUAUCUAUCCAGGCUUUGAGCUAUGCGCU
UGGAGGAGAUAUCAAUAAGGUGUUGGAAAAGCUCGG
AUACAGUGGAGGUGAUCUACUGGGCAUCUUAGAGAG
CAGAGGAAUAAAGGCCCGGAUAACUCACGUCGACACA
GAGUCCUACUUCAUUGUACUCAGUAUAGCCUAUCCGA
CGCUAUCCGAGAUUAAGGGGGUGAUUGUCCACCGGCU
AGAGGGGGUCUCGUACAACAUAGGCUCUCAAGAGUG
GUAUACCACUGUGCCCAAGUAUGUUGCAACCCAAGGG
UACCUUAUCUCGAAUUUUGAUGAGUCAUCAUGCACUU
UCAUGCCAGAGGGGACUGUGUGCAGCCAGAAUGCCUU
GUACCCGAUGAGUCCUCUGCUCCAAGAAUGCCUCCGG
GGGUCCACUAAGUCCUGUGCUCGUACACUCGUAUCCG
GGUCUUUCGGGAACCGGUUCAUUUUAUCACAGGGGA
ACCUAAUAGCCAAUUGUGCAUCAAUCCUUUGCAAGUG
UUACACAACAGGAACAAUCAUUAAUCAAGACCCUGAC
AAGAUCCUAACAUACAUUGCUGCCGAUCACUGCCCGG
UGGUCGAGGUGAAUGGCGUGACCAUCCAAGUCGGGA
GCAGGAGGUAUCCGGACGCUGUGUACUUGCACAGGAU
UGACCUCGGUCCUCCCAUAUCUUUGGAGAGGUUGGAC
GUAGGGACAAAUCUGGGGAAUGCAAUUGCUAAGUUG
GAGGAUGCCAAGGAAUUGUUGGAGUCAUCGGACCAG
AUAUUGAGGAGUAUGAAAGGUUUAUCGAGCACUAGU
AUAGUUUACAUCCUGAUUGCAGUGUGUCUUGGAGGA
UUGAUAGGGAUCCCCGCUUUAAUAUGUUGCUGCAGG
GGGCGUUGUAACAAGAAGGGAGAACAAGUUGGUAUG
UCAAGACCAGGCCUAAAGCCUGAUCUUACAGGAACAU
CAAAAUCCUAUGUAAGGUCACUCUGAUGAUAAUAGG
CUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCUUGGGC
CUCCCCCCAGCCCCUCCUCCCCUUCCUGCACCCGUACC
CCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGGC GC_F_MEASLES_D8
AUGGGUCUCAAGGUGAACGUCUCUGUCAUAUUCAUG 73 ORF Sequence, NT
GCAGUACUGUUAACUCUUCAAACACCCACCGGUCAAA
UCCAUUGGGGCAAUCUCUCUAAGAUAGGGGUGGUAG
GGGUAGGAAGUGCAAGCUACAAAGUUAUGACUCGUU
CCAGCCAUCAAUCAUUAGUCAUAAAGUUAAUGCCCAA
UAUAACUCUCCUCAACAAUUGCACGAGGGUAGGGAUU
GCAGAAUACAGGAGACUACUGAGAACAGUUCUGGAA
CCAAUUAGAGAUGCACUUAAUGCAAUGACCCAGAAUA
UAAGACCGGUUCAGAGUGUAGCUUCAAGUAGGAGAC
ACAAGAGAUUUGCGGGAGUUGUCCUGGCAGGUGCGG
CCCUAGGCGUUGCCACAGCUGCUCAAAUAACAGCCGG
UAUUGCACUUCACCAGUCCAUGCUGAACUCUCAAGCC
AUCGACAAUCUGAGAGCGAGCCUAGAAACUACUAAUC
AGGCAAUUGAGGCAAUCAGACAAGCAGGGCAGGAGA
UGAUAUUGGCUGUUCAGGGUGUCCAAGACUACAUCA
AUAAUGAGCUGAUACCGUCUAUGAAUCAACUAUCUU
GUGAUUUAAUCGGCCAGAAGCUAGGGCUCAAAUUGC
UCAGAUACUAUACAGAAAUCCUGUCAUUAUUUGGCCC
CAGCUUACGGGACCCCAUAUCUGCGGAGAUAUCUAUC
CAGGCUUUGAGCUAUGCGCUUGGAGGAGAUAUCAAU
AAGGUGUUGGAAAAGCUCGGAUACAGUGGAGGUGAU
CUACUGGGCAUCUUAGAGAGCAGAGGAAUAAAGGCCC
GGAUAACUCACGUCGACACAGAGUCCUACUUCAUUGU

ACUCAGUAUAGCCUAUCCGACGCUAUCCGAGAUUAAG
GGGGUGAUUGUCCACCGGCUAGAGGGGGUCUCGUACA
ACAUAGGCUCUCAAGAGUGGUAUACCACUGUGCCCAA
GUAUGUUGCAACCCAAGGGUACCUUAUCUCGAAUUUU
GAUGAGUCAUCAUGCACUUUCAUGCCAGAGGGGACUG
UGUGCAGCCAGAAUGCCUUGUACCCGAUGAGUCCUCU
GCUCCAAGAAUGCCUCCGGGGGUCCACUAAGUCCUGU
GCUCGUACACUCGUAUCCGGGUCUUUCGGGAACCGGU
UCAUUUUAUCACAGGGGAACCUAAUAGCCAAUUGUGC
AUCAAUCCUUUGCAAGUGUUACACAACAGGAACAAUC
AUUAAUCAAGACCCUGACAAGAUCCUAACAUACAUUG
CUGCCGAUCACUGCCCGGUGGUCGAGGUGAAUGGCGU
GACCAUCCAAGUCGGGAGCAGGAGGUAUCCGGACGCU
GUGUACUUGCACAGGAUUGACCUCGGUCCUCCCAUAU
CUUUGGAGAGGUUGGACGUAGGGACAAAUCUGGGGA
AUGCAAUUGCUAAGUUGGAGGAUGCCAAGGAAUUGU
UGGAGUCAUCGGACCAGAUAUUGAGGAGUAUGAAAG
GUUUAUCGAGCACUAGUAUAGUUUACAUCCUGAUUG
CAGUGUGUCUUGGAGGAUUGAUAGGGAUCCCCGCUU
UAAUAUGUUGCUGCAGGGGGCGUUGUAACAAGAAGG
GAGAACAAGUUGGUAUGUCAAGACCAGGCCUAAAGCC
UGAUCUUACAGGAACAUCAAAAUCCUAUGUAAGGUC ACUCUGA GC_F_MEASLES_D8
G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA 74 mRNA Sequence
UAUAAGAGCCACCAUGGGUCUCAAGGUGAACGUCUCU (assumes T100 tail)
GUCAUAUUCAUGGCAGUACUGUUAACUCUUCAAACAC Sequence Length:
CCACCGGUCAAAUCCAUUGGGGCAAUCUCUCUAAGAU 1925
AGGGGUGGUAGGGGUAGGAAGUGCAAGCUACAAAGU
UAUGACUCGUUCCAGCCAUCAAUCAUUAGUCAUAAAG
UUAAUGCCCAAUAUAACUCUCCUCAACAAUUGCACGA
GGGUAGGGAUUGCAGAAUACAGGAGACUACUGAGAA
CAGUUCUGGAACCAAUUAGAGAUGCACUUAAUGCAA
UGACCCAGAAUAUAAGACCGGUUCAGAGUGUAGCUUC
AAGUAGGAGACACAAGAGAUUUGCGGGAGUUGUCCU
GGCAGGUGCGGCCCUAGGCGUUGCCACAGCUGCUCAA
AUAACAGCCGGUAUUGCACUUCACCAGUCCAUGCUGA
ACUCUCAAGCCAUCGACAAUCUGAGAGCGAGCCUAGA
AACUACUAAUCAGGCAAUUGAGGCAAUCAGACAAGCA
GGGCAGGAGAUGAUAUUGGCUGUUCAGGGUGUCCAA
GACUACAUCAAUAAUGAGCUGAUACCGUCUAUGAAUC
AACUAUCUUGUGAUUUAAUCGGCCAGAAGCUAGGGC
UCAAAUUGCUCAGAUACUAUACAGAAAUCCUGUCAUU
AUUUGGCCCCAGCUUACGGGACCCCAUAUCUGCGGAG
AUAUCUAUCCAGGCUUUGAGCUAUGCGCUUGGAGGA
GAUAUCAAUAAGGUGUUGGAAAAGCUCGGAUACAGU
GGAGGUGAUCUACUGGGCAUCUUAGAGAGCAGAGGA
AUAAAGGCCCGGAUAACUCACGUCGACACAGAGUCCU
ACUUCAUUGUACUCAGUAUAGCCUAUCCGACGCUAUC
CGAGAUUAAGGGGGUGAUUGUCCACCGGCUAGAGGG
GGUCUCGUACAACAUAGGCUCUCAAGAGUGGUAUACC
ACUGUGCCCAAGUAUGUUGCAACCCAAGGGUACCUUA
UCUCGAAUUUUGAUGAGUCAUCAUGCACUUUCAUGCC
AGAGGGGACUGUGUGCAGCCAGAAUGCCUUGUACCCG
AUGAGUCCUCUGCUCCAAGAAUGCCUCCGGGGGUCCA
CUAAGUCCUGUGCUCGUACACUCGUAUCCGGGUCUUU

CGGGAACCGGUUCAUUUUAUCACAGGGGAACCUAAUA
GCCAAUUGUGCAUCAAUCCUUUGCAAGUGUUACACAA
CAGGAACAAUCAUUAAUCAAGACCCUGACAAGAUCCU
AACAUACAUUGCUGCCGAUCACUGCCCGGUGGUCGAG
GUGAAUGGCGUGACCAUCCAAGUCGGGAGCAGGAGG
UAUCCGGACGCUGUGUACUUGCACAGGAUUGACCUCG
GUCCUCCCAUAUCUUUGGAGAGGUUGGACGUAGGGAC
AAAUCUGGGGAAUGCAAUUGCUAAGUUGGAGGAUGC
CAAGGAAUUGUUGGAGUCAUCGGACCAGAUAUUGAG
GAGUAUGAAAGGUUUAUCGAGCACUAGUAUAGUUUA
CAUCCUGAUUGCAGUGUGUCUUGGAGGAUUGAUAGG
GAUCCCCGCUUUAAUAUGUUGCUGCAGGGGGCGUUGU
AACAAGAAGGGAGAACAAGUUGGUAUGUCAAGACCA
GGCCUAAAGCCUGAUCUUACAGGAACAUCAAAAUCCU
AUGUAAGGUCACUCUGAUGAUAAUAGGCUGGAGCCU
CGGUGGCCAAGCUUCUUGCCCCUUGGGCCUCCCCCCA
GCCCCUCCUCCCCUUCCUGCACCCGUACCCCCGUGGUC
UUUGAAUAAAGUCUGAGUGGGCGGCAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA AAAAAAAAAAAAAAAAAAUCUAG
GC_H_MEASLES_B3 UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC 75 Sequence, NT (5'
UCACUAUAGGGAAAUAAGAGAGAAAAGAAGAGUAAG UTR, ORF, 3'
AAGAAAUAUAAGAGCCACCAUGUCACCGCAACGAGAC UTR)
CGGAUAAAUGCCUUCUACAAAGAUAACCCUUAUCCCA Sequence Length:
AGGGAAGUAGGAUAGUUAUUAACAGAGAACAUCUUA 2065
UGAUUGACAGACCCUAUGUUCUGCUGGCUGUUCUGUU
CGUCAUGUUUCUGAGCUUGAUCGGAUUGCUGGCAAU
UGCAGGCAUUAGACUUCAUCGGGCAGCCAUCUACACC
GCGGAGAUCCAUAAAAGCCUCAGUACCAAUCUGGAUG
UGACUAACUCCAUCGAGCAUCAGGUCAAGGACGUGCU
GACACCACUCUUUAAAAUCAUCGGGGAUGAAGUGGGC
CUGAGAACACCUCAGAGAUUCACUGACCUAGUGAAAU
UCAUCUCGGACAAGAUUAAAUUCCUUAAUCCGGAUAG
GGAGUACGACUUCAGAGAUCUCACUUGGUGCAUCAAC
CCGCCAGAGAGGAUCAAACUAGAUUAUGAUCAAUACU
GUGCAGAUGUGGCUGCUGAAGAGCUCAUGAAUGCAU
UGGUGAACUCAACUCUACUGGAGACCAGAACAACCAC
UCAGUUCCUAGCUGUCUCAAAGGGAAACUGCUCAGGG
CCCACUACAAUCAGAGGUCAAUUCUCAAACAUGUCGC
UGUCCUUGUUGGACUUGUACUUAGGUCGAGGUUACA
AUGUGUCAUCUAUAGUCACUAUGACAUCCCAGGGAAU
GUAUGGGGGAACCUACCUAGUUGAAAAGCCUAAUCU
GAACAGCAAAGGGUCAGAGUUGUCACAACUGAGCAU
GUACCGAGUGUUUGAAGUAGGUGUGAUCAGAAACCC
GGGUUUGGGGGCUCCGGUGUUCCAUAUGACAAACUA
UUUUGAGCAACCAGUCAGUAAUGGUCUCGGCAACUGU
AUGGUGGCUUUGGGGGAGCUCAAACUCGCAGCCCUUU
GUCACGGGGACGAUUCUAUCAUAAUUCCCUAUCAGGG
AUCAGGGAAAGGUGUCAGCUUCCAGCUCGUCAAGCUG
GGUGUCUGGAAAUCCCCAACCGACAUGCAAUCCUGGG
UCCCCUUAUCAACGGAUGAUCCAGUGGUAGACAGGCU
UUACCUCUCAUCUCACAGAGGUGUCAUCGCUGACAAU
CAAGCAAAAUGGGCUGUCCCGACAACACGAACAGAUG
ACAAGUUGCGAAUGGAGACAUGCUUCCAGCAGGCGUG

UAAAGGUAAAAUCCAAGCACUCUGCGAGAAUCCCGAG
UGGGUACCAUUGAAGGAUAACAGGAUUCCUUCAUAC
GGGGUCCUGUCUGUUGAUCUGAGUCUGACGGUUGAG
CUUAAAAUCAAAAUUGCUUCGGGAUUCGGGCCAUUG
AUCACACACGGCUCAGGGAUGGACCUAUACAAAUCCA
ACUGCAACAAUGUGUAUUGGCUGACUAUUCCGCCAAU
GAGAAAUCUAGCCUUAGGCGUAAUCAACACAUUGGA
GUGGAUACCGAGAUUCAAGGUUAGUCCCAACCUCUUC
ACUGUCCCAAUUAAGGAAGCAGGCGAAGACUGCCAUG
CCCCAACAUACCUACCUGCGGAGGUGGACGGUGAUGU
CAAACUCAGUUCCAACCUGGUGAUUCUACCUGGUCAA
GAUCUCCAAUAUGUUUUGGCAACCUACGAUACCUCCA
GGGUUGAGCAUGCUGUGGUUUAUUACGUUUACAGCC
CAAGCCGCUCAUUUUCUUACUUUUAUCCUUUUAGGUU
GCCUAUAAAGGGGGUCCCAAUCGAACUACAAGUGGAA
UGCUUCACAUGGGAUCAAAAACUCUGGUGCCGUCACU
UCUGUGUGCUUGCGGACUCAGAAUCCGGUGGACUUAU
CACUCACUCUGGGAUGGUGGGCAUGGGAGUCAGCUGC
ACAGCUACCCGGGAAGAUGGAACCAAUCGCAGAUAAU
GAUAAUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGC
CCCUUGGGCCUCCCCCCAGCCCCUCCUCCCCUUCCUGC
ACCCGUACCCCCGUGGUCUUUGAAUAAAGUCUGAGUG GGCGGC GC_H_MEASLES_B3
AUGUCACCGCAACGAGACCGGAUAAAUGCCUUCUACA 76 ORF Sequence, NT
AAGAUAACCCUUAUCCCAAGGGAAGUAGGAUAGUUA
UUAACAGAGAACAUCUUAUGAUUGACAGACCCUAUG
UUCUGCUGGCUGUUCUGUUCGUCAUGUUUCUGAGCUU
GAUCGGAUUGCUGGCAAUUGCAGGCAUUAGACUUCA
UCGGGCAGCCAUCUACACCGCGGAGAUCCAUAAAAGC
CUCAGUACCAAUCUGGAUGUGACUAACUCCAUCGAGC
AUCAGGUCAAGGACGUGCUGACACCACUCUUUAAAAU
CAUCGGGGAUGAAGUGGGCCUGAGAACACCUCAGAGA

UUCACUGACCUAGUGAAAUUCAUCUCGGACAAGAUUA
AAUUCCUUAAUCCGGAUAGGGAGUACGACUUCAGAG
AUCUCACUUGGUGCAUCAACCCGCCAGAGAGGAUCAA
ACUAGAUUAUGAUCAAUACUGUGCAGAUGUGGCUGC
UGAAGAGCUCAUGAAUGCAUUGGUGAACUCAACUCU
ACUGGAGACCAGAACAACCACUCAGUUCCUAGCUGUC
UCAAAGGGAAACUGCUCAGGGCCCACUACAAUCAGAG
GUCAAUUCUCAAACAUGUCGCUGUCCUUGUUGGACUU
GUACUUAGGUCGAGGUUACAAUGUGUCAUCUAUAGU
CACUAUGACAUCCCAGGGAAUGUAUGGGGGAACCUAC
CUAGUUGAAAAGCCUAAUCUGAACAGCAAAGGGUCA
GAGUUGUCACAACUGAGCAUGUACCGAGUGUUUGAA
GUAGGUGUGAUCAGAAACCCGGGUUUGGGGGCUCCG
GUGUUCCAUAUGACAAACUAUUUUGAGCAACCAGUCA
GUAAUGGUCUCGGCAACUGUAUGGUGGCUUUGGGGG
AGCUCAAACUCGCAGCCCUUUGUCACGGGGACGAUUC
UAUCAUAAUUCCCUAUCAGGGAUCAGGGAAAGGUGU
CAGCUUCCAGCUCGUCAAGCUGGGUGUCUGGAAAUCC
CCAACCGACAUGCAAUCCUGGGUCCCCUUAUCAACGG
AUGAUCCAGUGGUAGACAGGCUUUACCUCUCAUCUCA
CAGAGGUGUCAUCGCUGACAAUCAAGCAAAAUGGGCU
GUCCCGACAACACGAACAGAUGACAAGUUGCGAAUGG

AGACAUGCUUCCAGCAGGCGUGUAAAGGUAAAAUCCA
AGCACUCUGCGAGAAUCCCGAGUGGGUACCAUUGAAG
GAUAACAGGAUUCCUUCAUACGGGGUCCUGUCUGUUG
AUCUGAGUCUGACGGUUGAGCUUAAAAUCAAAAUUG
CUUCGGGAUUCGGGCCAUUGAUCACACACGGCUCAGG
GAUGGACCUAUACAAAUCCAACUGCAACAAUGUGUAU
UGGCUGACUAUUCCGCCAAUGAGAAAUCUAGCCUUAG
GCGUAAUCAACACAUUGGAGUGGAUACCGAGAUUCA
AGGUUAGUCCCAACCUCUUCACUGUCCCAAUUAAGGA
AGCAGGCGAAGACUGCCAUGCCCCAACAUACCUACCU
GCGGAGGUGGACGGUGAUGUCAAACUCAGUUCCAACC
UGGUGAUUCUACCUGGUCAAGAUCUCCAAUAUGUUU
UGGCAACCUACGAUACCUCCAGGGUUGAGCAUGCUGU
GGUUUAUUACGUUUACAGCCCAAGCCGCUCAUUUUCU
UACUUUUAUCCUUUUAGGUUGCCUAUAAAGGGGGUC
CCAAUCGAACUACAAGUGGAAUGCUUCACAUGGGAUC
AAAAACUCUGGUGCCGUCACUUCUGUGUGCUUGCGGA
CUCAGAAUCCGGUGGACUUAUCACUCACUCUGGGAUG
GUGGGCAUGGGAGUCAGCUGCACAGCUACCCGGGAAG AUGGAACCAAUCGCAGAUAA
GC_H_MEASLES_B3 G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA 77 mRNA Sequence
UAUAAGAGCCACCAUGUCACCGCAACGAGACCGGAUA (assumes T100 Tail)
AAUGCCUUCUACAAAGAUAACCCUUAUCCCAAGGGAA Sequence Length:
GUAGGAUAGUUAUUAACAGAGAACAUCUUAUGAUUG 2126
ACAGACCCUAUGUUCUGCUGGCUGUUCUGUUCGUCAU
GUUUCUGAGCUUGAUCGGAUUGCUGGCAAUUGCAGG
CAUUAGACUUCAUCGGGCAGCCAUCUACACCGCGGAG
AUCCAUAAAAGCCUCAGUACCAAUCUGGAUGUGACUA
ACUCCAUCGAGCAUCAGGUCAAGGACGUGCUGACACC
ACUCUUUAAAAUCAUCGGGGAUGAAGUGGGCCUGAG
AACACCUCAGAGAUUCACUGACCUAGUGAAAUUCAUC
UCGGACAAGAUUAAAUUCCUUAAUCCGGAUAGGGAG
UACGACUUCAGAGAUCUCACUUGGUGCAUCAACCCGC
CAGAGAGGAUCAAACUAGAUUAUGAUCAAUACUGUG
CAGAUGUGGCUGCUGAAGAGCUCAUGAAUGCAUUGG
UGAACUCAACUCUACUGGAGACCAGAACAACCACUCA
GUUCCUAGCUGUCUCAAAGGGAAACUGCUCAGGGCCC
ACUACAAUCAGAGGUCAAUUCUCAAACAUGUCGCUGU
CCUUGUUGGACUUGUACUUAGGUCGAGGUUACAAUG
UGUCAUCUAUAGUCACUAUGACAUCCCAGGGAAUGUA
UGGGGGAACCUACCUAGUUGAAAAGCCUAAUCUGAAC
AGCAAAGGGUCAGAGUUGUCACAACUGAGCAUGUACC
GAGUGUUUGAAGUAGGUGUGAUCAGAAACCCGGGUU
UGGGGGCUCCGGUGUUCCAUAUGACAAACUAUUUUG
AGCAACCAGUCAGUAAUGGUCUCGGCAACUGUAUGGU
GGCUUUGGGGGAGCUCAAACUCGCAGCCCUUUGUCAC
GGGGACGAUUCUAUCAUAAUUCCCUAUCAGGGAUCAG
GGAAAGGUGUCAGCUUCCAGCUCGUCAAGCUGGGUGU
CUGGAAAUCCCCAACCGACAUGCAAUCCUGGGUCCCC
UUAUCAACGGAUGAUCCAGUGGUAGACAGGCUUUACC
UCUCAUCUCACAGAGGUGUCAUCGCUGACAAUCAAGC
AAAAUGGGCUGUCCCGACAACACGAACAGAUGACAAG
UUGCGAAUGGAGACAUGCUUCCAGCAGGCGUGUAAA
GGUAAAAUCCAAGCACUCUGCGAGAAUCCCGAGUGGG
UACCAUUGAAGGAUAACAGGAUUCCUUCAUACGGGG

UCCUGUCUGUUGAUCUGAGUCUGACGGUUGAGCUUA
AAAUCAAAAUUGCUUCGGGAUUCGGGCCAUUGAUCAC
ACACGGCUCAGGGAUGGACCUAUACAAAUCCAACUGC
AACAAUGUGUAUUGGCUGACUAUUCCGCCAAUGAGA
AAUCUAGCCUUAGGCGUAAUCAACACAUUGGAGUGG
AUACCGAGAUUCAAGGUUAGUCCCAACCUCUUCACUG
UCCCAAUUAAGGAAGCAGGCGAAGACUGCCAUGCCCC
AACAUACCUACCUGCGGAGGUGGACGGUGAUGUCAAA
CUCAGUUCCAACCUGGUGAUUCUACCUGGUCAAGAUC
UCCAAUAUGUUUUGGCAACCUACGAUACCUCCAGGGU
UGAGCAUGCUGUGGUUUAUUACGUUUACAGCCCAAGC
CGCUCAUUUUCUUACUUUUAUCCUUUUAGGUUGCCUA
UAAAGGGGGUCCCAAUCGAACUACAAGUGGAAUGCU
UCACAUGGGAUCAAAAACUCUGGUGCCGUCACUUCUG
UGUGCUUGCGGACUCAGAAUCCGGUGGACUUAUCACU
CACUCUGGGAUGGUGGGCAUGGGAGUCAGCUGCACAG
CUACCCGGGAAGAUGGAACCAAUCGCAGAUAAUGAUA
AUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCU
UGGGCCUCCCCCCAGCCCCUCCUCCCCUUCCUGCACCC
GUACCCCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCG
GCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUCUAG GC_H_MEASLES_D8
UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC 78 Sequence, NT (5'
UCACUAUAGGGAAAUAAGAGAGAAAAGAAGAGUAAG UTR, ORF, 3'
AAGAAAUAUAAGAGCCACCAUGUCACCACAACGAGAC UTR)
CGGAUAAAUGCCUUCUACAAAGACAACCCCCAUCCUA Sequence Length:
AGGGAAGUAGGAUAGUUAUUAACAGAGAACAUCUUA 2065
UGAUUGAUAGACCUUAUGUUUUGCUGGCUGUUCUAU
UCGUCAUGUUUCUGAGCUUGAUCGGGUUGCUAGCCAU
UGCAGGCAUUAGACUUCAUCGGGCAGCCAUCUACACC
GCAGAGAUCCAUAAAAGCCUCAGCACCAAUCUGGAUG
UAACUAACUCAAUCGAGCAUCAGGUUAAGGACGUGCU
GACACCACUCUUCAAGAUCAUCGGUGAUGAAGUGGGC
UUGAGGACACCUCAGAGAUUCACUGACCUAGUGAAGU
UCAUCUCUGACAAGAUUAAAUUCCUUAAUCCGGACAG
GGAAUACGACUUCAGAGAUCUCACUUGGUGUAUCAAC
CCGCCAGAGAGAAUCAAAUUGGAUUAUGAUCAAUAC
UGUGCAGAUGUGGCUGCUGAAGAACUCAUGAAUGCA
UUGGUGAACUCAACUCUACUGGAGACCAGGGCAACCA
AUCAGUUCCUAGCUGUCUCAAAGGGAAACUGCUCAGG
GCCCACUACAAUCAGAGGCCAAUUCUCAAACAUGUCG
CUGUCCCUGUUGGACUUGUAUUUAAGUCGAGGUUAC
AAUGUGUCAUCUAUAGUCACUAUGACAUCCCAGGGAA
UGUACGGGGGAACUUACCUAGUGGAAAAGCCUAAUC
UGAGCAGCAAAGGGUCAGAGUUGUCACAACUGAGCA
UGCACCGAGUGUUUGAAGUAGGUGUUAUCAGAAAUC
CGGGUUUGGGGGCUCCGGUAUUCCAUAUGACAAACUA
UCUUGAGCAACCAGUCAGUAAUGAUUUCAGCAACUGC
AUGGUGGCUUUGGGGGAGCUCAAGUUCGCAGCCCUCU
GUCACAGGGAAGAUUCUAUCACAAUUCCCUAUCAGGG
AUCAGGGAAAGGUGUCAGCUUCCAGCUUGUCAAGCUA
GGUGUCUGGAAAUCCCCAACCGACAUGCAAUCCUGGG
UCCCCCUAUCAACGGAUGAUCCAGUGAUAGACAGGCU

UUACCUCUCAUCUCACAGAGGCGUUAUCGCUGACAAU
CAAGCAAAAUGGGCUGUCCCGACAACACGGACAGAUG
ACAAGUUGCGAAUGGAGACAUGCUUCCAGCAGGCGUG
UAAGGGUAAAAUCCAAGCACUUUGCGAGAAUCCCGAG
UGGACACCAUUGAAGGAUAACAGGAUUCCUUCAUACG
GGGUCUUGUCUGUUGAUCUGAGUCUGACAGUUGAGC
UUAAAAUCAAAAUUGUUUCAGGAUUCGGGCCAUUGA
UCACACACGGUUCAGGGAUGGACCUAUACAAAUCCAA
CCACAACAAUAUGUAUUGGCUGACUAUCCCGCCAAUG
AAGAACCUGGCCUUAGGUGUAAUCAACACAUUGGAG
UGGAUACCGAGAUUCAAGGUUAGUCCCAACCUCUUCA
CUGUUCCAAUUAAGGAAGCAGGCGAGGACUGCCAUGC
CCCAACAUACCUACCUGCGGAGGUGGAUGGUGAUGUC
AAACUCAGUUCCAAUCUGGUGAUUCUACCUGGUCAAG
AUCUCCAAUAUGUUCUGGCAACCUACGAUACUUCCAG
AGUUGAACAUGCUGUAGUUUAUUACGUUUACAGCCC
AAGCCGCUCAUUUUCUUACUUUUAUCCUUUUAGGUUG
CCUGUAAGGGGGGUCCCCAUUGAAUUACAAGUGGAA
UGCUUCACAUGGGACCAAAAACUCUGGUGCCGUCACU
UCUGUGUGCUUGCGGACUCAGAAUCUGGUGGACAUA
UCACUCACUCUGGGAUGGUGGGCAUGGGAGUCAGCUG
CACAGCCACUCGGGAAGAUGGAACCAGCCGCAGAUAG
UGAUAAUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUG
CCCCUUGGGCCUCCCCCCAGCCCCUCCUCCCCUUCCUG
CACCCGUACCCCCGUGGUCUUUGAAUAAAGUCUGAGU GGGCGGC GC_H_MEASLES_D8
AUGUCACCACAACGAGACCGGAUAAAUGCCUUCUACA 79 ORF Sequence, NT
AAGACAACCCCCAUCCUAAGGGAAGUAGGAUAGUUAU
UAACAGAGAACAUCUUAUGAUUGAUAGACCUUAUGU
UUUGCUGGCUGUUCUAUUCGUCAUGUUUCUGAGCUU
GAUCGGGUUGCUAGCCAUUGCAGGCAUUAGACUUCAU
CGGGCAGCCAUCUACACCGCAGAGAUCCAUAAAAGCC
UCAGCACCAAUCUGGAUGUAACUAACUCAAUCGAGCA
UCAGGUUAAGGACGUGCUGACACCACUCUUCAAGAUC
AUCGGUGAUGAAGUGGGCUUGAGGACACCUCAGAGA
UUCACUGACCUAGUGAAGUUCAUCUCUGACAAGAUUA
AAUUCCUUAAUCCGGACAGGGAAUACGACUUCAGAGA
UCUCACUUGGUGUAUCAACCCGCCAGAGAGAAUCAAA
UUGGAUUAUGAUCAAUACUGUGCAGAUGUGGCUGCU
GAAGAACUCAUGAAUGCAUUGGUGAACUCAACUCUAC
UGGAGACCAGGGCAACCAAUCAGUUCCUAGCUGUCUC
AAAGGGAAACUGCUCAGGGCCCACUACAAUCAGAGGC
CAAUUCUCAAACAUGUCGCUGUCCCUGUUGGACUUGU
AUUUAAGUCGAGGUUACAAUGUGUCAUCUAUAGUCA
CUAUGACAUCCCAGGGAAUGUACGGGGGAACUUACCU
AGUGGAAAAGCCUAAUCUGAGCAGCAAAGGGUCAGA
GUUGUCACAACUGAGCAUGCACCGAGUGUUUGAAGU
AGGUGUUAUCAGAAAUCCGGGUUUGGGGGCUCCGGU
AUUCCAUAUGACAAACUAUCUUGAGCAACCAGUCAGU
AAUGAUUUCAGCAACUGCAUGGUGGCUUUGGGGGAG
CUCAAGUUCGCAGCCCUCUGUCACAGGGAAGAUUCUA
UCACAAUUCCCUAUCAGGGAUCAGGGAAAGGUGUCAG
CUUCCAGCUUGUCAAGCUAGGUGUCUGGAAAUCCCCA
ACCGACAUGCAAUCCUGGGUCCCCCUAUCAACGGAUG
AUCCAGUGAUAGACAGGCUUUACCUCUCAUCUCACAG

AGGCGUUAUCGCUGACAAUCAAGCAAAAUGGGCUGUC
CCGACAACACGGACAGAUGACAAGUUGCGAAUGGAGA
CAUGCUUCCAGCAGGCGUGUAAGGGUAAAAUCCAAGC
ACUUUGCGAGAAUCCCGAGUGGACACCAUUGAAGGAU
AACAGGAUUCCUUCAUACGGGGUCUUGUCUGUUGAUC
UGAGUCUGACAGUUGAGCUUAAAAUCAAAAUUGUUU
CAGGAUUCGGGCCAUUGAUCACACACGGUUCAGGGAU
GGACCUAUACAAAUCCAACCACAACAAUAUGUAUUGG
CUGACUAUCCCGCCAAUGAAGAACCUGGCCUUAGGUG
UAAUCAACACAUUGGAGUGGAUACCGAGAUUCAAGG
UUAGUCCCAACCUCUUCACUGUUCCAAUUAAGGAAGC
AGGCGAGGACUGCCAUGCCCCAACAUACCUACCUGCG
GAGGUGGAUGGUGAUGUCAAACUCAGUUCCAAUCUG
GUGAUUCUACCUGGUCAAGAUCUCCAAUAUGUUCUGG
CAACCUACGAUACUUCCAGAGUUGAACAUGCUGUAGU
UUAUUACGUUUACAGCCCAAGCCGCUCAUUUUCUUAC
UUUUAUCCUUUUAGGUUGCCUGUAAGGGGGGUCCCCA
UUGAAUUACAAGUGGAAUGCUUCACAUGGGACCAAA
AACUCUGGUGCCGUCACUUCUGUGUGCUUGCGGACUC
AGAAUCUGGUGGACAUAUCACUCACUCUGGGAUGGU
GGGCAUGGGAGUCAGCUGCACAGCCACUCGGGAAGAU GGAACCAGCCGCAGAUAG
GC_H_MEASLES_D8 G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA 80 mRNA Sequence
UAUAAGAGCCACCAUGUCACCACAACGAGACCGGAUA (assumes T100 tail)
AAUGCCUUCUACAAAGACAACCCCCAUCCUAAGGGAA Sequence Length:
GUAGGAUAGUUAUUAACAGAGAACAUCUUAUGAUUG 2126
AUAGACCUUAUGUUUUGCUGGCUGUUCUAUUCGUCA
UGUUUCUGAGCUUGAUCGGGUUGCUAGCCAUUGCAG
GCAUUAGACUUCAUCGGGCAGCCAUCUACACCGCAGA
GAUCCAUAAAAGCCUCAGCACCAAUCUGGAUGUAACU
AACUCAAUCGAGCAUCAGGUUAAGGACGUGCUGACAC
CACUCUUCAAGAUCAUCGGUGAUGAAGUGGGCUUGA
GGACACCUCAGAGAUUCACUGACCUAGUGAAGUUCAU
CUCUGACAAGAUUAAAUUCCUUAAUCCGGACAGGGAA
UACGACUUCAGAGAUCUCACUUGGUGUAUCAACCCGC
CAGAGAGAAUCAAAUUGGAUUAUGAUCAAUACUGUG
CAGAUGUGGCUGCUGAAGAACUCAUGAAUGCAUUGG
UGAACUCAACUCUACUGGAGACCAGGGCAACCAAUCA
GUUCCUAGCUGUCUCAAAGGGAAACUGCUCAGGGCCC
ACUACAAUCAGAGGCCAAUUCUCAAACAUGUCGCUGU
CCCUGUUGGACUUGUAUUUAAGUCGAGGUUACAAUG
UGUCAUCUAUAGUCACUAUGACAUCCCAGGGAAUGUA
CGGGGGAACUUACCUAGUGGAAAAGCCUAAUCUGAGC
AGCAAAGGGUCAGAGUUGUCACAACUGAGCAUGCACC
GAGUGUUUGAAGUAGGUGUUAUCAGAAAUCCGGGUU
UGGGGGCUCCGGUAUUCCAUAUGACAAACUAUCUUGA
GCAACCAGUCAGUAAUGAUUUCAGCAACUGCAUGGUG
GCUUUGGGGGAGCUCAAGUUCGCAGCCCUCUGUCACA
GGGAAGAUUCUAUCACAAUUCCCUAUCAGGGAUCAGG
GAAAGGUGUCAGCUUCCAGCUUGUCAAGCUAGGUGUC
UGGAAAUCCCCAACCGACAUGCAAUCCUGGGUCCCCC
UAUCAACGGAUGAUCCAGUGAUAGACAGGCUUUACCU
CUCAUCUCACAGAGGCGUUAUCGCUGACAAUCAAGCA
AAAUGGGCUGUCCCGACAACACGGACAGAUGACAAGU
UGCGAAUGGAGACAUGCUUCCAGCAGGCGUGUAAGG

GUAAAAUCCAAGCACUUUGCGAGAAUCCCGAGUGGAC
ACCAUUGAAGGAUAACAGGAUUCCUUCAUACGGGGUC
UUGUCUGUUGAUCUGAGUCUGACAGUUGAGCUUAAA
AUCAAAAUUGUUUCAGGAUUCGGGCCAUUGAUCACAC
ACGGUUCAGGGAUGGACCUAUACAAAUCCAACCACAA
CAAUAUGUAUUGGCUGACUAUCCCGCCAAUGAAGAAC

CUGGCCUUAGGUGUAAUCAACACAUUGGAGUGGAUA
CCGAGAUUCAAGGUUAGUCCCAACCUCUUCACUGUUC
CAAUUAAGGAAGCAGGCGAGGACUGCCAUGCCCCAAC
AUACCUACCUGCGGAGGUGGAUGGUGAUGUCAAACUC
AGUUCCAAUCUGGUGAUUCUACCUGGUCAAGAUCUCC
AAUAUGUUCUGGCAACCUACGAUACUUCCAGAGUUGA
ACAUGCUGUAGUUUAUUACGUUUACAGCCCAAGCCGC
UCAUUUUCUUACUUUUAUCCUUUUAGGUUGCCUGUA
AGGGGGGUCCCCAUUGAAUUACAAGUGGAAUGCUUC
ACAUGGGACCAAAAACUCUGGUGCCGUCACUUCUGUG
UGCUUGCGGACUCAGAAUCUGGUGGACAUAUCACUCA
CUCUGGGAUGGUGGGCAUGGGAGUCAGCUGCACAGCC
ACUCGGGAAGAUGGAACCAGCCGCAGAUAGUGAUAA
UAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCUU
GGGCCUCCCCCCAGCCCCUCCUCCCCUUCCUGCACCCG
UACCCCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGG
CAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUCUAG

TABLE-US-00015 TABLE 14 MeV Amino Acid Sequences SEQ ID Description Sequence NO:
GC_F_MEASLES_B3.1 MGLKVNVSAVFMAVLLTLQTPAGQIHWGNLSKIGVVG 47 ORF Sequence, AA
IGSASYKVMTRSSHQSLVIKLMPNITLLNNCTRVEIA
EYRRLLRTVLEPIRDALNAMTQNIRPVQSVASSRRHK
RFAGVVLAGAALGVATAAQITAGIALHRSMLNSQAID
NLRASLETTNQAIEAIRQAGQEMILAVQGVQDYINNE
LIPSMNQLSCDLIGQKLGLKLLRYYTEILSLFGPSLR
DPISAEISIQALSYALGGDINKVLEKLGYSGGDLLGI
LESRGIKARITHVDTESYFIVLSIAYPTLSEIKGVIV
HRLEGVSYNIGSQEWYTTVPKYVATQGYLISNFDESS
CTFMPEGTVCSQNALYPMSPLLQECLRGSTKSCARTL
VSGSFGNRFILSQGNLIANCASILCKCYTTGTIINQD
PDKILTYIAADRCPVVEVNGVTIQVGSRRYPDAVYLH
RIDLGPPISLERLDVGTNLGNAIAKLEDAKELLESSD
QILRSMKGLSSTSIVYILIAVCLGGLIGIPTLICCCR GRCNKKGEQVGMSRPGLKPDLTGTSKSYVRSL*
GC_F_MEASLES_D8 MGLKVNVSVIFMAVLLTLQTPTGQIHWGNLSKIGVVG 48 ORF Sequence, AA
VGSASYKVMTRSSHQSLVIKLMPNITLLNNCTRVGIA
EYRRLLRTVLEPIRDALNAMTQNIRPVQSVASSRRHK
RFAGVVLAGAALGVATAAQITAGIALHQSMLNSQAID
NLRASLETTNQAIEAIRQAGQEMILAVQGVQDYINNE
LIPSMNQLSCDLIGQKLGLKLLRYYTEILSLFGPSLR
DPISAEISIQALSYALGGDINKVLEKLGYSGGDLLGI
LESRGIKARITHVDTESYFIVLSIAYPTLSEIKGVIV
HRLEGVSYNIGSQEWYTTVPKYVATQGYLISNFDESS
CTFMPEGTVCSQNALYPMSPLLQECLRGSTKSCARTL
VSGSFGNRFILSQGNLIANCASILCKCYTTGTIINQD
PDKILTYIAADHCPVVEVNGVTIQVGSRRYPDAVYLH

RIDLGPPISLERLDVGTNLGNAIAKLEDAKELLESSD
QILRSMKGLSSTSIVYILIAVCLGGLIGIPALICCCR GRCNKKGEQVGMSRPGLKPDLTGTSKSYVRSL*
GC_H_MEASLES_B3 MSPQRDRINAFYKDNPYPKGSRIVINREHLMIDRPYV 49 ORF Sequence, AA
LLAVLFVMFLSLIGLLAIAGIRLHRAAIYTAEIHKSL
STNLDVTNSIEHQVKDVLTPLFKIIGDEVGLRTPQRF
TDLVKFISDKIKFLNPDREYDFRDLTWCINPPERIKL
DYDQYCADVAAEELMNALVNSTLLETRTTTQFLAVSK
GNCSGPTTIRGQFSNMSLSLLDLYLGRGYNVSSIVTM
TSQGMYGGTYLVEKPNLNSKGSELSQLSMYRVFEVGV
IRNPGLGAPVFHMTNYFEQPVSNGLGNCMVALGELKL
AALCHGDDSIIIPYQGSGKGVSFQLVKLGVWKSPTDM
QSWVPLSTDDPVVDRLYLSSHRGVIADNQAKWAVPTT
RTDDKLRMETCFQQACKGKIQALCENPEWVPLKDNRI
PSYGVLSVDLSLTVELKIKIASGFGPLITHGSGMDLY
KSNCNNVYWLTIPPMRNLALGVINTLEWIPRFKVSPN
LFTVPIKEAGEDCHAPTYLPAEVDGDVKLSSNLVILP
GQDLQYVLATYDTSRVEHAVVYYVYSPSRSFSYFYPF
RLPIKGVPIELQVECFTWDQKLWCRHFCVLADSESGG LITHSGMVGMGVSCTATREDGTNRR*
GC_H_MEASLES_D8 MSPQRDRINAFYKDNPHPKGSRIVINREHLMIDRPYV 50 ORF Sequence, AA
LLAVLFVMFLSLIGLLAIAGIRLHRAAIYTAEIHKSL
STNLDVTNSIEHQVKDVLTPLFKIIGDEVGLRTPQRF
TDLVKFISDKIKFLNPDREYDFRDLTWCINPPERIKL
DYDQYCADVAAEELMNALVNSTLLETRATNQFLAVSK
GNCSGPTTIRGQFSNMSLSLLDLYLSRGYNVSSIVTM
TSQGMYGGTYLVEKPNLSSKGSELSQLSMHRVFEVGV
IRNPGLGAPVFHMTNYLEQPVSNDFSNCMVALGELKF
AALCHREDSITIPYQGSGKGVSFQLVKLGVWKSPTDM
QSWVPLSTDDPVIDRLYLSSHRGVIADNQAKWAVPTT
RTDDKLRMETCFQQACKGKIQALCENPEWTPLKDNRI
PSYGVLSVDLSLTVELKIKIVSGFGPLITHGSGMDLY
KSNHNNMYWLTIPPMKNLALGVINTLEWIPRFKVSPN
LFTVPIKEAGEDCHAPTYLPAEVDGDVKLSSNLVILP
GQDLQYVLATYDTSRVEHAVVYYVYSPSRSFSYFYPF
RLPVRGVPIELQVECFTWDQKLWCRHFCVLADSESGG HITHSGMVGMGVSCTATREDGTSRR*

TABLE-US-00016 TABLE 15 MeV NCBI Accession Numbers (Amino Acid Sequences) Type Virus Name GenBank Accession hemagglutinin hemagglutinin [Measles virus strain Moraten] AAF85673.1 hemagglutinin hemagglutinin [Measles virus strain Rubeovax] AAF85689.1 hemagglutinin hemagglutinin [Measles virus] AAF89824.1 hemagglutinin hemagglutinin protein [Measles virus] CAA91369.1 hemagglutinin hemagglutinin [Measles virus] BAJ23068.1 hemagglutinin hemagglutinin protein [Measles virus] BAB39848.1 hemagglutinin hemagglutinin [Measles virus] AAA50551.1 hemagglutinin RecName: Full = Hemagglutinin glycoprotein P08362.1 hemagglutinin hemagglutinin [Measles virus] AAB63802.1 hemagglutinin hemagglutinin [Measles virus] AAA56650.1 hemagglutinin hemagglutinin [Measles virus] AAA56642.1 hemagglutinin hemagglutinin [Measles virus] AAA74936.1 hemagglutinin hemagglutinin protein [Measles virus] BAH56665.1 hemagglutinin hemagglutinin [Measles virus] ACC86105.1 hemagglutinin hemagglutinin [Measles virus strain Edmonston-Zagreb] AAF85697.1 hemagglutinin hemagglutinin [Measles virus] AAR89413.1 hemagglutinin hemagglutinin [Measles virus] AAA56653.1 hemagglutinin RecName: Full = Hemagglutinin glycoprotein P35971.1 hemagglutinin Hemagglutinin [Measles virus] CAB94916.1 hemagglutinin hemagglutinin [Measles virus] AAC03036.1 hemagglutinin hemagglutinin [Measles virus] AAF85681.1 hemagglutinin Hemagglutinin [Measles virus] CAB94927.1 hemagglutinin Hemagglutinin [Measles virus] CAB94925.1 hemagglutinin hemagglutinin protein [Measles virus] BAB39835.1 hemagglutinin Hemagglutinin [Measles virus] CAB94931.1 hemagglutinin hemagglutinin [Measles virus genotype A] AFO84712.1 hemagglutinin hemagglutinin [Measles virus] AAA56639.1 hemagglutinin Hemagglutinin [Measles virus] CAB94926.1 hemagglutinin hemagglutinin protein [Measles virus] BAB39836.1 hemagglutinin Hemagglutinin [Measles virus] CAB94929.1 hemagglutinin

RecName: Full = Hemagglutinin glycoprotein P06830.1 hemagglutinin Hemagglutinin [Measles virus] CAB94928.1 hemagglutinin hemagglutinin protein [Measles virus] BAB39837.1 hemagglutinin hemagglutinin [Measles virus] AAA74935.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43780.1 hemagglutinin hemagglutinin [Measles virus] BAA09952.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43815.1 hemagglutinin hemagglutinin [Measles virus] AAF28390.1 hemagglutinin Hemagglutinin [Measles virus] CAB94923.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43785.1 hemagglutinin hemagglutinin [Measles virus] ABD34001.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43782.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43781.1 hemagglutinin hemagglutinin [Measles virus] BAH22353.1 hemagglutinin hemagglutinin [Measles virus] AAC35878.2 hemagglutinin hemagglutinin protein [Measles virus] AAL86996.1 hemagglutinin hemagglutinin [Measles virus] CAA76066.2 hemagglutinin hemagglutinin [Measles virus] AAA46428.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43803.1 hemagglutinin Hemagglutinin [Measles virus] CAB94918.1 hemagglutinin hemagglutinin [Measles virus] AAF72162.1 hemagglutinin hemagglutinin [Measles virus] AAM70154.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43776.1 hemagglutinin hemagglutinin [Measles virus genotype D4] ACT78395.1 hemagglutinin hemagglutinin [Measles virus genotype D7] AAL02030.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43789.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43774.1 hemagglutinin Hemagglutinin [Measles virus] CAB94920.1 hemagglutinin Hemagglutinin [Measles virus] CAB94922.1 hemagglutinin hemagglutinin [Measles virus] ABB59491.1 hemagglutinin hemagglutinin protein [Measles virus] BAB39843.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43804.1 hemagglutinin hemagglutinin [Measles virus] AAX52048.1 hemagglutinin Hemagglutinin [Measles virus] CAB94930.1 hemagglutinin hemagglutinin [Measles virus] AAA74526.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43814.1 hemagglutinin hemagglutinin [Measles virus] ABB59493.1 hemagglutinin hemagglutinin [Measles virus genotype D4] AAL02019.1 hemagglutinin Hemagglutinin [Measles virus] CAB94919.1 hemagglutinin hemagglutinin protein [Measles virus] AAL86997.1 hemagglutinin hemagglutinin [Measles virus genotype C2] AAL02017.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43769.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43808.1 hemagglutinin hemagglutinin [Measles virus] BAO97032.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43805.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43777.1 hemagglutinin hemagglutinin [Measles virus] AAL67793.1 hemagglutinin hemagglutinin [Measles virus] AAF89816.1 hemagglutinin hemagglutinin [Measles virus genotype D4] AAL02020.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43786.1 hemagglutinin hemagglutinin protein [Measles virus strain AEP40452.1 MVi/New Jersey.USA/45.05] hemagglutinin hemagglutinin [Measles virus] AAA74531.1 hemagglutinin hemagglutinin [Measles virus] AAB63800.1 hemagglutinin hemagglutinin [Measles virus] AAO21711.1 hemagglutinin hemagglutinin [Measles virus genotype D8] ALE27189.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43810.1 hemagglutinin hemagglutinin [Measles virus] AAF89817.1 hemagglutinin hemagglutinin [Measles virus genotype D6] AAL02022.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43800.1 hemagglutinin hemagglutinin protein [Measles virus genotype B3] AGA17219.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43770.1 hemagglutinin hemagglutinin protein [Measles virus strain AEP40444.1 MVi/Texas.USA/4.07] hemagglutinin hemagglutinin [Measles virus] AAX52047.1 hemagglutinin hemagglutinin [Measles virus] AAB63794.1 hemagglutinin hemagglutinin [Measles virus] AAB63796.1 hemagglutinin hemagglutinin [Measles virus] AAA74528.1 hemagglutinin hemagglutinin [Measles virus] AAB63774.1 hemagglutinin hemagglutinin [Measles virus] AAB63795.1 hemagglutinin hemagglutinin [Measles virus] AAA74519.1 hemagglutinin hemagglutinin protein [Measles virus] CAB43778.1 fusion protein fusion protein [Measles virus strain Moraten] AAF85672.1 fasion protein fusion protein [Measles virus] AAA56645.1 fusion protein fusion protein [Measles virus strain Rubeovax] AAF85688.1 fusion protein fusion protein [Measles virus] AAF85680.1 fusion protein fusion protein [Measles virus] AEF30359.1 fusion protein fusion protein [Measles virus] BAA09957.1 fusion protein fusion protein [Measles virus] AAV84957.1 fusion protein fusion protein [Measles virus MeV-eGFP_Edm-tag] AII16636.1 fusion protein fusion protein [Measles virus] ABY58018.1 fusion protein fusion protein [Measles virus] BAA19838.1 fusion protein fusion protein [Measles virus] AAA56641.1 fusion protein F protein [Measles virus] ABK40529.1 fusion protein fusion protein [Measles virus] AAA56652.1 fusion protein fusion protein [Measles virus] ABY58017.1 fusion protein fusion protein [Measles virus] ABB71645.1 fusion protein fusion protein [Measles virus] NP_056922.1 fusion protein fusion protein [Measles virus strain AIK-C] AAF85664.1 fusion protein fusion protein [Measles virus] BAB60865.1 fusion protein fusion protein [Measles virus] BAA09950.1 fusion protein fusion protein [Measles virus strain AEP40403.1 MVi/New

York.USA/26.09/3] fusion protein fusion protein [Measles virus] AAA74934.1 fusion protein fusion protein [Measles virus] CAB38075.1 fusion protein fusion protein [Measles virus strain AEP40443.1 MVi/Texas.USA/4.07] fusion protein fusion protein [Measles virus] AAF02695.1 fusion protein fusion protein [Measles virus] AAF02696.1 fusion protein fusion protein [Measles virus] AAT99301.1 fusion protein fusion protein [Measles virus] ABB71661.1 fusion protein fusion protein [Measles virus] BAK08874.1 fusion protein fusion protein [Measles virus] AAF02697.1 fusion protein fusion protein [Measles virus genotype D4] AFY12704.1 fusion protein fusion protein [Measles virus strain AEP40467.1 MVi/California.USA/16.03] fusion protein fusion protein [Measles virus genotype D8] AHN07989.1 fusion protein fusion protein [Measles virus] AAA46421.1 fusion protein fusion protein [Measles virus] AAA56638.1 fusion protein fusion protein [Measles virus strain AEP40419.1 MVi/Virginia.USA/15.09] fusion protein fusion protein [Measles virus genotype D8] ALE27200.1 fusion protein fusion protein [Measles virus genotype D8] AFY12695.1 fusion protein fusion protein [Measles virus genotype D8] ALE27248.1 fusion protein fusion protein [Measles virus genotype D8] ALE27224.1 fusion protein fusion protein [Measles virus] AAT99300.1 fusion protein fusion protein [Measles virus] BAH96592.1 fusion protein fusion protein [Measles virus strain AEP40459.1 MVi/California.USA/8.04] fusion protein fusion protein [Measles virus genotype D8] AIG94081.1 fusion protein fusion protein [Measles virus] BAA09951.1 fusion protein fusion protein [Measles virus genotype D8] ALE27194.1 fusion protein fusion protein [Measles virus] BAA33871.1 fusion protein fusion protein [Measles virus strain AEP40427.1 MVi/Washington.USA/18.08/1] fusion protein fusion protein [Measles virus] ABY21182.1 fusion protein fusion protein [Measles virus genotype D8] ALE27284.1 fusion protein fusion protein [Measles virus] ACA09725.1 fusion protein fusion protein [Measles virus genotype D8] ALE27314.1 fusion protein fusion protein [Measles virus genotype G3] AFY12712.1 fusion protein fusion protein [Measles virus genotype D8] ALE27368.1 fusion protein RecName: Full = Fusion glycoprotein F0; Contains: P35973.1 RecName: Full = Fusion glycoprotein F2; Contains: RecName: Full = Fusion glycoprotein F1; Flags: Precursor fusion protein fusion protein [Measles virus genotype H1] AIG53713.1 unnamed protein product [Measles virus] CAA34588.1 fusion protein fusion protein [Measles virus] CAA76888.1 fusion protein fusion protein [Measles virus genotype B3.1] AIY55563.1 fusion protein fusion protein [Measles virus] ADO17330.1 fusion protein fusion protein [Measles virus genotype H1] AIG53703.1 fusion protein fusion protein [Measles virus genotype B3] AGA17208.1 fusion protein fusion protein [Measles virus] AAL29688.1 fusion protein fusion protein [Measles virus genotype H1] AIG53706.1 fusion protein fusion protein [Measles virus genotype H1] AIG53701.1 fusion protein fusion protein [Measles virus genotype B3] ALE27092.1 fusion protein fusion protein [Measles virus genotype H1] AIG53714.1 fusion protein fusion protein [Measles virus genotype H1] AIG53694.1 fusion protein fusion protein [Measles virus genotype H1] AIG53668.1 fusion protein fusion protein [Measles virus] ACC86094.1 fusion protein fusion protein [Measles virus genotype H1] AIG53670.1 fusion protein fusion protein [Measles virus genotype H1] AIG53707.1 fusion protein fusion protein [Measles virus genotype B3] AGA17216.1 fusion protein fusion protein [Measles virus genotype H1] AIG53671.1 fusion protein fusion protein [Measles virus strain AEP40451.1 MVi/New Jersey.USA/45.05] fusion protein fusion protein [Measles virus genotype H1] AIG53684.1 fusion protein fusion protein [Measles virus genotype H1] AIG53688.1 fusion protein fusion protein [Measles virus genotype B3] AGA17214.1 fusion protein fusion protein [Measles virus genotype H1] AIG53683.1 fusion protein fusion protein [Measles virus genotype H1] AIG53667.1 fusion protein fusion protein [Measles virus genotype H1] AIG53686.1 fusion protein fusion protein [Measles virus genotype H1] AIG53685.1 fusion protein fusion protein [Measles virus genotype H1] AIG53681.1 unnamed protein product [Measles virus] CAA34589.1 fusion protein fusion protein [Measles virus genotype H1] AIG53678.1 fusion protein fusion protein [Measles virus genotype H1] AIG53710.1 fusion protein fusion protein [Measles virus genotype H1] AIG53669.1 fusion protein fusion protein [Measles virus genotype H1] AIG53664.1 fusion protein fusion protein [Measles virus] AAA50547.1 fusion protein fusion protein [Measles virus genotype H1] AIG53679.1 fusion protein fusion protein [Measles virus genotype H1] AIG53709.1 fusion protein fusion protein [Measles virus genotype H1] AIG53672.1 fusion protein fusion protein [Measles virus genotype H1] AIG53697.1 fusion protein fusion protein [Measles virus genotype H1] AIG53689.1 fusion protein fusion protein [Measles virus genotype H1] AIG53676.1 fusion protein fusion protein [Measles virus genotype H1] AIG53675.1 fusion protein fusion protein [Measles virus genotype H1] AIG53663.1 fusion protein fusion protein [Measles virus] BAA19841.1 fusion protein fusion protein [Measles virus] AAF02701.1 fusion protein fusion protein [Measles virus genotype H1] AIG53680.1 fusion protein fusion protein [Measles virus genotype H1] AIG53674.1 C protein C protein [Measles virus strain Moraten] AAF85670.1 C protein RecName: Full = Protein C P03424.1 C protein C protein [Measles virus] ACN54404.1 C protein C protein [Measles virus]

ACN54412.1 C protein RecName: Full = Protein C P35977.1 C protein C protein [Measles virus] AAF85678.1 C protein C protein [Measles virus] ABD33998.1 C protein unnamed protein product [Measles virus] CAA34586.1 C protein C protein [Measles virus] BAJ51786.1 C protein C protein [Measles virus] BAA33869.1 C protein virulence factor [Measles virus] ABO69700.1 C protein C protein [Measles virus] NP_056920.1 C protein C protein [Measles virus] ADO17333.1 C protein C protein [Measles virus] ACC86082.1 C protein C protein [Measles virus] BAA33875.1 C protein C protein [Measles virus] ABY21189.1 C protein C protein [Measles virus] BAE98296.1 C protein C protein [Measles virus] ADU17782.1 C protein C protein [Measles virus strain AEP40417.1 MVi/Virginia.USA/15.09] C protein C protein [Measles virus] ADU17814.1 C protein C protein [Measles virus] ADU17798.1 C protein C protein [Measles virus genotype D4] AFY12700.1 C protein C protein [Measles virus] ADU17784.1 C protein C protein [Measles virus strain AEP40465.1 MVi/California.USA/16.03] C protein C protein [Measles virus] ABB71643.1 C protein C protein [Measles virus] AEI91027.1 C protein C protein [Measles virus] ADU17874.1 C protein C protein [Measles virus] ADU17903.1 C protein C protein [Measles virus] CAA34579.1 C protein C protein [Measles virus] ADU17790.1

C protein C protein [Measles virus] ADU17800.1 C protein C protein [Measles virus] ABB71667.1 C protein unnamed protein product [Measles virus] CAA34572.1 C protein C protein [Measles virus strain AEP40433.1 MVi/Arizona.USA/11.08/2] C protein C protein [Measles virus] ADU17830.1 C protein C protein [Measles virus] ADU17947.1 C protein C protein [Measles virus] ADU17818.1 C protein C protein [Measles virus strain AEP40449.1 MVi/New Jersey.USA/45.05] C protein C protein [Measles virus strain AEP40441.1 MVi/Texas.USA/4.07] C protein C protein [Measles virus] ADU17864.1 C protein C protein [Measles virus] ADU17838.1 C protein C protein [Measles virus] ADU17881.1 C protein C protein [Measles virus strain AEP40425.1 MVi/Washington.USA/18.08/1] C protein C protein [Measles virus] ADU17927.1 C protein C protein [Measles virus] ADU17953.1 C protein C protein [Measles virus] ADU17889.1 C protein C protein [Measles virus] ADU17963.1 C protein C protein [Measles virus] ADU17893.1 C protein C protein [Measles virus] ADU17820.1 C protein C protein [Measles virus] ABB71651.1 C protein C protein [Measles virus] ADU17786.1 C protein C protein [Measles virus] ADU17862.1 C protein C protein [Measles virus] ADU17923.1 C protein C protein [Measles virus] ADU17959.1 C protein C protein [Measles virus] ADU17951.1 C protein C protein [Measles virus] ADU17916.1 C protein C protein [Measles virus] ADU17957.1 C protein C protein [Measles virus] ADU17925.1 C protein C protein [Measles virus] ADU17901.1 C protein C protein [Measles virus] ADU17887.1 C protein C protein [Measles virus] ADU17832.1 C protein C protein [Measles virus] ADU17891.1 C protein C protein [Measles virus] ADU17961.1 C protein C protein [Measles virus] ADU17872.1 C protein C protein [Measles virus] ADU17929.1 C protein C protein [Measles virus] ADU17908.1 C protein C protein [Measles virus] ADU17910.1 C protein C protein [Measles virus] ADU17921.1 C protein C protein [Measles virus] ADU17824.1 C protein C protein [Measles virus strain AEP40473.1 MVi/Pennsylvania.USA/20.09] C protein C protein [Measles virus] ADU17828.1 C protein C protein [Measles virus] ADU17812.1 C protein C protein [Measles virus genotype D8] AFY12692.1 C protein nonstructural C protein [Measles virus] ABA59559.1 C protein RecName: Full = Protein C Q00794.1 C protein nonstructural C protein [Measles virus] ADO17934.1 C protein nonstructural C protein [Measles virus] ACJ66773.1 C protein C protein [Measles virus genotype G3] AFY12708.1 C protein RecName: Full = Protein C P26035.1 C protein C protein [Measles virus] BAA84128.1 nucleoprotein RecName: Full = Nucleoprotein; AltName: Q77M43.1 Full = Nucleocapsid protein; Short = NP; Short = Protein N nucleoprotein nucleocapsid protein [Measles virus strain Rubeovax] AAF85683.1 nucleoprotein RecName: Full = Nucleoprotein; AltName: Q89933.1 Full = Nucleocapsid protein; Short = NP; Short = Protein N nucleoprotein nucleocapsid protein [Measles virus strain AIK-C] AAF85659.1 nucleoprotein nucleoprotein [Measles virus] ABI54102.1 nucleoprotein nucleoprotein [Measles virus] AAA56643.1 nucleoprotein nucleoprotein [Measles virus] AAC03050.1 nucleoprotein nucleoprotein [Measles virus] AAA18990.1 nucleoprotein nucleoprotein [Measles virus] AAA56640.1 nucleoprotein RecName: Full = Nucleoprotein; AltName: P35972.1 Full = Nucleocapsid protein; Short = NP; Short = Protein N nucleoprotein RecName: Full=Nucleoprotein; AltName: P10050.1 Full = Nucleocapsid protein; Short = NP; Short = Protein N nucleoprotein N protein [Measles virus] BAB60956.1 nucleoprotein RecName: Full = Nucleoprotein; AltName: B1AAA7.1 Full = Nucleocapsid protein; Short = NP; Short = Protein N nucleoprotein nucleoprotein [Measles virus] AAA18991.1 nucleoprotein nucleoprotein [Measles virus] CAB46894.1 nucleoprotein nucleoprotein [Measles virus] CAB46871.1 nucleoprotein nucleoprotein [Measles virus] CAB46872.1 nucleoprotein

nucleoprotein [Measles virus] ABU49606.1 nucleoprotein nucleocapsid protein [Measles virus] AAA75494.1 nucleoprotein nucleoprotein [Measles virus] CAB46883.1 nucleoprotein nucleoprotein [Measles virus] CAB46892.1 nucleoprotein unnamed protein product [Measles virus] CAA34584.1 nucleoprotein nucleoprotein [Measles virus] AAA18997.1 nucleoprotein nucleoprotein [Measles virus] CAB46863.1 nucleoprotein nucleoprotein [Measles virus] AEF30352.1 nucleoprotein nucleoprotein [Measles virus] ABI54103.1 nucleoprotein nucleocapsid protein [Measles virus] AAA46433.1 nucleoprotein nucleoprotein [Measles virus] CAB46902.1 nucleoprotein nucleoprotein [Measles virus] CAB46873.1 nucleoprotein nucleoprotein [Measles virus] CAB46906.1 nucleoprotein nucleoprotein [Measles virus] AAA74547.1 nucleoprotein nucleoprotein [Measles virus] AAA74537.1 nucleoprotein nucleoprotein [Measles virus] CAB46862.1 nucleoprotein nucleocapsid protein [Measles virus] BAA09961.1 nucleoprotein nucleoprotein [Measles virus] AAO15875.1 nucleoprotein nucleoprotein [Measles virus] AAO15871.1 nucleoprotein nucleoprotein [Measles virus] CAB46882.1 nucleoprotein nucleoprotein [Measles virus] CAB60124.1 nucleoprotein nucleoprotein [Measles virus] ABI54104.1 nucleoprotein nucleoprotein [Measles virus] CAB46869.1 nucleoprotein nucleoprotein [Measles virus] CAB46880.1 nucleoprotein nucleoprotein [Measles virus] AAA74541.1 nucleoprotein nucleocapsid protein [Measles virus strain AEP40446.1 MVi/New Jersey.USA/45.05] nucleoprotein nucleoprotein [Measles virus] ABI54110.1 nucleoprotein nucleoprotein [Measles virus] CAB46903.1 nucleoprotein nucleoprotein [Measles virus] CAB46899.1 nucleoprotein nucleoprotein [Measles virus] CAB46901.1 nucleoprotein nucleocapsid protein [Measles virus] ABB71640.1 nucleoprotein nucleoprotein [Measles virus] CAB60113.1 nucleoprotein nucleoprotein [Measles virus] CAB60114.1 nucleoprotein nucleoprotein [Measles virus] CAB60116.1 nucleoprotein nucleoprotein [Measles virus] CAB46895.1 nucleoprotein nucleoprotein [Measles virus] CAB60121.1 nucleoprotein nucleoprotein [Measles virus] ABI54111.1 nucleoprotein nucleoprotein [Measles virus] CAB46889.1 nucleoprotein nucleoprotein [Measles virus] CAB46898.1 nucleoprotein nucleoprotein [Measles virus genotype B3] ALE27083.1 nucleoprotein nucleoprotein [Measles virus] CAB60118.1 nucleoprotein nucleocapsid protein [Measles virus] CAA34570.1 nucleoprotein nucleoprotein [Measles virus] AAC29443.1 nucleoprotein nucleocapsid protein [Measles virus strain AEP40422.1 MVi/Washington.USA/18.08/1] nucleoprotein nucleoprotein [Measles virus] AAO15872.1 nucleoprotein nucleoprotein [Measles virus] CAB46874.1 nucleoprotein nucleoprotein [Measles virus] AAA74550.1 nucleoprotein nucleocapsid protein [Measles virus] ABB71648.1 nucleoprotein nucleoprotein [Measles virus] CAB46900.1 nucleoprotein nucleoprotein [Measles virus] BAH22440.1 nucleoprotein nucleocapsid protein [Measles virus] AAA46432.1 nucleoprotein nucleocapsid protein [Measles virus] BAA33867.1 nucleoprotein nucleoprotein [Measles virus] AAA74539.1 nucleoprotein nucleoprotein [Measles virus] CAB60115.1 nucleoprotein nucleoprotein [Measles virus] CAB60123.1 nucleoprotein nucleocapsid protein [Measles virus] ABB71664.1 nucleoprotein nucleoprotein [Measles virus] CAB60125.1 nucleoprotein nucleoprotein [Measles virus] AAA74546.1 nucleoprotein nucleoprotein [Measles virus] CAB46886.1 nucleoprotein nucleoprotein [Measles virus] BAH22350.1 nucleoprotein nucleoprotein [Measles virus] CAB46867.1 nucleoprotein nucleocapsid protein [Measles virus] BAA09954.1 nucleoprotein nucleoprotein [Measles virus] AAO15873.1 nucleoprotein nucleocapsid protein [Measles virus] AEP95735.1 nucleoprotein nucleoprotein [Measles virus] AAL37726.1 nucleoprotein nucleoprotein [Measles virus] AAA74549.1 nucleoprotein RecName: Full = Nucleoprotein; AltName: P26030.1 Full = Nucleocapsid protein; Short = NP; Short = Protein N nucleoprotein nucleoprotein [Measles virus ETH55/99] AAK07777.1 nucleoprotein nucleoprotein [Measles virus genotype B3] AGA17238.1 nucleoprotein nucleoprotein [Measles virus] AEF30351.1 nucleoprotein nucleoprotein [Measles virus genotype B3] AGA17242.1 nucleoprotein nucleoprotein [Measles virus ETH54/98] AAK07776.1 nucleoprotein nucleoprotein [Measles virus] AAA74548.1 nucleoprotein nucleoprotein [Measles virus] AAA19221.1 nucleoprotein nucleoprotein [Measles virus] AAC03039.1 nucleoprotein nucleoprotein [Measles virus] AAA19223.1 nucleoprotein nucleoprotein [Measles virus genotype B3] AGA17241.1 nucleoprotein nucleoprotein [Measles virus] CAB60122.1 nucleoprotein nucleoprotein [Measles virus] CAC34599.1 nucleoprotein nucleoprotein [Measles virus] AAC03042.1 nucleoprotein nucleoprotein [Measles virus] CAC34604.1 nucleoprotein nucleoprotein [Measles virus] AAA74544.1 nucleoprotein nucleocapsid protein [Measles virus] NP_056918.1 V Protein RecName: Full = Non-structural protein V Q9IC37.1 V Protein RecName: Full = Non-structural protein V Q9EMA9.1 V Protein V protein [Measles virus] ACN54411.1 V Protein V protein [Measles virus] ACN54403.1 V Protein V protein [Measles virus] AEP95742.1 V Protein V protein [Measles virus strain AEP40416.1 MVi/Virginia.USA/15.09] V Protein V protein [Measles virus] ADU17801.1 V Protein V protein [Measles virus] ADU17849.1 V Protein V protein [Measles virus] ABB71642.1 V Protein V protein [Measles virus genotype D8] AFY12693.1 V Protein V protein [Measles virus] YP_003873249.2 V Protein V protein [Measles virus strain AEP40432.1 MVi/Arizona.USA/11.08/2] V Protein RecName: Full = Non-structural protein V P26036.1 V Protein V protein [Measles virus strain AEP40464.1 MVi/California.USA/16.03] V Protein V protein [Measles virus strain AEP40456.1 MVi/California.USA/8.04] V Protein V protein [Measles virus] ABY21188.1 V Protein V protein [Measles virus strain AEP40424.1 MVi/Washington.USA/18.08/1] V Protein V protein [Measles virus] BAH96581.1 V Protein V protein [Measles virus] ABB71666.1 V Protein RecName: Full = Non-structural protein V P60168.1 V Protein V protein [Measles virus] BAH96589.1 V Protein V protein [Measles virus] ADU17954.1 V Protein V protein [Measles virus strain AEP40400.1 MVi/New York.USA/26.09/3] V Protein V protein [Measles virus] ABY21196.1 V Protein virulence factor [Measles virus] ABO69701.1 V Protein V protein [Measles virus] ABB71650.1 V Protein V protein [Measles virus] ACC86086.1 V Protein V protein [Measles virus genotype D4] AFY12702.1 V Protein V protein [Measles virus strain AEP40448.1 MVi/New Jersey.USA/45.05] V Protein V protein [Measles virus] BAE98295.1 V Protein V protein [Measles virus] ACC86083.1 V Protein V protein [Measles virus] ACU5139.1 V Protein V protein [Measles virus] ADO17334.1 V Protein V protein [Measles virus] ADU17930.1 V Protein V protein [Measles virus genotype G3] AFY12710.1 V Protein V protein [Measles virus strain AEP40472.1 MVi/Pennsylvania.USA/20.09] V Protein phosphoprotein [Measles virus] ADU17839.1 V Protein V protein [Measles virus] ADU17894.1 V Protein V protein [Measles virus] ACN50010.1 V Protein V protein [Measles virus] ADU17892.1 unnamed protein product [Measles virus] CAA34585.1 V Protein V protein [Measles virus] ABD33997.1

TABLE-US-00017 TABLE 16 SEQ ID Name Sequence NO: Flagellin Nucleic Acid Sequences NT (5'
TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACTCACTAT 51 UTR, ORF,
AGGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAATATAAG 3' UTR)
AGCCACCATGGCACAAGTCATTAATACAAACAGCCTGTCGCTG
TTGACCCAGAATAACCTGAACAAATCCCAGTCCGCACTGGGCA
CTGCTATCGAGCGTTTGTCTTCCGGTCTGCGTATCAACAGCGCG
AAAGACGATGCGGCAGGACAGGCGATTGCTAACCGTTTTACCG
CGAACATCAAAGGTCTGACTCAGGCTTCCCGTAACGCTAACGA
CGGTATCTCCATTGCGCAGACCACTGAAGGCGCGCTGAACGAA
ATCAACAACAACCTGCAGCGTGTGCGTGAACTGGCGGTTCAGT
CTGCGAATGGTACTAACTCCCAGTCTGACCTCGACTCCATCCAG
GCTGAAATCACCCAGCGCCTGAACGAAATCGACCGTGTATCCG
GCCAGACTCAGTTCAACGGCGTGAAAGTCCTGGCGCAGGACAA
CACCCTGACCATCCAGGTTGGTGCCAACGACGGTGAAACTATC
GATATTGATTTAAAAGAAATCAGCTCTAAAACACTGGGACTTG
ATAAGCTTAATGTCCAAGATGCCTACACCCCGAAAGAAACTGC
TGTAACCGTTGATAAAACTACCTATAAAAATGGTACAGATCCT
ATTACAGCCCAGAGCAATACTGATATCCAAACTGCAATTGGCG
GTGGTGCAACGGGGGTTACTGGGGCTGATATCAAATTTAAAGA
TGGTCAATACTATTTAGATGTTAAAGGCGGTGCTTCTGCTGGTG
TTTATAAAGCCACTTATGATGAAACTACAAAGAAAGTTAATAT
TGATACGACTGATAAAACTCCGTTGGCAACTGCGGAAGCTACA
GCTATTCGGGGAACGGCCACTATAACCCACAACCAAATTGCTG
AAGTAACAAAAGAGGGTGTTGATACGACCACAGTTGCGGCTCA
ACTTGCTGCAGCAGGGGTTACTGGCGCCGATAAGGACAATACT
AGCCTTGTAAAACTATCGTTTGAGGATAAAAACGGTAAGGTTA
TTGATGGTGGCTATGCAGTGAAAATGGGCGACGATTTCTATGC
CGCTACATATGATGAGAAAACAGGTGCAATTACTGCTAAAACC
ACTACTTATACAGATGGTACTGGCGTTGCTCAAACTGGAGCTGT
GAAATTTGGTGGCGCAAATGGTAAATCTGAAGTTGTTACTGCT
ACCGATGGTAAGACTTACTTAGCAAGCGACCTTGACAAACATA
ACTTCAGAACAGGCGGTGAGCTTAAAGAGGTTAATACAGATAA
GACTGAAAACCCACTGCAGAAAATTGATGCTGCCTTGGCACAG
GTTGATACACTTCGTTCTGACCTGGGTGCGGTTCAGAACCGTTT

CAACTCCGCTATCACCAACCTGGGCAATACCGTAAATAACCTG
TCTTCTGCCCGTAGCCGTATCGAAGATTCCGACTACGCAACCGA
AGTCTCCAACATGTCTCGCGCGCAGATTCTGCAGCAGGCCGGT
ACCTCCGTTCTGGCGCAGGCGAACCAGGTTCCGCAAAACGTCC
TCTCTTTACTGCGTTGATAATAGGCTGGAGCCTCGGTGGCCATG
CTTCTTGCCCCTTGGGCCTCCCCCCAGCCCCTCCTCCCCTTCCTG
CACCCGTACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGG C ORF
ATGGCACAAGTCATTAATACAAACAGCCTGTCGCTGTTGACCC 52 Sequence,
AGAATAACCTGAACAAATCCCAGTCCGCACTGGGCACTGCTAT NT
CGAGCGTTTGTCTTCCGGTCTGCGTATCAACAGCGCGAAAGAC
GATGCGGCAGGACAGGCGATTGCTAACCGTTTTACCGCGAACA
TCAAAGGTCTGACTCAGGCTTCCCGTAACGCTAACGACGGTAT
CTCCATTGCGCAGACCACTGAAGGCGCGCTGAACGAAATCAAC
AACAACCTGCAGCGTGTGCGTGAACTGGCGGTTCAGTCTGCGA
ATGGTACTAACTCCCAGTCTGACCTCGACTCCATCCAGGCTGAA
ATCACCCAGCGCCTGAACGAAATCGACCGTGTATCCGGCCAGA
CTCAGTTCAACGGCGTGAAAGTCCTGGCGCAGGACAACACCCCT
GACCATCCAGGTTGGTGCCAACGACGGTGAAACTATCGATATT
GATTTAAAAGAAATCAGCTCTAAAACACTGGGACTTGATAAGC
TTAATGTCCAAGATGCCTACACCCCGAAAGAAACTGCTGTAAC
CGTTGATAAAACTACCTATAAAAATGGTACAGATCCTATTACA
GCCCAGAGCAATACTGATATCCAAACTGCAATTGGCGGTGGTG
CAACGGGGGTTACTGGGGCTGATATCAAATTTAAAGATGGTCA
ATACTATTTAGATGTTAAAGGCGGTGCTTCTGCTGGTGTTTATA
AAGCCACTTATGATGAAACTACAAAGAAAGTTAATATTGATAC
GACTGATAAAACTCCGTTGGCAACTGCGGAAGCTACAGCTATT
CGGGGAACGGCCACTATAACCCACAACCAAATTGCTGAAGTAA
CAAAAGAGGGTGTTGATACGACCACAGTTGCGGCTCAACTTGC
TGCAGCAGGGGTTACTGGCGCCGATAAGGACAATACTAGCCTT
GTAAAACTATCGTTTGAGGATAAAAACGGTAAGGTTATTGATG
GTGGCTATGCAGTGAAAATGGGCGACGATTTCTATGCCGCTAC
ATATGATGAGAAAACAGGTGCAATTACTGCTAAAACCACTACT
TATACAGATGGTACTGGCGTTGCTCAAACTGGAGCTGTGAAAT
TTGGTGGCGCAAATGGTAAATCTGAAGTTGTTACTGCTACCGAT
GGTAAGACTTACTTAGCAAGCGACCTTGACAAACATAACTTCA
GAACAGGCGGTGAGCTTAAAGAGGTTAATACAGATAAGACTG
AAAACCCACTGCAGAAAATTGATGCTGCCTTGGCACAGGTTGA
TACACTTCGTTCTGACCTGGGTGCGGTTCAGAACCGTTTCAACT
CCGCTATCACCAACCTGGGCAATACCGTAAATAACCTGTCTTCT
GCCCGTAGCCGTATCGAAGATTCCGACTACGCAACCGAAGTCT
CCAACATGTCTCGCGCGCAGATTCTGCAGCAGGCCGGTACCTC
CGTTCTGGCGCAGGCGAACCAGGTTCCGCAAAACGTCCTCTCTT TACTGCGT mRNA
G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAAUAUAA 53 Sequence
GAGCCACCAUGGCACAAGUCAUUAAUACAAACAGCCUGUCGC (assumes
UGUUGACCCAGAAUAACCUGAACAAAUCCCAGUCCGCACUGG T100 tail)
GCACUGCUAUCGAGCGUUUGUCUUCCGGUCUGCGUAUCAACA
GCGCGAAAGACGAUGCGGCAGGACAGGCGAUUGCUAACCGUU
UUACCGCGAACAUCAAAGGUCUGACUCAGGCUUCCCGUAACG
CUAACGACGGUAUCUCCAUUGCGCAGACCACUGAAGGCGCGC
UGAACGAAAUCAACAACAACCUGCAGCGUGUGCGUGAACUGG
CGGUUCAGUCUGCGAAUGGUACUAACUCCCAGUCUGACCUCG
ACUCCAUCCAGGCUGAAAUCACCCAGCGCCUGAACGAAAUCG
ACCGUGUAUCCGGCCAGACUCAGUUCAACGGCGUGAAAGUCC
UGGCGCAGGACAACACCCUGACCAUCCAGGUUGGUGCCAACG

ACGGUGAAACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUCU
AAAACACUGGGACUUGAUAAGCUUAAUGUCCAAGAUGCCUAC
ACCCCGAAAGAAACUGCUGUAACCGUUGAUAAAACUACCUAU
AAAAAUGGUACAGAUCCUAUUACAGCCCAGAGCAAUACUGAU
AUCCAAACUGCAAUUGGCGGUGGUGCAACGGGGGUUACUGG
GGCUGAUAUCAAAUUUAAAGAUGGUCAAUACUAUUUAGAUG
UUAAAGGCGGUGCUUCUGCUGGUGUUUAUAAAGCCACUUAU
GAUGAAACUACAAAGAAAGUUAAUAUUGAUACGACUGAUAA
AACUCCGUUGGCAACUGCGGAAGCUACAGCUAUUCGGGGAAC
GGCCACUAUAACCCACAACCAAAUUGCUGAAGUAACAAAAGA
GGGUGUUGAUACGACCACAGUUGCGGCUCAACUUGCUGCAGC
AGGGGUUACUGGCGCCGAUAAGGACAAUACUAGCCUUGUAA
AACUAUCGUUUGAGGAUAAAAACGGUAAGGUUAUUGAUGGU
GGCUAUGCAGUGAAAAUGGGCGACGAUUUCUAUGCCGCUACA
UAUGAUGAGAAAACAGGUGCAAUUACUGCUAAAACCACUAC
UUAUACAGAUGGUACUGGCGUUGCUCAAACUGGAGCUGUGA
AAUUUGGUGGCGCAAAUGGUAAAUCUGAAGUUGUUACUGCU
ACCGAUGGUAAGACUUACUUAGCAAGCGACCUUGACAAACAU
AACUUCAGAACAGGCGGUGAGCUUAAAGAGGUUAAUACAGA
UAAGACUGAAAACCCACUGCAGAAAAUUGAUGCUGCCUUGGC
ACAGGUUGAUACACUUCGUUCUGACCUGGGUGCGGUUCAGAA
CCGUUUCAACUCCGCUAUCACCAACCUGGGCAAUACCGUAAA
UAACCUGUCUUCUGCCCGUAGCCGUAUCGAAGAUUCCGACUA
CGCAACCGAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGCA
GCAGGCCGGUACCUCCGUUCUGGCGCAGGCGAACCAGGUUCC
GCAAAACGUCCUCUCUUUACUGCGUUGAUAAUAGGCUGGAGC
CUCGGUGGCCAUGCUUCUUGCCCCUUGGGCCUCCCCCCAGCC
CCUCCUCCCCUUCCUGCACCCGUACCCCCGUGGUCUUUGAAU
AAAGUCUGAGUGGGCGGCAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUCUAG Flagellin mRNA Sequences NT (5'
UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGACUCACU 81 UTR, ORF,
AUAGGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAAUAUA 3' UTR)
AGAGCCACCAUGGCACAAGUCAUUAAUACAAACAGCCUGUCG
CUGUUGACCCAGAAUAACCUGAACAAAUCCCAGUCCGCACUG
GGCACUGCUAUCGAGCGUUUGUCUUCCGGUCUGCGUAUCAAC
AGCGCGAAAGACGAUGCGGCAGGACAGGCGAUUGCUAACCGU
UUUACCGCGAACAUCAAAGGUCUGACUCAGGCUUCCCGUAAC
GCUAACGACGGUAUCUCCAUUGCGCAGACCACUGAAGGCGCG
CUGAACGAAAUCAACAACAACCUGCAGCGUGUGCGUGAACUG
GCGGUUCAGUCUGCGAAUGGUACUAACUCCCAGUCUGACCUC
GACUCCAUCCAGGCUGAAAUCACCCAGCGCCUGAACGAAAUC
GACCGUGUAUCCGGCCAGACUCAGUUCAACGGCGUGAAAGUC
CUGGCGCAGGACAACACCCUGACCAUCCAGGUUGGUGCCAAC
GACGGUGAAACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUC
UAAAACACUGGGACUUGAUAAGCUUAAUGUCCAAGAUGCCU
ACACCCCGAAAGAAACUGCUGUAACCGUUGAUAAAACUACCU
AUAAAAAUGGUACAGAUCCUAUUACAGCCCAGAGCAAUACUG
AUAUCCAAACUGCAAUUGGCGGUGGUGCAACGGGGGUUACU
GGGGCUGAUAUCAAAUUUAAAGAUGGUCAAUACUAUUUAGA
UGUUAAAGGCGGUGCUUCUGCUGGUGUUUAUAAAGCCACUU
AUGAUGAAACUACAAAGAAAGUUAAUAUUGAUACGACUGAU
AAAACUCCGUUGGCAACUGCGGAAGCUACAGCUAUUCGGGGA
ACGGCCACUAUAACCCACAACCAAAUUGCUGAAGUAACAAAA

GAGGGUGUUGAUACGACCACAGUUGCGGCUCAACUUGCUGCA
GCAGGGGUUACUGGCGCCGAUAAGGACAAUACUAGCCUUGUA
AAACUAUCGUUUGAGGAUAAAAACGGUAAGGUUAUUGAUGG
UGGCUAUGCAGUGAAAAUGGGCGACGAUUUCUAUGCCGCUAC
AUAUGAUGAGAAAACAGGUGCAAUUACUGCUAAAACCACUA
CUUAUACAGAUGGUACUGGCGUUGCUCAAACUGGAGCUGUG
AAAUUUGGUGGCGCAAAUGGUAAAUCUGAAGUUGUUACUGC
UACCGAUGGUAAGACUUACUUAGCAAGCGACCUUGACAAACA
UAACUUCAGAACAGGCGGUGAGCUUAAAGAGGUUAAUACAG
AUAAGACUGAAAACCCACUGCAGAAAAUUGAUGCUGCCUUGG
CACAGGUUGAUACACUUCGUUCUGACCUGGGUGCGGUUCAGA
ACCGUUUCAACUCCGCUAUCACCAACCUGGGCAAUACCGUAA
AUAACCUGUCUUCUGCCCGUAGCCGUAUCGAAGAUUCCGACU
ACGCAACCGAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGC
AGCAGGCCGGUACCUCCGUUCUGGCGCAGGCGAACCAGGUUC
CGCAAAACGUCCUCUCUUUACUGCGUUGAUAAUAGGCUGGAG
CCUCGGUGGCCAUGCUUCUUGCCCCUUGGGCCUCCCCCCAGC
CCCUCCUCCCCUUCCUGCACCCGUACCCCCGUGGUCUUUGAA UAAAGUCUGAGUGGGCGGC ORF
AUGGCACAAGUCAUUAAUACAAACAGCCUGUCGCUGUUGACC 82 Sequence,
CAGAAUAACCUGAACAAAUCCCAGUCCGCACUGGGCACUGCU NT
AUCGAGCGUUUGUCUUCCGGUCUGCGUAUCAACAGCGCGAAA
GACGAUGCGGCAGGACAGGCGAUUGCUAACCGUUUUACCGCG
AACAUCAAAGGUCUGACUCAGGCUUCCCGUAACGCUAACGAC
GGUAUCUCCAUUGCGCAGACCACUGAAGGCGCGCUGAACGAA
AUCAACAACAACCUGCAGCGUGUGCGUGAACUGGCGGUUCAG
UCUGCGAAUGGUACUAACUCCCAGUCUGACCUCGACUCCAUC
CAGGCUGAAAUCACCCAGCGCCUGAACGAAAUCGACCGUGUA
UCCGGCCAGACUCAGUUCAACGGCGUGAAAGUCCUGGCGCAG
GACAACACCCUGACCAUCCAGGUUGGUGCCAACGACGGUGAA
ACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUCUAAAACACU
GGGACUUGAUAAGCUUAAUGUCCAAGAUGCCUACACCCCGAA
AGAAACUGCUGUAACCGUUGAUAAAACUACCUAUAAAAAUG
GUACAGAUCCUAUUACAGCCCAGAGCAAUACUGAUAUCCAAA
CUGCAAUUGGCGGUGGUGCAACGGGGGUUACUGGGGCUGAU
AUCAAAUUUAAAGAUGGUCAAUACUAUUUAGAUGUUAAAGG
CGGUGCUUCUGCUGGUGUUUAUAAAGCCACUUAUGAUGAAA
CUACAAAGAAAGUUAAUAUUGAUACGACUGAUAAAACUCCG
UUGGCAACUGCGGAAGCUACAGCUAUUCGGGGAACGGCCACU
AUAACCCACAACCAAAUUGCUGAAGUAACAAAAGAGGGUGU
UGAUACGACCACAGUUGCGGCUCAACUUGCUGCAGCAGGGGU
UACUGGCGCCGAUAAGGACAAUACUAGCCUUGUAAAACUAUC
GUUUGAGGAUAAAAACGGUAAGGUUAUUGAUGGUGGCUAUG
CAGUGAAAAUGGGCGACGAUUUCUAUGCCGCUACAUAUGAU
GAGAAAACAGGUGCAAUUACUGCUAAAACCACUACUUAUACA
GAUGGUACUGGCGUUGCUCAAACUGGAGCUGUGAAAUUUGG
UGGCGCAAAUGGUAAAUCUGAAGUUGUUACUGCUACCGAUG
GUAAGACUUACUUAGCAAGCGACCUUGACAAACAUAACUUCA
GAACAGGCGGUGAGCUUAAAGAGGUUAAUACAGAUAAGACU
GAAAACCCACUGCAGAAAAUUGAUGCUGCCUUGGCACAGGUU
GAUACACUUCGUUCUGACCUGGGUGCGGUUCAGAACCGUUUC
AACUCCGCUAUCACCAACCUGGGCAAUACCGUAAAUAACCUG
UCUUCUGCCCGUAGCCGUAUCGAAGAUUCCGACUACGCAACC
GAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGCAGCAGGCC
GGUACCUCCGUUCUGGCGCAGGCGAACCAGGUUCCGCAAAAC GUCCUCUCUUUACUGCGU

mRNA G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAAUAUAA 83 Sequence
GAGCCACCAUGGCACAAGUCAUUAAUACAAACAGCCUGUCGC (assumes
UGUUGACCCAGAAUAACCUGAACAAAUCCCAGUCCGCACUGG T100 tail)
GCACUGCUAUCGAGCGUUUGUCUUCCGGUCUGCGUAUCAACA
GCGCGAAAGACGAUGCGGCAGGACAGGCGAUUGCUAACCGUU
UUACCGCGAACAUCAAAGGUCUGACUCAGGCUUCCCGUAACG
CUAACGACGGUAUCUCCAUUGCGCAGACCACUGAAGGCGCGC
UGAACGAAAUCAACAACAACCUGCAGCGUGUGCGUGAACUGG
CGGUUCAGUCUGCGAAUGGUACUAACUCCCAGUCUGACCUCG
ACUCCAUCCAGGCUGAAAUCACCCAGCGCCUGAACGAAAUCG
ACCGUGUAUCCGGCCAGACUCAGUUCAACGGCGUGAAAGUCC
UGGCGCAGGACAACACCCUGACCAUCCAGGUUGGUGCCAACG
ACGGUGAAACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUCU
AAAACACUGGGACUUGAUAAGCUUAAUGUCCAAGAUGCCUAC
ACCCCGAAAGAAACUGCUGUAACCGUUGAUAAAACUACCUAU
AAAAAUGGUACAGAUCCUAUUACAGCCCAGAGCAAUACUGAU
AUCCAAACUGCAAUUGGCGGUGGUGCAACGGGGGUUACUGG
GGCUGAUAUCAAAUUUAAAGAUGGUCAAUACUAUUUAGAUG
UUAAAGGCGGUGCUUCUGCUGGUGUUUAUAAAGCCACUUAU
GAUGAAACUACAAAGAAAGUUAAUAUUGAUACGACUGAUAA
AACUCCGUUGGCAACUGCGGAAGCUACAGCUAUUCGGGGAAC
GGCCACUAUAACCCACAACCAAAUUGCUGAAGUAACAAAAGA
GGGUGUUGAUACGACCACAGUUGCGGCUCAACUUGCUGCAGC
AGGGGUUACUGGCGCCGAUAAGGACAAUACUAGCCUUGUAA
AACUAUCGUUUGAGGAUAAAAACGGUAAGGUUAUUGAUGGU
GGCUAUGCAGUGAAAAUGGGCGACGAUUUCUAUGCCGCUACA
UAUGAUGAGAAAACAGGUGCAAUUACUGCUAAAACCACUAC
UUAUACAGAUGGUACUGGCGUUGCUCAAACUGGAGCUGUGA
AAUUUGGUGGCGCAAAUGGUAAAUCUGAAGUUGUUACUGCU
ACCGAUGGUAAGACUUACUUAGCAAGCGACCUUGACAAACAU
AACUUCAGAACAGGCGGUGAGCUUAAAGAGGUUAAUACAGA
UAAGACUGAAAACCCACUGCAGAAAAUUGAUGCUGCCUUGGC
ACAGGUUGAUACACUUCGUUCUGACCUGGGUGCGGUUCAGAA
CCGUUUCAACUCCGCUAUCACCAACCUGGGCAAUACCGUAAA
UAACCUGUCUUCUGCCCGUAGCCGUAUCGAAGAUUCCGACUA
CGCAACCGAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGCA
GCAGGCCGGUACCUCCGUUCUGGCGCAGGCGAACCAGGUUCC
GCAAAACGUCCUCUCUUUACUGCGUUGAUAAUAGGCUGGAGC

CUCGGUGGCCAUGCUUCUUGCCCCUUGGGCCUCCCCCCAGCC
CCUCCUCCCCUUCCUGCACCCGUACCCCCGUGGUCUUUGAAU
AAAGUCUGAGUGGGCGGCAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUCUAG

TABLE-US-00018 TABLE 17 Flagellin Amino Acid Sequences SEQ ID Name Sequence NO: ORF
MAQVINTNSLSLLTQNNLNKSQSALGTAIERLSSGLRINSAKDDAA 54 Sequence,
GQAIANRFTANIKGLTQASRNANDGISIAQTTEGALNEINNNLQRV AA
RELAVQSANGTNSQSDLDSIQAEITQRLNEIDRVSGQTQFNGVKVL
AQDNTLTIQVGANDGETIDIDLKEISSKTLGLDKLNVQDAYTPKET
AVTVDKTTYKNGTDPITAQSNTDIQTAIGGGATGVTGADIKFKDGQ
YYLDVKGGASAGVYKATYDETTKKVNIDTTDKTPLATAEATAIRGT
ATITHNQIAEVTKEGVDTTTVAAQLAAAGVTGADKDNTSLVKLSFE
DKNGKVIDGGYAVKMGDDFYAATYDEKTGAITAKTTTYTDGTGVAQ

TGAVKFGGANGKSEVVTATDGKTYLASDLDKHNFRTGGELKEVNTD
KTENPLQKIDAALAQVDTLRSDLGAVQNRFNSAITNLGNTVNNLSS
ARSRIEDSDYATEVSNMSRAQILQQAGTSVLAQANQVPQNVLSLLR Flagellin-
MAQVINTNSLSLLTQNNLNKSQSALGTAIERLSSGLRINSAKDDAA 55 GS linker-
GQAIANRFTANIKGLTQASRNANDGISIAQTTEGALNEINNNLQRV circumspor
RELAVQSANSTNSQSDLDSIQAEITQRLNEIDRVSGQTQFNGVKVL ozoite
AQDNTLTIQVGANDGETIDIDLKQINSQTLGLDTLNVQQKYKVSDT protein
AATVTGYADTTIALDNSTFKASATGLGGTDQKIDGDLKFDDTTGKY (CSP)
YAKVTVTGGTGKDGYYEVSVDKTNGEVTLAGGATSPLTGGLPATAT
EDVKNVQVANADLTEAKAALTAAGVTGTASVVKMSYTDNNGKTIDG
GLAVKVGDDYYSATQNKDGSISINTTKYTADDGTSKTALNKLGGAD
GKTEVVSIGGKTYAASKAEGHNFKAQPDLAEAAATTTENPLQKIDA
ALAQVDTLRSDLGAVQNRFNSAITNLGNTVNNLTSARSRIEDSDYA
TEVSNMSRAQILQQAGTSVLAQANQVPQNVLSLLRGGGGSGGGGSM
MAPDPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPN
ANPNANPNANPNANPNANPNANPNANPNANPNANPNKNNQGNGQGH
NMPNDPNRNVDENANANNAVKNNNNEEPSDKHIEQYLKKIKNSIST
EWSPCSVTCGNGIQVRIKPGSANKPKDELDYENDIEKKICKMEKCS SVFNVVNS Flagellin-
MMAPDPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANP 56 RPVT
NANPNANPNANPNANPNANPNANPNANPNANPNANPNKNNQGNGQG linker-
HNMPNDPNRNVDENANANNAVKNNNNEEPSDKHIEQYLKKIKNSIS circumspor
TEWSPCSVTCGNGIQVRIKPGSANKPKDELDYENDIEKKICKMEKC ozoite
SSVFNVVNSRPVTMAQVINTNSLSLLTQNNLNKSQSALGTAIERLS protein
SGLRINSAKDDAAGQAIANRFTANIKGLTQASRNANDGISIAQTTE (CSP)
GALNEINNNLQRVRELAVQSANSTNSQSDLDSIQAEITQRLNEIDR
VSGQTQFNGVKVLAQDNTLTIQVGANDGETIDIDLKQINSQTLGLD
TLNVQQKYKVSDTAATVTGYADTTIALDNSTFKASATGLGGTDQKI
DGDLKFDDTTGKYYAKVTVTGGTGKDGYYEVSVDKTNGEVTLAGGA
TSPLTGGLPATATEDVKNVQVANADLTEAKAALTAAGVTGTASVVK
MSYTDNNGKTIDGGLAVKVGDDYYSATQNKDGSISINTTKYTADDG
TSKTALNKLGGADGKTEVVSIGGKTYAASKAEGHNFKAQPDLAEAA
ATTTENPLQKIDAALAQVDTLRSDLGAVQNRFNSAITNLGNTVNNL
TSARSRIEDSDYATEVSNMSRAQILQQAGTSVLAQANQVPQNVLSL LR

TABLE-US-00019 TABLE 18 Human Metapneumovirus Mutant Amino Acid Sequences SEQ ID Strain
Sequence NO: HMPV_SC_ MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 85
DSCAV1_ VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS 4MMV
FVLGAIALGVAAAAAVTAGVAICKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLAFAVRELKDFVSKNLTRALNKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILCGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFNVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 86 DSTRIC_
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS 4MMV
FVLGAIALGVAAAAAVTAGVAICKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILCGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS

YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEHQWHVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 87 DM_Krarup_
VGDVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGS T74LD185P
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 88 TM_Krarup_
VGDVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGS T74LD185PD454N
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPENQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 89 4M_Krarup_
VGDVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGS T74LS170LD185P
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVLKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 90 5M_Krarup_
VGDVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGS T74LS170LD185PD454N
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVLKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPENQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLP 91 DM_Krarup_
VGDVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGS E51PT74L
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT

NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLP 92 TM_Krarup_
VGDVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGS E51PT74LD454N
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPENQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 93 StabilizeAlpha_
VGDVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGS T74L
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 94 StabilizeAlpha_
VGDLENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS V55L
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 95 StabilizeAlpha_
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS S170L
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVLKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 96 StabilizeAlpha_
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS T174W
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLWRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED

QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_SC_4M_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 97 StabilizeAlpha_
VGDLENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGS V55LT74LS170LT174W
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVLKNLWRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLP 98 ProlineStab_
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS E51P
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 99 ProlineStab_
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS D185P
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 100 ProlineStab_
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS D183P
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCPIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 101 ProlineStab_
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS E131P
FVLGAIALGVAAAAAVTAGVAIAKTIRLPSEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG

FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 102 ProlineStab_
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS D447P
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFPPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 103 TrimerRepulsionD454N
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPENQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 104 TrimerRepulsionE453N
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVV
RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPQDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN HMPV_
MSWKVVIIFSLLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLE 105 StabilizeAlphaF196W
VGDVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGS
FVLGAIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGN
GVRVLATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQWNRRFLNVV

RQFSDNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLENRAMVRRKG
FGILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLRED
QGWYCQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTT
NYPCKVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCS
YITNQDADTVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVA
LDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVIILIAVLGSSMILVSI
FIIIKKTKKPTGAPPELSGVTNNGFIPHN

TABLE-US-00020 TABLE 19 SEQ ID Strain Nucleic Acid Sequence NO: Human Metapneumovirus Mutant Nucleic Acid Sequences HMPV_SC_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 106

DSCAV1_4MMV CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCTGCAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CTTTGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCCTGAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGTGTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCAACGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_SC_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 107 DSTRIC_4MMV
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCTGCAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC

GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGTGTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGCACCAGTGGCATGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_SC_DM_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 108 Krarup_T74LD185P
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA
CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCGG
TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA
TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA
GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC
CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC
GGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCAG
CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG
ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG
CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA
CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC
TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC
GTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAGC
AGAGCAAAGAGTGCAACATCAACATCAGCACCACCAACT

ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_TM_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 109 Krarup_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74LD185PD454N
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA
CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCGG
TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA
TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA
GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC
CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC
GGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCAG
CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG
ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG
CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA
CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC
TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC
GTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAGC
AGAGCAAAGAGTGCAACATCAACATCAGCACCACCAACT
ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_4M_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 110 Krarup_

CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74LS170LD185P
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA
CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCGG
TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA
TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA
GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC
CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC
GGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCAG
CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG
ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG
CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA
CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC
TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC
GTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAGC
AGAGCAAAGAGTGCAACATCAACATCAGCACCACCAACT
ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_5M_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 111 Krarup_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74LS170LD185PD454N
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA
CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCGG

TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA
TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA
GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC
CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC
GGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCAG
CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG
ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG
CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA
CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC
TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC
GTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAGC
AGAGCAAAGAGTGCAACATCAACATCAGCACCACCAACT
ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG

GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_DM_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 112 Krarup_E51PT74L
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGCCTGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT

GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_TM_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 113 Krarup_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT E51PT74LD454N
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGCCTGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 114 StabilizeAlpha_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74L

CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 115 SC_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT StabilizeAlpha_
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG V55L
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACCTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG

AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 116 SC_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT StabilizeAlpha_
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG S170L
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT

ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 117 SC_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT StabilizeAlpha_
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG T174W
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGTGGCGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG

TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_SC_4M_

ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 118 StabilizeAlpha_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT V55LT74LS170LT174W
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACCTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC
TGTGGCGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 119 ProlineStab_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT E51P
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGCCTGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC

GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 120 ProlineStab_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT D185P
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC

TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 121 ProlineStab_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT D183P
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCCCTATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 122 ProlineStab_

CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT E131P
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGCCTAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_ ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 123 ProlineStab_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT D447P
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC

GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC

CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCCCACCTATCAAGT
TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 124 TrimerRepulsionD454N
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA

ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 125 TrimerRepulsionE453N
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTCAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG

ACCAACAATGGCTTCATCCCTCACAAC HMPV_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 126 StabilizeAlphaF196W
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTGGAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC Human Metapneumovirus mRNA Sequences HMPV_SC_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 127 DSCAV1_4MMV
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCUGCAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU

AGAGUGCUGGCCUUUGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCCUGAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GUGUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCAACGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 128 DSURIC_4MMV
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCUGCAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GUGUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA

UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGCACCAGUGGCAUGUGGCCCUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_DM_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 129 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74LD185P
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG

AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC

UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_UM_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 130 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74LD185PD454N
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGAACCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_4M_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 131 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74LS170LD185P
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG

CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACAA
GUGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_5M_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 132 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74LS170LD185PD454N
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACAA
GUGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA

CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGAACCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_DM_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 133 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA E51PU74L
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC

UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_UM_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 134 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA E51PU74LD454N
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGAACCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU

GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 135 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74L
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU

GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 136 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA V55L
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACCUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA

CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 137 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA S170L
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACAA
GUGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG

AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 138 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U174W
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGUGGCGGGCCAUUAACAAGAACAA
GUGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG

CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_4M_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 139 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA V55LU74LS170LU174W
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACCUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGCUUAAGAACCUGUGGCGGGCCAUUAACAAGAACAA
GUGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 140 ProlineSUab_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA E51P
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU

GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 141 ProlineSUab_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA D185P
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC

GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAGC

CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 142 ProlineSUab_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA D183P
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCCCUAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG

AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 143 ProlineSUab_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA E131P
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGCCUAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU

CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 144 ProlineSUab_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA D447P
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCCCACCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 145 UrimerRepulsionD454N
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA

GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGAACCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 146 UrimerRepulsionE453N
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC

AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UCAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 147 SUabilizeAlphaF196W
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU

GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUGGAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAAUCACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG

GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCCAGGUGGCCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC

EQUIVALENTS

[0841] Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the disclosure described herein. Such equivalents are intended to be encompassed by the following claims.

[0842] All references, including patent documents, disclosed herein are incorporated by reference in their entirety.

Sequence CWU 1

1

14711620DNAUnknownHuman metapneumovirus 1atgagctgga aggtggtgat tatcttcagc ctgctgatta cacctcaaca cggcctgaag 60gagagctacc tggaagagag ctgctccacc atcaccgagg gctacctgag cgtgctgcgg 120accggctggt acaccaacgt gttcaccctg gaggtgggcg acgtggagaa cctgacctgc 180agcgacggcc ctagcctgat caagaccgag ctggacctga ccaagagcgc tctgagagag 240ctgaagaccg tgtccgccga ccagctggcc agagaggaac agatcgagaa ccctcggcag 300agcagattcg tgctgggcgc catcgctctg ggagtcgccg ctgccgctgc agtgacagct 360ggagtggcca ttgctaagac catcagactg gaaagcgagg tgacagccat caacaatgcc 420ctgaagaaga ccaacgaggc cgtgagcacc ctgggcaatg gagtgagagt gctggccaca 480gccgtgcggg agctgaagga cttcgtgagc aagaacctga ccagagccat caacaagaac 540aagtgcgaca tcgatgacct gaagatggcc gtgagcttct cccagttcaa cagacggttc 600ctgaacgtgg tgagacagtt ctccgacaac gctggaatca cacctgccat tagcctggac 660ctgatgaccg acgccgagct ggctagagcc gtgcccaaca tgcccaccag cgctggccag 720atcaagctga tgctggagaa cagagccatg gtgcggagaa agggcttcgg catcctgatt 780ggggtgtatg gaagctccgt gatctacatg gtgcagctgc ccatcttcgg cgtgatcgac 840acaccctgct ggatcgtgaa ggccgctcct agctgctccg agaagaaagg aaactatgcc 900tgtctgctga gagaggacca gggctggtac tgccagaacg ccggaagcac agtgtactat 960cccaacgaga aggactgcga gaccagaggc gaccacgtgt tctgcgacac cgctgccgga 1020atcaacgtgg ccgagcagag caaggagtgc aacatcaaca tcagcacaac caactacccc 1080tgcaaggtga gcaccggacg gcaccccatc agcatggtgg ctctgagccc tctgggcgct 1140ctggtggcct gctataaggg cgtgtcctgt agcatcggca gcaatcgggt gggcatcatc 1200aagcagctga acaagggatg ctcctacatc accaaccagg acgccgacac cgtgaccatc 1260gacaacaccg tgtaccagct gagcaaggtg gagggcgagc agcacgtgat caagggcaga 1320cccgtgagct ccagcttcga ccccatcaag ttccctgagg accagttcaa cgtggccctg 1380gaccaggtgt ttgagaacat cgagaacagc caggccctgg tggaccagag caacagaatc 1440ctgtccagcg ctgagaaggg caacaccggc ttcatcattg tgatcattct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgagcatc ttcatcatta tcaagaagac caagaaaccc 1560accggagccc ctcctgagct gagcggcgtg accaacaatg gcttcattcc ccacaactga 162021620DNAUnknownHuman metapneumovirus 2atgtcttgga aagtgatgat catcatttcg ttactcataa caccccagca cgggctaaag 60gagagttatt tggaagaatc atgtagtact ataactgagg gatacctcag tgttttaaga 120acaggctggt acactaatgt cttcacatta gaagttggtg atgttgaaaa tcttacatgt 180actgatggac ctagcttaat caaaacagaa cttgatctaa caaaaagtgc tttaagggaa 240ctcaaaacag tctctgctga tcagttggcg agagaggagc aaattgaaaa tcccagacaa 300tcaagatttg tcttaggtgc gatagctctc ggagttgcta cagcagcagc agtcacagca 360ggcattgcaa tagccaaaac cataaggctt gagagtgagg tgaatgcaat taaaggtgct 420ctcaaacaaa ctaatgaagc agtatccaca ttagggaatg gtgtgcgggt cctagccact 480gcagtgagag agctaaaaga atttgtgagc aaaaacctga ctagtgcaat caacaggaac 540aaatgtgaca ttgctgatct gaagatggct gtcagcttca gtcaattcaa cagaagattt 600ctaaatgttg tgcggcagtt ttcagacaat gcagggataa caccagcaat atcattggac 660ctgatgactg atgctgagtt ggccagagct gtatcataca tgccaacatc tgcagggcag 720ataaaactga tgttggagaa ccgcgcaatg gtaaggagaa aaggatttgg aatcctgata 780ggggtctacg gaagctctgt gatttacatg gttcaattgc cgatctttgg tgtcatagat 840acaccttgtt ggatcatcaa ggcagctccc tcttgctcag aaaaaaacgg gaattatgct 900tgcctcctaa gagaggatca agggtggtat tgtaaaaatg caggatctac tgtttactac 960ccaaatgaaa aagactgcga aacaagaggt gatcatgttt tttgtgacac agcagcaggg

1020atcaatgttg ctgagcaatc aagagaatgc aacatcaaca tatctactac caactaccca 1080tgcaaagtca gcacaggaag acaccctata agcatggttg cactatcacc tctcggtgct 1140ttggtggctt gctataaagg ggtaagctgc tcgattggca gcaattgggt tggaatcatc 1200aaacaattac ccaaaggctg ctcatacata accaaccagg atgcagacac tgtaacaatt 1260gacaataccg tgtatcaact aagcaaagtt gaaggtgaac agcatgtaat aaaagggaga 1320ccagtttcaa gcagttttga tccaatcaag tttcctgagg atcagttcaa tgttgcgctt 1380gatcaagtct tcgaaagcat tgagaacagt caggcactag tggaccagtc aaacaaaatt 1440ctaaacagtg cagaaaaagg aaacactggt ttcattatcg tagtaatttt ggttgctgtt 1500cttggtctaa ccatgatttc agtgagcatc atcatcataa tcaagaaaac aaggaagccc 1560acaggagcac ctccagagct gaatggtgtc accaacggcg gtttcatacc acatagttag 162031620DNAUnknownHuman metapneumovirus 3atgtcttgga aagtgatgat tatcatttcg ttactcataa cacctcagca tggactaaaa 60gaaagttatt tagaagaatc atgtagtact ataactgaag gatatctcag tgttttaaga 120acaggttggt acaccaatgt ctttacatta gaagttggtg atgttgaaaa tcttacatgt 180actgatggac ctagcttaat caaaacagaa cttgacctaa ccaaaagtgc tttaagagaa 240ctcaaaacag tttctgctga tcagttagcg agagaagaac aaattgaaaa tcccagacaa 300tcaaggtttg tcctaggtgc aatagctctt ggagttgcca cagcagcagc agtcacagca 360ggcattgcaa tagccaaaac tataaggctt gagagtgaag tgaatgcaat caaaggtgct 420ctcaaaacaa ccaatgaggc agtatcaaca ctaggaaatg gagtgcgggt cctagccact 480gcagtaagag agctgaaaga atttgtgagc aaaaacctga ctagtgcgat caacaagaac 540aagtgtgaca ttgctgattt gaagatggct gtcagcttca gtcagttcaa cagaagattc 600ctaaatgttg tgcggcagtt ttcagacaat gcagggataa caccagcaat atcattggac 660ctgatgaatg atgctgagct ggccagagct gtatcataca tgccaacatc tgcaggacag 720ataaaactaa tgttagagaa ccgtgcaatg gtgaggagaa aaggatttgg aatcttgata 780ggggtctacg gaagctctgt gatttacatg gtccagctgc cgatctttgg tgtcataaat 840acaccttgtt ggataatcaa ggcagctccc tcttgttcag aaaaagatgg aaattatgct 900tgcctcctaa gagaggatca agggtggtat tgtaaaaatg caggatccac tgtttactac 960ccaaatgaaa aagactgcga aacaagaggt gatcatgttt tttgtgacac agcagcaggg 1020atcaatgttg ctgagcaatc aagagaatgc aacatcaaca tatctaccac caactaccca 1080tgcaaagtca gcacaggaag acaccctatc agcatggttg cactatcacc tctcggtgct 1140ttggtagctt gctacaaagg ggttagctgc tcgactggca gtaatcaggt tggaataatc 1200aaacaactac ctaaaggctg ctcatacata actaaccagg acgcagacac tgtaacaatt 1260gacaacactg tgtatcaact aagcaaagtt gagggtgaac agcatgtaat aaaagggaga 1320ccagtttcaa gcagttttga tccaatcagg tttcctgagg atcagttcaa tgttgcgctt 1380gatcaagtct ttgaaagcat tgaaaacagt caagcactag tggaccagtc aaacaaaatt 1440ctgaacagtg cagaaaaagg aaacactggt ttcattattg taataatttt gattgctgtt 1500cttgggttaa ccatgatttc agtgagcatc atcatcataa tcaaaaaaac aaggaagccc 1560acaggggcac ctccggagct gaatggtgtt accaacggcg gtttcatacc gcatagttag 162041725DNAHuman respiratory syncytial virus 4atggagttgc caatcctcaa aacaaatgca attaccacaa tccttgctgc agtcacactc 60tgtttcgctt ccagtcaaaa catcactgaa gaattttatc aatcaacatg cagtgcagtt 120agcaaaggct atcttagtgc tctaagaact ggttggtata ctagtgttat aactatagaa 180ttaagtaata tcaaggaaaa taagtgtaat ggaacagatg ctaaggtaaa attgataaaa 240caagaattag ataaatataa aaatgctgta acagaattgc agttgctcat gcaaagcaca 300ccagcagcca acaatcgagc cagaagagaa ctaccaaggt ttatgaatta tacactcaat 360aataccaaaa ataccaatgt aacattaagc aagaaaagga aaagaagatt tcttggcttt 420ttgttaggtg ttggatctgc aatcgccagt ggcattgctg tatctaaggt cctgcaccta 480gaaggggaag tgaacaaaat caaaagtgct ctactatcca caaacaaggc tgtagtcagc 540ttatcaaatg gagttagtgt cttaaccagc aaagtgttag acctcaaaaa ctatatagat 600aaacagttgt tacctattgt gaacaagcaa agctgcagca tatcaaacat tgaaactgtg 660atagagttcc aacaaaagaa caacagacta ctagagatta ccagggaatt tagtgttaat 720gcaggtgtaa ctacacctgt aagcacttat atgttaacta atagtgaatt attatcatta 780atcaatgata tgcctataac aaatgatcag aaaaagttaa tgtccaacaa tgttcaaata 840gttagacagc aaagttactc tatcatgtcc ataataaagg aggaagtctt agcatatgta 900gtacaattac cactatatgg tgtaatagat acaccctgtt ggaaactgca cacatcccct 960ctatgtacaa ccaacacaaa ggaagggtcc aacatctgct taacaagaac cgacagagga 1020tggtattgtg acaatgcagg atcagtatct ttcttcccac aagctgaaac atgtaaagtt 1080caatcgaatc gggtattttg tgacacaatg aacagtttaa cattaccaag tgaagtaaat 1140ctctgcaaca ttgacatatt caaccccaaa tatgattgca aaattatgac ttcaaaaaca 1200gatgtaagca gctccgttat cacatctcta ggagccattg tgtcatgcta tggcaaaact 1260aaatgtacag catccaataa aaatcgtggg atcataaaga cattttctaa cgggtgtgat 1320tatgtatcaa ataagggggt ggatactgtg tctgtaggta atacattata ttatgtaaat 1380aagcaagaag gcaaaagtct ctatgtaaaa ggtgaaccaa taataaattt ctatgaccca 1440ttagtgttcc cctctgatga atttgatgca tcaatatctc aagtcaatga gaagattaac 1500cagagcctag catttattcg taaatccgat gaattattac ataatgtaaa tgctggtaaa 1560tccaccacaa atatcatgat aactactata attatagtga ttatagtaat attgttatca 1620ttaattgcag ttggactgct cctatactgc aaggccagaa gcacaccagt cacactaagt 1680aaggatcaac tgagtggtat aaataatatt gcatttagta actga 17255539PRTUnknownHuman metapneumovirus isolate 5Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn

Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 5356539PRTUnknownHuman metapneumovirus 6Met Ser Trp Lys Val Met Ile Ile Ile Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Thr Ala Ala Ala Val Thr Ala Gly Ile Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Asn Ala Ile Lys Gly Ala Leu Lys Gln Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Glu Phe Val Ser Lys Asn Leu Thr Ser Ala 165 170 175Ile Asn Arg Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Ser Tyr Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Ile Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Asn Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Trp Val Gly Ile Ile385 390 395 400Lys Gln Leu Pro Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe 450 455 460Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Lys Ile465 470 475 480Leu Asn Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Val Ile 485 490 495Leu Val Ala Val Leu Gly Leu Thr Met Ile Ser Val Ser Ile Ile Ile 500 505 510Ile Ile Lys Lys Thr Arg Lys Pro Thr Gly Ala Pro Pro Glu Leu Asn 515 520 525Gly Val Thr Asn Gly Gly Phe Ile Pro His Ser 530 5357539PRTUnknownHuman metapneumovirus 7Met Ser Trp Lys Val Met Ile Ile Ile Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Thr Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Arg Gln Ser Arg Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Thr Ala Ala Ala Val Thr Ala Gly Ile Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Asn Ala Ile Lys Gly Ala Leu Lys Thr Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Glu Phe Val Ser Lys Asn Leu Thr Ser Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Ala Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Asn Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Ser Tyr Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265

270Leu Pro Ile Phe Gly Val Ile Asn Thr Pro Cys Trp Ile Ile Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Asp Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Lys Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Arg Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Thr Gly Ser Asn Gln Val Gly Ile Ile385 390 395 400Lys Gln Leu Pro Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Arg Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe 450 455 460Glu Ser Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Lys Ile465 470 475 480Leu Asn Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Leu Thr Met Ile Ser Val Ser Ile Ile Ile 500 505 510Ile Ile Lys Lys Thr Arg Lys Pro Thr Gly Ala Pro Pro Glu Leu Asn 515 520 525Gly Val Thr Asn Gly Gly Phe Ile Pro His Ser 530 5358574PRTHuman respiratory syncytial virus 8Met Glu Leu Pro Ile Leu Lys Thr Asn Ala Ile Thr Thr Ile Leu Ala1 5 10 15Ala Val Thr Leu Cys Phe Ala Ser Ser Gln Asn Ile Thr Glu Glu Phe 20 25 30Tyr Gln Ser Thr Cys Ser Ala Val Ser Lys Gly Tyr Leu Ser Ala Leu 35 40 45Arg Thr Gly Trp Tyr Thr Ser Val Ile Thr Ile Glu Leu Ser Asn Ile 50 55 60Lys Glu Asn Lys Cys Asn Gly Thr Asp Ala Lys Val Lys Leu Ile Lys65 70 75 80Gln Glu Leu Asp Lys Tyr Lys Asn Ala Val Thr Glu Leu Gln Leu Leu 85 90 95Met Gln Ser Thr Pro Ala Ala Asn Asn Arg Ala Arg Arg Glu Leu Pro 100 105 110Arg Phe Met Asn Tyr Thr Leu Asn Asn Thr Lys Asn Thr Asn Val Thr 115 120 125Leu Ser Lys Lys Arg Lys Arg Arg Phe Leu Gly Phe Leu Leu Gly Val 130 135 140Gly Ser Ala Ile Ala Ser Gly Ile Ala Val Ser Lys Val Leu His Leu145 150 155 160Glu Gly Glu Val Asn Lys Ile Lys Ser Ala Leu Leu Ser Thr Asn Lys 165 170 175Ala Val Val Ser Leu Ser Asn Gly Val Ser Val Leu Thr Ser Lys Val 180 185 190Leu Asp Leu Lys Asn Tyr Ile Asp Lys Gln Leu Leu Pro Ile Val Asn 195 200 205Lys Gln Ser Cys Ser Ile Ser Asn Ile Glu Thr Val Ile Glu Phe Gln 210 215 220Gln Lys Asn Asn Arg Leu Leu Glu Ile Thr Arg Glu Phe Ser Val Asn225 230 235 240Ala Gly Val Thr Thr Pro Val Ser Thr Tyr Met Leu Thr Asn Ser Glu 245 250 255Leu Leu Ser Leu Ile Asn Asp Met Pro Ile Thr Asn Asp Gln Lys Lys 260 265 270Leu Met Ser Asn Asn Val Gln Ile Val Arg Gln Gln Ser Tyr Ser Ile 275 280 285Met Ser Ile Ile Lys Glu Glu Val Leu Ala Tyr Val Val Gln Leu Pro 290 295 300Leu Tyr Gly Val Ile Asp Thr Pro Cys Trp Lys Leu His Thr Ser Pro305 310 315 320Leu Cys Thr Thr Asn Thr Lys Glu Gly Ser Asn Ile Cys Leu Thr Arg 325 330 335Thr Asp Arg Gly Trp Tyr Cys Asp Asn Ala Gly Ser Val Ser Phe Phe 340 345 350Pro Gln Ala Glu Thr Cys Lys Val Gln Ser Asn Arg Val Phe Cys Asp 355 360 365Thr Met Asn Ser Leu Thr Leu Pro Ser Glu Val Asn Leu Cys Asn Ile 370 375 380Asp Ile Phe Asn Pro Lys Tyr Asp Cys Lys Ile Met Thr Ser Lys Thr385 390 395 400Asp Val Ser Ser Ser Val Ile Thr Ser Leu Gly Ala Ile Val Ser Cys 405 410 415Tyr Gly Lys Thr Lys Cys Thr Ala Ser Asn Lys Asn Arg Gly Ile Ile 420 425 430Lys Thr Phe Ser Asn Gly Cys Asp Tyr Val Ser Asn Lys Gly Val Asp 435 440 445Thr Val Ser Val Gly Asn Thr Leu Tyr Tyr Val Asn Lys Gln Glu Gly 450 455 460Lys Ser Leu Tyr Val Lys Gly Glu Pro Ile Ile Asn Phe Tyr Asp Pro465 470 475 480Leu Val Phe Pro Ser Asp Glu Phe Asp Ala Ser Ile Ser Gln Val Asn 485 490 495Glu Lys Ile Asn Gln Ser Leu Ala Phe Ile Arg Lys Ser Asp Glu Leu 500 505 510Leu His Asn Val Asn Ala Gly Lys Ser Thr Thr Asn Ile Met Ile Thr 515 520 525Thr Ile Ile Ile Val Ile Ile Val Ile Leu Leu Ser Leu Ile Ala Val 530 535 540Gly Leu Leu Leu Tyr Cys Lys Ala Arg Ser Thr Pro Val Thr Leu Ser545 550 555 560Lys Asp Gln Leu Ser Gly Ile Asn Asn Ile Ala Phe Ser Asn 565 57091617DNAHuman parainfluenza virus 3 9atgccaattt caatactgtt aattattaca accatgatca tggcatcaca ctgccaaata 60gacatcacaa aactacagca tgtaggtgta ttggtcaaca gtcccaaagg gatgaagata 120tcacaaaact tcgaaacaag atatctaatc ctgagtctca taccaaaaat agaagattct 180aactcttgtg gtgaccaaca gatcaagcaa tacaagaggt tattggatag actgatcatt 240cctttatatg atggactaag attacagaag gatgtgatag tgactaatca agaatccaat 300gaaaacactg atcccagaac agaacgattc tttggagggg taattggaac tattgctcta 360ggagtagcaa cctcagcaca aattacagca gcagttgctc tggttgaagc caagcaggca 420agatcagaca ttgaaaaact caaggaagca atcagggaca caaataaagc agtgcagtca 480gttcagagct ctgtaggaaa tttgatagta gcaattaaat cagtccagga ttatgtcaac 540aaagaaatcg tgccatcgat tgcgagacta ggttgtgaag cagcaggact tcagttaggg 600attgcattaa cacagcatta ctcagaatta acaaatatat ttggtgataa cataggatcg 660ttacaagaaa aaggaataaa attacaaggt atagcatcat tataccgtac aaatatcaca 720gaaatattca caacatcaac agttgacaaa tatgatattt atgatctatt atttacagaa 780tcaataaagg tgagagttat agatgttgat ttgaatgatt actcaataac cctccaagtc 840agactccctt tattgaccag actgctgaac actcaaatct acaaagtaga ttccatatca 900tacaatatcc aaaatagaga atggtatatc cctcttccca gccatatcat gacgaaaggg 960gcatttctag gtggagcaga tgtcaaagaa tgcatagaag cattcagcag ttatatatgc 1020ccttctgatc caggatttgt actaaaccat gaaatggaga gctgtctatc aggaaacata 1080tcccaatgtc caagaaccac agtcacatca gacatagttc ctaggtatgc atttgtcaat 1140ggaggagtgg ttgcgaattg tataacaact acatgtacat gcaatggtat cggtaataga 1200atcaaccaac cacctgatca aggagtcaaa attataacac ataaagaatg taatacaata 1260ggtatcaacg gaatgctatt caacacaaac aaagaaggaa ctcttgcatt ctacacacca 1320gacgacataa cattaaacaa ttctgttgca cttgatccga ttgacatatc aatcgagctc 1380aacaaggcca aatcagatct tgaggaatca aaagaatgga taagaaggtc aaatcaaaag 1440ctagattcta ttggaagttg gcatcaatct agcactacaa tcatagttat tttgataatg 1500atgattatat tgtttataat taatataaca ataattacaa ttgcaattaa gtattacaga 1560attcaaaaga gaaatcgagt ggatcaaaat gataagccgt atgtattaac aaacaag 1617101716DNAHuman parainfluenza virus 3 10atggaatact ggaagcacac caaccacgga aaggatgctg gtaatgagct ggagacatcc 60acagccactc atggcaacaa gctcaccaac aagataacat atatattgtg gacgataacc 120ctggtgttat tatcaatagt cttcatcata gtgctaacta attccatcaa aagtgaaaag 180gcccgcgaat cattgctaca agacataaat aatgagttta tggaagttac agaaaagatc 240caagtggcat cggataatac taatgatcta atacagtcag gagtgaatac aaggcttctt 300acaattcaga gtcatgtcca gaattatata ccaatatcat tgacacaaca aatatcggat 360cttaggaaat tcattagtga aattacaatt agaaatgata atcaagaagt gccaccacaa 420agaataacac atgatgtggg tataaaacct ttaaatccag atgatttctg gagatgcacg 480tctggtcttc catctttgat gaaaactcca aaaataagat taatgccggg accaggatta 540ttagctatgc caacgactgt tgatggctgt gtcagaaccc cgtccttagt gataaatgat 600ctgatttatg cttacacctc aaatctaatt actcgaggtt gccaggatat agggaaatca 660tatcaagtat tacagatagg gataataact gtaaactcag acttggtacc tgacttaaat 720cctaggatct ctcatacctt caacataaat gacaatagaa agtcatgttc tctagcactc 780ctaaatacag atgtatatca actgtgttca accccaaaag ttgatgaaag atcagattat 840gcatcatcag gcatagaaga tattgtactt gatattgtca attatgatgg ctcaatctcg 900acaacaagat ttaagaataa taatataagt tttgatcaac catatgcggc attataccca 960tctgttggac cagggatata ctacaaaggc aaaataatat ttctcgggta tggaggtctt 1020gaacatccaa taaatgagaa tgcaatctgc aacacaactg ggtgtcctgg gaaaacacag 1080agagactgta atcaagcatc tcatagtcca tggttttcag atagaaggat ggtcaactct 1140ataattgttg ttgacaaggg cttgaactca gttccaaaat tgaaggtatg gacgatatct 1200atgagacaaa attactgggg gtcagaagga agattacttc tactaggtaa caagatctac 1260atatacacaa gatctacaag ttggcacagc aagttacaat taggaataat tgacattact 1320gactacagtg atataaggat aaaatggaca tggcataatg tgctatcaag accaggaaac 1380aatgaatgtc catggggaca ttcatgtccg gatggatgta taacgggagt atataccgat 1440gcatatccac tcaatcccac aggaagcatt gtatcatctg tcatattgga ctcacaaaaa 1500tcgagagtca acccagtcat aacttactca acagcaaccg aaagggtaaa cgagctggct 1560atccgaaaca aaacactctc agctgggtac acaacaacaa gctgcattac acactataac 1620aaagggtatt gttttcatat agtagaaata aatcataaaa gcttaaacac atttcaaccc 1680atgttgttca aaacagagat tccaaaaagc tgcagt 1716111716DNAArtificial SequenceSynthetic Polynucleotide 11atggaatact ggaagcacac caaccacggc aaggacgccg gcaacgagct ggaaaccagc 60acagccacac acggcaacaa gctgaccaac aagatcacct acatcctgtg gaccatcacc 120ctggtgctgc tgagcatcgt gttcatcatc gtgctgacca atagcatcaa gagcgagaag 180gccagagaga gcctgctgca ggacatcaac aacgagttca tggaagtgac cgagaagatc 240caggtggcca gcgacaacac caacgacctg atccagagcg gcgtgaacac ccggctgctg 300accatccaga gccacgtgca gaactacatc cccatcagcc tgacccagca gatcagcgac 360ctgcggaagt tcatcagcga gatcaccatc cggaacgaca accaggaagt gcccccccag 420agaatcaccc acgacgtggg catcaagccc ctgaaccccg acgatttctg gcggtgtaca 480agcggcctgc ccagcctgat gaagaccccc aagatccggc tgatgcctgg ccctggactg 540ctggccatgc ctaccacagt ggatggctgt gtgcggaccc ccagcctcgt gatcaacgat 600ctgatctacg cctacaccag caacctgatc acccggggct gccaggatat cggcaagagc 660taccaggtgc tgcagatcgg catcatcacc gtgaactccg acctggtgcc cgacctgaac 720cctcggatca gccacacctt caacatcaac gacaacagaa agagctgcag cctggctctg 780ctgaacaccg acgtgtacca gctgtgcagc acccccaagg tggacgagag aagcgactac 840gccagcagcg gcatcgagga tatcgtgctg gacatcgtga actacgacgg cagcatcagc 900accacccggt tcaagaacaa caacatcagc ttcgaccagc cctacgccgc cctgtaccct 960tctgtgggcc ctggcatcta ctacaagggc aagatcatct tcctgggcta cggcggcctg 1020gaacacccca tcaacgagaa cgccatctgc aacaccaccg gctgccctgg caagacccag 1080agagactgca atcaggccag ccacagcccc tggttcagcg accgcagaat ggtcaactct 1140atcatcgtgg tggacaaggg cctgaacagc gtgcccaagc tgaaagtgtg gacaatcagc 1200atgcgccaga actactgggg cagcgagggc agacttctgc tgctgggaaa caagatctac 1260atctacaccc ggtccaccag ctggcacagc aaactgcagc tgggaatcat cgacatcacc 1320gactacagcg acatccggat caagtggacc tggcacaacg tgctgagcag acccggcaac 1380aatgagtgcc cttggggcca cagctgcccc gatggatgta tcaccggcgt gtacaccgac 1440gcctaccccc tgaatcctac cggctccatc gtgtccagcg tgatcctgga cagccagaaa 1500agcagagtga accccgtgat cacatacagc accgccaccg agagagtgaa cgaactggcc 1560atcagaaaca agaccctgag cgccggctac accaccacaa gctgcatcac acactacaac 1620aagggctact gcttccacat cgtggaaatc aaccacaagt ccctgaacac cttccagccc 1680atgctgttca agaccgagat ccccaagagc tgctcc 1716121617DNAArtificial SequenceSynthetic Polynucleotide 12atgcccatca gcatcctgct gatcatcacc acaatgatca tggccagcca ctgccagatc 60gacatcacca agctgcagca cgtgggcgtg ctcgtgaaca gccccaaggg catgaagatc 120agccagaact tcgagacacg ctacctgatc ctgagcctga tccccaagat cgaggacagc 180aacagctgcg gcgaccagca gatcaagcag tacaagcggc tgctggacag actgatcatc 240cccctgtacg acggcctgcg gctgcagaaa gacgtgatcg tgaccaacca ggaaagcaac 300gagaacaccg acccccggac cgagagattc ttcggcggcg tgatcggcac aatcgccctg 360ggagtggcca caagcgccca gattacagcc gctgtggccc tggtggaagc caagcaggcc 420agaagcgaca tcgagaagct gaaagaggcc atccgggaca ccaacaaggc cgtgcagagc 480gtgcagtcca gcgtgggcaa tctgatcgtg gccatcaagt ccgtgcagga ctacgtgaac 540aaagaaatcg tgccctctat cgcccggctg ggctgtgaag ctgccggact gcagctgggc 600attgccctga cacagcacta cagcgagctg accaacatct tcggcgacaa catcggcagc 660ctgcaggaaa agggcattaa gctgcaggga atcgccagcc tgtaccgcac caacatcacc 720gagatcttca ccaccagcac cgtggataag tacgacatct acgacctgct gttcaccgag 780agcatcaaag tgcgcgtgat cgacgtggac ctgaacgact acagcatcac cctgcaagtg 840cggctgcccc tgctgaccag actgctgaac acccagatct acaaggtgga cagcatctcc 900tacaacatcc agaaccgcga gtggtacatc cctctgccca gccacattat gaccaagggc 960gcctttctgg gcggagccga cgtgaaagag tgcatcgagg ccttcagcag ctacatctgc 1020cccagcgacc ctggcttcgt gctgaaccac gagatggaaa gctgcctgag cggcaacatc 1080agccagtgcc ccagaaccac cgtgacctcc gacatcgtgc ccagatacgc cttcgtgaat 1140ggcggcgtgg tggccaactg catcaccacc acctgtacct gcaacggcat cggcaaccgg 1200atcaaccagc ctcccgatca gggcgtgaag attatcaccc acaaagagtg taacaccatc 1260ggcatcaacg gcatgctgtt caataccaac aaagagggca ccctggcctt ctacaccccc 1320gacgatatca ccctgaacaa ctccgtggct ctggacccca tcgacatctc catcgagctg 1380aacaaggcca agagcgacct ggaagagtcc aaagagtgga tccggcggag caaccagaag 1440ctggactcta tcggcagctg gcaccagagc agcaccacca tcatcgtgat cctgattatg 1500atgattatcc tgttcatcat caacattacc atcatcacta tcgccattaa gtactaccgg 1560atccagaaac ggaaccgggt ggaccagaat gacaagccct acgtgctgac aaacaag 161713539PRTHuman parainfluenza virus 3 13Met Pro Ile Ser Ile Leu Leu Ile Ile Thr Thr Met Ile Met Ala Ser1 5 10 15His Cys Gln Ile Asp Ile Thr Lys Leu Gln His Val Gly Val Leu Val 20 25 30Asn Ser Pro Lys Gly Met Lys Ile Ser Gln Asn Phe Glu Thr Arg Tyr 35 40 45Leu Ile Leu Ser Leu Ile Pro Lys Ile Glu Asp Ser Asn Ser Cys Gly 50 55 60Asp Gln Gln Ile Lys Gln Tyr Lys Arg Leu Leu Asp Arg Leu Ile Ile65 70 75 80Pro Leu Tyr Asp Gly Leu Arg Leu Gln Lys Asp Val Ile Val Thr Asn 85 90 95Gln Glu Ser Asn Glu Asn Thr Asp Pro Arg Thr Glu Arg Phe Phe Gly 100 105 110Gly Val Ile Gly Thr Ile Ala Leu Gly Val Ala Thr Ser Ala Gln Ile 115 120 125Thr Ala Ala Val Ala Leu Val Glu Ala Lys Gln Ala Arg Ser Asp Ile 130 135 140Glu Lys Leu Lys Glu Ala Ile Arg Asp Thr Asn Lys Ala Val Gln Ser145 150 155 160Val Gln Ser Ser Val Gly Asn Leu Ile Val Ala Ile Lys Ser Val Gln 165 170 175Asp Tyr Val Asn Lys Glu Ile Val Pro Ser Ile Ala Arg Leu Gly Cys 180 185 190Glu Ala Ala Gly Leu Gln Leu Gly Ile Ala Leu Thr Gln His Tyr Ser 195 200 205Glu Leu Thr Asn Ile Phe Gly Asp Asn Ile Gly Ser Leu Gln Glu Lys 210 215 220Gly Ile Lys Leu Gln Gly Ile Ala Ser Leu Tyr Arg Thr Asn Ile Thr225 230 235 240Glu Ile Phe Thr Thr Ser Thr Val Asp Lys Tyr Asp Ile Tyr Asp Leu 245 250 255Leu Phe Thr Glu Ser Ile Lys Val Arg Val Ile Asp Val Asp Leu Asn 260 265 270Asp Tyr Ser Ile Thr Leu Gln Val Arg Leu Pro Leu Leu Thr Arg Leu 275 280 285Leu Asn Thr Gln Ile Tyr Lys Val Asp Ser Ile Ser Tyr Asn Ile Gln 290 295 300Asn Arg Glu Trp Tyr Ile Pro Leu Pro Ser His Ile Met Thr Lys Gly305 310 315 320Ala Phe Leu Gly Gly Ala Asp Val Lys Glu Cys Ile Glu Ala Phe Ser 325 330 335Ser Tyr Ile Cys Pro Ser Asp Pro Gly Phe Val Leu Asn His Glu Met 340 345 350Glu Ser Cys Leu Ser Gly Asn Ile Ser Gln Cys Pro Arg Thr Thr Val 355 360 365Thr Ser Asp Ile Val Pro Arg Tyr Ala Phe Val Asn Gly Gly Val Val 370 375 380Ala Asn Cys Ile Thr Thr Thr Cys Thr Cys Asn Gly Ile Gly Asn Arg385 390 395 400Ile Asn Gln Pro Pro Asp Gln Gly Val Lys Ile Ile Thr His Lys Glu 405 410 415Cys Asn Thr Ile Gly Ile Asn Gly Met Leu Phe Asn Thr Asn Lys Glu 420 425 430Gly Thr Leu Ala Phe Tyr Thr Pro Asp Asp Ile Thr Leu Asn Asn Ser 435 440 445Val Ala Leu Asp Pro Ile Asp Ile Ser Ile Glu Leu Asn Lys Ala Lys 450 455 460Ser Asp Leu Glu Glu Ser Lys Glu Trp Ile Arg Arg Ser Asn Gln Lys465 470 475 480Leu Asp Ser Ile Gly Ser Trp His Gln Ser Ser Thr Thr Ile Ile Val

485 490 495Ile Leu Ile Met Met Ile Ile Leu Phe Ile Ile Asn Ile Thr Ile Ile 500 505 510Thr Ile Ala Ile Lys Tyr Tyr Arg Ile Gln Lys Arg Asn Arg Val Asp 515 520 525Gln Asn Asp Lys Pro Tyr Val Leu Thr Asn Lys 530 53514572PRTHuman parainfluenza virus 3 14Met Glu Tyr Trp Lys His Thr Asn His Gly Lys Asp Ala Gly Asn Glu1 5 10 15Leu Glu Thr Ser Thr Ala Thr His Gly Asn Lys Leu Thr Asn Lys Ile 20 25 30Thr Tyr Ile Leu Trp Thr Ile Thr Leu Val Leu Leu Ser Ile Val Phe 35 40 45Ile Ile Val Leu Thr Asn Ser Ile Lys Ser Glu Lys Ala Arg Glu Ser 50 55 60Leu Leu Gln Asp Ile Asn Asn Glu Phe Met Glu Val Thr Glu Lys Ile65 70 75 80Gln Val Ala Ser Asp Asn Thr Asn Asp Leu Ile Gln Ser Gly Val Asn 85 90 95Thr Arg Leu Leu Thr Ile Gln Ser His Val Gln Asn Tyr Ile Pro Ile 100 105 110Ser Leu Thr Gln Gln Ile Ser Asp Leu Arg Lys Phe Ile Ser Glu Ile 115 120 125Thr Ile Arg Asn Asp Asn Gln Glu Val Pro Pro Gln Arg Ile Thr His 130 135 140Asp Val Gly Ile Lys Pro Leu Asn Pro Asp Asp Phe Trp Arg Cys Thr145 150 155 160Ser Gly Leu Pro Ser Leu Met Lys Thr Pro Lys Ile Arg Leu Met Pro 165 170 175Gly Pro Gly Leu Leu Ala Met Pro Thr Thr Val Asp Gly Cys Val Arg 180 185 190Thr Pro Ser Leu Val Ile Asn Asp Leu Ile Tyr Ala Tyr Thr Ser Asn 195 200 205Leu Ile Thr Arg Gly Cys Gln Asp Ile Gly Lys Ser Tyr Gln Val Leu 210 215 220Gln Ile Gly Ile Ile Thr Val Asn Ser Asp Leu Val Pro Asp Leu Asn225 230 235 240Pro Arg Ile Ser His Thr Phe Asn Ile Asn Asp Asn Arg Lys Ser Cys 245 250 255Ser Leu Ala Leu Leu Asn Thr Asp Val Tyr Gln Leu Cys Ser Thr Pro 260 265 270Lys Val Asp Glu Arg Ser Asp Tyr Ala Ser Ser Gly Ile Glu Asp Ile 275 280 285Val Leu Asp Ile Val Asn Tyr Asp Gly Ser Ile Ser Thr Thr Arg Phe 290 295 300Lys Asn Asn Asn Ile Ser Phe Asp Gln Pro Tyr Ala Ala Leu Tyr Pro305 310 315 320Ser Val Gly Pro Gly Ile Tyr Tyr Lys Gly Lys Ile Ile Phe Leu Gly 325 330 335Tyr Gly Gly Leu Glu His Pro Ile Asn Glu Asn Ala Ile Cys Asn Thr 340 345 350Thr Gly Cys Pro Gly Lys Thr Gln Arg Asp Cys Asn Gln Ala Ser His 355 360 365Ser Pro Trp Phe Ser Asp Arg Arg Met Val Asn Ser Ile Ile Val Val 370 375 380Asp Lys Gly Leu Asn Ser Val Pro Lys Leu Lys Val Trp Thr Ile Ser385 390 395 400Met Arg Gln Asn Tyr Trp Gly Ser Glu Gly Arg Leu Leu Leu Leu Gly 405 410 415Asn Lys Ile Tyr Ile Tyr Thr Arg Ser Thr Ser Trp His Ser Lys Leu 420 425 430Gln Leu Gly Ile Ile Asp Ile Thr Asp Tyr Ser Asp Ile Arg Ile Lys 435 440 445Trp Thr Trp His Asn Val Leu Ser Arg Pro Gly Asn Asn Glu Cys Pro 450 455 460Trp Gly His Ser Cys Pro Asp Gly Cys Ile Thr Gly Val Tyr Thr Asp465 470 475 480Ala Tyr Pro Leu Asn Pro Thr Gly Ser Ile Val Ser Ser Val Ile Leu 485 490 495Asp Ser Gln Lys Ser Arg Val Asn Pro Val Ile Thr Tyr

Ser Thr Ala 500 505 510Thr Glu Arg Val Asn Glu Leu Ala Ile Arg Asn Lys Thr Leu Ser Ala 515 520 525Gly Tyr Thr Thr Thr Ser Cys Ile Thr His Tyr Asn Lys Gly Tyr Cys 530 535 540Phe His Ile Val Glu Ile Asn His Lys Ser Leu Asn Thr Phe Gln Pro545 550 555 560Met Leu Phe Lys Thr Glu Ile Pro Lys Ser Cys Ser 565 5701520PRTArtificial SequenceSynthetic Polypeptide 15Met Glu Thr Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro1 5 10 15Asp Thr Thr Gly 201618PRTArtificial SequenceSynthetic Polypeptide 16Met Asp Trp Thr Trp Ile Leu Phe Leu Val Ala Ala Ala Thr Arg Val1 5 10 15His Ser1724PRTArtificial SequenceSynthetic Polypeptide 17Met Leu Gly Ser Asn Ser Gly Gln Arg Val Val Phe Thr Ile Leu Leu1 5 10 15Leu Leu Val Ala Pro Ala Tyr Ser 201817PRTArtificial SequenceSynthetic Polypeptide 18Met Lys Cys Leu Leu Tyr Leu Ala Phe Leu Phe Ile Gly Val Asn Cys1 5 10 15Ala1915PRTArtificial SequenceSynthetic Polypeptide 19Met Trp Leu Val Ser Leu Ala Ile Val Thr Ala Cys Ala Gly Ala1 5 10 15204062DNAUnknownMiddle East respiratory syndrome coronavirus 20atgatacact cagtgtttct actgatgttc ttgttaacac ctacagaaag ttacgttgat 60gtagggccag attctgttaa gtctgcttgt attgaggttg atatacaaca gaccttcttt 120gataaaactt ggcctaggcc aattgatgtt tctaaggctg acggtattat ataccctcaa 180ggccgtacat attctaacat aactatcact tatcaaggtc tttttcccta tcagggagac 240catggtgata tgtatgttta ctctgcagga catgctacag gcacaactcc acaaaagttg 300tttgtagcta actattctca ggacgtcaaa cagtttgcta atgggtttgt cgtccgtata 360ggagcagctg ccaattccac tggcactgtt attattagcc catctaccag cgctactata 420cgaaaaattt accctgcttt tatgctgggt tcttcagttg gtaatttctc agatggtaaa 480atgggccgct tcttcaatca tactctagtt cttttgcccg atggatgtgg cactttactt 540agagcttttt attgtattct agagcctcgc tctggaaatc attgtcctgc tggcaattcc 600tatacttctt ttgccactta tcacactcct gcaacagatt gttctgatgg caattacaat 660cgtaatgcca gtctgaactc ttttaaggag tattttaatt tacgtaactg cacctttatg 720tacacttata acattaccga agatgagatt ttagagtggt ttggcattac acaaactgct 780caaggtgttc acctcttctc atctcggtat gttgatttgt acggcggcaa tatgtttcaa 840tttgccacct tgcctgttta tgatactatt aagtattatt ctatcattcc tcacagtatt 900cgttctatcc aaagtgatag aaaagcttgg gctgccttct acgtatataa acttcaaccg 960ttaactttcc tgttggattt ttctgttgat ggttatatac gcagagctat agactgtggt 1020tttaatgatt tgtcacaact ccactgctca tatgaatcct tcgatgttga atctggagtt 1080tattcagttt cgtctttcga agcaaaacct tctggctcag ttgtggaaca ggctgaaggt 1140gttgaatgtg atttttcacc tcttctgtct ggcacacctc ctcaggttta taatttcaag 1200cgtttggttt ttaccaattg caattataat cttaccaaat tgctttcact tttttctgtg 1260aatgatttta cttgtagtca aatatctcca gcagcaattg ctagcaactg ttattcttca 1320ctgattttgg attatttttc atacccactt agtatgaaat ccgatctcag tgttagttct 1380gctggtccaa tatcccagtt taattataaa cagtcctttt ctaatcccac atgtttgatc 1440ttagcgactg ttcctcataa ccttactact attactaagc ctcttaagta cagctatatt 1500aacaagtgct ctcgtcttct ttctgatgat cgtactgaag tacctcagtt agtgaacgct 1560aatcaatact caccctgtgt atccattgtc ccatccactg tgtgggaaga cggtgattat 1620tataggaaac aactatctcc acttgaaggt ggtggctggc ttgttgctag tggctcaact 1680gttgccatga ctgagcaatt acagatgggc tttggtatta cagttcaata tggtacagac 1740accaatagtg tttgccccaa gcttgaattt gctaatgaca caaaaattgc ctctcaatta 1800ggcaattgcg tggaatattc cctctatggt gtttcgggcc gtggtgtttt tcagaattgc 1860acagctgtag gtgttcgaca gcagcgcttt gtttatgatg cgtaccagaa tttagttggc 1920tattattctg atgatggcaa ctactactgt ctgcgtgctt gtgttagtgt tcctgtttct 1980gtcatctatg ataaagaaac taaaacccac gctactctat ttggtagtgt tgcatgtgaa 2040cacatttctt ctaccatgtc tcaatactcc cgttctacgc gatcaatgct taaacggcga 2100gattctacat atggcccct tcagacacct gttggttgtg tcctaggact tgttaattcc 2160tctttgttcg tagaggactg caagttgcct ctcggtcaat ctctctgtgc tcttcctgac 2220acacctagta ctctcacacc tcgcagtgtg cgctctgtgc caggtgaaat gcgcttggca 2280tccattgctt ttaatcatcc cattcaggtt gatcaactta atagtagtta ttttaaatta 2340agtataccca ctaatttttc ctttggtgtg actcaggagt acattcagac aaccattcag 2400aaagttactg ttgattgtaa acagtacgtt tgcaatggtt tccagaagtg tgagcaatta 2460ctgcgcgagt atggccagtt ttgttccaaa ataaaccagg ctctccatgg tgccaattta 2520cgccaggatg attctgtacg taatttgttt gcgagcgtga aaagctctca atcatctcct 2580atcataccag gttttggagg tgactttaat ttgacacttc tagaacctgt ttctatatct 2640actggcagtc gtagtgcacg tagtgctatt gaggatttgc tatttgacaa agtcactata 2700gctgatcctg gttatatgca aggttacgat gattgtatgc agcaaggtcc agcatcagct 2760cgtgatctta tttgtgctca atatgtggct ggttataaag tattacctcc tcttatggat 2820gttaatatgg aagccgcgta tacttcatct ttgcttggca gcatagcagg tgttggctgg 2880actgctggct tatcctcctt tgctgctatt ccatttgcac agagtatytt ttataggtta 2940aacggtgttg gcattactca acaggttctt tcagagaacc aaaagcttat tgccaataag 3000tttaatcagg ctctgggagc tatgcaaaca ggcttcacta caactaatga agcttttcgg 3060aaggttcagg atgctgtgaa caacaatgca caggctctat ccaaattagc tagcgagcta 3120tctaatactt ttggtgctat ttccgcctct attggagaca tcatacaacg tcttgatgtt 3180ctcgaacagg acgcccaaat agacagactt attaatggcc gtttgacaac actaaatgct 3240tttgttgcac agcagcttgt tcgttccgaa tcagctgctc tttccgctca attggctaaa 3300gataaagtca atgagtgtgt caaggcacaa tccaagcgtt ctggattttg cggtcaaggc 3360acacatatag tgtcctttgt tgtaaatgcc cctaatggcc tttactttat gcatgttggt 3420tattacccta gcaaccacat tgaggttgtt tctgcttatg gtctttgcga tgcagctaac 3480cctactaatt gtatagcccc tgttaatggc tactttatta aaactaataa cactaggatt 3540gttgatgagt ggtcatatac tggctcgtcc ttctatgcac ctgagcccat cacctctctt 3600aatactaagt atgttgcacc acaggtgaca taccaaaaca tttctactaa cctccctcct 3660cctcttctcg gcaattccac cgggattgac ttccaagatg agttggatga gtttttcaaa 3720aatgttagca ccagtatacc taattttggt tctctaacac agattaatac tacattactc 3780gatcttacct acgagatgtt gtctcttcaa caagttgtta aagcccttaa tgagtcttac 3840atagacctta aagagcttgg caattatact tattacaaca aatggccgtg gtacatttgg 3900cttggtttca ttgctgggct tgttgcctta gctctatgcg tcttcttcat actgtgctgc 3960actggttgtg gcacaaactg tatgggaaaa cttaagtgta atcgttgttg tgatagatac 4020gaggaatacg acctcgagcc gcataaggtt catgttcact aa 4062214062DNAArtificial SequenceSynthetic

Polynucleotide 21atgatacact cagtgtttct actgatgttc ttgttaacac ctacagaaag ttacgttgat 60gtagggccag attctgttaa gtctgcttgt attgaggttg atatacaaca gactttcttt 120gataaaactt ggcctaggcc aattgatgtt tctaaggctg acggtattat ataccctcaa 180ggccgtacat attctaacat aactatcact tatcaaggtc tttttcccta tcagggagac 240catggtgata tgtatgttta ctctgcagga catgctacag gcacaactcc acaaaagttg 300tttgtagcta actattctca ggacgtcaaa cagtttgcta atgggtttgt cgtccgtata 360ggagcagctg ccaattccac tggcactgtt attattagcc catctaccag cgctactata 420cgaaaaattt accctgcttt tatgctgggt tcttcagttg gtaatttctc agatggtaaa 480atgggccgct tcttcaatca tactctagtt cttttgcccg atggatgtgg cactttactt 540agagcttttt attgtattct ggagcctcgc tctggaaatc attgtcctgc tggcaattcc 600tatacttctt ttgccactta tcacactcct gcaacagatt gttctgatgg caattacaat 660cgtaatgcca gtctgaactc ttttaaggag tattttaatt tacgtaactg cacctttatg 720tacacttata acattaccga agatgagatt ttagagtggt ttggcattac acaaactgct 780caaggtgttc acctcttctc atctcggtat gttgatttgt acggcggcaa tatgtttcaa 840tttgccacct tgcctgttta tgatactatt aagtattatt ctatcattcc tcacagtatt 900cgttctatcc aaagtgatag aaaagcttgg gctgccttct acgtatataa acttcaaccg 960ttaactttcc tgttggattt ttctgttgat ggttatatac gcagagctat agactgtggt 1020tttaatgatt tgtcacaact ccactgctca tatgaatcct tcgatgttga atctggagtt 1080tattcagttt cgtctttcga agcaaaacct tctggctcag ttgtggaaca ggctgaaggt 1140gttgaatgtg atttttcacc tcttctgtct ggcacacctc ctcaggttta taatttcaag 1200cgtttggttt ttaccaattg caattataat cttaccaaat tgctttcact tttttctgtg 1260aatgatttta cttgtagtca aatatctcca gcagcaattg ctagcaactg ttattcttca 1320ctgattttgg attacttttc atacccactt agtatgaaat ccgatctcag tgttagttct 1380gctggtccaa tatcccagtt taattataaa cagtcctttt ctaatcccac atgtttgatt 1440ttagcgactg ttcctcataa ccttactact attactaagc ctcttaagta cagctatatt 1500aacaagtgct ctcgtcttct ttctgatgat cgtactgaag tacctcagtt agtgaacgct 1560aatcaatact caccctgtgt atccattgtc ccatccactg tgtgggaaga cggtgattat 1620tataggaaac aactatctcc acttgaaggt ggtggctggc ttgttgctag tggctcaact 1680gttgccatga ctgagcaatt acagatgggc tttggtatta cagttcaata tggtacagac 1740accaatagtg tttgccccaa gcttgaattt gctaatgaca caaaaaattgc ctctcaatta 1800ggcaattgcg tggaatattc cctctatggt gtttcgggcc gtggtgtttt tcagaattgc 1860acagctgtag gtgttcgaca gcagcgcttt gtttatgatg cgtaccagaa tttagttggc 1920tattattctg atgatggcaa ctactactgt ttgcgtgctt gtgttagtgt tcctgtttct 1980gtcatctatg ataaagaaac taaaacccac gctactctat ttggtagtgt tgcatgtgaa 2040cacatttctt ctaccatgtc tcaatactcc cgttctacgc gatcaatgct taaacggcga 2100gattctacat atggcccccct tcagacacct gttggttgtg tcctaggact tgttaattcc 2160tctttgttcg tagaggactg caagttgcct cttggtcaat ctctctgtgc tcttcctgac 2220acacctagta ctctcacacc tcgcagtgtg cgctctgttc caggtgaaat gcgcttggca 2280tccattgctt ttaatcatcc tattcaggtt gatcaactta atagtagtta ttttaaatta 2340agtataccca ctaatttttc ctttggtgtg actcaggagt acattcagac aaccattcag 2400aaagttactg ttgattgtaa acagtacgtt tgcaatggtt tccagaagtg tgagcaatta 2460ctgcgcgagt atggccagtt ttgttccaaa ataaaccagg ctctccatgg tgccaattta 2520cgccaggatg attctgtacg taatttgttt gcgagcgtga aaagctctca atcatctcct 2580atcataccag gttttggagg tgactttaat ttgacacttc tggaacctgt ttctatatct 2640actggcagtc gtagtgcacg tagtgctatt gaggatttgc tatttgacaa agtcactata 2700gctgatcctg gttatatgca aggttacgat gattgcatgc agcaaggtcc agcatcagct 2760cgtgatctta tttgtgctca atatgtggct ggttacaaag tattacctcc tcttatggat 2820gttaatatgg aagccgcgta tacttcatct ttgcttggca gcatagcagg tgttggctgg 2880actgctggct tatcctcctt tgctgctatt ccatttgcac agagtatctt ttataggtta 2940aacggtgttg gcattactca acaggttctt tcagagaacc aaaagcttat tgccaataag 3000tttaatcagg ctctgggagc tatgcaaaca ggcttcacta caactaatga agcttttcag 3060aaggttcagg atgctgtgaa caacaatgca caggctctat ccaaattagc tagcgagcta 3120tctaatactt ttggtgctat ttccgcctct attggagaca tcatacaacg tcttgatgtt 3180ctcgaacagg acgcccaaat agacagactt attaatggcc gtttgacaac actaaatgct 3240tttgttgcac agcagcttgt tcgttccgaa tcagctgctc tttccgctca attggctaaa 3300gataaagtca atgagtgtgt caaggcacaa tccaagcgtt ctggattttg cggtcaaggc 3360acacatatag tgtcctttgt tgtaaatgcc cctaatggcc tttacttcat gcatgttggt 3420tattacccta gcaaccacat tgaggttgtt tctgcttatg gtctttgcga tgcagctaac 3480cctactaatt gtatagcccc tgttaatggc tactttatta aaactaataa cactaggatt 3540gttgatgagt ggtcatatac tggctcgtcc ttctatgcac ctgagcccat tacctccctt 3600aatactaagt atgttgcacc acaggtgaca taccaaaaca tttctactaa cctccctcct 3660cctcttctcg gcaattccac cgggattgac ttccaagatg agttggatga gtttttcaaa 3720aatgttagca ccagtatacc taattttggt tccctaacac agattaatac tacattactc 3780gatcttacct acgagatgtt gtctcttcaa caagttgtta aagcccttaa tgagtcttac 3840atagacctta aagagcttgg caattatact tattacaaca aatggccgtg gtacatttgg 3900cttggtttca ttgctgggct tgttgcctta gctctatgcg tcttcttcat actgtgctgc 3960actggttgtg gcacaaactg tatgggaaaa cttaagtgta atcgttgttg tgatagatac 4020gaggaatacg acctcgagcc gcataaggtt catgttcact aa 4062221845DNAArtificial SequenceSynthetic Polynucleotide 22atgatccact ccgtgttcct cctcatgttc ctgttgaccc ccactgagtc agactgcaag 60ctcccgctgg gacagtccct gtgtgcgctg cctgacactc ctagcactct gaccccacgc 120tccgtgcggt cggtgcctgg cgaaatgcgg ctggcctcca tcgccttcaa tcacccaatc 180caagtggatc agctgaatag ctcgtatttc aagctgtcca tccccacgaa cttctcgttc 240ggggtcaccc aggagtacat ccagaccaca attcagaagg tcaccgtcga ttgcaagcaa 300tacgtgtgca acggcttcca gaagtgcgag cagctgctga gagaatacgg gcagttttgc 360agcaagatca accaggcgct gcatggagct aacttgcgcc aggacgactc cgtgcgcaac 420ctctttgcct ctgtgaagtc atcccagtcc tccccaatca tcccgggatt cggaggggac 480ttcaacctga ccctcctgga gcccgtgtcg atcagcaccg gtagcagatc ggcgcgctca 540gccattgaag atcttctgtt cgacaaggtc accatcgccg atccgggcta catgcaggga 600tacgacgact gtatgcagca gggaccagcc tccgcgaggg acctcatctg cgcgcaatac 660gtggccgggt acaaagtgct gcctcctctg atggatgtga acatggaggc cgcttatact 720tcgtccctgc tcggctctat cgccggcgtg gggtggaccg ccggcctgtc ctccttcgcc 780gctatcccct ttgcacaatc cattttctac cggctcaacg gcgtgggcat tactcaacaa 840gtcctgtcgg agaaccagaa gttgatcgca aacaagttca atcaggccct gggggccatg 900cagactggat tcactacgac taacgaagcg ttccagaagg tccaggacgc tgtgaacaac 960aacgcccagg cgctctcaaa gctggcctcc gaactcagca acaccttcgg agccatcagc 1020gcatcgatcg gtgacataat tcagcggctg gacgtgctgg agcaggacgc ccagatcgac 1080cgcctcatca acggacggct gaccaccttg aatgccttcg tggcacaaca gctggtccgg 1140agcgaatcag cggcactttc cgcccaactc gccaaggaca aagtcaacga atgcgtgaag 1200gcccagtcca agaggtccgg tttctgcggt caaggaaccc atattgtgtc cttcgtcgtg 1260aacgcgccca acggtctgta ctttatgcac gtcggctact acccgagcaa tcatatcgaa 1320gtggtgtccg cctacggcct gtgcgatgcc gctaacccca ctaactgtat tgcccctgtg 1380aacggatatt ttattaagac caacaacacc cgcattgtgg acgaatggtc atacaccggt 1440tcgtccttct acgcgcccga gcccatcact tcactgaaca ccaaatacgt ggctccgcaa 1500gtgacctacc agaacatctc caccaatttg ccgccgccgc tgctcggaaa cagcaccgga 1560attgatttcc aagatgaact ggacgaattc ttcaagaacg tgtccacttc cattcccaac 1620ttcggaagcc tgacacagat caacaccacc cttctcgacc tgacctacga gatgctgagc 1680cttcaacaag tggtcaaggc cctgaacgag agctacatcg acctgaagga gctgggcaac 1740tatacctact acaacaagtg gccggacaag attgaggaga ttctgtcgaa aatctaccac 1800attgaaaacg agatcgccag aatcaagaag cttatcggcg aagcc 1845234071DNAArtificial SequenceSynthetic Polynucleotide 23atggaaaccc ctgcccagct gctgttcctg ctgctgctgt ggctgcctga taccaccggc 60agctatgtgg acgtgggccc cgatagcgtg aagtccgcct gtatcgaagt ggacatccag 120cagaccttttt tcgacaagac ctggcccaga cccatcgacg tgtccaaggc cgacggcatc 180atctatccac aaggccggac ctacagcaac atcaccatta cctaccaggg cctgttccca 240tatcaaggcg

accacggcga tatgtacgtg tactctgccg gccacgccac cggcaccaca 300ccccagaaac tgttcgtggc caactacagc caggacgtga agcagttcgc caacggcttc 360gtcgtgcgga ttggcgccgc tgccaatagc accggcacag tgatcatcag ccccagcacc 420agcgccacca tccggaagat ctaccccgcc ttcatgctgg gcagctccgt gggcaatttc 480agcgacggca agatgggccg gttcttcaac cacaccctgg tgctgctgcc cgatggctgt 540ggcacactgc tgagagcctt ctactgcatc ctggaaccca gaagcggcaa ccactgccct 600gccggcaata gctacaccag cttcgccacc taccacacac ccgccaccga ttgctccgac 660ggcaactaca accggaacgc cagcctgaac agcttcaaag agtacttcaa cctgcggaac 720tgcaccttca tgtacaccta caatatcacc gaggacgaga tcctggaatg gttcggcatc 780acccagaccg cccagggcgt gcacctgttc agcagcagat acgtggacct gtacggcggc 840aacatgttcc agtttgccac cctgcccgtg tacgacacca tcaagtacta cagcatcatc 900ccccacagca tccggtccat ccagagcgac agaaaagcct gggccgcctt ctacgtgtac 960aagctgcagc ccctgacctt cctgctggac ttcagcgtgg acggctacat cagacgggcc 1020atcgactgcg gcttcaacga cctgagccag ctgcactgct cctacgagag cttcgacgtg 1080gaaagcggcg tgtacagcgt gtccagcttc gaggccaagc ctagcggcag cgtggtggaa 1140caggctgagg gcgtggaatg cgacttcagc cctctgctga gcggcacccc tccccaggtg 1200tacaacttca agcggctggt gttcaccaac tgcaattaca acctgaccaa gctgctgagc 1260ctgttctccg tgaacgactt cacctgtagc cagatcagcc ctgccgccat tgccagcaac 1320tgctacagca gcctgatcct ggactacttc agctaccccc tgagcatgaa gtccgatctg 1380agcgtgtcct ccgccggacc catcagccag ttcaactaca agcagagctt cagcaaccct 1440acctgcctga ttctggccac cgtgccccac aatctgacca ccatcaccaa gcccctgaag 1500tacagctaca tcaacaagtg cagcagactg ctgtccgacg accggaccga agtgccccag 1560ctcgtgaacg ccaaccagta cagcccctgc gtgtccatcg tgcccagcac cgtgtgggag 1620gacggcgact actacagaaa gcagctgagc cccctggaag gcggcggatg gctggtggct 1680tctggaagca cagtggccat gaccgagcag ctgcagatgg gctttggcat caccgtgcag 1740tacggcaccg acaccaacag cgtgtgcccc aagctggaat tcgccaatga caccaagatc 1800gccagccagc tgggaaactg cgtggaatac tccctgtatg gcgtgtccgg acggggcgtg 1860ttccagaatt gcacagcagt gggagtgcgg cagcagagat tcgtgtacga tgcctaccag 1920aacctcgtgg gctactacag cgacgacggc aattactact gcctgcgggc ctgtgtgtcc 1980gtgcccgtgt ccgtgatcta cgacaaagag acaaagaccc acgccacact gttcggctcc 2040gtggcctgcg agcacatcag ctccaccatg agccagtact cccgctccac ccggtccatg 2100ctgaagcgga gagatagcac ctacggcccc ctgcagacac ctgtgggatg tgtgctgggc 2160ctcgtgaaca gctccctgtt tgtggaagat tgcaagctgc ccctgggcca gagcctgtgt 2220gccctgccag ataccctag caccctgacc cctagaagcg tgcgctctgt gcccggcgaa 2280atgcggctgg cctctatcgc cttcaatcac cccatccagg tggaccagct gaactccagc 2340tacttcaagc tgagcatccc caccaacttc agcttcggcg tgacccagga gtacatccag 2400accacaatcc agaaagtgac cgtggactgc aagcagtacg tgtgcaacgg ctttcagaag 2460tgcgaacagc tgctgcgcga gtacggccag ttctgcagca agatcaacca ggccctgcac 2520ggcgccaacc tgagacagga tgacagcgtg cggaacctgt tcgccagcgt gaaaagcagc 2580cagtccagcc ccatcatccc tggcttcggc ggcgacttta acctgaccct gctggaacct 2640gtgtccatca gcaccggctc cagaagcgcc agatccgcca tcgaggacct gctgttcgac 2700aaagtgacca ttgccgaccc cggctacatg cagggctacg acgattgcat gcagcagggc 2760ccagccagcg ccagggatct gatctgtgcc cagtatgtgg ccggctacaa ggtgctgccc 2820cccctgatgg acgtgaacat ggaagccgcc tacacctcca gcctgctggg ctctattgct 2880ggcgtgggat ggacagccgg cctgtctagc tttgccgcca tccctttcgc ccagagcatc 2940ttctaccggc tgaacggcgt gggcatcaca caacaggtgc tgagcgagaa ccagaagctg 3000atcgccaaca agtttaacca ggcactgggc gccatgcaga ccggcttcac caccaccaac 3060gaggccttca gaaaggtgca ggacgccgtg aacaacaacg cccaggctct gagcaagctg 3120gcctccgagc tgagcaatac cttcggcgcc atcagcgcct ccatcggcga catcatccag 3180cggctggacg tgctggaaca ggacgcccag atcgaccggc tgatcaacgg cagactgacc 3240accctgaacg ccttcgtggc acagcagctc gtgcggagcg aatctgccgc tctgtctgct 3300cagctggcca aggacaaagt gaacgagtgc gtgaaggccc agtccaagcg gagcggcttt 3360tgtggccagg gcacccacat cgtgtccttc gtcgtgaatg cccccaacgg cctgtacttt 3420atgcacgtgg gctattaccc cagcaaccac atcgaggtgg tgtccgccta tggcctgtgc 3480gacgccgcca atcctaccaa ctgtatcgcc cccgtgaacg gctacttcat caagaccaac 3540aacacccgga tcgtggacga gtggtcctac acaggcagca gcttctacgc ccccgagccc 3600atcacctccc tgaacaccaa atacgtggcc ccccaagtga cataccagaa catctccacc

3660aacctgcccc ctccactgct gggaaattcc accggcatcg acttccagga cgagctggac 3720gagttcttca agaacgtgtc cacctccatc cccaacttcg gcagcctgac ccagatcaac 3780accactctgc tggacctgac ctacgagatg ctgtccctgc aacaggtcgt gaaagccctg 3840aacgagagct acatcgacct gaaagagctg ggcaactaca cctactacaa caagtggcct 3900tggtacattt ggctgggctt tatcgccggc ctggtggccc tggccctgtg cgtgttcttc 3960atcctgtgct gcaccggctg cggcaccaat tgcatgggca agctgaaatg caaccggtgc 4020tgcgacagat acgaggaata cgacctggaa cctcacaaag tgcatgtgca c 4071241353PRTUnknownMiddle East respiratory syndrome coronavirus 24Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu1 5 10 15Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu 20 25 30Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile 35 40 45Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr 50 55 60Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp65 70 75 80His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr 85 90 95Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe 100 105 110Ala Asn Gly Phe Val Val Arg Ile Gly Ala Ala Ala Asn Ser Thr Gly 115 120 125Thr Val Ile Ile Ser Pro Ser Thr Ser Ala Thr Ile Arg Lys Ile Tyr 130 135 140Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys145 150 155 160Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys 165 170 175Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly 180 185 190Asn His Cys Pro Ala Gly Asn Ser Tyr Thr Ser Phe Ala Thr Tyr His 195 200 205Thr Pro Ala Thr Asp Cys Ser Asp Gly Asn Tyr Asn Arg Asn Ala Ser 210 215 220Leu Asn Ser Phe Lys Glu Tyr Phe Asn Leu Arg Asn Cys Thr Phe Met225 230 235 240Tyr Thr Tyr Asn Ile Thr Glu Asp Glu Ile Leu Glu Trp Phe Gly Ile 245 250 255Thr Gln Thr Ala Gln Gly Val His Leu Phe Ser Ser Arg Tyr Val Asp 260 265 270Leu Tyr Gly Gly Asn Met Phe Gln Phe Ala Thr Leu Pro Val Tyr Asp 275 280 285Thr Ile Lys Tyr Tyr Ser Ile Ile Pro His Ser Ile Arg Ser Ile Gln 290 295 300Ser Asp Arg Lys Ala Trp Ala Ala Phe Tyr Val Tyr Lys Leu Gln Pro305 310 315 320Leu Thr Phe Leu Leu Asp Phe Ser Val Asp Gly Tyr Ile Arg Arg Ala 325 330 335Ile Asp Cys Gly Phe Asn Asp Leu Ser Gln Leu His Cys Ser Tyr Glu 340 345 350Ser Phe Asp Val Glu Ser Gly Val Tyr Ser Val Ser Ser Phe Glu Ala 355 360 365Lys Pro Ser Gly Ser Val Val Glu Gln Ala Glu Gly Val Glu Cys Asp 370 375 380Phe Ser Pro Leu Leu Ser Gly Thr Pro Pro Gln Val Tyr Asn Phe Lys385 390 395 400Arg Leu Val Phe Thr Asn Cys Asn Tyr Asn Leu Thr Lys Leu Leu Ser 405 410 415Leu Phe Ser Val Asn Asp Phe Thr Cys Ser Gln Ile Ser Pro Ala Ala 420 425 430Ile Ala Ser Asn Cys Tyr Ser Ser Leu Ile Leu Asp Tyr Phe Ser Tyr 435 440 445Pro Leu Ser Met Lys Ser Asp Leu Ser Val Ser Ser Ala Gly Pro Ile 450 455 460Ser Gln Phe Asn Tyr Lys Gln Ser Phe Ser Asn Pro Thr Cys Leu Ile465 470 475 480Leu Ala Thr Val Pro His Asn Leu Thr Thr Ile Thr Lys Pro Leu Lys 485 490 495Tyr Ser Tyr Ile Asn Lys Cys Ser Arg Leu Leu Ser Asp Asp Arg Thr 500 505 510Glu Val Pro Gln Leu Val Asn Ala Asn Gln Tyr Ser Pro Cys Val Ser 515 520 525Ile Val Pro Ser Thr Val Trp Glu Asp Gly Asp Tyr Tyr Arg Lys Gln 530 535 540Leu Ser Pro Leu Glu Gly Gly Gly Trp Leu Val Ala Ser Gly Ser Thr545 550 555 560Val Ala Met Thr Glu Gln Leu Gln Met Gly Phe Gly Ile Thr Val Gln 565 570 575Tyr Gly Thr Asp Thr Asn Ser Val Cys Pro Lys Leu Glu Phe Ala Asn 580 585 590Asp Thr Lys Ile Ala Ser Gln Leu Gly Asn Cys Val Glu Tyr Ser Leu 595 600 605Tyr Gly Val Ser Gly Arg Gly Val Phe Gln Asn Cys Thr Ala Val Gly 610 615 620Val Arg Gln Gln Arg Phe Val Tyr Asp Ala Tyr Gln Asn Leu Val Gly625 630 635 640Tyr Tyr Ser Asp Asp Gly Asn Tyr Tyr Cys Leu Arg Ala Cys Val Ser 645 650 655Val Pro Val Ser Val Ile Tyr Asp Lys Glu Thr Lys Thr His Ala Thr 660 665 670Leu Phe Gly Ser Val Ala Cys Glu His Ile Ser Ser Thr Met Ser Gln 675 680 685Tyr Ser Arg Ser Thr Arg Ser Met Leu Lys Arg Arg Asp Ser Thr Tyr 690 695 700Gly Pro Leu Gln Thr Pro Val Gly Cys Val Leu Gly Leu Val Asn Ser705 710 715 720Ser Leu Phe Val Glu Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys 725 730 735Ala Leu Pro Asp Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser 740 745 750Val Pro Gly Glu Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile 755 760 765Gln Val Asp Gln Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr 770 775 780Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln785 790 795 800Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys 805 810 815Cys Glu Gln Leu Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn 820 825 830Gln Ala Leu His Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn 835 840 845Leu Phe Ala Ser Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly 850 855 860Phe Gly Gly Asp Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser865 870 875 880Thr Gly Ser Arg Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp 885 890 895Lys Val Thr Ile Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys 900 905 910Met Gln Gln Gly Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr 915 920 925Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu 930 935 940Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp945 950 955 960Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile 965 970 975Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu 980 985 990Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met 995 1000 1005Gln Thr Gly Phe Thr Thr Thr Asn Glu Ala Phe Arg Lys Val Gln 1010 1015 1020Asp Ala Val Asn Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser 1025 1030 1035Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp 1040 1045 1050Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp 1055 1060 1065Arg Leu Ile Asn

Gly Arg Leu Thr Thr Leu Asn Ala Phe Val Ala 1070 1075 1080Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu 1085 1090 1095Ala Lys Asp Lys Val Asn Glu Cys Val Lys Ala Gln Ser Lys Arg 1100 1105 1110Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val 1115 1120 1125Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro 1130 1135 1140Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala 1145 1150 1155Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile 1160 1165 1170Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly 1175 1180 1185Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys 1190 1195 1200Tyr Val Ala Pro Gln Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu 1205 1210 1215Pro Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp 1220 1225 1230Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn 1235 1240 1245Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr 1250 1255 1260Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu 1265 1270 1275Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn 1280 1285 1290Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val 1295 1300 1305Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys 1310 1315 1320Gly Thr Asn Cys Met Gly Lys Leu Lys Cys Asn Arg Cys Cys Asp 1325 1330 1335Arg Tyr Glu Glu Tyr Asp Leu Glu Pro His Lys Val His Val His 1340 1345 1350251353PRTArtificial SequenceSynthetic Polypeptide 25Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu1 5 10 15Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu 20 25 30Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile 35 40 45Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr 50 55 60Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp65 70 75 80His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr 85 90 95Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe 100 105 110Ala Asn Gly Phe Val Val Arg Ile Gly Ala Ala Ala Asn Ser Thr Gly 115 120 125Thr Val Ile Ile Ser Pro Ser Thr Ser Ala Thr Ile Arg Lys Ile Tyr 130 135 140Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys145 150 155 160Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys 165 170 175Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly 180 185 190Asn His Cys Pro Ala Gly Asn Ser Tyr Thr Ser Phe Ala Thr Tyr His 195 200 205Thr Pro Ala Thr Asp Cys Ser Asp Gly Asn Tyr Asn Arg Asn Ala Ser 210 215 220Leu Asn Ser Phe Lys Glu Tyr Phe Asn Leu Arg Asn Cys Thr Phe Met225 230 235 240Tyr Thr Tyr Asn Ile Thr Glu Asp Glu Ile Leu Glu Trp Phe Gly Ile 245 250 255Thr Gln Thr Ala Gln Gly Val His Leu Phe Ser Ser Arg Tyr Val Asp 260 265 270Leu Tyr Gly Gly Asn Met Phe Gln Phe Ala Thr Leu Pro Val Tyr Asp 275 280 285Thr Ile Lys Tyr Tyr Ser Ile Ile Pro His Ser Ile Arg Ser Ile Gln 290 295 300Ser Asp Arg Lys Ala Trp Ala Ala Phe Tyr Val Tyr Lys Leu Gln Pro305 310 315 320Leu Thr Phe Leu Leu Asp Phe Ser Val Asp Gly Tyr Ile Arg Arg Ala 325 330 335Ile Asp Cys Gly Phe Asn Asp Leu Ser Gln Leu His Cys Ser Tyr Glu 340 345 350Ser Phe Asp Val Glu Ser Gly Val Tyr Ser Val Ser Ser Phe Glu Ala 355 360 365Lys Pro Ser Gly Ser Val Val Glu Gln Ala Glu Gly Val Glu Cys Asp 370 375 380Phe Ser Pro Leu Leu Ser Gly Thr Pro Pro Gln Val Tyr Asn Phe Lys385 390 395 400Arg Leu Val Phe Thr Asn Cys Asn Tyr Asn Leu Thr Lys Leu Leu Ser 405 410 415Leu Phe Ser Val Asn Asp Phe Thr Cys Ser Gln Ile Ser Pro Ala Ala 420 425 430Ile Ala Ser Asn Cys Tyr Ser Ser Leu Ile Leu Asp Tyr Phe Ser Tyr 435 440 445Pro Leu Ser Met Lys Ser Asp Leu Ser Val Ser Ser Ala Gly Pro Ile 450 455 460Ser Gln Phe Asn Tyr Lys Gln Ser

Phe Ser Asn Pro Thr Cys Leu Ile465 470 475 480Leu Ala Thr Val Pro His Asn Leu Thr Thr Ile Thr Lys Pro Leu Lys 485 490 495Tyr Ser Tyr Ile Asn Lys Cys Ser Arg Leu Leu Ser Asp Asp Arg Thr 500 505 510Glu Val Pro Gln Leu Val Asn Ala Asn Gln Tyr Ser Pro Cys Val Ser 515 520 525Ile Val Pro Ser Thr Val Trp Glu Asp Gly Asp Tyr Tyr Arg Lys Gln 530 535 540Leu Ser Pro Leu Glu Gly Gly Gly Trp Leu Val Ala Ser Gly Ser Thr545 550 555 560Val Ala Met Thr Glu Gln Leu Gln Met Gly Phe Gly Ile Thr Val Gln 565 570 575Tyr Gly Thr Asp Thr Asn Ser Val Cys Pro Lys Leu Glu Phe Ala Asn 580 585 590Asp Thr Lys Ile Ala Ser Gln Leu Gly Asn Cys Val Glu Tyr Ser Leu 595 600 605Tyr Gly Val Ser Gly Arg Gly Val Phe Gln Asn Cys Thr Ala Val Gly 610 615 620Val Arg Gln Gln Arg Phe Val Tyr Asp Ala Tyr Gln Asn Leu Val Gly625 630 635 640Tyr Tyr Ser Asp Asp Gly Asn Tyr Tyr Cys Leu Arg Ala Cys Val Ser 645 650 655Val Pro Val Ser Val Ile Tyr Asp Lys Glu Thr Lys Thr His Ala Thr 660 665 670Leu Phe Gly Ser Val Ala Cys Glu His Ile Ser Ser Thr Met Ser Gln 675 680 685Tyr Ser Arg Ser Thr Arg Ser Met Leu Lys Arg Arg Asp Ser Thr Tyr 690 695 700Gly Pro Leu Gln Thr Pro Val Gly Cys Val Leu Gly Leu Val Asn Ser705 710 715 720Ser Leu Phe Val Glu Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys 725 730 735Ala Leu Pro Asp Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser 740 745 750Val Pro Gly Glu Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile 755 760 765Gln Val Asp Gln Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr 770 775 780Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln785 790 795 800Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys 805 810 815Cys Glu Gln Leu Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn 820 825 830Gln Ala Leu His Gly Ala Asn Leu Arg Gln Asp Asp

Ser Val Arg Asn 835 840 845Leu Phe Ala Ser Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly 850 855 860Phe Gly Gly Asp Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser865 870 875 880Thr Gly Ser Arg Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp 885 890 895Lys Val Thr Ile Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys 900 905 910Met Gln Gln Gly Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr 915 920 925Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu 930 935 940Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp945 950 955 960Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile 965 970 975Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu 980 985 990Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met 995 1000 1005Gln Thr Gly Phe Thr Thr Thr Asn Glu Ala Phe Gln Lys Val Gln 1010 1015 1020Asp Ala Val Asn Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser 1025 1030 1035Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp 1040 1045 1050Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp 1055 1060 1065Arg Leu Ile Asn Gly Arg Leu Thr Thr Leu Asn Ala Phe Val Ala 1070 1075 1080Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu 1085 1090 1095Ala Lys Asp Lys Val Asn Glu Cys Val Lys Ala Gln Ser Lys Arg 1100 1105 1110Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val 1115 1120 1125Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro 1130 1135 1140Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala 1145 1150 1155Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile 1160 1165 1170Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly 1175 1180 1185Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys 1190 1195 1200Tyr Val Ala Pro Gln Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu 1205 1210 1215Pro Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp 1220 1225 1230Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn 1235 1240 1245Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr 1250 1255 1260Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu 1265 1270 1275Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn 1280 1285 1290Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val 1295 1300 1305Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys 1310 1315 1320Gly Thr Asn Cys Met Gly Lys Leu Lys Cys Asn Arg Cys Cys Asp 1325 1330 1335Arg Tyr Glu Glu Tyr Asp Leu Glu Pro His Lys Val His Val His 1340 1345 135026615PRTArtificial SequenceSynthetic Polypeptide 26Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu1 5 10 15Ser Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys Ala Leu Pro Asp 20 25 30Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser Val Pro Gly Glu 35 40 45Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile Gln Val Asp Gln 50 55 60Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr Asn Phe Ser Phe65 70 75 80Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln Lys Val Thr Val 85 90 95Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys Cys Glu Gln Leu 100 105 110Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn Gln Ala Leu His 115 120 125Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn Leu Phe Ala Ser 130 135 140Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly Phe Gly Gly Asp145 150 155 160Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser Thr Gly Ser Arg 165 170 175Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp Lys Val Thr Ile 180 185 190Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys Met Gln Gln Gly 195 200 205Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr Val Ala Gly Tyr 210 215 220Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu Ala Ala Tyr Thr225 230 235 240Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp Thr Ala Gly Leu 245 250 255Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile Phe Tyr Arg Leu 260 265 270Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu Asn Gln Lys Leu 275 280 285Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met Gln Thr Gly Phe 290 295 300Thr Thr Thr Asn Glu Ala Phe Gln Lys Val Gln Asp Ala Val Asn Asn305 310 315 320Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser Glu Leu Ser Asn Thr Phe 325 330 335Gly Ala Ile Ser Ala Ser Ile Gly Asp Ile Ile Gln Arg Leu Asp Val 340 345 350Leu Glu Gln Asp Ala Gln Ile Asp Arg Leu Ile Asn Gly Arg Leu Thr 355 360 365Thr Leu Asn Ala Phe Val Ala Gln Gln Leu Val Arg Ser Glu Ser Ala 370 375 380Ala Leu Ser Ala Gln Leu Ala Lys Asp Lys Val Asn Glu Cys Val Lys385 390 395 400Ala Gln Ser Lys Arg Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val 405 410 415Ser Phe Val Val Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly 420 425 430Tyr Tyr Pro Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys 435 440 445Asp Ala Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe 450 455 460Ile Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly465 470 475 480Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys Tyr 485 490 495Val Ala Pro Gln Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu Pro Pro 500 505 510Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp Glu Leu Asp 515 520 525Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn Phe Gly Ser Leu 530 535 540Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr Tyr Glu Met Leu Ser545 550 555 560Leu Gln Gln Val Val Lys Ala Leu Asn Glu Ser Tyr Ile Asp Leu Lys 565 570 575Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn Lys Trp Pro Asp Lys Ile Glu 580 585 590Glu Ile Leu Ser Lys Ile Tyr His Ile Glu Asn Glu Ile Ala Arg Ile 595 600 605Lys Lys Leu Ile Gly Glu Ala 610 615271353PRTUnknownMiddle East respiratory syndrome coronavirus 27Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu1 5 10 15Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys

Ser Ala Cys Ile Glu 20 25 30Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile 35 40 45Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr 50 55 60Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp65 70 75 80His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr 85 90 95Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe 100 105 110Ala Asn Gly Phe Val Val Arg Ile Gly Ala Ala Ala Asn Ser Thr Gly 115 120 125Thr Val Ile Ile Ser Pro Ser Thr Ser Ala Thr Ile Arg Lys Ile Tyr 130 135 140Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys145 150 155 160Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys 165 170 175Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly 180 185 190Asn His Cys Pro Ala Gly Asn Ser Tyr Thr Ser Phe Ala Thr Tyr His 195 200 205Thr Pro Ala Thr Asp Cys Ser Asp Gly Asn Tyr Asn Arg Asn Ala Ser 210 215 220Leu Asn Ser Phe Lys Glu Tyr Phe Asn Leu Arg Asn Cys Thr Phe Met225 230 235 240Tyr Thr Tyr Asn Ile Thr Glu Asp Glu Ile Leu Glu Trp Phe Gly Ile 245 250 255Thr Gln Thr Ala Gln Gly Val His Leu Phe Ser Ser Arg Tyr Val Asp 260 265 270Leu Tyr Gly Gly Asn Met Phe Gln Phe Ala Thr Leu Pro Val Tyr Asp 275 280 285Thr Ile Lys Tyr Tyr Ser Ile Ile Pro His Ser Ile Arg Ser Ile Gln 290 295 300Ser Asp Arg Lys Ala Trp Ala Ala Phe Tyr Val Tyr Lys Leu Gln Pro305 310 315 320Leu Thr Phe Leu Leu Asp Phe Ser Val Asp Gly Tyr Ile Arg Arg Ala 325 330 335Ile Asp Cys Gly Phe Asn Asp Leu Ser Gln Leu His Cys Ser Tyr Glu 340 345 350Ser Phe Asp Val Glu Ser Gly Val Tyr Ser Val Ser Ser Phe Glu Ala 355 360 365Lys Pro Ser Gly Ser Val Val Glu Gln Ala Glu Gly Val Glu Cys Asp 370 375 380Phe Ser Pro Leu Leu Ser Gly Thr Pro Pro Gln Val Tyr Asn Phe Lys385 390 395 400Arg Leu Val Phe Thr Asn Cys Asn Tyr Asn Leu Thr Lys Leu Leu Ser 405 410 415Leu Phe Ser Val Asn Asp Phe Thr Cys Ser Gln Ile Ser Pro Ala Ala 420 425 430Ile Ala Ser Asn Cys Tyr Ser Ser Leu Ile Leu Asp Tyr Phe Ser Tyr 435 440 445Pro Leu Ser Met Lys Ser Asp Leu Ser Val Ser Ser Ala Gly Pro Ile 450 455 460Ser Gln Phe Asn Tyr Lys Gln Ser Phe Ser Asn Pro Thr Cys Leu Ile465 470 475 480Leu Ala Thr Val Pro His Asn Leu Thr Thr Ile Thr Lys Pro Leu Lys 485 490 495Tyr Ser Tyr Ile Asn Lys Cys Ser Arg Leu Leu Ser Asp Asp Arg Thr 500 505 510Glu Val Pro Gln Leu Val Asn Ala Asn Gln Tyr Ser Pro Cys Val Ser 515 520 525Ile Val Pro Ser Thr Val Trp Glu Asp Gly Asp Tyr Tyr Arg Lys Gln 530 535 540Leu Ser Pro Leu Glu Gly Gly Gly Trp Leu Val Ala Ser Gly Ser Thr545 550 555 560Val Ala Met Thr Glu Gln Leu Gln Met Gly Phe Gly Ile Thr Val Gln 565 570 575Tyr Gly Thr Asp Thr Asn Ser Val Cys Pro Lys Leu Glu Phe Ala Asn 580 585 590Asp Thr Lys Ile Ala Ser Gln Leu Gly Asn Cys Val Glu Tyr Ser Leu 595 600 605Tyr Gly Val Ser Gly Arg Gly Val Phe Gln Asn Cys Thr Ala Val Gly 610 615 620Val Arg Gln Gln Arg Phe Val Tyr Asp Ala Tyr Gln Asn Leu Val Gly625 630 635 640Tyr Tyr Ser Asp Asp Gly Asn Tyr Tyr Cys Leu Arg Ala Cys Val Ser 645 650 655Val Pro Val Ser Val Ile Tyr Asp Lys Glu Thr Lys Thr His Ala Thr 660 665 670Leu Phe Gly Ser Val Ala Cys Glu His Ile Ser Ser Thr Met Ser Gln 675 680 685Tyr Ser Arg Ser Thr Arg Ser Met Leu Lys Arg Arg Asp Ser Thr Tyr 690 695 700Gly Pro Leu Gln Thr Pro Val Gly Cys Val Leu Gly Leu Val Asn Ser705 710 715 720Ser Leu Phe Val Glu Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys 725 730 735Ala Leu Pro Asp Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser 740 745 750Val Pro Gly Glu Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile 755 760 765Gln Val Asp Gln Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr 770 775 780Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln785 790 795 800Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys 805 810 815Cys Glu Gln Leu Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn 820 825 830Gln Ala Leu His Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn 835 840 845Leu Phe Ala Ser Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly 850 855 860Phe Gly Gly Asp Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser865 870 875 880Thr Gly Ser Arg Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp 885 890 895Lys Val Thr Ile Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys 900 905 910Met Gln Gln Gly Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr 915 920 925Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu 930 935 940Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser

Ile Ala Gly Val Gly Trp945 950 955 960Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile 965 970 975Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu 980 985 990Asn Gln Lys Leu Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met 995 1000 1005Gln Thr Gly Phe Thr Thr Thr Asn Glu Ala Phe Arg Lys Val Gln 1010 1015 1020Asp Ala Val Asn Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser 1025 1030 1035Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp 1040 1045 1050Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp 1055 1060 1065Arg Leu Ile Asn Gly Arg Leu Thr Thr Leu Asn Ala Phe Val Ala 1070 1075 1080Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu 1085 1090 1095Ala Lys Asp Lys Val Asn Glu Cys Val Lys Ala Gln Ser Lys Arg 1100 1105 1110Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val 1115 1120 1125Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro 1130 1135 1140Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala 1145 1150 1155Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile 1160 1165 1170Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly

1175 1180 1185Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys 1190 1195 1200Tyr Val Ala Pro His Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu 1205 1210 1215Pro Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp 1220 1225 1230Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn 1235 1240 1245Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr 1250 1255 1260Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu 1265 1270 1275Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn 1280 1285 1290Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val 1295 1300 1305Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys 1310 1315 1320Gly Thr Asn Cys Met Gly Lys Leu Lys Cys Asn Arg Cys Cys Asp 1325 1330 1335Arg Tyr Glu Glu Tyr Asp Leu Glu Pro His Lys Val His Val His 1340 1345 1350281353PRTUnknownMiddle East respiratory syndrome coronavirus 28Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu1 5 10 15Ser Tyr Val Asp Val Gly Pro Asp Ser Val Lys Ser Ala Cys Ile Glu 20 25 30Val Asp Ile Gln Gln Thr Phe Phe Asp Lys Thr Trp Pro Arg Pro Ile 35 40 45Asp Val Ser Lys Ala Asp Gly Ile Ile Tyr Pro Gln Gly Arg Thr Tyr 50 55 60Ser Asn Ile Thr Ile Thr Tyr Gln Gly Leu Phe Pro Tyr Gln Gly Asp65 70 75 80His Gly Asp Met Tyr Val Tyr Ser Ala Gly His Ala Thr Gly Thr Thr 85 90 95Pro Gln Lys Leu Phe Val Ala Asn Tyr Ser Gln Asp Val Lys Gln Phe 100 105 110Ala Asn Gly Phe Val Val Arg Ile Gly Ala Ala Ala Asn Ser Thr Gly 115 120 125Thr Val Ile Ile Ser Pro Ser Thr Ser Ala Thr Ile Arg Lys Ile Tyr 130 135 140Pro Ala Phe Met Leu Gly Ser Ser Val Gly Asn Phe Ser Asp Gly Lys145 150 155 160Met Gly Arg Phe Phe Asn His Thr Leu Val Leu Leu Pro Asp Gly Cys 165 170 175Gly Thr Leu Leu Arg Ala Phe Tyr Cys Ile Leu Glu Pro Arg Ser Gly 180 185 190Asn His Cys Pro Ala Gly Asn Ser Tyr Thr Ser Phe Ala Thr Tyr His 195 200 205Thr Pro Ala Thr Asp Cys Ser Asp Gly Asn Tyr Asn Arg Asn Ala Ser 210 215 220Leu Asn Ser Phe Lys Glu Tyr Phe Asn Leu Arg Asn Cys Thr Phe Met225 230 235 240Tyr Thr Tyr Asn Ile Thr Glu Asp Glu Ile Leu Glu Trp Phe Gly Ile 245 250 255Thr Gln Thr Ala Gln Gly Val His Leu Phe Ser Ser Arg Tyr Val Asp 260 265 270Leu Tyr Gly Gly Asn Met Phe Gln Phe Ala Thr Leu Pro Val Tyr Asp 275 280 285Thr Ile Lys Tyr Tyr Ser Ile Ile Pro His Ser Ile Arg Ser Ile Gln 290 295 300Ser Asp Arg Lys Ala Trp Ala Ala Phe Tyr Val Tyr Lys Leu Gln Pro305 310 315 320Leu Thr Phe Leu Leu Asp Phe Ser Val Asp Gly Tyr Ile Arg Arg Ala 325 330 335Ile Asp Cys Gly Phe Asn Asp Leu Ser Gln Leu His Cys Ser Tyr Glu 340 345 350Ser Phe Asp Val Glu Ser Gly Val Tyr Ser Val Ser Ser Phe Glu Ala 355 360 365Lys Pro Ser Gly Ser Val Val Glu Gln Ala Glu Gly Val Glu Cys Asp 370 375 380Phe Ser Pro Leu Leu Ser Gly Thr Pro Pro Gln Val Tyr Asn Phe Lys385 390 395 400Arg Leu Val Phe Thr Asn Cys Asn Tyr Asn Leu Thr Lys Leu Leu Ser 405 410 415Leu Phe Ser Val Asn Asp Phe Thr Cys Ser Gln Ile Ser Pro Ala Ala 420 425 430Ile Ala Ser Asn Cys Tyr Ser Ser Leu Ile Leu Asp Tyr Phe Ser Tyr 435 440 445Pro Leu Ser Met Lys Ser Asp Leu Ser Val Ser Ser Ala Gly Pro Ile 450 455 460Ser Gln Phe Asn Tyr Lys Gln Ser Phe Ser Asn Pro Thr Cys Leu Ile465 470 475 480Leu Ala Thr Val Pro His Asn Leu Thr Thr Ile Thr Lys Pro Leu Lys 485 490 495Tyr Ser Tyr Ile Asn Lys Cys Ser Arg Leu Leu Ser Asp Asp Arg Thr 500 505 510Glu Val Pro Gln Leu Val Asn Ala Asn Gln Tyr Ser Pro Cys Val Ser 515 520 525Ile Val Pro Ser Thr Val Trp Glu Asp Gly Asp Tyr Tyr Arg Lys Gln 530 535 540Leu Ser Pro Leu Glu Gly Gly Gly Trp Leu Val Ala Ser Gly Ser Thr545 550 555 560Val Ala Met Thr Glu Gln Leu Gln Met Gly Phe Gly Ile Thr Val Gln 565 570 575Tyr Gly Thr Asp Thr Asn Ser Val Cys Pro Lys Leu Glu Phe Ala Asn 580 585 590Asp Thr Lys Ile Ala Ser Gln Leu Gly Asn Cys Val Glu Tyr Ser Leu 595 600 605Tyr Gly Val Ser Gly Arg Gly Val Phe Gln Asn Cys Thr Ala Val Gly 610 615 620Val Arg Gln Gln Arg Phe Val Tyr Asp Ala Tyr Gln Asn Leu Val Gly625 630 635 640Tyr Tyr Ser Asp Asp Gly Asn Tyr Tyr Cys Leu Arg Ala Cys Val Ser 645 650 655Val Pro Val Ser Val Ile Tyr Asp Lys Glu Thr Lys Thr His Ala Thr 660 665 670Leu Phe Gly Ser Val Ala Cys Glu His Ile Ser Ser Thr Met Ser Gln 675 680 685Tyr Ser Arg Ser Thr Arg Ser Met Leu Lys Arg Arg Asp Ser Thr Tyr 690 695 700Gly Pro Leu Gln Thr Pro Val Gly Cys Val Leu Gly Leu Val Asn Ser705 710 715 720Ser Leu Phe Val Glu Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys 725 730 735Ala Leu Pro Asp Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser 740 745 750Val Pro Gly Glu Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile 755 760 765Gln Val Asp Gln Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr 770 775 780Asn Phe Ser Phe Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln785 790 795 800Lys Val Thr Val Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys 805 810 815Cys Glu Gln Leu Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn 820 825 830Gln Ala Leu His Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn 835 840 845Leu Phe Ala Ser Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly 850 855 860Phe Gly Gly Asp Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser865 870 875 880Thr Gly Ser Arg Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp 885 890 895Lys Val Thr Ile Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys 900 905 910Met Gln Gln Gly Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr 915 920 925Val Ala Gly Tyr Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu 930 935 940Ala Ala Tyr Thr Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp945 950 955 960Thr Ala Gly Leu Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile 965 970 975Phe Tyr Arg Leu Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu 980 985 990Asn Gln Lys Leu Ile Ala Asn Lys

Phe Asn Gln Ala Leu Gly Ala Met 995 1000 1005Gln Thr Gly Phe Thr Thr Thr Asn Glu Ala Phe Arg Lys Val Gln 1010 1015 1020Asp Ala Val Asn Asn Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser 1025 1030 1035Glu Leu Ser Asn Thr Phe Gly Ala Ile Ser Ala Ser Ile Gly Asp 1040 1045 1050Ile Ile Gln Arg Leu Asp Val Leu Glu Gln Asp Ala Gln Ile Asp 1055 1060 1065Arg Leu Ile Asn Gly Arg Leu Thr Thr Leu Asn Ala Phe Val Ala 1070 1075 1080Gln Gln Leu Val Arg Ser Glu Ser Ala Ala Leu Ser Ala Gln Leu 1085 1090 1095Ala Lys Asp Lys Val Asn Glu Cys Val Lys Ala Gln Ser Lys Arg 1100 1105 1110Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val Ser Phe Val Val 1115 1120 1125Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly Tyr Tyr Pro 1130 1135 1140Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys Asp Ala 1145 1150 1155Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe Ile 1160 1165 1170Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly 1175 1180 1185Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys 1190 1195 1200Tyr Val Ala Pro His Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu 1205 1210 1215Pro Pro Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp 1220 1225 1230Glu Leu Asp Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn 1235 1240 1245Phe Gly Ser Leu Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr 1250 1255 1260Tyr Glu Met Leu Ser Leu Gln Gln Val Val Lys Ala Leu Asn Glu 1265 1270 1275Ser Tyr Ile Asp Leu Lys Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn 1280 1285 1290Lys Trp Pro Trp Tyr Ile Trp Leu Gly Phe Ile Ala Gly Leu Val 1295 1300 1305Ala Leu Ala Leu Cys Val Phe Phe Ile Leu Cys Cys Thr Gly Cys 1310 1315 1320Gly Thr Asn Cys Met Gly Lys Leu Lys Cys Asn Arg Cys Cys Asp 1325 1330 1335Arg Tyr Glu Glu Tyr Asp Leu Glu Pro His Lys Val His Val His 1340 1345 1350291255PRTUnknownHuman SARS coronavirus 29Met Phe Ile Phe Leu Leu Phe Leu Thr Leu Thr Ser Gly Ser Asp Leu1 5 10 15Asp Arg Cys Thr Thr Phe Asp Asp Val Gln Ala Pro Asn Tyr Thr Gln 20 25 30His Thr Ser Ser Met Arg Gly Val Tyr Tyr Pro Asp Glu Ile Phe Arg 35 40 45Ser Asp Thr Leu Tyr Leu Thr Gln Asp Leu Phe Leu Pro Phe Tyr Ser 50 55 60Asn Val Thr Gly Phe His Thr Ile Asn His Thr Phe Gly Asn Pro Val65 70 75 80Ile Pro Phe Lys Asp Gly Ile Tyr Phe Ala Ala Thr Glu Lys Ser Asn 85 90 95Val Val Arg Gly Trp Val Phe Gly Ser Thr Met Asn Asn Lys Ser Gln 100 105 110Ser Val Ile Ile Ile Asn Asn Ser Thr Asn Val Val Ile Arg Ala Cys 115 120 125Asn Phe Glu Leu Cys Asp Asn Pro Phe Phe Ala Val Ser Lys Pro Met 130 135 140Gly Thr Gln Thr His Thr Met Ile Phe Asp Asn Ala Phe Asn Cys Thr145 150 155 160Phe Glu Tyr Ile Ser Asp Ala Phe Ser Leu Asp Val Ser Glu Lys Ser 165 170 175Gly Asn Phe Lys His Leu Arg Glu Phe Val Phe Lys Asn Lys Asp Gly 180 185 190Phe Leu Tyr Val Tyr Lys Gly Tyr Gln Pro Ile Asp Val Val Arg Asp 195 200 205Leu Pro Ser Gly Phe Asn Thr Leu Lys Pro Ile Phe Lys Leu Pro Leu 210 215 220Gly Ile Asn Ile Thr Asn Phe Arg Ala Ile Leu Thr Ala Phe Ser Pro225 230 235 240Ala Gln Asp Ile Trp Gly Thr Ser Ala Ala Ala Tyr Phe Val Gly Tyr 245 250 255Leu Lys Pro Thr Thr Phe Met Leu Lys Tyr Asp Glu Asn Gly Thr Ile 260 265 270Thr Asp Ala Val Asp Cys Ser Gln Asn Pro Leu Ala Glu Leu Lys Cys 275 280 285Ser Val Lys Ser Phe Glu Ile Asp Lys Gly Ile Tyr Gln Thr Ser Asn 290 295 300Phe Arg Val Val Pro Ser Gly Asp Val Val Arg Phe Pro Asn Ile Thr305 310 315 320Asn Leu Cys Pro Phe Gly Glu Val Phe Asn Ala Thr Lys Phe Pro Ser 325 330 335Val Tyr Ala Trp Glu Arg Lys Lys Ile Ser Asn Cys Val Ala Asp Tyr 340 345 350Ser Val Leu Tyr Asn Ser Thr Phe Phe Ser Thr Phe Lys Cys Tyr Gly 355 360 365Val Ser Ala Thr Lys Leu Asn Asp Leu Cys Phe Ser Asn Val Tyr Ala 370 375 380Asp Ser Phe Val Val Lys Gly Asp Asp Val Arg Gln Ile Ala Pro Gly385 390 395 400Gln Thr Gly Val Ile Ala Asp Tyr Asn Tyr Lys Leu Pro Asp Asp Phe 405 410 415Met Gly Cys Val Leu Ala Trp Asn Thr Arg Asn Ile Asp Ala Thr Ser 420 425 430Thr Gly Asn Tyr Asn Tyr Lys Tyr Arg Tyr Leu Arg His Gly Lys Leu 435 440 445Arg Pro Phe Glu Arg Asp Ile Ser Asn Val Pro Phe Ser Pro Asp Gly 450 455 460Lys Pro Cys Thr Pro Pro Ala Leu Asn Cys Tyr Trp Pro Leu Asn Asp465 470 475 480Tyr Gly Phe Tyr Thr Thr Thr Gly Ile Gly Tyr Gln Pro Tyr Arg Val 485 490 495Val Val Leu Ser Phe Glu Leu Leu Asn Ala Pro Ala Thr Val Cys Gly 500 505 510Pro Lys Leu Ser Thr Asp Leu Ile Lys Asn Gln Cys Val Asn Phe Asn 515 520 525Phe Asn Gly Leu Thr Gly Thr Gly Val Leu Thr Pro Ser Ser Lys Arg 530 535 540Phe Gln Pro Phe Gln Gln Phe Gly Arg Asp Val Ser Asp Phe Thr Asp545 550 555 560Ser Val Arg Asp Pro Lys Thr Ser Glu Ile Leu Asp Ile Ser Pro Cys 565 570 575Ser Phe Gly Gly Val Ser Val Ile Thr Pro Gly Thr Asn Ala Ser Ser 580 585 590Glu Val Ala Val Leu Tyr Gln Asp Val Asn Cys Thr Asp Val Ser Thr 595 600 605Ala Ile His Ala Asp Gln Leu Thr Pro Ala Trp Arg Ile Tyr Ser Thr 610 615 620Gly Asn Asn Val Phe Gln Thr Gln Ala Gly Cys Leu Ile Gly Ala Glu625 630 635 640His Val Asp Thr Ser Tyr Glu Cys Asp Ile Pro Ile Gly Ala Gly Ile 645 650 655Cys Ala Ser Tyr His Thr Val Ser Leu Leu Arg Ser Thr Ser Gln Lys 660 665 670Ser Ile Val Ala Tyr Thr Met Ser Leu Gly Ala Asp Ser Ser Ile Ala 675 680 685Tyr Ser Asn Asn Thr Ile Ala

Ile Pro Thr Asn Phe Ser Ile Ser Ile 690 695 700Thr Thr Glu Val Met Pro Val Ser Met Ala Lys Thr Ser Val Asp Cys705 710 715 720Asn Met Tyr Ile Cys Gly Asp Ser Thr Glu Cys Ala Asn Leu Leu Leu 725 730 735Gln Tyr Gly Ser Phe Cys Thr Gln Leu Asn Arg Ala Leu Ser Gly Ile 740 745 750Ala Ala Glu Gln Asp Arg Asn Thr Arg Glu Val Phe Ala Gln Val Lys 755 760 765Gln Met Tyr Lys Thr Pro Thr Leu Lys Tyr Phe Gly Gly Phe Asn Phe

770 775 780Ser Gln Ile Leu Pro Asp Pro Leu Lys Pro Thr Lys Arg Ser Phe Ile785 790 795 800Glu Asp Leu Leu Phe Asn Lys Val Thr Leu Ala Asp Ala Gly Phe Met 805 810 815Lys Gln Tyr Gly Glu Cys Leu Gly Asp Ile Asn Ala Arg Asp Leu Ile 820 825 830Cys Ala Gln Lys Phe Asn Gly Leu Thr Val Leu Pro Pro Leu Leu Thr 835 840 845Asp Asp Met Ile Ala Ala Tyr Thr Ala Ala Leu Val Ser Gly Thr Ala 850 855 860Thr Ala Gly Trp Thr Phe Gly Ala Gly Ala Ala Leu Gln Ile Pro Phe865 870 875 880Ala Met Gln Met Ala Tyr Arg Phe Asn Gly Ile Gly Val Thr Gln Asn 885 890 895Val Leu Tyr Glu Asn Gln Lys Gln Ile Ala Asn Gln Phe Asn Lys Ala 900 905 910Ile Ser Gln Ile Gln Glu Ser Leu Thr Thr Thr Ser Thr Ala Leu Gly 915 920 925Lys Leu Gln Asp Val Val Asn Gln Asn Ala Gln Ala Leu Asn Thr Leu 930 935 940Val Lys Gln Leu Ser Ser Asn Phe Gly Ala Ile Ser Ser Val Leu Asn945 950 955 960Asp Ile Leu Ser Arg Leu Asp Lys Val Glu Ala Glu Val Gln Ile Asp 965 970 975Arg Leu Ile Thr Gly Arg Leu Gln Ser Leu Gln Thr Tyr Val Thr Gln 980 985 990Gln Leu Ile Arg Ala Ala Glu Ile Arg Ala Ser Ala Asn Leu Ala Ala 995 1000 1005Thr Lys Met Ser Glu Cys Val Leu Gly Gln Ser Lys Arg Val Asp 1010 1015 1020Phe Cys Gly Lys Gly Tyr His Leu Met Ser Phe Pro Gln Ala Ala 1025 1030 1035Pro His Gly Val Val Phe Leu His Val Thr Tyr Val Pro Ser Gln 1040 1045 1050Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His Glu Gly Lys 1055 1060 1065Ala Tyr Phe Pro Arg Glu Gly Val Phe Val Phe Asn Gly Thr Ser 1070 1075 1080Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile Thr 1085 1090 1095Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly 1100 1105 1110Ile Ile Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro Glu Leu Asp 1115 1120 1125Ser Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn His Thr Ser 1130 1135 1140Pro Asp Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val 1145 1150 1155Val Asn Ile Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys 1160 1165 1170Asn Leu Asn Glu Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr 1175 1180 1185Glu Gln Tyr Ile Lys Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile 1190 1195 1200Ala Gly Leu Ile Ala Ile Val Met Val Thr Ile Leu Leu Cys Cys 1205 1210 1215Met Thr Ser Cys Cys Ser Cys Leu Lys Gly Ala Cys Ser Cys Gly 1220 1225 1230Ser Cys Cys Lys Phe Asp Glu Asp Asp Ser Glu Pro Val Leu Lys 1235 1240 1245Gly Val Lys Leu His Tyr Thr 1250 1255301353PRTHuman coronavirus 30Met Phe Leu Ile Leu Leu Ile Ser Leu Pro Thr Ala Phe Ala Val Ile1 5 10 15Gly Asp Leu Lys Cys Thr Ser Asp Asn Ile Asn Asp Lys Asp Thr Gly 20 25 30Pro Pro Pro Ile Ser Thr Asp Thr Val Asp Val Thr Asn Gly Leu Gly 35 40 45Thr Tyr Tyr Val Leu Asp Arg Val Tyr Leu Asn Thr Thr Leu Phe Leu 50 55 60Asn Gly Tyr Tyr Pro Thr Ser Gly Ser Thr Tyr Arg Asn Met Ala Leu65 70 75 80Lys Gly Ser Val Leu Leu Ser Arg Leu Trp Phe Lys Pro Pro Phe Leu 85 90 95Ser Asp Phe Ile Asn Gly Ile Phe Ala Lys Val Lys Asn Thr Lys Val 100 105 110Ile Lys Asp Arg Val Met Tyr Ser Glu Phe Pro Ala Ile Thr Ile Gly 115 120 125Ser Thr Phe Val Asn Thr Ser Tyr Ser Val Val Val Gln Pro Arg Thr 130 135 140Ile Asn Ser Thr Gln Asp Gly Asp Asn Lys Leu Gln Gly Leu Leu Glu145 150 155 160Val Ser Val Cys Gln Tyr Asn Met Cys Glu Tyr Pro Gln Thr Ile Cys 165 170 175His Pro Asn Leu Gly Asn His Arg Lys Glu Leu Trp His Leu Asp Thr 180 185 190Gly Val Val Ser Cys Leu Tyr Lys Arg Asn Phe Thr Tyr Asp Val Asn 195 200 205Ala Asp Tyr Leu Tyr Phe His Phe Tyr Gln Glu Gly Gly Thr Phe Tyr 210 215 220Ala Tyr Phe Thr Asp Thr Gly Val Val Thr Lys Phe Leu Phe Asn Val225 230 235 240Tyr Leu Gly Met Ala Leu Ser His Tyr Tyr Val Met Pro Leu Thr Cys 245 250 255Asn Ser Lys Leu Thr Leu Glu Tyr Trp Val Thr Pro Leu Thr Ser Arg 260 265 270Gln Tyr Leu Leu Ala Phe Asn Gln Asp Gly Ile Ile Phe Asn Ala Glu 275 280 285Asp Cys Met Ser Asp Phe Met Ser Glu Ile Lys Cys Lys Thr Gln Ser 290 295 300Ile Ala Pro Pro Thr Gly Val Tyr Glu Leu Asn Gly Tyr Thr Val Gln305 310 315 320Pro Ile Ala Asp Val Tyr Arg Arg Lys Pro Asn Leu Pro Asn Cys Asn 325 330 335Ile Glu Ala Trp Leu Asn Asp Lys Ser Val Pro Ser Pro Leu Asn Trp 340 345 350Glu Arg Lys Thr Phe Ser Asn Cys Asn Phe Asn Met Ser Ser Leu Met 355 360 365Ser Phe Ile Gln Ala Asp Ser Phe Thr Cys Asn Asn Ile Asp Ala Ala 370 375 380Lys Ile Tyr Gly Met Cys Phe Ser Ser Ile Thr Ile Asp Lys Phe Ala385 390 395 400Ile Pro Asn Gly Arg Lys Val Asp Leu Gln Leu Gly Asn Leu Gly Tyr 405 410 415Leu Gln Ser Phe Asn Tyr Arg Ile Asp Thr Thr Ala Thr Ser Cys Gln 420 425 430Leu Tyr Tyr Asn Leu Pro Ala Ala Asn Val Ser Val Ser Arg Phe Asn 435 440 445Pro Ser Thr Trp Asn Lys Arg Phe Gly Phe Ile Glu Asp Ser Val Phe 450 455 460Lys Pro Arg Pro Ala Gly Val Leu Thr Asn His Asp Val Val Tyr Ala465 470 475 480Gln His Cys Phe Lys Ala Pro Lys Asn Phe Cys Pro Cys Lys Leu Asn 485 490 495Gly Ser Cys Val Gly Ser Gly Pro Gly Lys Asn Asn Gly Ile Gly Thr 500 505 510Cys Pro Ala Gly Thr Asn Tyr Leu Thr Cys Asp Asn Leu Cys Thr Pro 515 520 525Asp Pro Ile Thr Phe Thr Gly Thr Tyr Lys Cys Pro Gln Thr Lys Ser 530 535 540Leu Val Gly Ile Gly Glu His Cys Ser Gly Leu Ala Val Lys Ser Asp545 550 555 560Tyr Cys Gly Gly Asn Ser Cys Thr Cys Arg Pro Gln Ala Phe Leu Gly 565 570 575Trp Ser Ala Asp Ser Cys Leu Gln Gly Asp Lys Cys Asn Ile Phe Ala 580 585 590Asn Phe Ile Leu His Asp Val Asn Ser Gly Leu Thr Cys Ser Thr Asp 595 600 605Leu Gln Lys Ala Asn Thr Asp Ile Ile Leu Gly Val Cys Val Asn Tyr 610 615 620Asp Leu Tyr Gly Ile Leu Gly Gln Gly Ile Phe Val Glu Val Asn Ala625 630 635 640Thr Tyr Tyr Asn Ser Trp Gln Asn Leu Leu Tyr Asp Ser Asn Gly Asn 645 650 655Leu Tyr Gly Phe Arg Asp Tyr Ile Ile Asn Arg Thr Phe Met Ile Arg 660 665 670Ser Cys Tyr Ser Gly Arg Val Ser Ala Ala Phe His Ala Asn Ser Ser 675 680 685Glu Pro Ala Leu Leu Phe

Arg Asn Ile Lys Cys Asn Tyr Val Phe Asn 690 695 700Asn Ser Leu Thr Arg Gln Leu Gln Pro Ile Asn Tyr Phe Asp Ser Tyr705 710 715 720Leu Gly Cys Val Val Asn Ala Tyr Asn Ser Thr Ala Ile Ser Val Gln 725 730 735Thr Cys Asp Leu Thr Val Gly Ser Gly Tyr Cys Val Asp Tyr Ser Lys 740 745 750Asn Arg Arg Ser Arg Gly Ala Ile Thr Thr Gly Tyr Arg Phe Thr Asn 755 760 765Phe Glu Pro Phe Thr Val Asn Ser Val Asn Asp Ser Leu Glu Pro Val 770 775 780Gly Gly Leu Tyr Glu Ile Gln Ile Pro Ser Glu Phe Thr Ile Gly Asn785 790 795 800Met Val Glu Phe Ile Gln Thr Ser Ser Pro Lys Val Thr Ile Asp Cys 805 810 815Ala Ala Phe Val Cys Gly Asp Tyr Ala Ala Cys Lys Ser Gln Leu Val 820 825 830Glu Tyr Gly Ser Phe Cys Asp Asn Ile Asn Ala Ile Leu Thr Glu Val 835 840 845Asn Glu Leu Leu Asp Thr Thr Gln Leu Gln Val Ala Asn Ser Leu Met 850 855 860Asn Gly Val Thr Leu Ser Thr Lys Leu Lys Asp Gly Val Asn Phe Asn865 870 875 880Val Asp Asp Ile Asn Phe Ser Pro Val Leu Gly Cys Leu Gly Ser Glu 885 890 895Cys Ser Lys Ala Ser Ser Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp 900 905 910Lys Val Lys Leu Ser Asp Val Gly Phe Val Glu Ala Tyr Asn Asn Cys 915 920 925Thr Gly Gly Ala Glu Ile Arg Asp Leu Ile Cys Val Gln Ser Tyr Lys 930 935 940Gly Ile Lys Val Leu Pro Pro Leu Leu Ser Glu Asn Gln Ile Ser Gly945 950 955 960Tyr Thr Leu Ala Ala Thr Ser Ala Ser Leu Phe Pro Pro Trp Thr Ala 965 970 975Ala Ala Gly Val Pro Phe Tyr Leu Asn Val Gln Tyr Arg Ile Asn Gly 980 985 990Leu Gly Val Thr Met Asp Val Leu Ser Gln Asn Gln Lys Leu Ile Ala 995 1000 1005Asn Ala Phe Asn Asn Ala Leu Tyr Ala Ile Gln Glu Gly Phe Asp 1010 1015 1020Ala Thr Asn Ser Ala Leu Val Lys Ile Gln Ala Val Val Asn Ala 1025 1030 1035Asn Ala Glu Ala Leu Asn Asn Leu Leu Gln Gln Leu Ser Asn Arg 1040 1045 1050Phe Gly Ala Ile Ser Ala Ser Leu Gln Glu Ile Leu Ser Arg Leu 1055 1060 1065Asp Ala Leu Glu Ala Glu Ala Gln Ile Asp Arg Leu Ile Asn Gly 1070 1075 1080Arg Leu Thr Ala Leu Asn Ala Tyr Val Ser Gln Gln Leu Ser Asp 1085 1090 1095Ser Thr Leu Val Lys Phe Ser Ala Ala Gln Ala Met Glu Lys Val 1100 1105 1110Asn Glu Cys Val Lys Ser Gln Ser Ser Arg Ile Asn Phe Cys Gly 1115 1120 1125Asn Gly Asn His Ile Ile Ser Leu Val Gln Asn Ala Pro Tyr Gly 1130 1135 1140Leu Tyr Phe Ile His Phe Ser Tyr Val Pro Thr Lys Tyr Val Thr 1145 1150 1155Ala Arg Val Ser Pro Gly Leu Cys Ile Ala Gly Asp Arg Gly Ile 1160 1165 1170Ala Pro Lys Ser Gly Tyr Phe Val Asn Val Asn Asn Thr Trp Met 1175 1180 1185Tyr Thr Gly Ser Gly Tyr Tyr Tyr Pro Glu Pro Ile Thr Glu Asn 1190 1195 1200Asn Val Val Val Met Ser Thr Cys Ala Val Asn Tyr Thr Lys Ala 1205 1210 1215Pro Tyr Val Met Leu Asn Thr Ser Ile Pro Asn Leu Pro Asp Phe 1220 1225 1230Lys Glu Glu Leu Asp Gln Trp Phe Lys Asn Gln Thr Ser Val Ala 1235 1240 1245Pro Asp Leu Ser Leu Asp Tyr Ile Asn Val Thr Phe Leu Asp Leu 1250 1255 1260Gln Val Glu Met Asn Arg Leu Gln Glu Ala Ile Lys Val Leu Asn 1265 1270 1275Gln Ser Tyr Ile Asn Leu Lys Asp Ile Gly Thr Tyr Glu Tyr Tyr 1280 1285 1290Val Lys Trp Pro Trp Tyr Val Trp Leu Leu Ile Cys Leu Ala Gly 1295 1300 1305Val Ala Met Leu Val Leu Leu Phe Phe Ile Cys Cys Cys Thr Gly 1310 1315 1320Cys Gly Thr Ser Cys Phe Lys Lys Cys Gly Gly Cys Cys Asp Asp 1325 1330 1335Tyr Thr Gly Tyr Gln Glu Leu Val Ile Lys Thr Ser His Asp Asp 1340 1345 1350311351PRTHuman coronavirus 31Met Phe Leu Ile Ile Phe Ile Leu Pro Thr Thr Leu Ala Val Ile Gly1 5 10 15Asp Phe Asn Cys Thr Asn Ser Phe Ile Asn Asp Tyr Asn Lys Thr Ile 20 25 30Pro Arg Ile Ser Glu Asp Val Val Asp Val Ser Leu Gly Leu Gly Thr 35 40 45Tyr Tyr Val Leu Asn Arg Val Tyr Leu Asn Thr Thr Leu Leu Phe Thr 50 55 60Gly Tyr Phe Pro Lys Ser Gly Ala Asn Phe Arg Asp Leu Ala Leu Lys65 70 75 80Gly Ser Ile Tyr Leu Ser Thr Leu Trp Tyr Lys Pro Pro Phe Leu Ser 85 90 95Asp Phe Asn Asn Gly Ile Phe Ser Lys Val Lys Asn Thr Lys Leu Tyr 100 105 110Val Asn Asn Thr Leu Tyr Ser Glu Phe Ser Thr Ile Val Ile Gly Ser 115 120 125Val Phe Val Asn Thr Ser Tyr Thr Ile Val Val Gln Pro His Asn Gly 130 135 140Ile Leu Glu Ile Thr Ala Cys Gln Tyr Thr Met Cys Glu Tyr Pro His145 150 155 160Thr Val Cys Lys Ser Lys Gly Ser Ile Arg Asn Glu Ser Trp His Ile 165 170 175Asp Ser Ser Glu Pro Leu Cys Leu Phe Lys Lys Asn Phe Thr Tyr Asn 180 185 190Val Ser Ala Asp Trp Leu Tyr Phe His Phe Tyr Gln Glu Arg Gly Val 195 200 205Phe Tyr Ala Tyr Tyr Ala Asp Val Gly Met Pro Thr Thr Phe Leu Phe 210 215 220Ser Leu Tyr Leu Gly Thr Ile Leu Ser His Tyr Tyr Val Met Pro Leu225 230 235 240Thr Cys Asn Ala Ile Ser Ser Asn Thr Asp Asn Glu Thr Leu Glu Tyr 245 250 255Trp Val Thr Pro Leu Ser Arg Arg Gln Tyr Leu Leu Asn Phe Asp Glu 260 265 270His Gly Val Ile Thr Asn Ala Val Asp Cys Ser Ser Ser Phe Leu Ser 275 280 285Glu Ile Gln Cys Lys Thr Gln Ser Phe Ala Pro Asn Thr Gly Val Tyr 290 295 300Asp Leu Ser Gly Phe Thr Val Lys Pro Val Ala Thr Val Tyr Arg Arg305 310 315 320Ile Pro Asn Leu Pro Asp Cys Asp Ile Asp Asn Trp Leu Asn Asn Val 325 330 335Ser Val Pro Ser Pro Leu Asn Trp Glu Arg Arg Ile Phe Ser Asn Cys 340 345 350Asn Phe Asn Leu Ser Thr Leu Leu Arg Leu Val His Val Asp Ser Phe 355 360 365Ser Cys Asn Asn Leu Asp Lys Ser Lys Ile Phe Gly Ser Cys Phe Asn 370 375 380Ser Ile Thr Val Asp Lys Phe Ala Ile Pro Asn Arg Arg Arg Asp Asp385 390 395 400Leu Gln Leu Gly Ser Ser Gly Phe Leu Gln Ser Ser Asn Tyr Lys Ile 405 410 415Asp Ile Ser Ser Ser Ser Cys Gln Leu Tyr Tyr Ser Leu Pro Leu Val 420 425 430Asn Val Thr Ile Asn Asn Phe Asn Pro Ser Ser Trp Asn Arg Arg Tyr 435 440 445Gly Phe Gly Ser Phe Asn Leu Ser Ser Tyr Asp Val Val Tyr Ser Asp 450 455 460His Cys Phe Ser Val Asn Ser Asp Phe Cys Pro Cys Ala Asp Pro Ser465 470 475 480Val Val Asn Ser Cys Ala Lys Ser Lys Pro Pro Ser Ala Ile Cys Pro 485 490 495Ala Gly Thr Lys Tyr Arg His Cys Asp

Leu Asp Thr Thr Leu Tyr Val 500 505 510Lys Asn Trp Cys Arg Cys Ser Cys Leu Pro Asp Pro Ile Ser Thr Tyr 515 520 525Ser Pro Asn Thr Cys Pro Gln Lys Lys Val Val Val Gly Ile Gly Glu 530

535 540His Cys Pro Gly Leu Gly Ile Asn Glu Glu Lys Cys Gly Thr Gln Leu545 550 555 560Asn His Ser Ser Cys Phe Cys Ser Pro Asp Ala Phe Leu Gly Trp Ser 565 570 575Phe Asp Ser Cys Ile Ser Asn Asn Arg Cys Asn Ile Phe Ser Asn Phe 580 585 590Ile Phe Asn Gly Ile Asn Ser Gly Thr Thr Cys Ser Asn Asp Leu Leu 595 600 605Tyr Ser Asn Thr Glu Ile Ser Thr Gly Val Cys Val Asn Tyr Asp Leu 610 615 620Tyr Gly Ile Thr Gly Gln Gly Ile Phe Lys Glu Val Ser Ala Ala Tyr625 630 635 640Tyr Asn Asn Trp Gln Asn Leu Leu Tyr Asp Ser Asn Gly Asn Ile Ile 645 650 655Gly Phe Lys Asp Phe Leu Thr Asn Lys Thr Tyr Thr Ile Leu Pro Cys 660 665 670Tyr Ser Gly Arg Val Ser Ala Ala Phe Tyr Gln Asn Ser Ser Ser Pro 675 680 685Ala Leu Leu Tyr Arg Asn Leu Lys Cys Ser Tyr Val Leu Asn Asn Ile 690 695 700Ser Phe Ile Ser Gln Pro Phe Tyr Phe Asp Ser Tyr Leu Gly Cys Val705 710 715 720Leu Asn Ala Val Asn Leu Thr Ser Tyr Ser Val Ser Ser Cys Asp Leu 725 730 735Arg Met Gly Ser Gly Phe Cys Ile Asp Tyr Ala Leu Pro Ser Ser Arg 740 745 750Arg Lys Arg Arg Gly Ile Ser Ser Pro Tyr Arg Phe Val Thr Phe Glu 755 760 765Pro Phe Asn Val Ser Phe Val Asn Asp Ser Val Glu Thr Val Gly Gly 770 775 780Leu Phe Glu Ile Gln Ile Pro Thr Asn Phe Thr Ile Ala Gly His Glu785 790 795 800Glu Phe Ile Gln Thr Ser Ser Pro Lys Val Thr Ile Asp Cys Ser Ala 805 810 815Phe Val Cys Ser Asn Tyr Ala Ala Cys His Asp Leu Leu Ser Glu Tyr 820 825 830Gly Thr Phe Cys Asp Asn Ile Asn Ser Ile Leu Asn Glu Val Asn Asp 835 840 845Leu Leu Asp Ile Thr Gln Leu Gln Val Ala Asn Ala Leu Met Gln Gly 850 855 860Val Thr Leu Ser Ser Asn Leu Asn Thr Asn Leu His Ser Asp Val Asp865 870 875 880Asn Ile Asp Phe Lys Ser Leu Leu Gly Cys Leu Gly Ser Gln Cys Gly 885 890 895Ser Ser Ser Arg Ser Leu Leu Glu Asp Leu Leu Phe Asn Lys Val Lys 900 905 910Leu Ser Asp Val Gly Phe Val Glu Ala Tyr Asn Asn Cys Thr Gly Gly 915 920 925Ser Glu Ile Arg Asp Leu Leu Cys Val Gln Ser Phe Asn Gly Ile Lys 930 935 940Val Leu Pro Pro Ile Leu Ser Glu Thr Gln Ile Ser Gly Tyr Thr Thr945 950 955 960Ala Ala Thr Val Ala Ala Met Phe Pro Pro Trp Ser Ala Ala Ala Gly 965 970 975Val Pro Phe Ser Leu Asn Val Gln Tyr Arg Ile Asn Gly Leu Gly Val 980 985 990Thr Met Asp Val Leu Asn Lys Asn Gln Lys Leu Ile Ala Asn Ala Phe 995 1000 1005Asn Lys Ala Leu Leu Ser Ile Gln Asn Gly Phe Thr Ala Thr Asn 1010 1015 1020Ser Ala Leu Ala Lys Ile Gln Ser Val Val Asn Ala Asn Ala Gln 1025 1030 1035Ala Leu Asn Ser Leu Leu Gln Gln Leu Phe Asn Lys Phe Gly Ala 1040 1045 1050Ile Ser Ser Ser Leu Gln Glu Ile Leu Ser Arg Leu Asp Asn Leu 1055 1060 1065Glu Ala Gln Val Gln Ile Asp Arg Leu Ile Asn Gly Arg Leu Thr 1070 1075 1080Ala Leu Asn Ala Tyr Val Ser Gln Gln Leu Ser Asp Ile Thr Leu 1085 1090 1095Ile Lys Ala Gly Ala Ser Arg Ala Ile Glu Lys Val Asn Glu Cys 1100 1105 1110Val Lys Ser Gln Ser Pro Arg Ile Asn Phe Cys Gly Asn Gly Asn 1115 1120 1125His Ile Leu Ser Leu Val Gln Asn Ala Pro Tyr Gly Leu Leu Phe 1130 1135 1140Ile His Phe Ser Tyr Lys Pro Thr Ser Phe Lys Thr Val Leu Val 1145 1150 1155Ser Pro Gly Leu Cys Leu Ser Gly Asp Arg Gly Ile Ala Pro Lys 1160 1165 1170Gln Gly Tyr Phe Ile Lys Gln Asn Asp Ser Trp Met Phe Thr Gly 1175 1180 1185Ser Ser Tyr Tyr Tyr Pro Glu Pro Ile Ser Asp Lys Asn Val Val 1190 1195 1200Phe Met Asn Ser Cys Ser Val Asn Phe Thr Lys Ala Pro Phe Ile 1205 1210 1215Tyr Leu Asn Asn Ser Ile Pro Asn Leu Ser Asp Phe Glu Ala Glu 1220 1225 1230Leu Ser Leu Trp Phe Lys Asn His Thr Ser Ile Ala Pro Asn Leu 1235 1240 1245Thr Phe Asn Ser His Ile Asn Ala Thr Phe Leu Asp Leu Tyr Tyr 1250 1255 1260Glu Met Asn Val Ile Gln Glu Ser Ile Lys Ser Leu Asn Ser Ser 1265 1270 1275Phe Ile Asn Leu Lys Glu Ile Gly Thr Tyr Glu Met Tyr Val Lys 1280 1285 1290Trp Pro Trp Tyr Ile Trp Leu Leu Ile Val Ile Leu Phe Ile Ile 1295 1300 1305Phe Leu Met Ile Leu Phe Phe Ile Cys Cys Cys Thr Gly Cys Gly 1310 1315 1320Ser Ala Cys Phe Ser Lys Cys His Asn Cys Cys Asp Glu Tyr Gly 1325 1330 1335Gly His Asn Asp Phe Val Ile Lys Ala Ser His Asp Asp 1340 1345 135032526PRTArtificial SequenceSynthetic Polypeptide 32Met Phe Ile Phe Leu Leu Phe Leu Thr Leu Thr Ser Gly Ser Asp Leu1 5 10 15Asp Arg Ala Leu Ser Gly Ile Ala Ala Glu Gln Asp Arg Asn Thr Arg 20 25 30Glu Val Phe Ala Gln Val Lys Gln Met Tyr Lys Thr Pro Thr Leu Lys 35 40 45Tyr Phe Gly Gly Phe Asn Phe Ser Gln Ile Leu Pro Asp Pro Leu Lys 50 55 60Pro Thr Lys Arg Ser Phe Ile Glu Asp Leu Leu Phe Asn Lys Val Thr65 70 75 80Leu Ala Asp Ala Gly Phe Met Lys Gln Tyr Gly Glu Cys Leu Gly Asp 85 90 95Ile Asn Ala Arg Asp Leu Ile Cys Ala Gln Lys Phe Asn Gly Leu Thr 100 105 110Val Leu Pro Pro Leu Leu Thr Asp Asp Met Ile Ala Ala Tyr Thr Ala 115 120 125Ala Leu Val Ser Gly Thr Ala Thr Ala Gly Trp Thr Phe Gly Ala Gly 130 135 140Ala Ala Leu Gln Ile Pro Phe Ala Met Gln Met Ala Tyr Arg Phe Asn145 150 155 160Gly Ile Gly Val Thr Gln Asn Val Leu Tyr Glu Asn Gln Lys Gln Ile 165 170 175Ala Asn Gln Phe Asn Lys Ala Ile Ser Gln Ile Gln Glu Ser Leu Thr 180 185 190Thr Thr Ser Thr Ala Leu Gly Lys Leu Gln Asp Val Val Asn Gln Asn 195 200 205Ala Gln Ala Leu Asn Thr Leu Val Lys Gln Leu Ser Ser Asn Phe Gly 210 215 220Ala Ile Ser Ser Val Leu Asn Asp Ile Leu Ser Arg Leu Asp Lys Val225 230 235 240Glu Ala Glu Val Gln Ile Asp Arg Leu Ile Thr Gly Arg Leu Gln Ser 245 250 255Leu Gln Thr Tyr Val Thr Gln Gln Leu Ile Arg Ala Ala Glu Ile Arg 260 265 270Ala Ser Ala Asn Leu Ala Ala Thr Lys Met Ser Glu

Cys Val Leu Gly 275 280 285Gln Ser Lys Arg Val Asp Phe Cys Gly Lys Gly Tyr His Leu Met Ser 290 295 300Phe Pro Gln Ala Ala Pro His Gly Val Val Phe Leu His Val Thr Tyr305 310 315 320Val Pro Ser Gln Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His 325 330 335Glu Gly Lys Ala Tyr Phe Pro Arg Glu Gly Val Phe Val Phe Asn Gly 340 345 350Thr Ser Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile 355 360 365Thr Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly 370 375 380Ile Ile Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro Glu Leu Asp Ser385 390 395 400Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn His Thr Ser Pro Asp 405 410 415Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val Val Asn Ile 420 425 430Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys Asn Leu Asn Glu 435 440 445Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr Glu Gln Tyr Ile Lys 450 455 460Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile Ala Gly Leu Ile Ala Ile465 470 475 480Val Met Val Thr Ile Leu Leu Cys Cys Met Thr Ser Cys Cys Ser Cys 485 490 495Leu Lys Gly Ala Cys Ser Cys Gly Ser Cys Cys Lys Phe Asp Glu Asp 500 505 510Asp Ser Glu Pro Val Leu Lys Gly Val Lys Leu His Tyr Thr 515 520 52533588PRTArtificial SequenceSynthetic Polypeptide 33Met Ile His Ser Val Phe Leu Leu Met Phe Leu Leu Thr Pro Thr Glu1 5 10 15Ser Asp Cys Lys Leu Pro Leu Gly Gln Ser Leu Cys Ala Leu Pro Asp 20 25 30Thr Pro Ser Thr Leu Thr Pro Arg Ser Val Arg Ser Val Pro Gly Glu 35 40 45Met Arg Leu Ala Ser Ile Ala Phe Asn His Pro Ile Gln Val Asp Gln 50 55 60Leu Asn Ser Ser Tyr Phe Lys Leu Ser Ile Pro Thr Asn Phe Ser Phe65 70 75 80Gly Val Thr Gln Glu Tyr Ile Gln Thr Thr Ile Gln Lys Val Thr Val 85 90 95Asp Cys Lys Gln Tyr Val Cys Asn Gly Phe Gln Lys Cys Glu Gln Leu 100 105 110Leu Arg Glu Tyr Gly Gln Phe Cys Ser Lys Ile Asn Gln Ala Leu His 115 120 125Gly Ala Asn Leu Arg Gln Asp Asp Ser Val Arg Asn Leu Phe Ala Ser 130 135 140Val Lys Ser Ser Gln Ser Ser Pro Ile Ile Pro Gly Phe Gly Gly Asp145 150 155 160Phe Asn Leu Thr Leu Leu Glu Pro Val Ser Ile Ser Thr Gly Ser Arg 165 170 175Ser Ala Arg Ser Ala Ile Glu Asp Leu Leu Phe Asp Lys Val Thr Ile 180 185 190Ala Asp Pro Gly Tyr Met Gln Gly Tyr Asp Asp Cys Met Gln Gln Gly 195 200 205Pro Ala Ser Ala Arg Asp Leu Ile Cys Ala Gln Tyr Val Ala Gly Tyr 210 215 220Lys Val Leu Pro Pro Leu Met Asp Val Asn Met Glu Ala Ala Tyr Thr225 230 235 240Ser Ser Leu Leu Gly Ser Ile Ala Gly Val Gly Trp Thr Ala Gly Leu 245 250 255Ser Ser Phe Ala Ala Ile Pro Phe Ala Gln Ser Ile Phe Tyr Arg Leu 260 265 270Asn Gly Val Gly Ile Thr Gln Gln Val Leu Ser Glu Asn Gln Lys Leu 275 280 285Ile Ala Asn Lys Phe Asn Gln Ala Leu Gly Ala Met Gln Thr Gly Phe 290 295 300Thr Thr Thr Asn Glu Ala Phe Gln Lys Val Gln Asp Ala Val Asn Asn305 310 315 320Asn Ala Gln Ala Leu Ser Lys Leu Ala Ser Glu Leu Ser Asn Thr Phe 325 330 335Gly Ala Ile Ser Ala Ser Ile Gly Asp Ile Ile Gln Arg Leu Asp Val 340 345 350Leu Glu Gln Asp Ala Gln Ile Asp Arg Leu Ile Asn Gly Arg Leu Thr 355 360 365Thr Leu Asn Ala Phe Val Ala Gln Gln Leu Val Arg Ser Glu Ser Ala 370 375 380Ala Leu Ser Ala Gln Leu Ala Lys Asp Lys Val Asn Glu Cys Val Lys385 390 395 400Ala Gln Ser Lys Arg Ser Gly Phe Cys Gly Gln Gly Thr His Ile Val 405 410 415Ser Phe Val Val Asn Ala Pro Asn Gly Leu Tyr Phe Met His Val Gly 420 425 430Tyr Tyr Pro Ser Asn His Ile Glu Val Val Ser Ala Tyr Gly Leu Cys 435 440 445Asp Ala Ala Asn Pro Thr Asn Cys Ile Ala Pro Val Asn Gly Tyr Phe 450 455 460Ile Lys Thr Asn Asn Thr Arg Ile Val Asp Glu Trp Ser Tyr Thr Gly465 470 475 480Ser Ser Phe Tyr Ala Pro Glu Pro Ile Thr Ser Leu Asn Thr Lys Tyr 485 490 495Val Ala Pro Gln Val Thr Tyr Gln Asn Ile Ser Thr Asn Leu Pro Pro 500 505 510Pro Leu Leu Gly Asn Ser Thr Gly Ile Asp Phe Gln Asp Glu Leu Asp 515 520 525Glu Phe Phe Lys Asn Val Ser Thr Ser Ile Pro Asn Phe Gly Ser Leu 530 535 540Thr Gln Ile Asn Thr Thr Leu Leu Asp Leu Thr Tyr Glu Met Leu Ser545 550 555 560Leu Gln Gln Val Val Lys Ala Leu Asn Glu Ser Tyr Ile Asp Leu Lys 565 570 575Glu Leu Gly Asn Tyr Thr Tyr Tyr Asn Lys Trp Pro 580 58534526PRTArtificial SequenceSynthetic Polypeptide 34Met Phe Ile Phe Leu Leu Phe Leu Thr Leu Thr Ser Gly Ser Asp Leu1 5 10 15Asp Arg Ala Leu Ser Gly Ile Ala Ala Glu Gln Asp Arg Asn Thr Arg 20 25 30Glu Val Phe Ala Gln Val Lys Gln Met Tyr Lys Thr Pro Thr Leu Lys 35 40 45Tyr Phe Gly Gly Phe Asn Phe Ser Gln Ile Leu Pro Asp Pro Leu Lys 50 55 60Pro Thr Lys Arg Ser Phe Ile Glu Asp Leu Leu Phe Asn Lys Val Thr65 70 75 80Leu Ala Asp Ala Gly Phe Met Lys Gln Tyr Gly Glu Cys Leu Gly Asp 85 90 95Ile Asn Ala Arg Asp Leu Ile Cys Ala Gln Lys Phe Asn Gly Leu Thr 100 105 110Val Leu Pro Pro Leu Leu Thr Asp Asp Met Ile Ala Ala Tyr Thr Ala 115 120 125Ala Leu Val Ser Gly Thr Ala Thr Ala Gly Trp Thr Phe Gly Ala Gly 130 135 140Ala Ala Leu Gln Ile Pro Phe Ala Met Gln Met Ala Tyr Arg Phe Asn145 150 155 160Gly Ile Gly Val Thr Gln Asn Val Leu Tyr Glu Asn Gln Lys Gln Ile 165 170 175Ala Asn Gln Phe Asn Lys Ala Ile Ser Gln Ile Gln Glu Ser Leu Thr 180 185 190Thr Thr Ser Thr Ala Leu Gly Lys Leu Gln Asp Val Val Asn Gln Asn 195 200 205Ala Gln Ala Leu Asn Thr Leu Val Lys Gln Leu Ser Ser Asn Phe Gly 210 215 220Ala Ile Ser Ser Val Leu Asn Asp Ile Leu Ser Arg Leu Asp Lys Val225 230 235 240Glu Ala Glu Val Gln Ile Asp Arg Leu Ile Thr Gly Arg Leu Gln Ser 245 250 255Leu Gln Thr Tyr Val Thr Gln Gln Leu Ile Arg Ala Ala Glu Ile Arg 260 265 270Ala Ser Ala Asn Leu Ala Ala Thr Lys Met Ser Glu Cys Val Leu Gly 275 280 285Gln Ser Lys Arg Val Asp Phe Cys Gly Lys Gly Tyr His Leu Met Ser 290 295 300Phe Pro Gln Ala Ala Pro His Gly Val Val Phe Leu His Val Thr Tyr305 310 315 320Val Pro Ser Gln Glu Arg Asn Phe Thr Thr Ala Pro Ala Ile Cys His 325 330 335Glu Gly Lys Ala Tyr Phe Pro Arg

Glu Gly Val Phe Val Phe Asn Gly 340 345 350Thr Ser Trp Phe Ile Thr Gln Arg Asn Phe Phe Ser Pro Gln Ile Ile 355 360 365Thr Thr Asp Asn Thr Phe Val Ser Gly Asn Cys Asp Val Val Ile Gly 370 375 380Ile Ile Asn Asn Thr Val Tyr Asp Pro Leu Gln Pro Glu Leu Asp Ser385 390 395 400Phe Lys Glu Glu Leu Asp Lys Tyr Phe Lys Asn His Thr Ser Pro Asp 405 410 415Val Asp Leu Gly Asp Ile Ser Gly Ile Asn Ala Ser Val Val Asn Ile 420 425 430Gln Lys Glu Ile Asp Arg Leu Asn Glu Val Ala Lys Asn Leu Asn Glu 435 440 445Ser Leu Ile Asp Leu Gln Glu Leu Gly Lys Tyr Glu Gln Tyr Ile Lys 450 455 460Trp Pro Trp Tyr Val Trp Leu Gly Phe Ile Ala Gly Leu Ile Ala Ile465 470 475 480Val Met Val Thr Ile Leu Leu Cys Cys Met Thr Ser Cys Cys Ser Cys 485 490 495Leu Lys Gly Ala Cys Ser Cys Gly Ser Cys Cys Lys Phe Asp Glu Asp 500 505 510Asp Ser Glu Pro Val Leu Lys Gly Val Lys Leu His Tyr Thr 515

520 525351864DNAArtificial SequenceSynthetic Polynucleotide 35tcaagctttt ggaccctcgt acagaagcta atacgactca ctatagggaa ataagagaga 60aaagaagagt aagaagaaat ataagagcca ccatgggtct caaggtgaac gtctctgccg 120tattcatggc agtactgtta actctccaaa cacccgccgg tcaaattcat tggggcaatc 180tctctaagat aggggtagta ggaataggaa gtgcaagcta caaagttatg actcgttcca 240gccatcaatc attagtcata aaattaatgc ccaatataac tctcctcaat aactgcacga 300gggtagagat tgcagaatac aggagactac taagaacagt tttggaacca attagggatg 360cacttaatgc aatgacccag aacataaggc cggttcagag cgtagcttca agtaggagac 420acaagagatt tgcgggagta gtcctggcag gtgcggccct aggtgttgcc acagctgctc 480agataacagc cggcattgca cttcaccggt ccatgctgaa ctctcaggcc atcgacaatc 540tgagagcgag cctggaaact actaatcagg caattgaggc aatcagacaa gcagggcagg 600agatgatatt ggctgttcag ggtgtccaag actacatcaa taatgagctg ataccgtcta 660tgaaccagct atcttgtgat ctaatcggtc agaagctcgg gctcaaattg cttagatact 720atacagaaat cctgtcatta tttggcccca gcctacggga ccccatatct gcggagatat 780ctatccaggc tttgagttat gcacttggag gagatatcaa taaggtgtta gaaaagctcg 840gatacagtgg aggcgattta ctaggcatct tagagagcag aggaataaag gctcggataa 900ctcacgtcga cacagagtcc tacttcatag tcctcagtat agcctatccg acgctgtccg 960agattaaggg ggtgattgtc caccggctag agggggtctc gtacaacata ggctctcaag 1020agtggtatac cactgtgccc aagtatgttg caacccaagg gtaccttatc tcgaattttg 1080atgagtcatc atgtactttc atgccagagg ggactgtgtg cagccaaaat gccttgtacc 1140cgatgagtcc tctgctccaa gaatgcctcc gggggtccac caagtcctgt gctcgtacac 1200tcgtatccgg gtcttttggg aaccggttca ttttatcaca agggaaccta atagccaatt 1260gtgcatcaat tctttgtaag tgttacacaa caggtacgat tattaatcaa gaccctgaca 1320agatcctaac atacattgct gccgatcgct gcccggtagt cgaggtgaac ggcgtgacca 1380tccaagtcgg gagcaggagg tatccagacg ctgtgtactt gcacagaatt gacctcggtc 1440ctcccatatc attggagagg ttggacgtag ggacaaatct ggggaatgca attgccaaat 1500tggaggatgc caaggaattg ttggaatcat cggaccagat attgagaagt atgaaaggtt 1560tatcgagcac tagcatagtc tacatcctga ttgcagtgtg tcttggaggg ttgataggga 1620tccccacttt aatatgttgc tgcagggggc gttgtaacaa aaagggagaa caagttggta 1680tgtcaagacc aggcctaaag cctgacctta caggaacatc aaaatcctat gtaagatcgc 1740tttgatgata ataggctgga gcctcggtgg ccaagcttct tgccccttgg gcctcccccc 1800agcccctcct ccccttcctg cacccgtacc cccgtggtct ttgaataaag tctgagtggg 1860cggc 1864361653DNAArtificial SequenceSynthetic Polynucleotide 36atgggtctca aggtgaacgt ctctgccgta ttcatggcag tactgttaac tctccaaaca 60cccgccggtc aaattcattg gggcaatctc tctaagatag gggtagtagg aataggaagt 120gcaagctaca aagttatgac tcgttccagc catcaatcat tagtcataaa attaatgccc 180aatataactc tcctcaataa ctgcacgagg gtagagattg cagaatacag gagactacta 240agaacagttt tggaaccaat tagggatgca cttaatgcaa tgacccagaa cataaggccg 300gttcagagcg tagcttcaag taggagacac aagagatttg cgggagtagt cctggcaggt 360gcggccctag gtgttgccac agctgctcag ataacagccg gcattgcact tcaccggtcc 420atgctgaact ctcaggccat cgacaatctg agagcgagcc tggaaactac taatcaggca 480attgaggcaa tcagacaagc agggcaggag atgatattgg ctgttcaggg tgtccaagac 540tacatcaata atgagctgat accgtctatg aaccagctat cttgtgatct aatcggtcag 600aagctcgggc tcaaattgct tagatactat acagaaatcc tgtcattatt tggccccagc 660ctacgggacc ccatatctgc ggagatatct atccaggctt tgagttatgc acttggagga 720gatatcaata aggtgttaga aaagctcgga tacagtggag gcgatttact aggcatctta 780gagagcagag gaataaaggc tcggataact cacgtcgaca cagagtccta cttcatagtc 840ctcagtatag cctatccgac gctgtccgag attaaggggg tgattgtcca ccggctagag 900ggggtctcgt acaacatagg ctctcaagag tggtatacca ctgtgcccaa gtatgttgca 960acccaagggt accttatctc gaattttgat gagtcatcat gtactttcat gccagagggg 1020actgtgtgca gccaaaatgc cttgtacccg atgagtcctc tgctccaaga atgcctccgg 1080gggtccacca agtcctgtgc tcgtacactc gtatccgggt cttttgggaa ccggttcatt 1140ttatcacaag ggaacctaat agccaattgt gcatcaattc tttgtaagtg ttacacaaca 1200ggtacgatta ttaatcaaga ccctgacaag atcctaacat acattgctgc cgatcgctgc 1260ccggtagtcg aggtgaacgg cgtgaccatc caagtcggga gcaggaggta tccagacgct 1320gtgtacttgc acagaattga cctcggtcct cccatatcat tggagaggtt ggacgtaggg 1380acaaatctgg ggaatgcaat tgccaaattg gaggatgcca aggaattgtt ggaatcatcg 1440gaccagatat tgagaagtat gaaaggttta tcgagcacta gcatagtcta catcctgatt 1500gcagtgtgtc ttggagggtt gatagggatc cccactttaa tatgttgctg cagggggcgt 1560tgtaacaaaa agggagaaca agttggtatg tcaagaccag gcctaaagcc tgaccttaca 1620ggaacatcaa aatcctatgt aagatcgctt tga 1653371925DNAArtificial SequenceSynthetic Polynucleotide 37ggggaaataa gagagaaaag aagagtaaga agaaatataa gagccaccat gggtctcaag 60gtgaacgtct ctgccgtatt catggcagta ctgttaactc tccaaacacc cgccggtcaa 120attcattggg gcaatctctc taagataggg gtagtaggaa taggaagtgc aagctacaaa 180gttatgactc gttccagcca tcaatcatta gtcataaaat taatgcccaa tataactctc 240ctcaataact gcacgagggt agagattgca gaatacagga gactactaag aacagttttg

300gaaccaatta gggatgcact taatgcaatg acccagaaca taaggccggt tcagagcgta 360gcttcaagta ggagacacaa gagatttgcg ggagtagtcc tggcaggtgc ggccctaggt 420gttgccacag ctgctcagat aacagccggc attgcacttc accggtccat gctgaactct 480caggccatcg acaatctgag agcgagcctg gaaactacta atcaggcaat tgaggcaatc 540agacaagcag ggcaggagat gatattggct gttcagggtg tccaagacta catcaataat 600gagctgatac cgtctatgaa ccagctatct tgtgatctaa tcggtcagaa gctcgggctc 660aaattgctta gatactatac agaaatcctg tcattatttg gccccagcct acgggacccc 720atatctgcgg agatatctat ccaggctttg agttatgcac ttggaggaga tatcaataag 780gtgttagaaa agctcggata cagtggaggc gatttactag gcatcttaga gagcagagga 840ataaaggctc ggataactca cgtcgacaca gagtcctact tcatagtcct cagtatagcc 900tatccgacgc tgtccgagat taagggggtg attgtccacc ggctagaggg ggtctcgtac 960aacataggct ctcaagagtg gtataccact gtgcccaagt atgttgcaac ccaagggtac 1020cttatctcga attttgatga gtcatcatgt actttcatgc cagaggggac tgtgtgcagc 1080caaaatgcct tgtacccgat gagtcctctg ctccaagaat gcctccgggg gtccaccaag 1140tcctgtgctc gtacactcgt atccgggtct tttgggaacc ggttcatttt atcacaaggg 1200aacctaatag ccaattgtgc atcaattctt tgtaagtgtt acacaacagg tacgattatt 1260aatcaagacc ctgacaagat cctaacatac attgctgccg atcgctgccc ggtagtcgag 1320gtgaacggcg tgaccatcca agtcgggagc aggaggtatc cagacgctgt gtacttgcac 1380agaattgacc tcggtcctcc catatcattg gagaggttgg acgtagggac aaatctgggg 1440aatgcaattg ccaaattgga ggatgccaag gaattgttgg aatcatcgga ccagatattg 1500agaagtatga aaggtttatc gagcactagc atagtctaca tcctgattgc agtgtgtctt 1560ggagggttga tagggatccc cactttaata tgttgctgca gggggcgttg taacaaaaag 1620ggagaacaag ttggtatgtc aagaccaggc ctaaagcctg accttacagg aacatcaaaa 1680tcctatgtaa gatcgctttg atgataatag gctggagcct cggtggccaa gcttcttgcc 1740ccttgggcct ccccccagcc cctcctcccc ttcctgcacc cgtacccccg tggtctttga 1800ataaagtctg agtgggcggc aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920tctag 1925381864DNAArtificial SequenceSynthetic Polynucleotide 38tcaagctttt ggaccctcgt acagaagcta atacgactca ctatagggaa ataagagaga 60aaagaagagt aagaagaaat ataagagcca ccatgggtct caaggtgaac gtctctgtca 120tattcatggc agtactgtta actcttcaaa cacccaccgg tcaaatccat tggggcaatc 180tctctaagat aggggtggta ggggtaggaa gtgcaagcta caaagttatg actcgttcca 240gccatcaatc attagtcata aagttaatgc ccaatataac tctcctcaac aattgcacga 300gggtagggat tgcagaatac aggagactac tgagaacagt tctggaacca attagagatg 360cacttaatgc aatgacccag aatataagac cggttcagag tgtagcttca agtaggagac 420acaagagatt tgcgggagtt gtcctggcag gtgcggccct aggcgttgcc acagctgctc 480aaataacagc cggtattgca cttcaccagt ccatgctgaa ctctcaagcc atcgacaatc 540tgagagcgag cctagaaact actaatcagg caattgaggc aatcagacaa gcagggcagg 600agatgatatt ggctgttcag ggtgtccaag actacatcaa taatgagctg ataccgtcta 660tgaatcaact atcttgtgat ttaatcggcc agaagctagg gctcaaattg ctcagatact 720atacagaaat cctgtcatta tttggcccca gcttacggga ccccatatct gcggagatat 780ctatccaggc tttgagctat gcgcttggag gagatatcaa taaggtgttg gaaaagctcg 840gatacagtgg aggtgatcta ctgggcatct tagagagcag aggaataaag gcccggataa 900ctcacgtcga cacagagtcc tacttcattg tactcagtat agcctatccg acgctatccg 960agattaaggg ggtgattgtc caccggctag agggggtctc gtacaacata ggctctcaag 1020agtggtatac cactgtgccc aagtatgttg caacccaagg gtaccttatc tcgaattttg 1080atgagtcatc atgcactttc atgccagagg ggactgtgtg cagccagaat gccttgtacc 1140cgatgagtcc tctgctccaa gaatgcctcc gggggtccac taagtcctgt gctcgtacac 1200tcgtatccgg gtctttcggg aaccggttca ttttatcaca ggggaaccta atagccaatt 1260gtgcatcaat cctttgcaag tgttacacaa caggaacaat cattaatcaa gaccctgaca 1320agatcctaac atacattgct gccgatcact gcccggtggt cgaggtgaat ggcgtgacca 1380tccaagtcgg gagcaggagg tatccggacg ctgtgtactt gcacaggatt gacctcggtc 1440ctcccatatc tttggagagg ttggacgtag ggacaaatct ggggaatgca attgctaagt 1500tggaggatgc caaggaattg ttggagtcat cggaccagat attgaggagt atgaaaggtt 1560tatcgagcac tagtatagtt tacatcctga ttgcagtgtg tcttggagga ttgataggga 1620tccccgcttt aatatgttgc tgcagggggc gttgtaacaa gaagggagaa caagttggta 1680tgtcaagacc aggcctaaag cctgatctta caggaacatc aaaatcctat gtaaggtcac 1740tctgatgata ataggctgga gcctcggtgg ccaagcttct tgccccttgg gcctcccccc 1800agcccctcct ccccttcctg cacccgtacc cccgtggtct ttgaataaag tctgagtggg 1860cggc 1864391653DNAArtificial SequenceSynthetic Polynucleotide 39atgggtctca aggtgaacgt ctctgtcata ttcatggcag tactgttaac tcttcaaaca 60cccaccggtc aaatccattg gggcaatctc tctaagatag gggtggtagg ggtaggaagt 120gcaagctaca aagttatgac tcgttccagc catcaatcat tagtcataaa gttaatgccc 180aatataactc tcctcaacaa ttgcacgagg gtagggattg cagaatacag gagactactg 240agaacagttc tggaaccaat tagagatgca cttaatgcaa tgacccagaa tataagaccg 300gttcagagtg tagcttcaag taggagacac aagagatttg cgggagttgt cctggcaggt 360gcggccctag gcgttgccac agctgctcaa ataacagccg gtattgcact tcaccagtcc 420atgctgaact ctcaagccat cgacaatctg agagcgagcc tagaaactac taatcaggca 480attgaggcaa tcagacaagc agggcaggag atgatattgg ctgttcaggg tgtccaagac 540tacatcaata atgagctgat accgtctatg aatcaactat cttgtgattt aatcggccag 600aagctagggc tcaaattgct cagatactat acagaaatcc tgtcattatt tggccccagc 660ttacgggacc ccatatctgc ggagatatct atccaggctt tgagctatgc gcttggagga 720gatatcaata aggtgttgga aaagctcgga tacagtggag gtgatctact gggcatctta 780gagagcagag gaataaaggc ccggataact cacgtcgaca cagagtccta cttcattgta 840ctcagtatag cctatccgac gctatccgag attaaggggg tgattgtcca ccggctagag 900ggggtctcgt acaacatagg ctctcaagag tggtatacca ctgtgcccaa gtatgttgca 960acccaagggt accttatctc gaattttgat gagtcatcat gcactttcat gccagagggg 1020actgtgtgca gccagaatgc cttgtacccg atgagtcctc tgctccaaga atgcctccgg 1080gggtccacta agtcctgtgc tcgtacactc gtatccgggt ctttcgggaa ccggttcatt 1140ttatcacagg ggaacctaat agccaattgt gcatcaatcc tttgcaagtg ttacacaaca 1200ggaacaatca ttaatcaaga ccctgacaag atcctaacat acattgctgc cgatcactgc 1260ccggtggtcg aggtgaatgg cgtgaccatc caagtcggga gcaggaggta tccggacgct 1320gtgtacttgc acaggattga cctcggtcct cccatatctt tggagaggtt ggacgtaggg 1380acaaatctgg ggaatgcaat tgctaagttg gaggatgcca aggaattgtt ggagtcatcg 1440gaccagatat tgaggagtat gaaaggttta tcgagcacta gtatagttta catcctgatt 1500gcagtgtgtc ttggaggatt gatagggatc cccgctttaa tatgttgctg cagggggcgt 1560tgtaacaaga agggagaaca agttggtatg tcaagaccag gcctaaagcc tgatcttaca 1620ggaacatcaa aatcctatgt aaggtcactc tga 1653401925DNAArtificial SequenceSynthetic Polynucleotide 40ggggaaataa gagagaaaag aagagtaaga agaaatataa gagccaccat gggtctcaag 60gtgaacgtct ctgtcatatt catggcagta ctgttaactc ttcaaacacc caccggtcaa 120atccattggg gcaatctctc taagataggg gtggtagggg taggaagtgc aagctacaaa 180gttatgactc gttccagcca tcaatcatta gtcataaagt taatgcccaa tataactctc 240ctcaacaatt gcacgagggt agggattgca gaatacagga gactactgag aacagttctg 300gaaccaatta gagatgcact taatgcaatg acccagaata taagaccggt tcagagtgta 360gcttcaagta ggagacacaa gagatttgcg ggagttgtcc tggcaggtgc ggccctaggc 420gttgccacag ctgctcaaat aacagccggt attgcacttc accagtccat gctgaactct 480caagccatcg acaatctgag agcgagccta gaaactacta atcaggcaat tgaggcaatc 540agacaagcag ggcaggagat gatattggct gttcagggtg tccaagacta catcaataat 600gagctgatac cgtctatgaa tcaactatct tgtgatttaa tcggccagaa gctagggctc 660aaattgctca gatactatac agaaatcctg tcattatttg gccccagctt acgggacccc 720atatctgcgg agatatctat ccaggctttg agctatgcgc ttggaggaga tatcaataag 780gtgttggaaa agctcggata cagtggaggt gatctactgg gcatcttaga gagcagagga 840ataaaggccc ggataactca cgtcgacaca gagtcctact tcattgtact cagtatagcc 900tatccgacgc tatccgagat taagggggtg attgtccacc ggctagaggg ggtctcgtac 960aacataggct ctcaagagtg gtataccact gtgcccaagt atgttgcaac ccaagggtac 1020cttatctcga attttgatga gtcatcatgc actttcatgc cagaggggac tgtgtgcagc 1080cagaatgcct tgtacccgat gagtcctctg ctccaagaat gcctccgggg gtccactaag 1140tcctgtgctc gtacactcgt atccgggtct ttcgggaacc ggttcatttt atcacagggg 1200aacctaatag ccaattgtgc atcaatcctt tgcaagtgtt acacaacagg aacaatcatt 1260aatcaagacc ctgacaagat cctaacatac attgctgccg atcactgccc ggtggtcgag 1320gtgaatggcg tgaccatcca agtcgggagc aggaggtatc cggacgctgt gtacttgcac 1380aggattgacc tcggtcctcc catatctttg gagaggttgg acgtagggac aaatctgggg 1440aatgcaattg ctaagttgga ggatgccaag gaattgttgg agtcatcgga ccagatattg 1500aggagtatga aaggtttatc gagcactagt atagtttaca tcctgattgc agtgtgtctt 1560ggaggattga tagggatccc cgctttaata tgttgctgca gggggcgttg taacaagaag 1620ggagaacaag ttggtatgtc aagaccaggc ctaaagcctg atcttacagg aacatcaaaa 1680tcctatgtaa ggtcactctg atgataatag gctggagcct cggtggccaa gcttcttgcc 1740ccttgggcct ccccccagcc cctcctcccc ttcctgcacc cgtacccccg tggtctttga 1800ataaagtctg agtgggcggc aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920tctag 1925412065DNAArtificial SequenceSynthetic Polynucleotide 41tcaagctttt ggaccctcgt acagaagcta atacgactca ctatagggaa ataagagaga 60aaagaagagt aagaagaaat ataagagcca ccatgtcacc gcaacgagac cggataaatg 120ccttctacaa agataaccct tatcccaagg gaagtaggat agttattaac agagaacatc 180ttatgattga cagaccctat gttctgctgg ctgttctgtt cgtcatgttt ctgagcttga 240tcggattgct ggcaattgca ggcattagac ttcatcgggc agccatctac accgcggaga 300tccataaaag cctcagtacc aatctggatg tgactaactc catcgagcat caggtcaagg 360acgtgctgac accactcttt aaaatcatcg gggatgaagt gggcctgaga acacctcaga 420gattcactga cctagtgaaa ttcatctcgg acaagattaa attccttaat ccggataggg 480agtacgactt cagagatctc acttggtgca tcaacccgcc agagaggatc aaactagatt 540atgatcaata ctgtgcagat gtggctgctg aagagctcat gaatgcattg gtgaactcaa 600ctctactgga gaccagaaca accactcagt tcctagctgt ctcaaaggga aactgctcag 660ggcccactac aatcagaggt caattctcaa acatgtcgct gtccttgttg gacttgtact 720taggtcgagg ttacaatgtg tcatctatag tcactatgac atcccaggga atgtatgggg 780gaacctacct agttgaaaag cctaatctga acagcaaagg gtcagagttg tcacaactga 840gcatgtaccg agtgtttgaa gtaggtgtga tcagaaaccc gggtttgggg gctccggtgt 900tccatatgac aaactatttt gagcaaccag tcagtaatgg tctcggcaac tgtatggtgg 960ctttggggga gctcaaactc gcagcccttt gtcacgggga cgattctatc ataattccct 1020atcagggatc agggaaaggt gtcagcttcc agctcgtcaa gctgggtgtc tggaaatccc 1080caaccgacat gcaatcctgg gtccccttat caacggatga tccagtggta gacaggcttt 1140acctctcatc tcacagaggt gtcatcgctg acaatcaagc aaaatgggct gtcccgacaa 1200cacgaacaga tgacaagttg cgaatggaga catgcttcca gcaggcgtgt aaaggtaaaa 1260tccaagcact ctgcgagaat cccgagtggg taccattgaa ggataacagg attccttcat 1320acggggtcct gtctgttgat ctgagtctga cggttgagct taaaatcaaa attgcttcgg 1380gattcgggcc attgatcaca cacggctcag ggatggacct atacaaatcc aactgcaaca 1440atgtgtattg gctgactatt ccgccaatga gaaatctagc cttaggcgta atcaacacat 1500tggagtggat accgagattc aaggttagtc ccaacctctt cactgtccca attaaggaag 1560caggcgaaga ctgccatgcc ccaacatacc tacctgcgga ggtggacggt gatgtcaaac 1620tcagttccaa cctggtgatt ctacctggtc aagatctcca atatgttttg gcaacctacg 1680atacctccag ggttgagcat gctgtggttt attacgttta cagcccaagc cgctcatttt 1740cttactttta tccttttagg ttgcctataa agggggtccc aatcgaacta caagtggaat 1800gcttcacatg ggatcaaaaa ctctggtgcc gtcacttctg tgtgcttgcg gactcagaat 1860ccggtggact tatcactcac tctgggatgg tgggcatggg agtcagctgc acagctaccc 1920gggaagatgg aaccaatcgc agataatgat aataggctgg agcctcggtg gccaagcttc 1980ttgccccttg ggcctccccc cagcccctcc tccccttcct gcacccgtac cccgtggtc 2040tttgaataaa gtctgagtgg gcggc 2065421854DNAArtificial SequenceSynthetic Polynucleotide 42atgtcaccgc aacgagaccg gataaatgcc ttctacaaag ataaccctta tcccaaggga 60agtaggatag ttattaacag agaacatctt atgattgaca gaccctatgt tctgctggct 120gttctgttcg tcatgtttct gagcttgatc ggattgctgg caattgcagg cattagactt 180catcgggcag ccatctacac cgcggagatc cataaaagcc tcagtaccaa tctggatgtg 240actaactcca tcgagcatca ggtcaaggac gtgctgacac cactctttaa aatcatcggg 300gatgaagtgg gcctgagaac acctcagaga ttcactgacc tagtgaaatt catctcggac

360aagattaaat tccttaatcc ggatagggag tacgacttca gagatctcac ttggtgcatc 420aacccgccag agaggatcaa actagattat gatcaatact gtgcagatgt ggctgctgaa 480gagctcatga atgcattggt gaactcaact ctactggaga ccagaacaac cactcagttc 540ctagctgtct caaagggaaa ctgctcaggg cccactacaa tcagaggtca attctcaaac 600atgtcgctgt ccttgttgga cttgtactta ggtcgaggtt acaatgtgtc atctatagtc 660actatgacat cccagggaat gtatggggga acctacctag ttgaaaagcc taatctgaac 720agcaaagggt cagagttgtc acaactgagc atgtaccgag tgtttgaagt aggtgtgatc 780agaaacccgg gtttgggggc tccggtgttc catatgacaa actattttga gcaaccagtc 840agtaatggtc tcggcaactg tatggtggct ttgggggagc tcaaactcgc agccctttgt 900cacggggacg attctatcat aattccctat cagggatcag ggaaaggtgt cagcttccag 960ctcgtcaagc tgggtgtctg gaaatcccca accgacatgc aatcctgggt ccccttatca 1020acggatgatc cagtggtaga caggctttac ctctcatctc acagaggtgt catcgctgac 1080aatcaagcaa aatgggctgt cccgacaaca cgaacagatg acaagttgcg aatggagaca 1140tgcttccagc aggcgtgtaa aggtaaaatc caagcactct gcgagaatcc cgagtgggta 1200ccattgaagg ataacaggat tccttcatac ggggtcctgt ctgttgatct gagtctgacg 1260gttgagctta aaatcaaaat tgcttcggga ttcgggccat tgatcacaca cggctcaggg 1320atggacctat

acaaatccaa ctgcaacaat gtgtattggc tgactattcc gccaatgaga 1380aatctagcct taggcgtaat caacacattg gagtggatac cgagattcaa ggttagtccc 1440aacctcttca ctgtcccaat taaggaagca ggcgaagact gccatgcccc aacataccta 1500cctgcggagg tggacggtga tgtcaaactc agttccaacc tggtgattct acctggtcaa 1560gatctccaat atgttttggc aacctacgat acctccaggg ttgagcatgc tgtggtttat 1620tacgtttaca gcccaagccg ctcattttct tacttttatc cttttaggtt gcctataaag 1680ggggtcccaa tcgaactaca agtggaatgc ttcacatggg atcaaaaact ctggtgccgt 1740cacttctgtg tgcttgcgga ctcagaatcc ggtggactta tcactcactc tgggatggtg 1800ggcatgggag tcagctgcac agctacccgg gaagatggaa ccaatcgcag ataa 1854432126DNAArtificial SequenceSynthetic Polynucleotide 43ggggaaataa gagagaaaag aagagtaaga agaaatataa gagccaccat gtcaccgcaa 60cgagaccgga taaatgcctt ctacaaagat aacccttatc ccaagggaag taggatagtt 120attaacagag aacatcttat gattgacaga ccctatgttc tgctggctgt tctgttcgtc 180atgtttctga gcttgatcgg attgctggca attgcaggca ttagacttca tcgggcagcc 240atctacaccg cggagatcca taaaagcctc agtaccaatc tggatgtgac taactccatc 300gagcatcagg tcaaggacgt gctgacacca ctctttaaaa tcatcgggga tgaagtgggc 360ctgagaacac ctcagagatt cactgaccta gtgaaattca tctcggacaa gattaaattc 420cttaatccgg atagggagta cgacttcaga gatctcactt ggtgcatcaa cccgccagag 480aggatcaaac tagattatga tcaatactgt gcagatgtgg ctgctgaaga gctcatgaat 540gcattggtga actcaactct actggagacc agaacaacca ctcagttcct agctgtctca 600aagggaaact gctcagggcc cactacaatc agaggtcaat tctcaaacat gtcgctgtcc 660ttgttggact tgtacttagg tcgaggttac aatgtgtcat ctatagtcac tatgacatcc 720cagggaatgt atgggggaac ctacctagtt gaaaagccta atctgaacag caaagggtca 780gagttgtcac aactgagcat gtaccgagtg tttgaagtag gtgtgatcag aaacccgggt 840ttgggggctc cggtgttcca tatgacaaac tattttgagc aaccagtcag taatggtctc 900ggcaactgta tggtggcttt gggggagctc aaactcgcag ccctttgtca cggggacgat 960tctatcataa ttccctatca gggatcaggg aaaggtgtca gcttccagct cgtcaagctg 1020ggtgtctgga aatccccaac cgacatgcaa tcctgggtcc ccttatcaac ggatgatcca 1080gtggtagaca ggctttacct ctcatctcac agaggtgtca tcgctgacaa tcaagcaaaa 1140tgggctgtcc cgacaacacg aacagatgac aagttgcgaa tggagacatg cttccagcag 1200gcgtgtaaag gtaaaatcca agcactctgc gagaatcccg agtgggtacc attgaaggat 1260aacaggattc cttcatacgg ggtcctgtct gttgatctga gtctgacggt tgagcttaaa 1320atcaaaattg cttcgggatt cgggccattg atcacacacg gctcagggat ggacctatac 1380aaatccaact gcaacaatgt gtattggctg actattccgc caatgagaaa tctagcctta 1440ggcgtaatca acacattgga gtggataccg agattcaagg ttagtcccaa cctcttcact 1500gtcccaatta aggaagcagg cgaagactgc catgccccaa catacctacc tgcggaggtg 1560gacggtgatg tcaaactcag ttccaacctg gtgattctac ctggtcaaga tctccaatat 1620gttttggcaa cctacgatac ctccagggtt gagcatgctg tggtttatta cgtttacagc 1680ccaagccgct cattttctta cttttatcct tttaggttgc ctataaaggg ggtcccaatc 1740gaactacaag tggaatgctt cacatgggat caaaaactct ggtgccgtca cttctgtgtg 1800cttgcggact cagaatccgg tggacttatc actcactctg ggatggtggg catgggagtc 1860agctgcacag ctacccggga agatggaacc aatcgcagat aatgataata ggctggagcc 1920tcggtggcca agcttcttgc cccttgggcc tccccccagc ccctcctccc cttcctgcac 1980ccgtaccccc gtggtctttg aataaagtct gagtgggcgg caaaaaaaaa aaaaaaaaaa 2040aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100aaaaaaaaaa aaaaaaaaaa atctag 2126442065DNAArtificial SequenceSynthetic Polynucleotide 44tcaagctttt ggaccctcgt acagaagcta atacgactca ctatagggaa ataagagaga 60aaagaagagt aagaagaaat ataagagcca ccatgtcacc acaacgagac cggataaatg 120ccttctacaa agacaacccc catcctaagg gaagtaggat agttattaac agagaacatc 180ttatgattga tagaccttat gttttgctgg ctgttctatt cgtcatgttt ctgagcttga 240tcgggttgct agccattgca ggcattagac ttcatcgggc agccatctac accgcagaga 300tccataaaag cctcagcacc aatctggatg taactaactc aatcgagcat caggttaagg 360acgtgctgac accactcttc aagatcatcg gtgatgaagt gggcttgagg acacctcaga 420gattcactga cctagtgaag ttcatctctg acaagattaa attccttaat ccggacaggg 480aatacgactt cagagatctc acttggtgta tcaacccgcc agagagaatc aaattggatt 540atgatcaata ctgtgcagat gtggctgctg aagaactcat gaatgcattg gtgaactcaa 600ctctactgga gaccagggca accaatcagt tcctagctgt ctcaaaggga aactgctcag 660ggcccactac aatcagaggc caattctcaa acatgtcgct gtccctgttg gacttgtatt 720taagtcgagg ttacaatgtg tcatctatag tcactatgac atcccaggga atgtacgggg 780gaacttacct agtggaaaag cctaatctga gcagcaaagg gtcagagttg tcacaactga 840gcatgcaccg agtgtttgaa gtaggtgtta tcagaaatcc gggtttgggg gctccggtat 900tccatatgac aaactatctt gagcaaccag tcagtaatga tttcagcaac tgcatggtgg 960ctttggggga gctcaagttc gcagccctct gtcacaggga agattctatc acaattccct 1020atcagggatc agggaaaggt gtcagcttcc agcttgtcaa gctaggtgtc tggaaatccc 1080caaccgacat gcaatcctgg gtccccctat caacggatga tccagtgata gacaggcttt 1140acctctcatc tcacagaggc gttatcgctg acaatcaagc aaaatgggct gtcccgacaa 1200cacggacaga tgacaagttg cgaatggaga catgcttcca gcaggcgtgt aagggtaaaa 1260tccaagcact ttgcgagaat cccgagtgga caccattgaa ggataacagg attccttcat 1320acggggtctt gtctgttgat ctgagtctga cagttgagct taaaatcaaa attgtttcag 1380gattcgggcc attgatcaca cacggttcag ggatggacct atacaaatcc aaccacaaca 1440atatgtattg gctgactatc ccgccaatga agaacctggc cttaggtgta atcaacacat 1500tggagtggat accgagattc aaggttagtc ccaacctctt cactgttcca attaaggaag 1560caggcgagga ctgccatgcc ccaacatacc tacctgcgga ggtggatggt gatgtcaaac 1620tcagttccaa tctggtgatt ctacctggtc aagatctcca atatgttctg gcaacctacg 1680atacttccag agttgaacat gctgtagttt attacgttta cagcccaagc cgctcatttt 1740cttactttta tccttttagg ttgcctgtaa ggggggtccc cattgaatta caagtggaat 1800gcttcacatg ggaccaaaaa ctctggtgcc gtcacttctg tgtgcttgcg gactcagaat 1860ctggtggaca tatcactcac tctgggatgg tgggcatggg agtcagctgc acagccactc 1920gggaagatgg aaccagccgc agatagtgat aataggctgg agcctcggtg gccaagcttc 1980ttgccccttg ggcctccccc cagcccctcc tccccttcct gcacccgtac ccccgtggtc 2040tttgaataaa gtctgagtgg gcggc 2065451854DNAArtificial SequenceSynthetic Polynucleotide 45atgtcaccac aacgagaccg gataaatgcc ttctacaaag acaacccccca tcctaaggga 60agtaggatag ttattaacag agaacatctt atgattgata gaccttatgt tttgctggct 120gttctattcg tcatgtttct gagcttgatc gggttgctag ccattgcagg cattagactt 180catcgggcag ccatctacac cgcagagatc cataaaagcc tcagcaccaa tctggatgta 240actaactcaa tcgagcatca ggttaaggac gtgctgacac cactcttcaa gatcatcggt 300gatgaagtgg gcttgaggac acctcagaga ttcactgacc tagtgaagtt catctctgac 360aagattaaat tccttaatcc ggacagggaa tacgacttca gagatctcac ttggtgtatc 420aacccgccag agagaatcaa attggattat gatcaatact gtgcagatgt ggctgctgaa 480gaactcatga atgcattggt gaactcaact ctactggaga ccagggcaac caatcagttc 540ctagctgtct caaagggaaa ctgctcaggg cccactacaa tcagaggcca attctcaaac 600atgtcgctgt ccctgttgga cttgtattta agtcgaggtt acaatgtgtc atctatagtc 660actatgacat cccagggaat gtacgggggga acttacctag tggaaaagcc taatctgagc 720agcaaagggt cagagttgtc acaactgagc atgcaccgag tgtttgaagt aggtgttatc 780agaaatccgg gtttgggggc tccggtattc catatgacaa actatcttga gcaaccagtc 840agtaatgatt tcagcaactg catggtggct ttgggggagc tcaagttcgc agccctctgt 900cacagggaag attctatcac aattccctat cagggatcag ggaaaggtgt cagcttccag 960cttgtcaagc taggtgtctg gaaatcccca accgacatgc aatcctgggt ccccctatca 1020acggatgatc cagtgataga caggctttac ctctcatctc acagaggcgt tatcgctgac 1080aatcaagcaa aatgggctgt cccgacaaca cggacagatg acaagttgcg aatggagaca 1140tgcttccagc aggcgtgtaa gggtaaaatc caagcacttt gcgagaatcc cgagtggaca 1200ccattgaagg ataacaggat tccttcatac ggggtcttgt ctgttgatct gagtctgaca 1260gttgagctta aaatcaaaat tgtttcagga ttcgggccat tgatcacaca cggttcaggg 1320atggacctat acaaatccaa ccacaacaat atgtattggc tgactatccc gccaatgaag 1380aacctggcct taggtgtaat caacacattg gagtggatac cgagattcaa ggttagtccc 1440aacctcttca ctgttccaat taaggaagca ggcgaggact gccatgcccc aacataccta 1500cctgcggagg tggatggtga tgtcaaactc agttccaatc tggtgattct acctggtcaa 1560gatctccaat atgttctggc aacctacgat acttccagag ttgaacatgc tgtagtttat 1620tacgtttaca gcccaagccg ctcattttct tacttttatc cttttaggtt gcctgtaagg 1680ggggtcccca ttgaattaca agtggaatgc ttcacatggg accaaaaact ctggtgccgt 1740cacttctgtg tgcttgcgga ctcagaatct ggtggacata tcactcactc tgggatggtg 1800ggcatgggag tcagctgcac agccactcgg gaagatggaa ccagccgcag atag 1854462126DNAArtificial SequenceSynthetic Polynucleotide 46ggggaaataa gagagaaaag aagagtaaga agaaatataa gagccaccat gtcaccacaa 60cgagaccgga taaatgcctt ctacaaagac aacccccatc ctaagggaag taggatagtt 120attaacagag aacatcttat gattgataga ccttatgttt tgctggctgt tctattcgtc 180atgtttctga gcttgatcgg gttgctagcc attgcaggca ttagacttca tcgggcagcc 240atctacaccg cagagatcca taaaagcctc agcaccaatc tggatgtaac taactcaatc 300gagcatcagg ttaaggacgt gctgacacca ctcttcaaga tcatcggtga tgaagtgggc 360ttgaggacac ctcagagatt cactgaccta gtgaagttca tctctgacaa gattaaattc 420cttaatccgg acagggaata cgacttcaga gatctcactt ggtgtatcaa cccgccagag 480agaatcaaat tggattatga tcaatactgt gcagatgtgg ctgctgaaga actcatgaat 540gcattggtga actcaactct actggagacc agggcaacca atcagttcct agctgtctca 600aagggaaact gctcagggcc cactacaatc agaggccaat tctcaaacat gtcgctgtcc 660ctgttggact tgtatttaag tcgaggttac aatgtgtcat ctatagtcac tatgacatcc 720cagggaatgt acggggggaac ttacctagtg gaaaagccta atctgagcag caaagggtca 780gagttgtcac aactgagcat gcaccgagtg tttgaagtag gtgttatcag aaatccgggt 840ttgggggctc cggtattcca tatgacaaac tatcttgagc aaccagtcag taatgatttc 900agcaactgca tggtggcttt gggggagctc aagttcgcag ccctctgtca cagggaagat 960tctatcacaa ttccctatca gggatcaggg aaaggtgtca gcttccagct tgtcaagcta 1020ggtgtctgga aatccccaac cgacatgcaa tcctgggtcc ccctatcaac ggatgatcca 1080gtgatagaca ggctttacct ctcatctcac agaggcgtta tcgctgacaa tcaagcaaaa 1140tgggctgtcc cgacaacacg gacagatgac aagttgcgaa tggagacatg cttccagcag 1200gcgtgtaagg gtaaaatcca agcactttgc gagaatcccg agtggacacc attgaaggat 1260aacaggattc cttcatacgg ggtcttgtct gttgatctga gtctgacagt tgagcttaaa 1320atcaaaattg tttcaggatt cgggccattg atcacacacg gttcagggat ggacctatac 1380aaatccaacc acaacaatat gtattggctg actatcccgc caatgaagaa cctggcctta 1440ggtgtaatca acacattgga gtggataccg agattcaagg ttagtcccaa cctcttcact 1500gttccaatta aggaagcagg cgaggactgc catgccccaa catacctacc tgcggaggtg 1560gatggtgatg tcaaactcag ttccaatctg gtgattctac ctggtcaaga tctccaatat 1620gttctggcaa cctacgatac ttccagagtt gaacatgctg tagtttatta cgtttacagc 1680ccaagccgct cattttctta cttttatcct tttaggttgc ctgtaagggg ggtccccatt 1740gaattacaag tggaatgctt cacatgggac caaaaactct ggtgccgtca cttctgtgtg 1800cttgcggact cagaatctgg tggacatatc actcactctg ggatggtggg catgggagtc 1860agctgcacag ccactcggga agatggaacc agccgcagat agtgataata ggctggagcc

1920tcggtggcca agcttcttgc cccttgggcc tccccccagc ccctcctccc cttcctgcac 1980ccgtaccccc gtggtctttg aataaagtct gagtgggcgg caaaaaaaaa aaaaaaaaaa 2040aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100aaaaaaaaaa aaaaaaaaaa atctag 212647550PRTArtificial SequenceSynthetic Polypeptide 47Met Gly Leu Lys Val Asn Val Ser Ala Val Phe Met Ala Val Leu Leu1 5 10 15Thr Leu Gln Thr Pro Ala Gly Gln Ile His Trp Gly Asn Leu Ser Lys 20 25 30Ile Gly Val Val Gly Ile Gly Ser Ala Ser Tyr Lys Val Met Thr Arg 35 40 45Ser Ser His Gln Ser Leu Val Ile Lys Leu Met Pro Asn Ile Thr Leu 50 55 60Leu Asn Asn Cys Thr Arg Val Glu Ile Ala Glu Tyr Arg Arg Leu Leu65 70 75 80Arg Thr Val Leu Glu Pro Ile Arg Asp Ala Leu Asn Ala Met Thr Gln 85 90 95Asn Ile Arg Pro Val Gln Ser Val Ala Ser Ser Arg Arg His Lys Arg 100 105 110Phe Ala Gly Val Val Leu Ala Gly Ala Ala Leu Gly Val Ala Thr Ala 115 120 125Ala Gln Ile Thr Ala Gly Ile Ala Leu His Arg Ser Met Leu Asn Ser 130 135 140Gln Ala Ile Asp Asn Leu Arg Ala Ser Leu Glu Thr Thr Asn Gln Ala145 150 155 160Ile Glu Ala Ile Arg Gln Ala Gly Gln Glu Met Ile Leu Ala Val Gln 165 170 175Gly Val Gln Asp Tyr Ile Asn Asn Glu Leu Ile Pro Ser Met Asn Gln 180 185 190Leu Ser Cys Asp Leu Ile Gly Gln Lys Leu Gly Leu Lys Leu Leu Arg 195 200 205Tyr Tyr Thr Glu Ile Leu Ser Leu Phe Gly Pro Ser Leu Arg Asp Pro 210 215 220Ile Ser Ala Glu Ile Ser Ile Gln Ala Leu Ser Tyr Ala Leu Gly Gly225 230 235 240Asp Ile Asn Lys Val Leu Glu Lys Leu Gly Tyr Ser Gly Gly Asp Leu 245 250 255Leu Gly Ile Leu Glu Ser Arg Gly Ile Lys Ala Arg Ile Thr His Val 260 265 270Asp Thr Glu Ser Tyr Phe Ile Val Leu Ser Ile Ala Tyr Pro Thr Leu 275 280 285Ser Glu Ile Lys Gly Val Ile Val His Arg Leu Glu Gly Val Ser Tyr 290 295 300Asn Ile Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Ala305 310 315 320Thr Gln Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe 325 330 335Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser 340 345 350Pro Leu Leu Gln Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 355 360 365Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly 370 375 380Asn Leu Ile Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr385 390 395 400Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala 405 410 415Ala Asp Arg Cys Pro Val Val Glu Val Asn Gly Val Thr Ile Gln Val 420 425 430Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu 435 440 445Gly Pro Pro Ile Ser Leu Glu Arg Leu Asp Val Gly Thr Asn Leu Gly 450 455 460Asn Ala Ile Ala Lys Leu Glu Asp Ala Lys Glu Leu Leu Glu Ser Ser465 470 475 480Asp Gln Ile Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 485 490 495Tyr Ile Leu Ile Ala Val Cys Leu Gly Gly Leu Ile Gly Ile Pro Thr 500 505 510Leu Ile Cys Cys Cys Arg Gly Arg Cys Asn Lys Lys Gly Glu Gln Val 515 520 525Gly Met Ser Arg Pro Gly Leu Lys Pro Asp Leu Thr Gly Thr Ser Lys 530 535 540Ser Tyr Val Arg Ser Leu545 55048550PRTArtificial SequenceSynthetic Polypeptide 48Met Gly Leu Lys Val Asn Val Ser Val Ile Phe Met Ala Val Leu Leu1 5 10 15Thr Leu Gln Thr Pro Thr Gly Gln Ile His Trp Gly Asn Leu Ser Lys 20 25 30Ile Gly Val Val Gly Val Gly Ser Ala Ser Tyr Lys Val Met Thr Arg 35 40 45Ser Ser His Gln Ser Leu Val Ile Lys Leu Met Pro Asn Ile Thr Leu 50 55 60Leu Asn Asn Cys Thr Arg Val Gly Ile Ala Glu Tyr Arg Arg Leu Leu65 70 75 80Arg Thr Val Leu Glu Pro Ile Arg Asp Ala Leu Asn Ala Met Thr Gln 85 90 95Asn Ile Arg Pro Val Gln Ser Val Ala Ser Ser Arg Arg His Lys Arg 100 105 110Phe Ala Gly Val Val Leu Ala Gly Ala Ala Leu Gly Val Ala Thr Ala 115 120 125Ala Gln Ile Thr Ala Gly Ile Ala Leu His Gln Ser Met Leu Asn Ser 130 135 140Gln Ala Ile Asp Asn Leu Arg Ala Ser Leu Glu Thr Thr Asn Gln Ala145 150 155 160Ile Glu Ala Ile Arg Gln Ala Gly Gln Glu Met Ile Leu Ala Val Gln 165 170 175Gly Val Gln Asp Tyr Ile Asn Asn Glu Leu Ile Pro Ser Met Asn Gln 180 185 190Leu Ser Cys Asp Leu Ile Gly Gln Lys Leu Gly Leu Lys Leu Leu Arg 195 200 205Tyr Tyr Thr Glu Ile Leu Ser Leu Phe Gly Pro Ser Leu Arg Asp Pro 210 215 220Ile Ser Ala Glu Ile Ser Ile Gln Ala Leu Ser Tyr Ala Leu Gly Gly225 230 235 240Asp Ile Asn Lys Val Leu Glu Lys Leu Gly Tyr Ser Gly Gly Asp Leu 245 250 255Leu Gly Ile Leu Glu Ser Arg Gly Ile Lys Ala Arg Ile Thr His Val 260 265 270Asp Thr Glu Ser Tyr Phe Ile Val Leu Ser Ile Ala Tyr Pro Thr Leu 275 280 285Ser Glu Ile Lys Gly Val Ile Val His Arg Leu Glu Gly Val Ser Tyr 290 295 300Asn Ile Gly Ser Gln Glu Trp Tyr Thr Thr Val Pro Lys Tyr Val Ala305 310 315 320Thr Gln Gly Tyr Leu Ile Ser Asn Phe Asp Glu Ser Ser Cys Thr Phe 325 330 335Met Pro Glu Gly Thr Val Cys Ser Gln Asn Ala Leu Tyr Pro Met Ser 340 345 350Pro Leu Leu Gln Glu Cys Leu Arg Gly Ser Thr Lys Ser Cys Ala Arg 355 360 365Thr Leu Val Ser Gly Ser Phe Gly Asn Arg Phe Ile Leu Ser Gln Gly 370 375 380Asn Leu Ile Ala Asn Cys Ala Ser Ile Leu Cys Lys Cys Tyr Thr Thr385 390 395 400Gly Thr Ile Ile Asn Gln Asp Pro Asp Lys Ile Leu Thr Tyr Ile Ala 405 410 415Ala Asp His Cys Pro Val Val Glu Val Asn

Gly Val Thr Ile Gln Val 420 425 430Gly Ser Arg Arg Tyr Pro Asp Ala Val Tyr Leu His Arg Ile Asp Leu 435 440 445Gly Pro Pro Ile Ser Leu Glu Arg Leu Asp Val Gly Thr Asn Leu Gly 450 455 460Asn Ala Ile Ala Lys Leu Glu Asp Ala Lys Glu Leu Leu Glu Ser Ser465 470 475 480Asp Gln Ile Leu Arg Ser Met Lys Gly Leu Ser Ser Thr Ser Ile Val 485 490 495Tyr Ile Leu Ile Ala Val Cys Leu Gly Gly Leu Ile Gly Ile Pro Ala 500 505 510Leu Ile Cys Cys Cys Arg Gly Arg Cys Asn Lys Lys Gly Glu Gln Val 515 520 525Gly Met Ser Arg Pro Gly Leu Lys Pro

Asp Leu Thr Gly Thr Ser Lys 530 535 540Ser Tyr Val Arg Ser Leu545 55049617PRTArtificial SequenceSynthetic Polypeptide 49Met Ser Pro Gln Arg Asp Arg Ile Asn Ala Phe Tyr Lys Asp Asn Pro1 5 10 15Tyr Pro Lys Gly Ser Arg Ile Val Ile Asn Arg Glu His Leu Met Ile 20 25 30Asp Arg Pro Tyr Val Leu Leu Ala Val Leu Phe Val Met Phe Leu Ser 35 40 45Leu Ile Gly Leu Leu Ala Ile Ala Gly Ile Arg Leu His Arg Ala Ala 50 55 60Ile Tyr Thr Ala Glu Ile His Lys Ser Leu Ser Thr Asn Leu Asp Val65 70 75 80Thr Asn Ser Ile Glu His Gln Val Lys Asp Val Leu Thr Pro Leu Phe 85 90 95Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr 100 105 110Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp 115 120 125Arg Glu Tyr Asp Phe Arg Asp Leu Thr Trp Cys Ile Asn Pro Pro Glu 130 135 140Arg Ile Lys Leu Asp Tyr Asp Gln Tyr Cys Ala Asp Val Ala Ala Glu145 150 155 160Glu Leu Met Asn Ala Leu Val Asn Ser Thr Leu Leu Glu Thr Arg Thr 165 170 175Thr Thr Gln Phe Leu Ala Val Ser Lys Gly Asn Cys Ser Gly Pro Thr 180 185 190Thr Ile Arg Gly Gln Phe Ser Asn Met Ser Leu Ser Leu Leu Asp Leu 195 200 205Tyr Leu Gly Arg Gly Tyr Asn Val Ser Ser Ile Val Thr Met Thr Ser 210 215 220Gln Gly Met Tyr Gly Gly Thr Tyr Leu Val Glu Lys Pro Asn Leu Asn225 230 235 240Ser Lys Gly Ser Glu Leu Ser Gln Leu Ser Met Tyr Arg Val Phe Glu 245 250 255Val Gly Val Ile Arg Asn Pro Gly Leu Gly Ala Pro Val Phe His Met 260 265 270Thr Asn Tyr Phe Glu Gln Pro Val Ser Asn Gly Leu Gly Asn Cys Met 275 280 285Val Ala Leu Gly Glu Leu Lys Leu Ala Ala Leu Cys His Gly Asp Asp 290 295 300Ser Ile Ile Ile Pro Tyr Gln Gly Ser Gly Lys Gly Val Ser Phe Gln305 310 315 320Leu Val Lys Leu Gly Val Trp Lys Ser Pro Thr Asp Met Gln Ser Trp 325 330 335Val Pro Leu Ser Thr Asp Asp Pro Val Val Asp Arg Leu Tyr Leu Ser 340 345 350Ser His Arg Gly Val Ile Ala Asp Asn Gln Ala Lys Trp Ala Val Pro 355 360 365Thr Thr Arg Thr Asp Asp Lys Leu Arg Met Glu Thr Cys Phe Gln Gln 370 375 380Ala Cys Lys Gly Lys Ile Gln Ala Leu Cys Glu Asn Pro Glu Trp Val385 390 395 400Pro Leu Lys Asp Asn Arg Ile Pro Ser Tyr Gly Val Leu Ser Val Asp 405 410 415Leu Ser Leu Thr Val Glu Leu Lys Ile Lys Ile Ala Ser Gly Phe Gly 420 425 430Pro Leu Ile Thr His Gly Ser Gly Met Asp Leu Tyr Lys Ser Asn Cys 435 440 445Asn Asn Val Tyr Trp Leu Thr Ile Pro Pro Met Arg Asn Leu Ala Leu 450 455 460Gly Val Ile Asn Thr Leu Glu Trp Ile Pro Arg Phe Lys Val Ser Pro465 470 475 480Asn Leu Phe Thr Val Pro Ile Lys Glu Ala Gly Glu Asp Cys His Ala 485 490 495Pro Thr Tyr Leu Pro Ala Glu Val Asp Gly Asp Val Lys Leu Ser Ser 500 505 510Asn Leu Val Ile Leu Pro Gly Gln Asp Leu Gln Tyr Val Leu Ala Thr 515 520 525Tyr Asp Thr Ser Arg Val Glu His Ala Val Val Tyr Tyr Val Tyr Ser 530 535 540Pro Ser Arg Ser Phe Ser Tyr Phe Tyr Pro Phe Arg Leu Pro Ile Lys545 550 555 560Gly Val Pro Ile Glu Leu Gln Val Glu Cys Phe Thr Trp Asp Gln Lys 565 570 575Leu Trp Cys Arg His Phe Cys Val Leu Ala Asp Ser Glu Ser Gly Gly 580 585 590Leu Ile Thr His Ser Gly Met Val Gly Met Gly Val Ser Cys Thr Ala 595 600 605Thr Arg Glu Asp Gly Thr Asn Arg Arg 610 61550617PRTArtificial SequenceSynthetic Polypeptide 50Met Ser Pro Gln Arg Asp Arg Ile Asn Ala Phe Tyr Lys Asp Asn Pro1 5 10 15His Pro Lys Gly Ser Arg Ile Val Ile Asn Arg Glu His Leu Met Ile 20 25 30Asp Arg Pro Tyr Val Leu Leu Ala Val Leu Phe Val Met Phe Leu Ser 35 40 45Leu Ile Gly Leu Leu Ala Ile Ala Gly Ile Arg Leu His Arg Ala Ala 50 55 60Ile Tyr Thr Ala Glu Ile His Lys Ser Leu Ser Thr Asn Leu Asp Val65 70 75 80Thr Asn Ser Ile Glu His Gln Val Lys Asp Val Leu Thr Pro Leu Phe 85 90 95Lys Ile Ile Gly Asp Glu Val Gly Leu Arg Thr Pro Gln Arg Phe Thr 100 105 110Asp Leu Val Lys Phe Ile Ser Asp Lys Ile Lys Phe Leu Asn Pro Asp 115 120 125Arg Glu Tyr Asp Phe Arg Asp Leu Thr Trp Cys Ile Asn Pro Pro Glu 130 135 140Arg Ile Lys Leu Asp Tyr Asp Gln Tyr Cys Ala Asp Val Ala Ala Glu145 150 155 160Glu Leu Met Asn Ala Leu Val Asn Ser Thr Leu Leu Glu Thr Arg Ala 165 170 175Thr Asn Gln Phe Leu Ala Val Ser Lys Gly Asn Cys Ser Gly Pro Thr 180 185 190Thr Ile Arg Gly Gln Phe Ser Asn Met Ser Leu Ser Leu Leu Asp Leu 195 200 205Tyr Leu Ser Arg Gly Tyr Asn Val Ser Ser Ile Val Thr Met Thr Ser 210 215 220Gln Gly Met Tyr Gly Gly Thr Tyr Leu Val Glu Lys Pro Asn Leu Ser225 230 235 240Ser Lys Gly Ser Glu Leu Ser Gln Leu Ser Met His Arg Val Phe Glu 245 250 255Val Gly Val Ile Arg Asn Pro Gly Leu Gly Ala Pro Val Phe His Met 260 265 270Thr Asn Tyr Leu Glu Gln Pro Val Ser Asn Asp Phe Ser Asn Cys Met 275 280 285Val Ala Leu Gly Glu Leu Lys Phe Ala Ala Leu Cys His Arg Glu Asp 290 295 300Ser Ile Thr Ile Pro Tyr Gln Gly Ser Gly Lys Gly Val Ser Phe Gln305 310 315 320Leu Val Lys Leu Gly Val Trp Lys Ser Pro Thr Asp Met Gln Ser Trp 325 330 335Val Pro Leu Ser Thr Asp Asp Pro Val Ile Asp Arg Leu Tyr Leu Ser 340 345 350Ser His Arg Gly Val Ile Ala Asp Asn Gln Ala Lys Trp Ala Val Pro 355 360 365Thr Thr Arg Thr Asp Asp Lys Leu Arg Met Glu Thr Cys Phe Gln Gln 370 375 380Ala Cys Lys Gly Lys Ile Gln Ala Leu Cys Glu Asn Pro Glu Trp Thr385 390 395 400Pro Leu Lys Asp Asn Arg Ile Pro Ser Tyr Gly Val Leu Ser Val Asp 405 410 415Leu Ser Leu Thr Val Glu Leu Lys Ile Lys Ile Val Ser Gly Phe Gly 420 425 430Pro Leu Ile Thr His Gly Ser Gly Met Asp Leu Tyr Lys Ser Asn His 435 440 445Asn Asn Met Tyr Trp Leu Thr Ile Pro Pro Met Lys Asn Leu Ala Leu 450 455 460Gly Val Ile Asn Thr Leu Glu Trp Ile Pro Arg Phe Lys Val Ser Pro465 470 475 480Asn Leu Phe Thr Val Pro Ile Lys Glu Ala Gly Glu Asp Cys His Ala 485 490 495Pro Thr Tyr Leu Pro Ala Glu Val Asp Gly Asp Val Lys Leu Ser Ser 500 505 510Asn Leu Val Ile Leu Pro Gly Gln Asp Leu Gln Tyr Val Leu Ala Thr 515 520 525Tyr Asp Thr Ser Arg Val Glu His Ala Val Val

Tyr Tyr Val Tyr Ser 530 535 540Pro Ser Arg Ser Phe Ser Tyr Phe Tyr Pro Phe Arg Leu Pro Val Arg545 550 555 560Gly Val Pro Ile Glu Leu Gln Val Glu Cys Phe Thr Trp Asp Gln Lys 565 570 575Leu Trp Cys Arg His Phe Cys Val Leu Ala Asp Ser Glu Ser Gly Gly 580 585 590His Ile Thr His Ser Gly Met Val Gly Met Gly Val Ser Cys Thr Ala 595 600 605Thr Arg Glu Asp Gly Thr Ser Arg Arg 610 615511729DNAArtificial SequenceSynthetic Polynucleotide 51tcaagctttt ggaccctcgt acagaagcta atacgactca ctatagggaa ataagagaga 60aaagaagagt aagaagaaat ataagagcca ccatggcaca agtcattaat acaaacagcc 120tgtcgctgtt gacccagaat aacctgaaca aatcccagtc cgcactgggc actgctatcg 180agcgtttgtc ttccggtctg cgtatcaaca gcgcgaaaga cgatgcggca ggacaggcga 240ttgctaaccg ttttaccgcg aacatcaaag gtctgactca ggcttcccgt aacgctaacg 300acggtatctc cattgcgcag accactgaag gcgcgctgaa cgaaatcaac aacaacctgc 360agcgtgtgcg tgaactggcg gttcagtctg cgaatggtac taactcccag tctgacctcg 420actccatcca ggctgaaatc acccagcgcc tgaacgaaat cgaccgtgta tccggccaga 480ctcagttcaa cggcgtgaaa gtcctggcgc aggacaacac cctgaccatc caggttggtg 540ccaacgacgg tgaaactatc gatattgatt taaaagaaat cagctctaaa acactgggac 600ttgataagct taatgtccaa gatgcctaca ccccgaaaga aactgctgta accgttgata 660aaactaccta taaaaatggt acagatccta ttacagccca gagcaatact gatatccaaa 720ctgcaattgg cggtggtgca acgggggtta ctggggctga tatcaaattt aaagatggtc 780aatactattt agatgttaaa ggcggtgctt ctgctggtgt ttataaagcc acttatgatg 840aaactacaaa gaaagttaat attgatacga ctgataaaac tccgttggca actgcggaag 900ctacagctat tcggggaacg gccactataa cccacaacca aattgctgaa gtaacaaaag 960agggtgttga tacgaccaca gttgcggctc aacttgctgc agcaggggtt actggcgccg 1020ataaggacaa tactagcctt gtaaaactat cgtttgagga taaaaacggt aaggttattg 1080atggtggcta tgcagtgaaa atgggcgacg atttctatgc cgctacatat gatgagaaaa 1140caggtgcaat tactgctaaa accactactt atacagatgg tactggcgtt gctcaaactg 1200gagctgtgaa atttggtggc gcaaatggta aatctgaagt tgttactgct accgatggta 1260agacttactt agcaagcgac cttgacaaac ataacttcag aacaggcggt gagcttaaag 1320aggttaatac agataagact gaaaacccac tgcagaaaat tgatgctgcc ttggcacagg 1380ttgatacact tcgttctgac ctgggtgcgg ttcagaaccg tttcaactcc gctatcacca 1440acctgggcaa taccgtaaat aacctgtctt ctgcccgtag ccgtatcgaa gattccgact 1500acgcaaccga agtctccaac atgtctcgcg cgcagattct gcagcaggcc ggtacctccg 1560ttctggcgca ggcgaaccag gttccgcaaa acgtcctctc tttactgcgt tgataatagg 1620ctggagcctc ggtggccatg cttcttgccc cttgggcctc cccccagccc ctcctcccct 1680tcctgcaccc gtacccccgt ggtctttgaa taaagtctga gtgggcggc 1729521518DNAArtificial SequenceSynthetic Polynucleotide 52atggcacaag tcattaatac aaacagcctg tcgctgttga cccagaataa cctgaacaaa 60tcccagtccg cactgggcac tgctatcgag cgtttgtctt ccggtctgcg tatcaacagc 120gcgaaagacg atgcggcagg acaggcgatt gctaaccgtt ttaccgcgaa catcaaaggt 180ctgactcagg cttcccgtaa cgctaacgac ggtatctcca ttgcgcagac cactgaaggc 240gcgctgaacg aaatcaacaa caacctgcag cgtgtgcgtg aactggcggt tcagtctgcg 300aatggtacta actcccagtc tgacctcgac tccatccagg ctgaaatcac ccagcgcctg 360aacgaaatcg accgtgtatc cggccagact cagttcaacg gcgtgaaagt cctggcgcag 420gacaacaccc tgaccatcca ggttggtgcc aacgacggtg aaactatcga tattgattta 480aaagaaatca gctctaaaac actgggactt gataagctta atgtccaaga tgcctacacc 540ccgaaagaaa ctgctgtaac cgttgataaa actacctata aaaatggtac agatcctatt 600acagcccaga gcaatactga tatccaaact gcaattggcg gtggtgcaac gggggttact 660ggggctgata tcaaatttaa agatggtcaa tactatttag atgttaaagg cggtgcttct 720gctggtgttt ataaagccac ttatgatgaa actacaaaga aagttaatat tgatacgact 780gataaaactc cgttggcaac tgcggaagct acagctattc ggggaacggc cactataacc 840cacaaccaaa ttgctgaagt aacaaaagag ggtgttgata cgaccacagt tgcggctcaa 900cttgctgcag caggggttac tggcgccgat aaggacaata ctagccttgt aaaactatcg 960tttgaggata aaaacggtaa ggttattgat ggtggctatg cagtgaaaat gggcgacgat 1020ttctatgccg ctacatatga tgagaaaaca ggtgcaatta ctgctaaaac cactacttat 1080acagatggta ctggcgttgc tcaaactgga gctgtgaaat ttggtggcgc aaatggtaaa 1140tctgaagttg ttactgctac cgatggtaag acttacttag caagcgacct tgacaaacat 1200aacttcagaa caggcggtga gcttaaagag gttaatacag ataagactga aaacccactg 1260cagaaaattg atgctgcctt ggcacaggtt gatacacttc gttctgacct gggtgcggtt 1320cagaaccgtt tcaactccgc tatcaccaac ctgggcaata ccgtaaataa cctgtcttct 1380gcccgtagcc gtatcgaaga ttccgactac gcaaccgaag tctccaacat gtctcgcgcg 1440cagattctgc agcaggccgg tacctccgtt ctggcgcagg cgaaccaggt tccgcaaaac 1500gtcctctctt tactgcgt 1518531790RNAArtificial SequenceSynthetic Polynucleotide 53ggggaaauaa gagagaaaag aagaguaaga agaaauauaa gagccaccau ggcacaaguc 60auuaauacaa acagccuguc gcuguugacc cagaauaacc ugaacaaauc ccaguccgca 120cugggcacug cuaucgagcg uuugucuucc ggucugcgua ucaacagcgc gaaagacgau 180gcggcaggac aggcgauugc uaaccguuuu accgcgaaca ucaaaggucu gacucaggcu 240ucccguaacg cuaacgacgg uaucuccauu gcgcagacca cugaaggcgc gcugaacgaa 300aucaacaaca accugcagcg ugugcgugaa cuggcgguuc agucugcgaa ugguacuaac 360ucccagucug accucgacuc cauccaggcu gaaaucaccc agcgccugaa cgaaaucgac 420cguguauccg gccagacuca guucaacggc gugaaagucc uggcgcagga caacacccug 480accauccagg uuggugccaa cgacggugaa acuaucgaua uugauuuaaa agaaaucagc 540ucuaaaacac ugggacuuga uaagcuuaau guccaagaug ccuacacccc gaaagaaacu 600gcuguaaccg uugauaaaac uaccuauaaa aaugguacag auccuauuac agcccagagc 660aauacugaua uccaaacugc aauuggcggu ggugcaacgg ggguuacugg ggcugauauc 720aaauuuaaag auggucaaua cuauuuagau guuaaaggcg gugcuucugc ugguguuuau 780aaagccacuu augaugaaac uacaaagaaa guuaauauug auacgacuga uaaaacuccg 840uuggcaacug cggaagcuac agcuauucgg ggaacggcca cuauaaccca caaccaaauu 900gcugaaguaa caaaagaggg uguugauacg accacaguug cggcucaacu ugcugcagca 960gggguuacug gcgccgauaa ggacaauacu agccuuguaa aacuaucguu ugaggauaaa 1020aacgguaagg uuauugaugg uggcuaugca gugaaaaugg gcgacgauuu cuaugccgcu 1080acauaugaug agaaaacagg ugcaauuacu gcuaaaacca cuacuuauac agaugguacu 1140ggcguugcuc aaacuggagc ugugaaauuu gguggcgcaa augguaaauc ugaaguuguu 1200acugcuaccg augguaagac uuacuuagca agcgaccuug acaaacauaa cuucagaaca 1260ggcggugagc uuaaagaggu uaauacagau aagacugaaa acccacugca gaaaauugau 1320gcugccuugg cacagguuga uacacuucgu ucugaccugg gugcgguuca gaaccguuuc 1380aacuccgcua ucaccaaccu gggcaauacc guaaauaacc ugucuucugc ccguagccgu 1440aucgaagauu ccgacuacgc aaccgaaguc uccaacaugu cucgcgcgca gauucugcag 1500caggccggua ccuccguucu ggcgcaggcg aaccagguuc cgcaaaacgu ccucucuuua 1560cugcguugau aauaggcugg agccucggug gccaugcuuc uugccccuug ggccuccccc 1620cagccccucc uccccuuccu gcacccguac ccccgugguc uuugaauaaa gucugagugg 1680gcggcaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaucuag 179054506PRTArtificial SequenceSynthetic Polypeptide 54Met Ala Gln Val Ile Asn Thr Asn Ser Leu Ser Leu Leu Thr Gln Asn1 5 10 15Asn Leu Asn Lys Ser Gln Ser Ala Leu Gly Thr Ala Ile Glu Arg Leu 20 25 30Ser Ser Gly Leu Arg Ile Asn Ser Ala Lys Asp Asp Ala Ala Gly Gln 35 40 45Ala Ile Ala Asn Arg Phe Thr Ala Asn Ile Lys Gly Leu Thr Gln Ala 50 55 60Ser Arg Asn Ala Asn Asp Gly Ile Ser Ile Ala Gln Thr Thr Glu Gly65 70 75 80Ala Leu Asn Glu Ile Asn Asn Asn Leu Gln Arg Val Arg Glu Leu Ala 85 90 95Val Gln Ser Ala Asn Gly Thr Asn Ser Gln Ser Asp Leu Asp Ser Ile 100 105 110Gln Ala Glu Ile Thr Gln Arg Leu Asn Glu Ile Asp Arg Val Ser Gly 115 120 125Gln Thr Gln Phe Asn Gly Val Lys Val Leu Ala Gln Asp Asn Thr Leu 130 135 140Thr Ile Gln Val Gly Ala Asn Asp Gly Glu Thr Ile Asp Ile Asp Leu145 150 155 160Lys Glu Ile Ser Ser Lys Thr Leu Gly Leu Asp Lys Leu Asn Val Gln 165 170 175Asp Ala Tyr Thr Pro Lys Glu Thr Ala Val Thr Val Asp Lys Thr Thr 180 185 190Tyr Lys Asn Gly Thr Asp Pro Ile Thr Ala Gln Ser Asn Thr Asp Ile 195 200 205Gln Thr Ala Ile Gly Gly Gly Ala Thr Gly Val Thr Gly Ala Asp Ile 210 215 220Lys Phe Lys Asp Gly Gln Tyr Tyr Leu Asp Val Lys

Gly Gly Ala Ser225 230 235 240Ala Gly Val Tyr Lys Ala Thr Tyr Asp Glu Thr Thr Lys Lys Val Asn 245 250 255Ile Asp Thr Thr Asp Lys Thr Pro Leu Ala Thr Ala Glu Ala Thr Ala 260 265 270Ile Arg Gly Thr Ala Thr Ile Thr His Asn Gln Ile Ala Glu Val Thr 275 280 285Lys Glu Gly Val Asp Thr Thr Thr Val Ala Ala Gln Leu Ala Ala Ala 290 295 300Gly Val Thr Gly Ala Asp Lys Asp Asn Thr Ser Leu Val Lys Leu Ser305 310 315 320Phe Glu Asp Lys Asn Gly Lys Val Ile Asp Gly Gly Tyr Ala Val Lys 325 330 335Met Gly Asp Asp Phe Tyr Ala Ala Thr Tyr Asp Glu Lys Thr Gly Ala 340 345 350Ile Thr Ala Lys Thr Thr Thr Tyr Thr Asp Gly Thr Gly Val Ala Gln 355 360 365Thr Gly Ala Val Lys Phe Gly Gly Ala Asn Gly Lys Ser Glu Val Val 370 375 380Thr Ala Thr Asp Gly Lys Thr Tyr Leu Ala Ser Asp Leu Asp Lys His385 390 395 400Asn Phe Arg Thr Gly Gly Glu Leu Lys Glu Val Asn Thr Asp Lys Thr 405 410 415Glu Asn Pro Leu Gln Lys Ile Asp Ala Ala Leu Ala Gln Val Asp Thr 420 425 430Leu Arg Ser Asp Leu Gly Ala Val Gln Asn Arg Phe Asn Ser Ala Ile 435 440 445Thr Asn Leu Gly Asn Thr Val Asn Asn Leu Ser Ser Ala Arg Ser Arg 450 455 460Ile Glu Asp Ser Asp Tyr Ala Thr Glu Val Ser Asn Met Ser Arg Ala465 470 475 480Gln Ile Leu Gln Gln Ala Gly Thr Ser Val Leu Ala Gln Ala Asn Gln 485 490 495Val Pro Gln Asn Val Leu Ser Leu Leu Arg 500 50555698PRTArtificial SequenceSynthetic Polypeptide 55Met Ala Gln Val Ile Asn Thr Asn Ser Leu Ser Leu Leu Thr Gln Asn1 5 10 15Asn Leu Asn Lys Ser Gln Ser Ala Leu Gly Thr Ala Ile Glu Arg Leu 20 25 30Ser Ser Gly Leu Arg Ile Asn Ser Ala Lys Asp Asp Ala Ala Gly Gln 35 40 45Ala Ile Ala Asn Arg Phe Thr Ala Asn Ile Lys Gly Leu Thr Gln Ala 50 55 60Ser Arg Asn Ala Asn Asp Gly Ile Ser Ile Ala Gln Thr Thr Glu Gly65 70 75 80Ala Leu Asn Glu Ile Asn Asn Asn Leu Gln Arg Val Arg Glu Leu Ala 85 90 95Val Gln Ser Ala Asn Ser Thr Asn Ser Gln Ser Asp Leu Asp Ser Ile 100 105 110Gln Ala Glu Ile Thr Gln Arg Leu Asn Glu Ile Asp Arg Val Ser Gly 115 120 125Gln Thr Gln Phe Asn Gly Val Lys Val Leu Ala Gln Asp Asn Thr Leu 130 135 140Thr Ile Gln Val Gly Ala Asn Asp Gly Glu Thr Ile Asp Ile Asp Leu145 150 155 160Lys Gln Ile Asn Ser Gln Thr Leu Gly Leu Asp Thr Leu Asn Val Gln 165 170 175Gln Lys Tyr Lys Val Ser Asp Thr Ala Ala Thr Val Thr Gly Tyr Ala 180 185 190Asp Thr Thr Ile Ala Leu Asp Asn Ser Thr Phe Lys Ala Ser Ala Thr 195 200 205Gly Leu Gly Gly Thr Asp Gln Lys Ile Asp Gly Asp Leu Lys Phe Asp 210 215 220Asp Thr Thr Gly Lys Tyr Tyr Ala Lys Val Thr Val Thr Gly Gly Thr225 230 235 240Gly Lys Asp Gly Tyr Tyr Glu Val Ser Val Asp Lys Thr Asn Gly Glu 245 250 255Val Thr Leu Ala Gly Gly Ala Thr Ser Pro Leu Thr Gly Gly Leu Pro 260 265 270Ala Thr Ala Thr Glu Asp Val Lys Asn Val Gln Val Ala Asn Ala Asp 275 280 285Leu Thr Glu Ala Lys Ala Ala Leu Thr Ala Ala Gly Val Thr Gly Thr 290 295 300Ala Ser Val Val Lys Met Ser Tyr Thr Asp Asn Asn Gly Lys Thr Ile305 310 315 320Asp Gly Gly Leu Ala Val Lys Val Gly Asp Asp Tyr Tyr Ser Ala Thr 325 330 335Gln Asn Lys Asp Gly Ser Ile Ser Ile Asn Thr Thr Lys Tyr Thr Ala 340 345 350Asp Asp Gly Thr Ser Lys Thr Ala Leu Asn Lys Leu Gly Gly Ala Asp 355 360 365Gly Lys Thr Glu Val Val Ser Ile Gly Gly Lys Thr Tyr Ala Ala Ser 370 375 380Lys Ala Glu Gly His Asn Phe Lys Ala Gln Pro Asp Leu Ala Glu Ala385 390 395 400Ala Ala Thr Thr Thr Glu Asn Pro Leu Gln Lys Ile Asp Ala Ala Leu 405 410

415Ala Gln Val Asp Thr Leu Arg Ser Asp Leu Gly Ala Val Gln Asn Arg 420 425 430Phe Asn Ser Ala Ile Thr Asn Leu Gly Asn Thr Val Asn Asn Leu Thr 435 440 445Ser Ala Arg Ser Arg Ile Glu Asp Ser Asp Tyr Ala Thr Glu Val Ser 450 455 460Asn Met Ser Arg Ala Gln Ile Leu Gln Gln Ala Gly Thr Ser Val Leu465 470 475 480Ala Gln Ala Asn Gln Val Pro Gln Asn Val Leu Ser Leu Leu Arg Gly 485 490 495Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Met Ala Pro Asp Pro Asn 500 505 510Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn 515 520 525Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn 530 535 540Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn545 550 555 560Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn 565 570 575Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Lys Asn Asn Gln 580 585 590Gly Asn Gly Gln Gly His Asn Met Pro Asn Asp Pro Asn Arg Asn Val 595 600 605Asp Glu Asn Ala Asn Ala Asn Asn Ala Val Lys Asn Asn Asn Asn Glu 610 615 620Glu Pro Ser Asp Lys His Ile Glu Gln Tyr Leu Lys Lys Ile Lys Asn625 630 635 640Ser Ile Ser Thr Glu Trp Ser Pro Cys Ser Val Thr Cys Gly Asn Gly 645 650 655Ile Gln Val Arg Ile Lys Pro Gly Ser Ala Asn Lys Pro Lys Asp Glu 660 665 670Leu Asp Tyr Glu Asn Asp Ile Glu Lys Lys Ile Cys Lys Met Glu Lys 675 680 685Cys Ser Ser Val Phe Asn Val Val Asn Ser 690 69556692PRTArtificial SequenceSynthetic Polypeptide 56Met Met Ala Pro Asp Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala1 5 10 15Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala 20 25 30Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala 35 40 45Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala 50 55 60Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala Asn Pro Asn Ala65 70 75 80Asn Pro Asn Lys Asn Asn Gln Gly Asn Gly Gln Gly His Asn Met Pro 85 90 95Asn Asp Pro Asn Arg Asn Val Asp Glu Asn Ala Asn Ala Asn Asn Ala 100 105 110Val Lys Asn Asn Asn Asn Glu Glu Pro Ser Asp Lys His Ile Glu Gln 115 120 125Tyr Leu Lys Lys Ile Lys Asn Ser Ile Ser Thr Glu Trp Ser Pro Cys 130 135 140Ser Val Thr Cys Gly Asn Gly Ile Gln Val Arg Ile Lys Pro Gly Ser145 150 155 160Ala Asn Lys Pro Lys Asp Glu Leu Asp Tyr Glu Asn Asp Ile Glu Lys 165 170 175Lys Ile Cys Lys Met Glu Lys Cys Ser Ser Val Phe Asn Val Val Asn 180 185 190Ser Arg Pro Val Thr Met Ala Gln Val Ile Asn Thr Asn Ser Leu Ser 195 200 205Leu Leu Thr Gln Asn Asn Leu Asn Lys Ser Gln Ser Ala Leu Gly Thr 210 215 220Ala Ile Glu Arg Leu Ser Ser Gly Leu Arg Ile Asn Ser Ala Lys Asp225 230 235 240Asp Ala Ala Gly Gln Ala Ile Ala Asn Arg Phe Thr Ala Asn Ile Lys 245 250 255Gly Leu Thr Gln Ala Ser Arg Asn Ala Asn Asp Gly Ile Ser Ile Ala 260 265 270Gln Thr Thr Glu Gly Ala Leu Asn Glu Ile Asn Asn Asn Leu Gln Arg 275 280 285Val Arg Glu Leu Ala Val Gln Ser Ala Asn Ser Thr Asn Ser Gln Ser 290 295 300Asp Leu Asp Ser Ile Gln Ala Glu Ile Thr Gln Arg Leu Asn Glu Ile305 310 315 320Asp Arg Val Ser Gly Gln Thr Gln Phe Asn Gly Val Lys Val Leu Ala 325 330 335Gln Asp Asn Thr Leu Thr Ile Gln Val Gly Ala Asn Asp Gly Glu Thr 340 345 350Ile Asp Ile Asp Leu Lys Gln Ile Asn Ser Gln Thr Leu Gly Leu Asp 355 360 365Thr Leu Asn Val Gln Gln Lys Tyr Lys Val Ser Asp Thr Ala Ala Thr 370 375 380Val Thr Gly Tyr Ala Asp Thr Thr Ile Ala Leu Asp Asn Ser Thr Phe385 390 395 400Lys Ala Ser Ala Thr Gly Leu Gly Gly Thr Asp Gln Lys Ile Asp Gly 405 410 415Asp Leu Lys Phe Asp Asp Thr Thr Gly Lys Tyr Tyr Ala Lys Val Thr 420 425 430Val Thr Gly Gly Thr Gly Lys Asp Gly Tyr Tyr Glu Val Ser Val Asp 435 440 445Lys Thr Asn Gly Glu Val Thr Leu Ala Gly Gly Ala Thr Ser Pro Leu 450 455 460Thr Gly Gly Leu Pro Ala Thr Ala Thr Glu Asp Val Lys Asn Val Gln465 470 475 480Val Ala Asn Ala Asp Leu Thr Glu Ala Lys Ala Ala Leu Thr Ala Ala 485 490 495Gly Val Thr Gly Thr Ala Ser Val Val Lys Met Ser Tyr Thr Asp Asn 500 505 510Asn Gly Lys Thr Ile Asp Gly Gly Leu Ala Val Lys Val Gly Asp Asp 515 520 525Tyr Tyr Ser Ala Thr Gln Asn Lys Asp Gly Ser Ile Ser Ile Asn Thr 530 535 540Thr Lys Tyr Thr Ala Asp Asp Gly Thr Ser Lys Thr Ala Leu Asn Lys545 550 555 560Leu Gly Gly Ala Asp Gly Lys Thr Glu Val Val Ser Ile Gly Gly Lys 565 570 575Thr Tyr Ala Ala Ser Lys Ala Glu Gly His Asn Phe Lys Ala Gln Pro 580 585 590Asp Leu Ala Glu Ala Ala Ala Thr Thr Thr Glu Asn Pro Leu Gln Lys 595 600 605Ile Asp Ala Ala Leu Ala Gln Val Asp Thr Leu Arg Ser Asp Leu Gly 610 615 620Ala Val Gln Asn Arg Phe Asn Ser Ala Ile Thr Asn Leu Gly Asn Thr625 630 635 640Val Asn Asn Leu Thr Ser Ala Arg Ser Arg Ile Glu Asp Ser Asp Tyr 645 650 655Ala Thr Glu Val Ser Asn Met Ser Arg Ala Gln Ile Leu Gln Gln Ala 660 665 670Gly Thr Ser Val Leu Ala Gln Ala Asn Gln Val Pro Gln Asn Val Leu 675 680 685Ser Leu Leu Arg 690571620RNAUnknownHuman metapneumovirus 57augagcugga agguggugau uaucuucagc cugcugauua caccucaaca cggccugaag 60gagagcuacc uggaagagag cugcuccacc aucaccgagg gcuaccugag cgugcugcgg 120accggcuggu acaccaacgu guucacccug gaggugggcg acguggagaa ccugaccugc 180agcgacggcc cuagccugau caagaccgag cuggaccuga ccaagagcgc ucugagagag 240cugaagaccg uguccgccga ccagcuggcc agagaggaac agaucgagaa cccucggcag 300agcagauucg ugcugggcgc caucgcucug ggagucgccg cugccgcugc agugacagcu 360ggaguggcca uugcuaagac caucagacug gaaagcgagg ugacagccau caacaaugcc 420cugaagaaga ccaacgaggc cgugagcacc cugggcaaug gagugagagu gcuggccaca 480gccgugcggg agcugaagga cuucgugagc aagaaccuga ccagagccau caacaagaac 540aagugcgaca ucgaugaccu gaagauggcc gugagcuucu cccaguucaa cagacgguuc 600cugaacgugg ugagacaguu cuccgacaac gcuggaauca caccugccau uagccuggac 660cugaugaccg acgccgagcu ggcuagagcc gugcccaaca ugcccaccag cgcuggccag 720aucaagcuga ugcuggagaa cagagccaug gugcggagaa agggcuucgg cauccugauu 780ggggguguaug gaagcuccgu gaucuacaug gugcagcugc ccaucuucgg cgugaucgac 840acacccugcu ggaucgugaa ggccgcuccu agcugcuccg agaagaaagg aaacuaugcc 900ugucugcuga gagaggacca gggcugguac ugccagaacg ccggaagcac aguguacuau 960cccaacgaga aggacugcga gaccagaggc gaccacgugu ucugcgacac cgcugccgga 1020aucaacgugg ccgagcagag caaggagugc aacaucaaca ucagcacaac caacuacccc 1080ugcaagguga gcaccggacg gcaccccauc agcauggugg cucugagccc ucugggcgcu 1140cugguggccu gcuauaaggg cguguccugu agcaucggca gcaaucgggu gggcaucauc 1200aagcagcuga acaagggaug cuccuacauc accaaccagg acgccgacac cgugaccauc 1260gacaacaccg uguaccagcu gagcaaggug gagggcgagc agcacgugau caagggcaga 1320cccgugagcu ccagcuucga ccccaucaag uucccugagg accaguucaa cguggcccug 1380gaccaggugu uugagaacau cgagaacagc caggcccugg uggaccagag caacagaauc 1440cuguccagcg cugagaaggg caacaccggc uucaucauug ugaucauucu gaucgccgug 1500cugggcagcu ccaugauccu ggugagcauc uucaucauua ucaagaagac caagaaaccc 1560accggagccc cuccugagcu gagcggcgug accaacaaug gcuucauucc ccacaacuga 1620581620RNAUnknownHuman metapneumovirus 58augucuugga aagugaugau caucauuucg uuacucauaa caccccagca cgggcuaaag 60gagaguuauu uggaagaauc auguaguacu auaacugagg gauaccucag uguuuuaaga 120acaggcuggu acacuaaugu cuucacauua gaaguuggug auguugaaaa ucuuacaugu 180acugauggac cuagcuuaau caaaacagaa cuugaucuaa caaaaagugc uuuaagggaa 240cucaaaacag ucucugcuga ucaguuggcg agagaggagc aaauugaaaa ucccagacaa 300ucaagauuug ucuuaggugc gauagcucuc ggaguugcua cagcagcagc agucacagca 360ggcauugcaa uagccaaaac cauaaggcuu gagagugagg ugaaugcaau uaaaggugcu 420cucaaacaaa cuaaugaagc aguauccaca uuagggaaug gugugcgggu ccuagccacu 480gcagugagag agcuaaaaga auuugugagc aaaaaccuga cuagugcaau caacaggaac 540aaaugugaca uugcugaucu gaagauggcu gucagcuuca gucaauucaa cagaagauuu 600cuaaauguug ugcggcaguu uucagacaau gcagggauaa caccagcaau aucauuggac 660cugaugacug augcugaguu ggccagagcu guaucauaca ugccaacauc ugcagggcag 720auaaaacuga uguuggagaa ccgcgcaaug guaaggagaa aaggauuugg aauccugaua 780ggggucuacg gaagcucugu gauuuacaug guucaauugc cgaucuuugg ugucauagau 840acaccuuguu ggaucaucaa ggcagcuccc ucuugcucag aaaaaaacgg gaauuaugcu 900ugccuccuaa gagaggauca aggggugguau uguaaaaaug caggaucuac uguuuacuac 960ccaaaugaaa aagacugcga aacaagaggu gaucauguuu uuugugacac agcagcaggg 1020aucaauguug cugagcaauc aagagaaugc aacaucaaca uaucuacuac caacuaccca 1080ugcaaaguca gcacaggaag acacccuaua agcaugguug cacuaucacc ucucggugcu 1140uugguggcuu gcuauaaagg gguaagcugc ucgauuggca gcaauugggu uggaaucauc 1200aaacaauuac ccaaaggcug cucauacaua accaaccagg augcagacac uguaacaauu 1260gacaauaccg uguaucaacu aagcaaaguu gaaggugaac agcauguaau aaaagggaga 1320ccaguuucaa gcaguuuuga uccaaucaag uuuccugagg aucaguucaa uguugcgcuu 1380gaucaagucu ucgaaagcau ugagaacagu caggcacuag uggaccaguc aaacaaaauu 1440cuaaacagug cagaaaaagg aaacacuggu uucauuaucg uaguaauuuu gguugcuguu 1500cuuggucuaa ccaugauuuc agugagcauc aucaucauaa ucaagaaaac aaggaagccc 1560acaggagcac cuccagagcu gaauggugu accaacggcg guuucauacc acauaguuag 1620591620RNAUnknownHuman metapneumovirus 59augucuugga aagugaugau uaucauuucg uuacucauaa caccucagca uggacuaaaa 60gaaaguuauu uagaagaauc auguaguacu auaacugaag gauaucucag uguuuuaaga 120acagguuggu acaccaaugu cuuuacauua gaaguuggug auguugaaaa ucuuacaugu 180acugauggac cuagcuuaau caaaacagaa cuugaccuaa ccaaaagugc uuuaagagaa 240cucaaaacag uuucugcuga ucaguuagcg agagaagaac aaauugaaaa ucccagacaa 300ucaagguuug uccuaggugc aauagcucuu ggaguugcca cagcagcagc agucacagca 360ggcauugcaa uagccaaaac uauaaggcuu gagagugaag ugaaugcaau caaaggugcu 420cucaaaacaa ccaaugaggc aguaucaaca cuaggaaaug gagugcgggu ccuagccacu 480gcaguaagag agcugaaaga auuugugagc aaaaaccuga cuagugcgau caacaagaac 540aagugugaca uugcugauuu gaagauggcu gucagcuuca gucaguucaa cagaagauuc 600cuaaauguug ugcggcaguu uucagacaau gcagggauaa caccagcaau aucauuggac 660cugaugaaug augcugagcu ggccagagcu guaucauaca ugccaacauc ugcaggacag 720auaaaaacuaa uguuagagaa ccgugcaaug gugaggagaa aaggauuugg aaucuugaua 780ggggucuacg gaagcucugu gauuuacaug guccagcugc cgaucuuugg ugucauaaau 840acaccuuguu ggauaaucaa ggcagcuccc ucuuguucag aaaaagaugg aaauuaugcu 900ugccuccuaa gagaggauca agggguggua uguaaaaaug caggauccac uguuuacuac 960ccaaaugaaa aagacugcga aacaagaggu gaucauguuu uuugugacac agcagcaggg 1020aucaauguug cugagcaauc aagagaaugc aacaucaaca uaucuaccac caacuaccca 1080ugcaaaguca gcacaggaag acacccuauc agcaugguug cacuaucacc ucucggugcu 1140uugguagcuu gcuacaaagg gguuagcugc ucgacuggca guaaucaggu uggaauaauc 1200aaacaacuac cuaaaggcug cucauacaua acuaaccagg acgcagacac uguaacaauu 1260gacaacacug uguaucaacu aagcaaaguu gagggugaac agcauguaau aaaagggaga 1320ccaguuucaa gcaguuuuga uccaaucagg uuuccugagg aucaguucaa uguugcgcuu 1380gaucaagucu uugaaagcau ugaaaacagu caagcacuag uggaccaguc aaacaaaauu 1440cugaacagug cagaaaaagg aaacacuggu uucauuauug uaauaauuuu gauugcuguu 1500cuuggguuaa ccaugauuuc agugagcauc aucaucauaa ucaaaaaaac aaggaagccc 1560acaggggcac cuccggagcu gaauggugu accaacggcg guuucauacc gcauaguuag 1620601725RNAHuman respiratory syncytial virus 60auggaguugc caauccucaa aacaaaugca auuaccacaa uccuugcugc agucacacuc 60uguuucgcuu ccagucaaaa caucacugaa gaauuuuauc aaucaacaug cagugcaguu 120agcaaaggcu aucuuagugc ucuaagaacu gguugguaua cuaguguuau aacuauagaa 180uuaaguaaua ucaaggaaaa uaaguguaau ggaacagaug cuaagguaaa auugauaaaa 240caagaauuag auaaauauaa aaaugcugua acagaauugc aguugcucau gcaaagcaca 300ccagcagcca acaaucgagc cagaagagaa cuaccaaggu uuaugaauua uacacucaau 360aauaccaaaa auaccaaugu aacauuaagc aagaaaagga aaagaagauu ucuuggcuuu 420uuguuaggug uuggaucugc aaucgccagu ggcauugcug uaucuaaggu ccugcaccua 480gaaggggaag ugaacaaaau caaaagugcu cuacuaucca caaacaaggc uguagucagc 540uuaucaaaug gaguuagugu cuuaaccagc aaaguguuag accucaaaaa cuauauagau 600aaacaguugu uaccuauugu gaacaagcaa agcugcagca uaucaaacau ugaaacugug 660auagaguucc aacaaaagaa caacagacua cuagagauua ccagggaauu uaguguuaau 720gcaggguguaa cuacaccugu aagcacuuau auguuaacua auagugaauu auuaucauua 780aucaaugaua ugccuauaac aaaugaucag aaaaaguuaa uguccaacaa uguucaaaua 840guuagacagc aaaguuacuc uaucaugucc auaauaaagg aggaagucuu agcauaugua 900guacaauuac cacuauaugg uguaauagau acacccuguu ggaaacugca cacaucccu 960cuauguacaa ccaacacaaa ggaagggucc aacaucugcu uaacaagaac cgacagagga 1020ugguauugug acaaugcagg aucaguaucu uucuucccac aagcugaaac auguaaaguu 1080caaucgaauc ggguauuuug ugacacaaug aacaguuuaa cauuaccaag ugaaguaaau 1140cucugcaaca uugacauauu caaccccaaa uaugauugca aaauuaugac uucaaaaaca 1200gauguaagca gcuccguuau cacaucucua ggagccauug ugucaugcua uggcaaaacu 1260aaauguacag cauccaauaa aaaucguggg aucauaaaga cauuuucuaa cggguguguau 1320uauguaucaa auaaggggu ggauacugug ucuguaggua auacauuaua uuauguaaau 1380aagcaagaag gcaaaagucu cuauguaaaa ggugaaccaa uaauaaauuu cuaugaccca 1440uuaguguucc ccucugauga auuugaugca ucaauaucuc aagucaauga gaagauuaac 1500cagagccuag cauuuauucg uaaauccgau gaauuauuac auaauguaaa ugcugguaaa 1560uccaccacaa auaucaugau aacuacuaua auuauaguga uuauaguaau auuguuauca 1620uuaauugcag uuggacugcu ccuauacugc aaggccagaa gcacaccagu cacacuaagu 1680aaggaucaac ugagugguau aaauaauauu gcauuuagua acuga 1725611617RNAHuman parainfluenza virus 3 61augccaauuu caauacuguu aauuauuaca accaugauca uggcaucaca cugccaaaua 60gacaucacaa aacuacagca uguaggugua uuggucaaca gucccaaagg gaugaagaua 120ucacaaaacu ucgaaacaag auaucuaauc cugagucuca uaccaaaaau agaagauucu 180aacucuugug gugaccaaca gaucaagcaa uacaagaggu uauuggauag acugaucauu 240ccuuuauaug auggacuaag auuacagaag gaugugauag ugacuaauca agaauccaau 300gaaaacacug aucccagaac agaacgauuc uuuggagggg uaauuggaac uauugcucua 360ggaguagcaa ccucagcaca aauuacagca gcaguugcuc ugguugaagc caagcaggca 420agaucagaca uugaaaaacu caaggaagca aucagggaca caaauaaagc agugcaguca 480guucagagcu cuguaggaaa uuugauagua gcaauuaaau caguccagga uuaugucaac 540aaagaaaucg ugccaucgau ugcgagacua gguugugaag cagcaggacu ucaguuaggg 600auugcauuaa cacagcauua cucagaauua acaaauauau uuggugauaa cauaggaucg 660uuacaagaaa aaggaauaaa auuacaaggu auagcaucau uauaccguac aaauaucaca 720gaaauauuca caacaucaac aguugacaaa uaugauauuu augaucuauu auuuacagaa 780ucaauaaagg ugagaguuau agauguugau uugaaugauu acucaauaac ccuccaaguc 840agacucccuu uauugaccag acugcugaac acucaaaucu acaaaguaga uuccauauca 900uacaauaucc aaaauagaga augguauauc ccucuuccca gccauaucau gacgaaaggg 960gcauuucuag guggagcaga ugucaaagaa ugcauagaag cauucagcag uuauauaugc 1020ccuucugauc caggauuugu acuaaaccau gaaauggaga gcugucuauc aggaaacaua 1080ucccaauguc caagaaccac agucacauca gacauaguuc cuagguaugc auuugucaau 1140ggaggagugg uugcgaauug uauaacaacu acauguacau gcaaugguau cgguaauaga 1200aucaaccaac caccugauca aggagucaaa auuauaacac auaaagaaug uaauacaaua 1260gguaucaacg gaaugcuauu caacacaaac aaagaaggaa cucuugcauu cuacacacca 1320gacgacauaa cauuaaacaa uucuguugca cuugauccga uugacauauc aaucgagcuc 1380aacaaggcca aaucagaucu ugaggaauca aaagaaugga uaagaagguc aaaucaaaag 1440cuagauucua uuggaaguug gcaucaaucu agcacuacaa ucauaguuau uuugauaaug 1500augauuauau uguuuauaau uaauauaaca auaauuacaa uugcaauuaa guauuacaga 1560auucaaaaga gaaaucgagu ggaucaaaau gauaagccgu auguauuaac aaacaag 1617621716RNAHuman parainfluenza virus 3 62auggaauacu ggaagcacac caaccacgga aaggaugcug guaaugagcu ggagacaucc 60acagccacuc auggcaacaa gcucaccaac aagauaacau auauauugug gacgauaacc 120cugguguuau uaucaauagu cuucaucaua gugcuaacua auuccaucaa aagugaaaag 180gcccgcgaau cauugcuaca agacauaaau aaugaguuua uggaaguuac agaaaagauc 240caaguggcau cggauaauac uaaugaucua auacagucag gagugaauac aaggcuucuu 300acaauucaga gucauguccca gaauuauaua ccaauaucau ugacacaaca aauaucggau 360cuuaggaaau ucauuaguga aauuacaauu agaaaugaua aucaagaagu gccaccacaa 420agaauaacac augauguggg uauaaaaccu uuaaauccag augauuucug gagaugcacg 480ucuggucuuc caucuuugau gaaaacucca aaaauaagau uaaugccggg accaggauua 540uuagcuaugc caacgacugu ugauggcugu gucagaaccc cguccuuagu gauaaaugau 600cugauuuaug cuuacaccuc aaaucuaauu acucgagguu gccaggauau agggaaauca 660uaucaaguau uacagauagg gauaauaacu guaaacucag acuugguacc ugacuuaaau 720ccuaggaucu cucauaccuu caacauaaau gacaauagaa agucauguuc ucuagcacuc 780cuaaauacag auguauauca acuguguuca accccaaaag uugaugaaag aucagauuau 840gcaucaucag gcauagaaga uauuguacuu gauauuguca auuaugaugg cucaaucucg 900acaacaagau uuaagaauaa uaauauaagu uuugaucaac cauaugcggc auuauaccca 960ucuguuggac cagggauaua cuacaaaggc aaaauaauau uucucgggua uggaggucuu 1020gaacauccaa uaaaugagaa ugcaaucugc aacacaacug gguguccugg gaaaacacag 1080agagacugua aucaagcauc ucauagucca ugguuuucag auagaaggau ggucaacucu 1140auaauuguug uugacaaggg cuugaacuca guuccaaaau ugaagguaug gacgauaucu 1200augagacaaa auuacugggg gucagaagga agauuacuuc uacuagguaa caagaucuac 1260auauacacaa gaucuacaag uuggcacagc aaguuacaau uaggaauaau ugacauuacu 1320gacuacagug auauaaggau aaaauggaca uggcauaaug ugcuaucaag accaggaaac 1380aaugaauguc cauggggaca uucauguccg gauggaugua uaacgggagu auauaccgau 1440gcauauccac ucaaucccac aggaagcauu guaucaucug ucauauugga cucacaaaaa 1500ucgagaguca acccagucau aacuuacuca acagcaaccg aaaggguaaa cgagcuggcu 1560auccgaaaca aaacacucuc agcuggguac acaacaacaa gcugcauuac acacuauaac 1620aaaggguauu guuuucauau aguagaaaua aaucauaaaa gcuuaaacac auuucaaccc 1680auguuguuca aaacagagau uccaaaaagc ugcagu 1716631716RNAArtificial SequenceSynthetic Polynucleotide 63auggaauacu ggaagcacac caaccacggc aaggacgccg gcaacgagcu ggaaaccagc 60acagccacac acggcaacaa gcugaccaac aagaucaccu acauccugug gaccaucacc 120cuggugcugc ugagcaucgu guucaucauc gugcugacca auagcaucaa gagcgagaag 180gccagagaga gccugcugca ggacaucaac aacgaguuca uggaagugac cgagaagauc 240cagguggcca gcgacaacac caacgaccug auccagagcg gcgugaacac ccggcugcug 300accauccaga gccacgugca gaacuacauc cccaucagcc ugacccagca gaucagcgac 360cugcggaagu ucaucagcga gaucaccauc cggaacgaca accaggaagu gcccccccag 420agaaucaccc acgacguggg caucaagccc cugaaccccg acgauuucug gcgguguaca 480agcggccugc ccagccugau gaagaccccc aagauccggc ugaugccugg cccuggacug 540cuggccaugc cuaccacagu ggauggcugu gugcggaccc ccagccucgu gaucaacgau 600cugaucuacg ccuacaccag caaccugauc acccggggcu gccaggauau cggcaagagc 660uaccaggugc ugcagaucgg caucaucacc gugaacuccg accuggugcc cgaccugaac 720ccucggauca gccacaccuu caacaucaac gacaacagaa agagcugcag ccuggcucug 780cugaacaccg acguguacca gcugugcagc acccccaagg uggacgagag aagcgacuac 840gccagcagcg gcaucgagga uaucgugcug gacaucguga acuacgacgg cagcaucagc 900accacccggu ucaagaacaa caacaucagc uucgaccagc ccuacgccgc ccuguacccu 960ucugugggcc cuggcaucua cuacaagggc aagaucaucu uccugggcua cggcggccug 1020gaacacccca ucaacgagaa cgccaucugc aacaccaccg gcugcccugg caagacccag 1080agagacugca aucaggccag ccacagcccc ugguucagcg accgcagaau ggucaacucu 1140aucaucgugg uggacaaggg ccugaacagc gugcccaagc ugaaagugug gacaaucagc 1200augcgccaga acuacugggg cagcgagggc agacuucugc ugcugggaaa caagaucuac 1260aucuacaccc gguccaccag cuggcacagc aaacugcagc ugggaaucau cgacaucacc 1320gacuacagcg acauccggau caaguggacc uggcacaacg ugcugagcag acccggcaac 1380aaugagugcc cuuggggcca cagcugcccc gauggaugua ucaccggcgu guacaccgac 1440gccuaccccc ugaauccuac cggcuccauc guguccagcg ugauccugga cagccagaaa 1500agcagaguga accccgugau cacauacagc accgccaccg agagagugaa cgaacuggcc 1560aucagaaaca agacccugag cgccggcuac accaccacaa gcugcaucac acacuacaac 1620aagggcuacu gcuuccacau cguggaaauc aaccacaagu cccugaacac cuuccagccc 1680augcuguuca agaccgagau ccccaagagc ugcucc 1716641617RNAArtificial SequenceSynthetic Polynucleotide 64augcccauca gcauccugcu gaucaucacc acaaugauca uggccagcca cugccagauc 60gacaucacca agcugcagca cgugggcgug cucgugaaca gccccaaggg caugaagauc 120agccagaacu ucgagacacg cuaccugauc cugagccuga uccccaagau cgaggacagc 180aacagcugcg gcgaccagca gaucaagcag uacaagcggc ugcuggacag acugaucauc 240ccccuguacg acggccugcg gcugcagaaa gacgugaucg ugaccaacca ggaaagcaac 300gagaacaccg acccccggac cgagagauuc uucggcggcg ugaucggcac aaucgcccug 360ggaguggcca caagcgccca gauuacagcc gcuguggccc ugguggaagc caagcaggcc 420agaagcgaca ucgagaagcu gaaagaggcc auccgggaca ccaacaaggc cgugcagagc 480gugcagucca gcgugggcaa ucugaucgug gccaucaagu ccgugcagga cuacgugaac 540aaagaaaucg ugcccucuau cgcccggcug ggcugugaag cugccggacu gcagcugggc 600auugcccuga cacagcacua cagcgagcug accaacaucu ucggcgacaa caucggcagc 660cugcaggaaa agggcauuaa gcugcaggga aucgccagcc uguaccgcac caacaucacc 720gagaucuuca ccaccagcac cguggauaag uacgacaucu acgaccugcu guucaccgag 780agcaucaaag ugcgcgugau cgacguggac cugaacgacu acagcaucac ccugcaagug 840cggcugcccc ugcugaccag acugcugaac acccagaucu acaaggugga cagcaucucc 900uacaacaucc agaaccgcga gugguacauc ccucugccca gccacauuau gaccaagggc 960gccuuucugg gcggagccga cgugaaagag ugcaucgagg ccuucagcag cuacaucugc 1020cccagcgacc cuggcuucgu gcugaaccac gagauggaaa gcugccugag cggcaacauc 1080agccagugcc ccagaaccac cgugaccucc gacaucgugc ccagauacgc cuucgugaau 1140ggcggcgugg uggccaacug caucaccacc accuguaccu gcaacggcau cggcaaccgg 1200aucaaccagc cucccgauca gggcgugaag auuaucaccc acaaagagug uaacaccauc 1260ggcaucaacg gcaugcuguu caauaccaac aaagagggca cccuggccuu cuacaccccc 1320gacgauauca cccugaacaa cuccguggcu cuggaccccа ucgacaucuc caucgagcug 1380aacaaggcca agagcgaccu ggaagagucc aaagagugga uccggcggag caaccagaag 1440cuggacucua ucggcagcug gcaccagagc agcaccacca ucaucgugau ccugauuaug 1500augauuaucc uguucaucau caacauuacc aucaucacua ucgccauuaa guacuaccgg 1560auccagaaac ggaaccgggu ggaccagaau gacaagcccu acgugcugac aaacaag 1617654062RNAUnknownMiddle East respiratory syndrome coronavirus 65augauacacu caguguuucu acugauguuc uuguuaacac cuacagaaag uuacguugau 60guagggccag auucuguuaa gucugcuugu auugagguug auauacaaca gaccuucuuu 120gauaaaacuu ggccuaggcc aauugauguu ucuaaggcug acgguauuau auacccucaa 180ggccguacau auucuaacau aacuaucacu uaucaagguc uuuuucccua ucagggagac 240cauggugaua uguauguuua cucugcagga caugcuacag gcacaacucc acaaaaguug 300uuuguagcua acuauucuca ggacgucaaa caguuugcua augguuuugu cguccguaua 360ggagcagcug ccaauuccac uggcacuguu auuauuagcc caucuaccag cgcuacuaua 420cgaaaaauuu acccugcuuu uaugcugggu ucuucaguug guaauuucuc agaugguaaa 480augggccgcu ucuucaauca uacucuaguu cuuuugcccg auggaugugg cacuuuacuu 540agagcuuuuu auuguauucu agagccucgc ucuggaaauc auuguccugc uggcaauucc 600uauacuucuu uugccacuua ucacacuccu gcaacagauu guucugaugg caauuacaau 660cguaaugcca gucugaacuc uuuuaaggag uauuuuaauu uacguaacug caccuuuaug 720uacacuuaua acauuaccga agaugagauu uuagaguggu uuggcauuac acaaacugcu 780caagguguuc accucuucuc aucucgguau guugauuugu acggcggcaa uauguuucaa 840uuugccaccu ugccuguuua ugauacuauu aaguauuauu cuaucauucc ucacaguauu 900cguucuaucc aaagugauag aaaagcuugg gcugccuucu acguauauaa acuucaaccg 960uuaacuuucc uguuggauuu uucuguugau gguuauauac gcagagcuau agacuguggu 1020uuuaaugauu ugucacaacu ccacugcuca uaugaauccu ucgauguuga aucuggaguu 1080uauucaguuu cgucuuucga agcaaaaccu ucuggcucag uuguggaaca ggcugaaggu 1140guugaaugug auuuuucacc ucuucugucu ggcacaccuc cucagguuua uaauuucaag 1200cguuugguuu uuaccaauug caauuauaau cuuaccaaau ugcuuucacu uuuuucugug 1260aaugauuuua cuuguaguca aauaucucca gcagcaauug cuagcaacug uuauucuuca 1320cugauuuugg auuauuuuuc auacccacuu aguaugaaau ccgaucucag uguuaguucu 1380gcugguccaa uaucccaguu uaauuauaaa caguccuuuu cuaaucccac auguuugauc 1440uuagcgacug uuccucauaa ccuuacuacu auuacuaagc cucuuaagua cagcuauauu 1500aacaagugcu cucgucuucu uucugaugau cguacugaag uaccucaguu agugaacgcu 1560aaucaauacu cacccugugu auccauuguc ccauccacug ugugggaaga cggugauuau 1620uauaggaaac aacuaucucc acuugaaggu gguggcuggc uuguugcuag uggcucaacu 1680guugccauga cugagcaauu acagaugggc uuugguauua caguucaaua ugguacagac 1740accaauagug uuugccccaa gcuugaauuu gcuaaugaca caaaaauugc cucucaauua 1800ggcaauugcg uggaauauuc ccucuauggu guuucgggcc gugguguuuu ucagaauugc 1860acagcuguag guguucgaca gcagcgcuuu guuuaugaug cguaccagaa uuuaguuggc 1920uauuauucug augauggcaa cuacuacugu cugcgugcuu guguuagugu uccuguuucu 1980gucaucuaug auaaagaaac uaaaacccac gcuacucuau uugguagugu ugcaugugaa 2040cacauuucuu cuaccauguc ucaauacucc cguucuacgc gaucaaugcu uaaacggcga 2100gauucuacau auggcccccu ucagacaccu guugguugug uccuaggacu uguuaauucc 2160ucuuuguucg uagaggacug caaguugccu cucggucaau cucucugugc ucuuccugac 2220acaccuagua cucucacacc ucgcagugug cgcucugugc caggugaaau gcgcuuggca 2280uccauugcuu uuaaucaucc cauucagguu gaucaacuua auaguaguua uuuuaaauua 2340aguauaccca cuaauuuuuc cuuuggugug acucaggagu acauucagac aaccauucag 2400aaaguuacug uugauuguaa acaguacguu ugcaugguu uccagaagug ugagcaauua 2460cugcgcgagu auggccaguu uuguuccaaa auaaaccagg cucuccaugg ugccaauuua 2520cgccaggaug auucuguacg uaauuuguuu gcgagcguga aagcucuca aucaucuccu 2580aucauaccag guuuuggagg ugacuuuaau uugacacuuc uagaaccugu uucuauaucu 2640acuggcaguc guagugcacg uagugcuauu gaggauuugc uauuugacaa agucacuaua 2700gcugauccug guuauaugca agguuacgau gauuguaugc agcaagguccc agcaucagcu 2760cgugaucuua uuugugcuca auauguggcu gguuauaaag uauuaccucc ucuuauggau 2820guuaauaugg aagccgcgua uacuucaucu uugcuuggca gcauagcagg uguuggcugg 2880acugcuggcu uauccuccuu ugcugcuauu ccauuugcac agaguauyuu uuauagguua 2940aacgguguug gcauuacuca acagguucuu ucagagaacc aaaagcuuau ugccaauaag 3000uuuaaucagg cucugggagc uaugcaaaca ggcuucacua caacuaauga agcuuuucgg 3060aagguucagg augcugugaa caacaaugca caggcucuau ccaaauuagc uagcgagcua 3120ucuaauacuu uuggugcuau uuccgccucu auuggagaca ucauacaacg ucuugauguu 3180cucgaacagg acgcccaaau agacagacuu auuaauggcc guuugacaac acuaaaugcu 3240uuuguugcac agcagcuugu ucguuccgaa ucagcugcuc uuuccgcuca auuggcuaaa 3300gauaaaguca augaguguguu caaggcacaa uccaagcguu cuggauuuug cggucaaggc 3360acacauauag uguccuuugu uguaaaugcc ccuaauggcc uuuacuuuau gcauguuggu 3420uauuacccua gcaaccacau ugagguuguu ucugcuuaug gucuuugcga ugcagcuaac 3480ccuacuaauu guauagcccc uguuaauggc uacuuuauua aacuaauaa cacuaggauu 3540guugaugagu ggucauauac uggcucgucc uucuaugcac cugagcccau caccucucuu 3600aauacuaagu auguugcacc acaggugaca uaccaaaaca uuucuacuaa ccucccuccu 3660ccucuucucg gcaauuccac cgggauugac uucccagaug aguuggauga guuuuucaaa 3720aauguuagca ccaguauacc uaauuuuggu ucucuaacac agauuaauac uacauuacuc 3780gaucuuaccu acgagauguu gucucuucaa caaguuguua aagcccuuaa ugagucuuac 3840auagaccuua aagagcuugg caauuauacu uauuacaaca aauggccgug guacauuugg 3900cuugguuuca uugcugggcu uguugccuua gcucuaugcg ucuucuucau acugugcugc 3960acugguugug gcacaaacug uaugggaaaa cuuaagugua aucguuguug ugauagauac 4020gaggaauacg accucgagcc gcauaagguu cauguucacu aa 4062664062RNAArtificial SequenceSynthetic Polynucleotide 66augauacacu caguguuucu acugauguuc uuguuaacac cuacagaaag uuacguugau 60guagggccag auucuguuaa gucugcuugu auugagguug auauacaaca gacuuucuuu 120gauaaaacuu ggccuaggcc aauugauguu ucuaaggcug acgguauuau auacccucaa 180ggccguacau auucuaacau aacuaucacu uaucaagguc uuuuucccua ucagggagac 240cauggugaua uguauguuua cucugcagga caugcuacag gcacaacucc acaaaaguug 300uuuguagcua acuauucuca ggacgucaaa caguuugcua augggguugu cguccguaua 360ggagcagcug ccaauuccac uggcacuguu auuauuagcc caucuaccag cgcuacuaua 420cgaaaaauuu acccugcuuu uaugcugggu ucuucaguug guaauuucuc agaugguaaa 480augggccgcu ucuucaauca uacucuaguu cuuuugcccg auggaugugg cacuuuacuu 540agagcuuuuu auuguauucu ggagccucgc ucuggaaauc auuguccugc uggcaauucc 600uauacuucuu uugccacuua ucacacuccu gcaacagauu guucugaugg caauuacaau 660cguaaugcca gucugaacuc uuuuaaggag uauuuuaauu uacguaacug caccuuuaug 720uacacuuaua acauuaccga agaugagauu uuagaguggu uuggcauuac acaaacugcu 780caagguguuc accucuucuc aucucgguau guugauuugu acggcggcaa uauguuucaa 840uuugccaccu ugccuguuua ugauacuauu aaguauuauu cuaucauucc ucacaguauu 900cguucuaucc aaagugauag aaaagcuugg gcugccuucu acguauauaa acuucaaccg 960uuaacuuucc uguuggauuu uucuguugau gguuauauac gcagagcuau agacuguggu 1020uuuaaugauu ugucacaacu ccacugcuca uaugaauccu ucgauguuga aucuggaguu 1080uauucaguuu cgucuuucga agcaaaaccu ucuggcucag uuguggaaca ggcugaaggu 1140guugaaugug auuuuucacc ucuucugucu ggcacaccuc cucagguuua uaauuucaag 1200cguuugguuu uuaccaauug caauuauaau cuuaccaaau ugcuuucacu uuuuucugug 1260aaugauuuua cuuguaguca aauaucucca gcagcaauug cuagcaacug uuauucuuca 1320cugauuuugg auuacuuuuc auacccacuu aguaugaaau ccgaucucag uguuaguucu 1380gcugguccaa uaucccaguu uaauuauaaa caguccuuuu cuaaucccac auguuugauu 1440uuagcgacug uuccucauaa ccuuacuacu auuacuaagc cucuuaagua cagcuauauu 1500aacaagugcu cucgucuucu uucugaugau cguacugaag uaccucaguu agugaacgcu 1560aaucaauacu cacccugugu auccauuguc ccauccacug uguggggaaga cggugauuau 1620uauaggaaac aacuaucucc acuugaaggu gguggcuggc uuguugcuag uggcucaacu 1680guugccauga cugagcaauu acagaugggc uuugguauua caguucaaua ugguacagac 1740accaauagug uuugccccaa gcuugaauuu gcuaaugaca caaaaauugc cucucaauua 1800ggcaauugcg uggaauauuc ccucuauggu guuucgggcc gugguguuuu ucagaauugc 1860acagcuguag guguucgaca gcagcgcuuu guuuaugaug cguaccagaa uuuaguuggc 1920uauuauucug augauggcaa cuacuacugu uugcgugcuu guguuagugu uccuguuucu 1980gucaucuaug auaaagaaac uaaaacccac gcuacucuau uugguagugu ugcaugugaa 2040cacauuucuu

cuaccauguc ucaauacucc cguucuacgc gaucaaugcu uaaacggcga 2100gauucuacau auggcccccu ucagacaccu guugguugug uccuaggacu uguuaauucc 2160ucuuuguucg uagaggacug caaguugccu cuuggucaau cucucugugc ucuuccugac 2220acaccuagua cucucacacc ucgcagugug cgcucuguuc caggugaaau gcgcuuggca 2280uccauugcuu uuaaucaucc uauucagguu gaucaacuua auaguaguua uuuuaaauua 2340aguauaccca cuaauuuuuc cuuuggugug acucaggagu acauucagac aaccauucag 2400aaaguuacug uugauuguaa acaguacguu ugcaauggu uccagaagug ugagcaauua 2460cugcgcgagu auggccaguu uuguuccaaa auaaaccagg cucuccaugg ugccaauuua 2520cgccaggaug auucuguacg uaauuuguuu gcgagcguga aaagcucuca aucaucuccu 2580aucauaccag guuuuggagg ugacuuuaau uugacacuuc uggaaccugu uucuauaucu 2640acuggcaguc guagugcacg uagugcuauu gaggauuugc uauuugacaa agucacuaua 2700gcugauccug guuauaugca agguuacgau gauugcaugc agcaagguccc agcaucagcu 2760cgugaucuua uuugugcuca auauguggcu gguuacaaag uauuaccucc ucuuauggau 2820guuaauaugg aagccgcgua uacuucaucu uugcuuggca gcauagcagg uguuggcugg 2880acugcuggcu uauccuccuu ugcugcuauu ccauuugcac agaguaucuu uuauagguua 2940aacgguguug gcauuacuca acagguucuu ucagagaacc aaaagcuuau ugccaauaag 3000uuuaaucagg cucugggagc uaugcaaaca ggcuucacua caacuaauga agcuuuucag 3060aagguucagg augcugugaa caacaaugca caggcucuau ccaaauuagc uagcgagcua 3120ucuaauacuu uuggugcuau uuccgccucu auuggagaca ucauacaacg ucuugauguu 3180cucgaacagg acgcccaaau agacagacuu auuaauggcc guuugacaac acuaaaugcu 3240uuuguugcac agcagcuugu ucguuccgaa ucagcugcuc uuuccgcuca auuggcuaaa 3300gauaaaguca augagugugu caaggcacaa uccaagcguu cuggauuuug cggucaaggc 3360acacauauag uguccuuugu uguaaaugcc ccuaauggcc uuuacuucau gcauguuggu 3420uauuacccua gcaaccacau ugagguuguu ucugcuuaug gucuuugcga ugcagcuaac 3480ccuacuaauu guauagcccc uguuaauggc uacuuuauua aaacuaauaa cacuaggauu 3540guugaugagu ggucauauac uggcucgucc uucuaugcac cugagcccau uaccucccuu 3600aauacuaagu auguugcacc acaggugaca uaccaaaaca uuucuacuaa ccucccuccu 3660ccucuucucg gcaauuccac cgggauugac uuccaagaug aguuggauga guuuuucaaa 3720aauguuagca ccaguauacc uaauuuuggu ucccuaacac agauuaauac uacauuacuc 3780gaucuuaccu acgagauguu gucucuucaa caaguuguua aagcccuuaa ugagucuuac 3840auagaccuua aagagcuugg caauuauacu uauuacaaca aauggccgug guacauuugg 3900cuugguuuca uugcugggcu uguugccuua gcucuaugcg ucuucuucau acugugcugc 3960acugguugug gcacaaacug uaugggaaaa cuuaagugua aucguuguug ugauagauac 4020gaggaauacg accucgagcc gcauaagguu cauguucacu aa 4062671845RNAArtificial SequenceSynthetic Polynucleotide 67augauccacu ccguguuccu ccucauguuc cuguugaccc ccacugaguc agacugcaag 60cucccgcugg gacagucccu gugugcgcug ccugacacuc cuagcacucu gaccccacgc 120uccgugcggu cggugccugg cgaaaugcgg cuggccucca ucgccuucaa ucacccaauc 180caaguggauc agcugaauag cucguauuuc aagcugucca uccccacgaa cuucucguuc 240ggggucaccc aggaguacau ccagaccaca auucagaagg ucaccgucga uugcaagcaa 300uacgugugca acggcuucca gaagugcgag cagcugcuga gagaauacgg gcaguuuugc 360agcaagauca accaggcgcu gcauggagcu aacuugcgcc aggacgacuc cgugcgcaac 420cucuuugccu cugugaaguc aucccagucc uccccaauca ucccgggauu cggaggggac 480uucaaccuga cccuccugga gcccgugucg aucagcaccg guagcagauc ggcgcgcuca 540gccauugaag aucuucuguu cgacaagguc accaucgccg auccgggcua caugcaggga 600uacgacgacu guaugcagca gggaccagcc uccgcgaggg accucaucug cgcgcaauac 660guggccgggu acaaagugcu gccuccucug auggauguga acauggaggc cgcuuauacu 720ucgucccugc ucggcucuau cgccggcgug ggguggaccg ccggccuguc cuccuucgcc 780gcuauccccu uugcacaauc cauuuucuac cggcucaacg gcgugggcau uacucaacaa 840guccugucgg agaaccagaa guugaucgca aacaaguuca aucaggcccu gggggccaug 900cagacuggau ucacuacgac uaacgaagcg uuccagaagg uccaggacgc ugugaacaac 960aacgcccagg cgcucucaaa gcuggccucc gaacucagca acaccuucgg agccaucagc 1020gcaucgaucg gugacauaau ucagcggcug gacgugcugg agcaggacgc ccagaucgac 1080cgccucauca acggacggcu gaccaccuug aaugccuucg uggcacaaca gcugguccgg 1140agcgaaucag cggcacuuuc cgcccaacuc gccaaggaca aagucaacga augcgugaag 1200gcccagucca agagguccgg uuucugcggu caaggaaccc auauuguguc cuucgucgug 1260aacgcgccca acggucugua cuuuaugcac gucggcuacu acccgagcaa ucauaucgaa 1320guggguguccg ccuacggccu gugcgaugcc gcuaacccca cuaacuguau ugccccugug 1380aacggauauu uuauuaagac caacaacacc cgcauugugg acgaaugguc auacaccggu 1440ucguccuucu acgcgcccga gcccaucacu ucacugaaca ccaaauacgu ggcuccgcaa 1500gugaccuacc agaacaucuc caccaauuug ccgccgccgc ugcucggaaa cagcaccgga 1560auugauuucc aagaugaacu ggacgaauuc uucaagaacg uguccacuuc cauucccaac 1620uucggaagcc ugacacagau caacaccacc cuucucgacc ugaccuacga gaugcugagc 1680cuucaacaag uggucaaggc ccugaacgag agcuacaucg accugaagga gcugggcaac 1740uauaccuacu acaacaagug gccggacaag auugaggaga uucugucgaa aaucuaccac 1800auugaaaacg agaucgccag aaucaagaag cuuaucggcg aagcc 1845684071RNAArtificial SequenceSynthetic Polynucleotide 68auggaaaccc cugcccagcu gcuguuccug cugcugcugu ggcugccuga uaccaccggc 60agcuaugugg acgugggccc cgauagcgug aaguccgccu guaucgaagu ggacauccag 120cagaccuuuu ucgacaagac cuggcccaga cccaucgacg uguccaaggc cgacggcauc 180aucuauccac aaggccggac cuacagcaac aucaccauua ccuaccaggg ccuguuccca 240uaucaaggcg accacggcga uauguacgug uacucugccg gccacgccac cggcaccaca 300ccccagaaac uguucguggc caacuacagc caggacguga agcaguucgc caacggcuuc 360gucgugcgga uuggcgccgc ugccaauagc accggcacag ugaucaucag ccccagcacc 420agcgccacca uccggaagau cuaccccgcc uucaugcugg gcagcuccgu gggcaauuuc 480agcgacggca agaugggccg guucuucaac cacacccugg ugcugcugcc cgauggcugu 540ggcacacugc ugagagccuu cuacugcauc cuggaaccca gaagcggcaa ccacugcccu 600gccggcaaua gcuacaccag cuucgccacc uaccacacac ccgccaccga uugcuccgac 660ggcaacuaca accggaacgc cagccugaac agcuucaaag aguacuucaa ccugcggaac 720ugcaccuuca uguacaccua caauaucacc gaggacgaga uccuggaaug guucggcauc 780acccagaccg cccagggcgu gcaccuguuc agcagcagau acguggaccu guacggcggc 840aacauguucc aguuugccac ccugcccgug uacgacacca ucaaguacua cagcaucauc 900ccccacagca uccgguccau ccagagcgac agaaaagccu gggccgccuu cuacguguac 960aagcugcagc cccugaccuu ccugcuggac uucagcgugg acggcuacau cagacgggcc 1020aucgacugcg gcuucaacga ccugagccag cugcacugcu ccuacgagag cuucgacgug 1080gaaagcggcg uguacagcgu guccagcuuc gaggccaagc cuagcggcag cgugguggaa 1140caggcugagg gcguggaaug cgacuucagc ccucugcuga gcggcacccc uccccaggug 1200uacaacuuca agcggcuggu guucaccaac ugcaauuaca accugaccaa gcugcugagc 1260cuguucuccg ugaacgacuu caccuguagc cagaucagcc cugccgccau ugccagcaac 1320ugcuacagca gccugauccu ggacuacuuc agcuaccccc ugagcaugaa guccgaucug 1380agcguguccu ccgccggacc caucagccag uucaacuaca agcagagcuu cagcaacccu 1440accugccuga uucuggccac cgugccccac aaucugacca ccaucaccaa gccccugaag 1500uacagcuaca ucaacaagug cagcagacug cuguccgacg accggaccga agugccccag 1560cucgugaacg ccaaccagua cagccccugc guguccaucg ugcccagcac cgugugggag 1620gacggcgacu acuacagaaa gcagcugagc ccccuggaag gcggcggaug gcugguggcu 1680ucuggaagca caguggccau gaccgagcag cugcagaugg gcuuuggcau caccgugcag 1740uacggcaccg acaccaacag cgugugcccc aagcuggaau ucgccaauga caccaagauc 1800gccagccagc ugggaaacug cguggaauac ucccuguaug gcguguccgg acggggcgug 1860uuccagaauu gcacagcagu gggagugcgg cagcagagau ucguguacga ugccuaccag 1920aaccucgugg gcuacuacag cgacgacggc aauuacuacu gccugcgggc cugugugucc 1980gugcccgugu ccgugaucua cgacaaagag acaaagaccc acgccacacu guucggcucc 2040guggccugcg agcacaucag cuccaccaug agccaguacu cccgcuccac ccgguccaug 2100cugaagcgga gagauagcac cuacggcccc cugcagacac cugugggaug ugugcugggc 2160cucgugaaca gcucccuguu uguggaagau ugcaagcugc cccugggcca gagccugugu 2220gcccugccag auaccccuag cacccugacc ccuagaagcg ugcgcucugu gcccggcgaa 2280augcggcugg ccucuaucgc cuucaaucac cccauccagg uggaccagcu gaacuccagc 2340uacuucaagc ugagcauccc caccaacuuc agcuucggcg ugacccagga guacauccag 2400accacaaucc agaaagugac cguggacugc aagcaguacg ugugcaacgg cuuucagaag 2460ugcgaacagc ugcugcgcga guacggccag uucugcagca agaucaacca ggcccugcac 2520ggcgccaacc ugagacagga ugacagcgug cggaaccugu ucgccagcgu gaaaagcagc 2580caguccagcc ccaucauccc uggcuucggc ggcgacuuua accugacccu gcuggaaccu 2640guguccauca gcaccggcuc cagaagcgcc agauccgcca ucgaggaccu gcuguucgac 2700aaagugacca uugccgaccc cggcuacaug cagggcuacg acgauugcau gcagcagggc 2760ccagccagcg ccagggaucu gaucugugcc caguaugugg ccggcuacaa ggugcugccc 2820ccccugaugg acgugaacau ggaagccgcc uacaccucca gccugcuggg cucuauugcu 2880ggcgugggau ggacagccgg ccugucuagc uuugccgcca ucccuuucgc ccagagcauc 2940uucuaccggc ugaacggcgu gggcaucaca caacaggugc ugagcgagaa ccagaagcug 3000aucgccaaca aguuuaacca ggcacugggc gccaugcaga ccggcuucac caccaccaac 3060gaggccuuca gaaaggugca ggacgccgug aacaacaacg cccaggcucu gagcaagcug 3120gccuccgagc ugagcaauac cuucggcgcc aucagcgccu ccaucggcga caucauccag 3180cggcuggacg ugcuggaaca ggacgcccag aucgaccggc ugaucaacgg cagacugacc 3240acccugaacg ccuucguggc acagcagcuc gugcggagcg aaucugccgc ucugucugcu 3300cagcuggcca aggacaaagu gaacgagugc gugaaggccc aguccaagcg gagcggcuuu 3360uguggccagg gcacccacau cguguccuuc gucgugaaug ccccaacgg ccuguacuuu 3420augcacgugg gcuauuaccc cagcaaccac aucgaggugg uguccgccua uggccugugc 3480gacgccgcca auccuaccaa cuguaucgcc cccgugaacg gcuacuucau caagaccaac 3540aacacccgga ucguggacga gugguccuac acaggcagca gcuucuacgc ccccgagccc 3600aucaccuccc ugaacaccaa auacguggcc ccccaaguga cauaccagaa caucuccacc 3660aaccugcccc cuccacugcu gggaaauucc accggcaucg acuuccagga cgagcuggac 3720gaguucuuca agaacguguc caccuccauc cccaacuucg gcagccugac ccagaucaac 3780accacucugc uggaccugac cuacgagaug cugucccugc aacaggucgu gaaagcccug 3840aacgagagcu acaucgaccu gaaagagcug gggaacuaca ccuacuacaa caaguggccu 3900ugguacauuu ggcugggcuu uaucgccggc cugguggccc uggcccugug cguguucuuc 3960auccugugcu gcaccggcug cggcaccaau ugcaugggca agcugaaaug caaccggugc 4020ugcgacagau acgaggaaua cgaccuggaa ccucacaaag ugcaugugca c 4071691864RNAArtificial SequenceSynthetic Polynucleotide 69ucaagcuuuu ggacccucgu acagaagcua auacgacuca cuauagggaa auaagagaga 60aaagaagagu aagaagaaau auaagagcca ccaugggucu caaggugaac gucucugccg 120uauucauggc aguacuguua acucuccaaa cacccgccgg ucaaauucau uggggcaauc 180ucucuaagau agggguagua ggaauaggaa gugcaagcua caaaguuaug acucguucca 240gccaucaauc auuagucaua aaauuaaugc ccaauauaac ucuccucaau aacugcacga 300ggguagagau ugcagaauac aggagacuac uaagaacagu uuuggaacca auuagggaug 360cacuuaaugc aaugacccag aacauaaggc cgguucagag cguagcuuca aguaggagac 420acaagagauu ugcgggagua guccuggcag gugcggcccu agguguugcc acagcugcuc 480agauaacagc cggcauugca cuucaccggu ccaugcugaa cucucaggcc aucgacaauc 540ugagagcgag ccuggaaacu acuaaucagg caauugaggc aaucagacaa gcagggcagg 600agaugauauu ggcuguucag ggguguccaag acuacaucaa uaaugagcug auaccgucua 660ugaaccagcu aucuugugau cuaaucgguc agaagcucgg gcucaaauug cuuagauacu 720auacagaaau ccugucauua uuuggcccca gccuacggga ccccauaucu gcggagauau 780cuauccaggc uuugaguuau gcacuuggag gagauaucaa uaagguguua gaaaagcucg 840gauacagugg aggcgauuua cuaggcaucu uagagagcag aggaauaaag gcucggauaa 900cucacgucga cacagagucc uacuucauag uccucaguau agccuauccg acgcuguccg 960agauuaaggg ggugauuguc caccggcuag agggggucuc guacaacaua ggcucucaag 1020agugguauac cacugugccc aaguauguug caacccaagg guaccuuauc ucgaauuuug 1080augagucauc auguacuuuc augccagagg ggacugugug cagccaaaau gccuuguacc 1140cgaugagucc ucugcuccaa gaaugccucc gggggguccac caaguccugu gcucguacac 1200ucguauccgg gucuuuuggg aaccgguuca uuuuaucaca agggaaccua auagccaauu 1260gugcaucaau ucuuuguaag uguuacacaa cagguacgau uauuaaucaa gacccugaca 1320agauccuaac auacauugcu gccgaucgcu gcccgguagu cgaggugaac ggcgugacca 1380uccaagucgg gagcaggagg uauccagacg cuguguacuu gcacagaauu gaccucgguc 1440cucccauauc auuggagagg uuggacguag ggacaaaucu ggggaaugca auugccaaau 1500uggaggaugc caaggaauug uuggaaucau cggaccagau auugagaagu augaaagguu 1560uaucgagcac uagcauaguc uacauccuga uugcagugug ucuuggaggg uugauaggga 1620ucccccacuuu aauauguugc ugcaggggggc guuguaacaa aaagggagaa caaguuggua 1680ugucaagacc aggccuaaag ccugaccuua caggaacauc aaaauccuau guaagaucgc 1740uuugaugaua auaggcugga gccucggugg ccaagcuucu ugccccuugg gccucccccc 1800agccccuccu ccccuuccug cacccguacc cccguggucu uugaauaaag ucugaguggg 1860cggc 1864701653RNAArtificial SequenceSynthetic Polynucleotide 70augggucuca aggugaacgu cucugccgua uucauggcag uacuguuaac ucuccaaaca 60cccgccgguc aaauucauug gggcaaucuc ucuaagauag ggguaguagg aauaggaagu 120gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa auuaaugccc 180aauauaacuc uccucaauaa cugcacgagg guagagauug cagaauacag gagacuacua 240agaacaguuu uggaaccaau uagggaugca cuuaaugcaa ugacccagaa cauaaggccg 300guucagagcg uagcuucaag uaggagacac aagagauuug cgggaguagu ccuggcaggu 360gcggcccuag guguugccac agcugcucag auaacagccg gcauugcacu ucaccggucc 420augcugaacu cucaggccau cgacaaucug agagcgagcc uggaaacuac uaaucaggca 480auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagac 540uacaucaaua augagcugau accgucuaug aaccagcuau cuugugaucu aaucggucag 600aagcucgggc ucaaauugcu uagauacuau acagaaaucc ugucauuauu uggccccagc 660cuacgggacc ccauaucugc ggagauaucu auccaggcuu ugaguuaugc acuuggagga 720gauaucaaua agguguuaga aaagcucgga uacaguggag gcgauuuacu aggcaucuua 780gagagcagag gaauaaaggc ucggauaacu cacgucgaca cagaguccua cuucauaguc 840cucaguauag ccuauccgac gcuguccgag auuaaggggg ugauugucca ccggcuagag 900ggggucucgu acaacauagg cucucaagag ugguauacca cugugcccaa guauguugca 960acccaagggu accuuaucuc gaauuuugau gagucaucau guacuuucau gccagagggg 1020acugugugca gccaaaaugc cuuguacccg augaguccuc ugcuccaaga augccuccgg 1080ggguccacca aguccugugc ucguacacuc guauccgggu cuuuugggaa ccgguucauu 1140uuaucacaag ggaaccuaau agccaauugu gcaucaauuc uuuguaagug uuacacaaca 1200gguacgauua uuaaucaaga cccugacaag auccuaacau acauugcugc cgaucgcugc 1260ccgguagucg aggugaacgg cgugaccauc caagucggga gcaggaggua uccagacgcu 1320guguacuugc acagaauuga ccucgguccu cccauaucau uggagagguu ggacguaggg 1380acaaaucugg ggaaugcaau ugccaaauug gaggaugcca aggaauuguu ggaaucaucg 1440gaccagauau ugagaaguau gaaagguuua ucgagcacua gcauagucua cauccugauu 1500gcagugugu c uuggagggu u gauagggauc cccacuuuaa uauguugcug caggggggcgu 1560uguaacaaaa agggagaaca aguugguaug ucaagaccag gccuaaagcc ugaccuuaca 1620ggaacaucaa aauccuaugu aagaucgcuu uga 1653711925RNAArtificial SequenceSynthetic Polynucleotide 71ggggaaauaa gagagaaaag aagaguaaga agaaauauaa gagccaccau gggucucaag 60gugaacgucu cugccguauu cauggcagua cuguuaacuc uccaaacacc cgccggucaa 120auucauuggg gcaaucucuc uaagauaggg guaguaggaa uaggaagugc aagcuacaaa 180guuaugacuc guuccagcca ucaaucauua gucauaaaau uaaugcccaa uauaacucuc 240cucaauaacu gcacgagggu agagauugca gaauacagga gacuacuaag aacaguuuug 300gaaccaauua gggaugcacu uaaugcaaug acccagaaca uaaggccggu ucagagcgua 360gcuucaagua ggagacacaa gagauuugcg ggaguagucc uggcaggugc ggcccuaggu 420guugccacag cugcucagau aacagccggc auugcacuuc accgguccau gcugaacucu 480caggccaucg acaaucugag agcgagccug gaaacuacua aucaggcaau ugaggcaauc 540agacaagcag ggcaggagau gauauuggcu guucagggug uccaagacua caucaauaau 600gagcugauac cgucuaugaa ccagcuaucu ugugaucuaa ucggucagaa gcucgggcuc 660aaauugcuua gauacuauac agaaauccug ucauuauuug gccccagccu acgggacccc 720auaucugcgg agauaucuau ccaggcuuug aguuaugcac uuggaggaga uaucaauaag 780guguuagaaa agcucggaua caguggaggc gauuuacuag gcaucuuaga gagcagagga 840auaaaggcuc ggauaacuca cgucgacaca gaguccuacu ucauaguccu caguauagcc 900uauccgacgc uguccgagau uaaggggggug auuguccacc ggcuagaggg ggucucguac 960aacauaggcu cucaagagug guauaccacu gugcccaagu auguugcaac ccaaggguac 1020cuuaucucga auuuugauga gucaucaugu acuuucaugc cagaggggac ugugugcagc 1080caaaaugccu uguacccgau gaguccucug cuccaagaau gccuccgggg guccaccaag 1140uccugugcuc guacacucgu auccgggucu uuugggaacc gguucauuuu aucacaaggg 1200aaccuaauag ccaauugugc aucaauucuu uguaaguguu acacaacagg uacgauuauu 1260aaucaagacc cugacaagau ccuaacauac auugcugccg aucgcugccc gguagucgag 1320gugaacggcg ugaccaucca agucgggagc aggagguauc cagacgcugu guacuugcac 1380agaauugacc ucgguccucc cauaucauug gagagguugg acguagggac aaaucugggg 1440aaugcaauug ccaaauugga ggaugccaag gaauuguugg aaucaucgga ccagauauug 1500agaaguauga aagguuuauc gagcacuagc auagucuaca uccugauugc agugugucuu 1560ggaggguuga uagggauccc cacuuuaaua uguugcugca gggggcguug uaacaaaaag 1620ggagaacaag uugguauguc aagaccaggc cuaaagccug accuuacagg aacaucaaaa 1680uccuauguaa gaucgcuuug augauaauag gcuggagccu cgguggccaa gcuucuugcc 1740ccuugggccu ccccccagcc ccuccucccc uuccugcacc cguacccccg uggucuuuga 1800auaaagucug agugggcggc aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920ucuag 1925721864RNAArtificial SequenceSynthetic Polynucleotide 72ucaagcuuuu ggacccucgu acagaagcua auacgacuca cuauagggaa auaagagaga 60aaagaagagu aagaagaaau auaagagcca ccaugggucu caaggugaac gucucuguca 120uauucauggc aguacuguua acucuucaaa cacccaccgg ucaaauccau uggggcaauc 180ucucuaagau agggguggua gggguaggaa gugcaagcua caaaguuaug acucguucca 240gccaucaauc auuagucaua aaguuaaugc ccaauauaac ucuccucaac aauugcacga 300ggguagggau ugcagaauac aggagacuac ugagaacagu ucuggaacca auuagagaug 360cacuuaaugc aaugacccag aauauaagac cgguucagag uguagcuuca aguaggagac 420acaagagauu ugcgggaguu guccuggcag gugcggcccu aggcguugcc acagcugcuc 480aaauaacagc cgguauugca cuucaccagu ccaugcugaa cucucaagcc aucgacaauc 540ugagagcgag ccuagaaacu acuaaucagg caauugaggc aaucagacaa gcagggcagg 600agaugauauu ggcuguucag ggguguccaag acuacaucaa uaaugagcug auaccgucua 660ugaaucaacu aucuugugau uuaaucggcc agaagcuagg gcucaaauug cucagauacu 720auacagaaau ccugucauua uuuggcccca gcuuacggga ccccauaucu gcggagauau 780cuauccaggc uuugagcuau gcgcuuggag gagauaucaa uaagguguug gaaaagcucg 840gauacagugg aggugaucua cugggcaucu uagagagcag aggaauaaag gcccggauaa 900cucacgucga cacagagucc uacuucauug uacucaguau agccuauccg acgcuauccg 960agauuaaggg ggugauuguc caccggcuag agggggucuc guacaacaua ggcucucaag 1020agugguauac cacugugccc aaguauguug caacccaagg guaccuuauc ucgaauuuug 1080augagucauc augcacuuuc augccagagg ggacugugug cagccagaau gccuuguacc 1140cgaugagucc

ucugcuccaa gaaugccucc gggggguccac uaaguccugu gcucguacac 1200ucguauccgg gucuuucggg aaccgguuca uuuuaucaca ggggaaccua auagccaauu 1260gugcaucaau ccuuugcaag uguuacacaa caggaacaau cauuaaucaa gacccugaca 1320agauccuaac auacauugcu gccgaucacu gcccggguggu cgaggugaau ggcgugacca 1380uccaagucgg gagcaggagg uauccggacg cuguguacuu gcacaggauu gaccucgguc 1440cucccauauc uuuggagagg uuggacguag ggacaaaucu ggggaaugca auugcuaagu 1500uggaggaugc caaggaauug uuggagucau cggaccagau auugaggagu augaaagguu 1560uaucgagcac uaguauaguu uacauccuga uugcagugug ucuuggagga uugauaggga 1620ucccgcuuu aauauguugc ugcagggggc guuguaacaa gaagggagaa caaguuggua 1680ugucaagacc aggccuaaag ccugaucuua caggaacauc aaaauccuau guaaggucac 1740ucugaugaua auaggcugga gccucggugg ccaagcuucu ugccccuugg gccuccccc 1800agccccuccu ccccuuccug cacccguacc cccgugcucu uugaauaaag ucugaguggg 1860cggc 1864731653RNAArtificial SequenceSynthetic Polynucleotide 73augggucuca aggugaacgu cucugucaua uucauggcag uacuguuaac ucuucaaaca 60cccaccgguc aaauccauug gggcaaucuc ucuaagauag ggguggguagg gguaggaagu 120gcaagcuaca aaguuaugac ucguuccagc caucaaucau uagucauaaa guuaaugccc 180aauauaacuc uccucaacaa uugcacgagg guagggauug cagaauacag gagacuacug 240agaacaguuc uggaaccaau uagagaugca cuuaaugcaa ugacccagaa uauaagaccg 300guucagagug uagcuucaag uaggagacac aagagauuug cgggaguugu ccuggcaggu 360gcggcccuag gcguugccac agcugcucaa auaacagccg guauugcacu ucaccagucc 420augcugaacu cucaagccau cgacaaucug agagcgagcc uagaaacuac uaaucaggca 480auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagac 540uacaucaaua augagcugau accgucuaug aaucaacuau cuugugauuu aaucggccag 600aagcuagggc ucaaauugcu cagauacuau acagaaaucc ugucauuauu uggccccagc 660uuacgggacc ccauaucugc ggagauaucu auccaggcuu ugagcuaugc gcuuggagga 720gauaucaaua agguguugga aaagcucgga uacaguggag gugaucuacu gggcaucuua 780gagagcagag gaauaaaggc ccggauaacu cacgucgaca cagaguccua cuucauugua 840cucaguauag ccuauccgac gcuauccgag auuaaggggg ugauugucca ccggcuagag 900ggggucucgu acaacauagg cucucaagag ugguauacca cugugcccaa guauguugca 960acccaagggu accuuaucuc gaauuuugau gagucaucau gcacuuucau gccagagggg 1020acugugugca gccagaaugc cuuguacccg augaguccuc ugcuccaaga augccuccgg 1080ggguccacua aguccugugc ucguacacuc guauccgggu cuuucgggaa ccgguucauu 1140uuaucacagg ggaaccuaau agccaauugu gcaucaaucc uuugcaagug uuacacaaca 1200ggaacaauca uuaaucaaga cccugacaag auccuaacau acauugcugc cgaucacugc 1260ccgguggucg aggugaaugg cgugaccauc caagucggga gcaggaggua uccggacgcu 1320guguacuugc acaggauuga ccucggcccu cccauaucuu uggagagguu ggacguaggg 1380acaaaucugg ggaaugcaau ugcuaaguug gaggaugcca aggaauuguu ggagucaucg 1440gaccagauau ugaggaguau gaaagguuua ucgagcacua guauaguuua cauccugauu 1500gcagugugu c uuggaggauu gauagggauc cccgcuuuaa uauguugcug caggggggcgu 1560uguaacaaga agggagaaca aguugguaug ucaagaccag gccuaaagcc ugaucuuaca 1620ggaacaucaa aauccuaugu aaggucacuc uga 1653741925RNAArtificial SequenceSynthetic Polynucleotide 74ggggaaauaa gagagaaaag aagaguaaga agaaauauaa gagccaccau gggucucaag 60gugaacgucu cugucauauu cauggcagua cuguuaacuc uucaaacacc caccggucaa 120auccauuggg gcaaucucuc uaagauaggg gugguagggg uaggaagugc aagcuacaaa 180guuaugacuc guuccagcca ucaaucauua gucauaaagu uaaugcccaa uauaacucuc 240cucaacaauu gcacgagggu agggauugca gaauacagga gacuacugag aacaguucug 300gaaccaauua gagaugcacu uaaugcaaug acccagaaua uaagaccggu ucagagugua 360gcuucaagua ggagacacaa gagauuugcg ggaguugucc uggcaggugc ggcccuaggc 420guugccacag cugcucaaau aacagccggu auugcacuuc accaguccau gcugaacucu 480caagccaucg acaaucugag agcgagccua gaaacuacua aucaggcaau ugaggcaauc 540agacaagcag ggcaggagau gauauuggcu guucagggug uccaagacua caucaauaau 600gagcugauac cgucuaugaa ucaacuaucu ugugauuuaa ucggccagaa gcuagggcuc 660aaauugcuca gauacuauac agaaauccug ucauuauuug gccccagcuu acgggacccc 720auaucugcgg agauaucuau ccaggcuuug agcuaugcgc uuggaggaga uaucaauaag 780guguuggaaa agcucggaua caguggaggu gaucuacugg gcaucuuaga gagcagagga 840auaaaggccc ggauaacuca cgucgacaca gaguccuacu ucauuguacu caguauagcc 900uauccgacgc uauccgagau uaaggggggug auuguccacc ggcuagaggg ggucucguac 960aacauaggcu cucaagagug guauaccacu gugcccaagu auguugcaac ccaaggguac 1020cuuaucucga auuuugauga gucaucaugc acuuucaugc cagaggggac ugugugcagc 1080cagaaugccu uguacccgau gaguccucug cuccaagaau gccuccgggg guccacuaag 1140uccugugcuc guacacucgu auccgggucu uucgggaacc gguucauuuu aucacagggg 1200aaccuaauag ccaauugugc aucaauccuu ugcaaguguu acacaacagg aacaaucauu 1260aaucaagacc cugacaagau ccuaacauac auugcugccg aucacugccc gguggucgag 1320gugaauggcg ugaccaucca agucgggagc aggagguauc cggacgcugu guacuugcac 1380aggauugacc ucgguccucc cauaucuuug gagagguugg acguagggac aaaucugggg 1440aaugcaauug cuaaguugga ggaugccaag gaauuguugg agucaucgga ccagauauug 1500aggaguauga aagguuuauc gagcacuagu auaguuuaca uccugauugc agugugucuu 1560ggaggauuga uagggauccc cgcuuuaaua uguugcugca gggggcguug uaacaagaag 1620ggagaacaag uugguauguc aagaccaggc cuaaagccug aucuuacagg aacaucaaaa 1680uccuauguaa ggucacucug augauaauag gcuggagccu cgguggccaa gcuucuugcc 1740ccuugggccu ccccccagcc ccuccucccc uuccugcacc cguacccccg uggucuuuga 1800auaaagucug agugggcggc aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1920ucuag 1925752065RNAArtificial SequenceSynthetic Polynucleotide 75ucaagcuuuu ggacccucgu acagaagcua auacgacuca cuauagggaa auaagagaga 60aaagaagagu aagaagaaau auaagagcca ccaugucacc gcaacgagac cggauaaaug 120ccuucuacaa agauaacccu uaucccaagg gaaguaggau aguuauuaac agagaacauc 180uuaugauuga cagacccuau guucugcugg cuguucuguu cgucauguuu cugagcuuga 240ucggauugcu ggcaauugca ggcauuagac uucaucgggc agccaucuac accgcggaga 300uccauaaaag ccucaguacc aaucuggaug ugacuaacuc caucgagcau caggucaagg 360acgugcugac accacucuuu aaaaucaucg gggaugaagu gggccugaga acaccucaga 420gauucacuga ccuagugaaa uucaucucgg acaagauuaa auuccuuaau ccggauaggg 480aguacgacuu cagagaucuc acuuggugca ucaacccgcc agagaggauc aaacuagauu 540augaucaaua cugugcagau guggcugcug aagagcucau gaaugcauug gugaacucaa 600cucuacugga gaccagaaca accacucagu uccuagcugu cucaaaggga aacugcucag 660ggcccacuac aaucagaggu caauucucaa acaugucgcu gucuuguug gacuuguacu 720uaggucgagg uuacaaugug ucaucuauag ucacuaugac aucccaggga auguaugggg 780gaaccuaccu aguugaaaag ccuaaucuga acagcaaagg gucagaguug ucacaacuga 840gcauguaccg aguguuugaa guaggugugа ucagaaaccc ggguuugggg gcuccggugu 900uccauaugac aaacuauuuu gagcaaccag ucaguaaugg ucucggcaac uguauggugg 960cuuuggggga gcucaaacuc gcagcccuuu gucacgggga cgauucuauc auaaauuccu 1020aucagggauc agggaaaggu gucagcuucc agcucgucaa gcugggguguc uggaaauccc 1080caaccgacau gcaauccugg gucccuuau caacggauga uccaguggua gacaggcuuu 1140accucucauc ucacagaggu gucaucgcug acaaucaagc aaaaugggcu gucccgacaa 1200cacgaacaga ugacaaguug cgaauggaga caugcuucca gcaggcgugu aaagguaaaa 1260uccaagcacu cugcgagaau cccgaguggg uaccauugaa ggauaacagg auuccuucau 1320acgggguccu gucuguugau cugagucuga cgguugagcu uaaaaucaaa auugcuucgg 1380gauucgggcc auugaucaca cacggcucag ggauggaccu auacaaaucc aacugcaaca 1440auguguauug gcugacuauu ccgccaauga gaaaucuagc cuuaggcgua aucaacacau 1500uggaguggau accgagauuc aagguuaguc ccaaccucuu cacuguccca auuaaggaag 1560caggcgaaga cugccaugcc ccaacauacc uaccugcgga ggguggacggu gaugucaaac 1620ucaguuccaa ccuggugauu cuaccugguc aagaucucca auauguuuug gcaaccuacg 1680auaccuccag gguugagcau gcugugguuu auuacguuua cagcccaagc cgcucauuuu 1740cuuacuuuua uccuuuuagg uugccuauaa agggggucccc aaucgaacua caaguggaau 1800gcuucacaug ggaucaaaaa cucuggugcc gucacuucug ugugcuugcg gacucagaau 1860ccgguggacu uaucacucac ucugggaugg ugggcauggg agucagcugc acagcuaccc 1920gggaagaugg aaccaaucgc agauaaugau aauaggcugg agccucggug gccaagcuuc 1980uugccccuug ggccuccccc cagccccucc ucccuucccu gcacccguac ccccguggguc 2040uuugaauaaa gucugagugg gcggc 2065761854RNAArtificial SequenceSynthetic Polynucleotide 76augucaccgc aacgagaccg gauaaaugcc uucuacaaag auaacccuua ucccaaggga 60aguaggauag uuauuaacag agaacaucuu augauugaca gacccuaugu ucugcuggcu 120guucuguucg ucauguuucu gagcuugauc ggauugcugg caauugcagg cauuagacuu 180caucgggcag ccaucuacac cgcggagauc cauaaaagcc ucaguaccaa ucuggaugug 240acuaacucca ucgagcauca ggucaaggac gugcugacac cacucuuuaa aaucaucggg 300gaugaagugg gccugagaac accucagaga uucacugacc uagugaaauu caucucggac 360aagauuaaau uccuuaaucc ggauagggag uacgacuuca gagaucucac uuggugcauc 420aacccgccag agaggaucaa acuagauuau gaucaauacu gugcagaugu ggcugcugaa 480gagcucauga augcauuggu gaacucaacu cuacuggaga ccagaacaac cacucaguuc 540cuagcugucu caaagggaaa cugcucaggg cccacuacaa ucagagguca auucucaaac 600augucgcugu ccuuguugga cuuguacuua ggucgagguu acaaugugc aucuauaguc 660acuaugacau cccagggaau guaugggga accuaccuag uugaaaagcc uaaucugaac 720agcaaagggu cagaguuguc acaacugagc auguaccgag uguuugaagu aggugugauc 780agaaacccgg guuuggggc uccgguguuc cauaugacaa acuauuuuga gcaaccaguc 840aguaaugguc ucggcaacug uaugguggcu uugggggagc ucaaacucgc agcccuuugu 900cacggggacg auucuaucau aaauucccuau cagggaucag ggaaaggugu cagcuuccag 960cucgucaagc ugggugucug gaaaucccca accgacaugc aauccugggu ccccuuauca 1020acggaugauc cagugguaga caggcuuuac cucucaucuc acagaggugu caucgcugac 1080aaucaagcaa aaugggcugu cccgacaaca cgaacagaug acaaguugcg aauggagaca 1140ugcuuccagc aggcguguaa agguaaaauc caagcacucu gcgagaaucc cgagugggua 1200ccauugaagg auaacaggau uccuucauac gggguccugu cuguugaucu gagucugacg 1260guugagcuua aaaucaaaau ugcuucggga uucgggccau ugaucacaca cggcucaggg 1320auggaccuau acaaauccaa cugcaacaau guguauuggc ugacuauucc gccaaugaga 1380aaucuagccu uaggcguaau caacacauug gaguggauac cgagauucaa gguuaguccc 1440aaccucuuca cugucccaau uaaggaagca ggcgaagacu gccaugcccc aacauaccua 1500ccugcggagg uggacgguga ugucaaacuc aguuccaacc uggugauucu accuggucaa 1560gaucuccaau auguuuuggc aaccuacgau accuccaggg uugagcaugc ugugguuuau 1620uacguuuaca gcccaagccg cucauuuucu uacuuuuauc cuuuuagguu gccuauaaag 1680gggguccсaa ucgaacuaca aguggaaugc uucacauggg aucaaaaacu cuggugccgu 1740cacuucugug ugcuugcgga cucagaaucc gguggacuua ucacucacuc ugggauggug 1800ggcaugggag ucagcugcac agcuacccgg gaagauggaa ccaaucgcag auaa 1854772126RNAArtificial SequenceSynthetic Polynucleotide 77ggggaaauaa gagagaaaag aagaguaaga agaaauauaa gagccaccau gucaccgcaa 60cgagaccgga uaaaugccuu cuacaaagau aacccuuauc ccaagggaag uaggauaguu 120auuaacagag aacaucuuau gauugacaga cccuauguuc ugcuggcugu ucuguucguc 180auguuucuga gcuugaucgg auugcuggca auugcaggca uuagacuuca ucgggcagcc 240aucuacaccg cggagaucca uaaaagccuc aguaccaauc uggaugugac uaacuccauc 300gagcaucagg ucaaggacgu gcugacacca cucuuuaaaa ucaucgggga ugaagugggc 360cugagaacac cucagagauu cacugaccua gugaaauuca ucucggacaa gauuaaauuc 420cuuaauccgg auagggagua cgacuucaga gaucucacuu ggugcaucaa cccgccagag 480aggaucaaac uagauuauga ucaauacugu gcagaugugg cugcugaaga gcucaugaau 540gcauugguga acucaacucu acuggagacc agaacaacca cucaguuccu agcugucuca 600aagggaaacu gcucagggcc cacuacaauc agaggucaau ucucaaacau gucgcugucc 660uuguuggacu uguacuuagg ucgagguuac aaugugucau cuauagucac uaugacaucc 720cagggaaugu augggggaac cuaccuaguu gaaaagccua aucugaacag caaaggguca 780gaguugucac aacugagcau guaccgagug uuugaaguag gugugaucag aaacccgggu 840uugggggcuc cgguguucca uaugacaaac uauuuugagc aaccagucag uaauggucuc 900ggcaacugua ugguggcuuu gggggagcuc aaacucgcag cccuuuguca cggggacgau 960ucuaucauaa uucccuauca gggaucaggg aaagguguca gcuuccagcu cgucaagcug 1020ggugucugga aaucccaac cgacaugcaa uccugggucc ccuuaucaac ggaugaucca 1080gugguagaca ggcuuuaccu cucaucucac agagguguca ucgcugacaa ucaagcaaaa 1140ugggcugucc cgacaacacg aacagaugac aaguugcgaa uggagacaug cuuccagcag 1200gcguguaaag guaaaaucca agcacucugc gagaaucccg aguggguacc auugaaggau 1260aacaggauuc cuucauacgg gguccugucu guugaucuga gucugacggu ugagcuuaaa 1320aucaaaauug cuucgggauu cgggccauug aucacacacg gcucagggau ggaccuauac 1380aaauccaacu gcaacaaugu guauuggcug acuauuccgc caaugagaaa ucuagccuua 1440ggcguaauca acacauugga guggauaccg agauucaagg uuagucccaa ccucuucacu 1500gucccaauua aggaagcagg cgaagacugc caugccccaa cauaccuacc ugcggaggug 1560gacggugaug ucaaacucag uuccaaccug gugauucuac cuggucaaga ucuccaauau 1620guuuuggcaa ccuacgauac cuccagggu gagcaugcug ugguuuauua cguuuacagc 1680ccaagccgcu cauuuucuua cuuuuauccu uuuagguugc cuauaaaggg ggucccaauc 1740gaacuacaag uggaaugcuu cacaugggau caaaaacucu ggugccguca cuucugugug 1800cuugcggacu cagaauccgg uggacuuauc acucacucug ggaugguggg caugggaguc 1860agcugcacag cuacccggga agauggaacc aaucgcagau aaugauaaua ggcuggagcc 1920ucgguggcca agcuucuugc cccuugggcc uccccccagc cccuccuccc cuuccugcac 1980ccguaccccc guggucuuug aauaaagucu gagugggcgg caaaaaaaaa aaaaaaaaaa 2040aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100aaaaaaaaaa aaaaaaaaaa aucuag 2126782065RNAArtificial SequenceSynthetic Polynucleotide 78ucaagcuuuu ggacccucgu acagaagcua auacgacuca cuauagggaa auaagagaga 60aaagaagagu aagaagaaau auaagagcca ccaugucacc acaacgagac cggauaaaug 120ccuucuacaa agacaacccc cauccuaagg gaaguaggau aguuauuaac agagaacauc 180uuaugauuga uagaccuuau guuuugcugg cuguucuauu cgucauguuu cugagcuuga 240ucggguugcu agccauugca ggcauuagac uucaucgggc agccaucuac accgcagaga 300uccauaaaag ccucagcacc aaucuggaug uaacuaacuc aaucgagcau cagguuaagg 360acgugcugac accacucuuc aagaucaucg gugaugaagu gggcuugagg acaccucaga 420gauucacuga ccuagugaag uucaucucug acaagauuaa auuccuuaau ccggacaggg 480aauacgacuu cagagaucuc acuuggugua ucaacccgcc agagagaauc aaauuggauu 540augaucaaua cugugcagau guggcugcug aagaacucau gaaugcauug gugaacucaa 600cucuacugga gaccagggca accaaucagu uccuagcugu cucaaaggga aacugcucag 660ggcccacuac aaucagaggc caauucucaa acaugucgcu gucccuguug gacuuguauu 720uaagucgagg uuacaaugug ucaucuauag ucacuaugac aucccaggga auguacgggg 780gaacuuaccu aguggaaaag ccuaaucuga gcagcaaagg gucagaguug ucacaacuga 840gcaugcaccg aguguuugaa guagguguua ucagaaaucc ggguuugggg gcuccgguau 900uccauaugac aaacuaucuu gagcaaccag ucaguaauga uuucagcaac ugcauggugg 960cuuuggggga gcucaaguuc gcagcccucu gucacaggga agauucuauc acaauucccu 1020aucagggauc agggaaaggu gucagcuucc agcuugucaa gcuagguguc uggaaauccc 1080caaccgacau gcaauccugg gucccccuau caacggauga uccagugaua gacaggcuuu 1140accucucauc ucacagaggc guuaucgcug acaaucaagc aaaaugggcu gucccgacaa 1200cacggacaga ugacaaguug cgaauggaga caugcuucca gcaggcgugu aaggguaaaa 1260uccaagcacu uugcgagaau cccgagugga caccauugaa ggauaacagg auuccuucau 1320acggggucuu gucuguugau cugagucuga caguugagcu uaaaaucaaa auuguuucag 1380gauucgggcc auugaucaca cacgguucag ggauggaccu auacaaaucc aaccacaaca 1440auauguauug gcugacuauc ccgccaauga agaaccuggc cuuaggugua aucaacacau 1500uggaguggau accgagauuc aagguuaguc ccaaccucuu cacuguucca auuaaggaag 1560caggcgagga cugccaugcc ccaacauacc uaccugcgga gguggauggu gaugucaaac 1620ucaguuccaa ucuggugauu cuaccugguc aagaucucca auauguucug gcaaccuacg 1680auacuuccag aguugaacau gcuguaguuu auuacguuua cagcccaagc cgcucauuuu 1740cuuacuuuua uccuuuuagg uugccuguaa ggggggaccc cauugaauua caaguggaau 1800gcuucacaug ggaccaaaaa cucuggugcc gucacuucug ugugcuugcg gacucagaau 1860cugguggaca uaucacucac ucugggaugg ugggcauggg agucagcugc acagccacuc 1920gggaagaugg aaccagccgc agauagugau aauaggcugg agccucggug gccaagcuuc 1980uugccccuug ggccuccccc cagccccucc ucccuuccu gcacccguac ccccgugguc 2040uuugaauaaa gucugagugg gcggc 2065791854RNAArtificial SequenceSynthetic Polynucleotide 79augucaccac aacgagaccg gauaaaugcc uucuacaaag acaaccccca uccuaaggga 60aguaggauag uuauuaacag agaacaucuu augauugaua gaccuuaugu uuugcuggcu 120guucuauucg ucauguuucu gagcuugauc ggguugcuag ccauugcagg cauuagacuu 180caucgggcag ccaucuacac cgcagagauc cauaaaagcc ucagcaccaa ucuggaugua 240acuaacucaa ucgagcauca gguuaaggac gugcugacac cacucuucaa gaucaucggu 300gaugaagugg gcuugaggac accucagaga uucacugacc uagugaaguu caucucugac 360aagauuaaau uccuuaaucc ggacagggaa uacgacuuca gagaucucac uugguguauc 420aacccgccag agagaaucaa auuggauuau gaucaauacu gugcagaugu ggcugcugaa 480gaacucauga augcauuggu gaacucaacu cuacuggaga ccagggcaac caaucaguuc 540cuagcugucu caaagggaaa cugcucaggg cccacuacaa ucagaggcca auucucaaac 600augucgcugu cccuguugga cuuguauuua agucgagguu acaaugugucaucuauaguc 660acuaugacau cccagggaau guacggggga acuuaccuag uggaaaagcc uaaucugagc 720agcaaagggu cagaguuguc acaacugagc augcaccgag uguuugaagu aggguguuauc 780agaaauccgg guuuggggc uccgguauuc cauaugacaa acuaucuuga gcaaccaguc 840aguaaugauu ucagcaacug cauggugcu uugggggagc ucaaguucgc agcccucugu 900cacagggaag auucuaucac aauucccuau cagggaucag ggaaaggugu cagcuuccag 960cuugucaagc uaggugucug gaaaucccca accgacaugc aauccugggu cccccuauca 1020acggaugauc cagugauaga caggcuuuac cucucaucuc acagaggcgu uaucgcugac 1080aaucaagcaa aaugggcugu cccgacaaca cggacagaug acaaguugcg aauggagaca 1140ugcuuccagc aggcguguaa ggguaaaauc caagcacuuu gcgagaaucc cgaguggaca 1200ccauugaagg auaacaggau uccuucauac ggggucuugu cuguugaucu gagucugaca 1260guugagcuua aaaucaaaau uguuucagga uucgggccau ugaucacaca cgguucaggg 1320auggaccuau acaaauccaa ccacaacaau auguauuggc ugacuauccc gccaaugaag 1380aaccuggccu uaggguguaau caacacauug gaguggauac cgagauucaa gguuaguccc 1440aaccucuuca cuguuccaau uaaggaagca ggcgaggacu gccaugcccc aacauaccua 1500ccugcggagg uggauggugag ugucaaacuc aguuccaauc uggugauucu accuggucaa 1560gaucuccaau auguucuggc aaccuacgau acuuccagag uugaacaugc uguaguuuau 1620uacguuuaca gcccaagccg cucauuuucu uacuuuuauc cuuuuagguu gccuguaagg 1680ggggucccca uugaauuaca aguggaaugc uucacauggg accaaaaacu cuggugccgu 1740cacuucugug ugcuugcgga cucagaaucu gguggacaua ucacucacuc ugggauggug 1800ggcaugggag ucagcugcac agccacucgg gaagauggaa ccagccgcag auag 1854802126RNAArtificial SequenceSynthetic Polynucleotide 80ggggaaauaa gagagaaaag aagaguaaga agaaauauaa gagccaccau gucaccacaa 60cgagaccgga

uaaaugccuu cuacaaagac aacccccauc cuaagggaag uaggauaguu 120auuaacagag aacaucuuau gauugauaga ccuuauguuu ugcuggcugu ucuauucguc 180auguuucuga gcuugaucgg guugcuagcc auugcaggca uuagacuuca ucgggcagcc 240aucuacaccg cagagaucca uaaaagccuc agcaccaauc uggauguaac uaacucaauc 300gagcaucagg uuaaggacgu gcugacacca cucuucaaga ucaucggugaugaagugggc 360uugaggacac cucagagauu cacugaccua gugaaguuca ucucugacaa gauuaaauuc 420cuuaauccgg acagggaaua cgacuucaga gaucucacuu gguguaucaa cccgccagag 480agaaucaaau uggauuauga ucaauacugu gcagaugugg cugcugaaga acucaugaau 540gcauugguga acucaacucu acuggagacc agggcaacca aucaguuccu agcugucuca 600aagggaaacu gcucagggcc cacuacaauc agaggccaau ucucaaacau gucgcugucc 660cuguuggacu uguauuuaag ucgagguuac aaugugucau cuauagucac uaugacaucc 720cagggaaugu acgggggaac uuaccuagug gaaaagccua aucugagcag caaaggguca 780gaguugucac aacugagcau gcaccgagug uuugaaguag guguuaucag aaauccgggu 840uuggggggcuc cgguauucca uaugacaaac uaucuugagc aaccagucag uaaugauuuc 900agcaacugca ugguggcuuu gggggagcuc aaguucgcag cccucuguca cagggaagau 960ucuaucacaa uucccuauca gggaucaggg aaagguguca gcuuccagcu ugucaagcua 1020ggugucugga aauccccaac cgacaugcaa uccugggucc cccuaucaac ggaugaucca 1080gugauagaca ggcuuuaccu cucaucucac agaggcguua ucgcugacaa ucaagcaaaa 1140ugggcugucc cgacaacacg gacagaugac aaguugcgaa uggagacaug cuuccagcag 1200gcguguaagg guaaaaucca agcacuuugc gagaaucccg aguggacacc auugaaggau 1260aacaggauuc cuucauacgg ggucuugucu guugaucuga gucugacagu ugagcuuaaa 1320aucaaaauug uuucaggauu cgggccauug aucacacacg guucagggau ggaccuauac 1380aaauccaacc acaacaauau guauuggcug acuaucccgc caaugaagaa ccuggccuua 1440ggguguaauca acacauugga guggauaccg agauucaagg uuagucccaa ccucuucacu 1500guuccaauua aggaagcagg cgaggacugc caugccccaa cauaccuacc ugcggaggug 1560gauggugaug ucaaacucag uuccaaucug gugauucuac cuggucaaga ucuccaauau 1620guucuggcaa ccuacgauac uuccagaguu gaacaugcug uaguuuauua cguuuacagc 1680ccaagccgcu cauuuucuua cuuuuauccu uuuagguugc cuguaagggg ggucccccauu 1740gaauuacaag uggaaugcuu cacaugggac caaaaacucu ggugccguca cuucugugug 1800cuugcggacu cagaaucugg uggacauauc acucacucug ggaugguggg caugggaguc 1860agcugcacag ccacucggga agauggaacc agccgcagau agugauaaua ggcuggagcc 1920ucgguggcca agcuucuugc cccuugggcc ucccccccagc cccucucccc cuuccugcac 1980ccguaccccc guggucuuug aauaaagucu gagugggcgg caaaaaaaaa aaaaaaaaaa 2040aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100aaaaaaaaaa aaaaaaaaaa aucuag 2126811729RNAArtificial SequenceSynthetic Polynucleotide 81ucaagcuuuu ggacccucgu acagaagcua auacgacuca cuauagggaa auaagagaga 60aaagaagagu aagaagaaau auaagagcca ccauggcaca agucauuaau acaaacagcc 120ugucgcuguu gacccagaau aaccugaaca aaucccaguc cgcacugggc acugcuaucg 180agcguuuguc uuccggucug cguaucaaca gcgcgaaaga cgaugcggca ggacaggcga 240uugcuaaccg uuuuaccgcg aacaucaaag gucugacuca ggcuucccgu aacgcuaacg 300acgguaucuc cauugcgcag accacugaag gcgcgcugaa cgaaaucaac aacaaccugc 360agcgugugcg ugaacuggcg guucagucug cgaaugguac uaacucccag ucugaccucg 420acuccaucca ggcugaaauc acccagcgcc ugaacgaaau cgaccgugua uccggccaga 480cucaguucaa cggcgugaaa guccuggcgc aggacaacac ccugaccauc cagguuggug 540ccaacgacgg ugaaacuauc gauauugauu uaaaagaaau cagcucuaaa acacugggac 600uugauaagcu uaauguccaa gaugccuaca ccccgaaaga aacugcugua accguugaua 660aaacuaccua uaaaaauggu acagauccua uuacagccca gagcaauacu gauauccaaa 720cugcaauugg cgguggugca acgggggguua cuggggcuga uaucaaauuu aaagaugguc 780aauacuauuu agauguuaaa ggcggugcuu cugcuggugu uuauaaagcc acuuaugaug 840aaacuacaaa gaaaguuaau auugauacga cugauaaaac uccguuggca acugcggaag 900cuacagcuau ucggggaacg gccacuauaa cccacaacca aauugcugaa guaacaaaag 960aggguguuga uacgaccaca guugcggcuc aacuugcugc agcaggggguu acuggcgccg 1020auaaggacaa uacuagccuu guaaaacuau cguuugagga uaaaaacggu aagguuauug 1080auggugggcua ugcagugaaa augggcgacg auuucuaugc cgcuacauau gaugagaaaa 1140caggugcaau uacugcuaaa accacuacuu auacagaugg uacuggcguu gcucaaacug 1200gagcugugaa auuuggugc gcaaauggua aaucugaagu uguuacugcu accgauggua 1260agacuuacuu agcaagcgac cuugacaaac auaacuucag aacaggcggu gagcuuaaag 1320agguuaauac agauaagacu gaaaacccac ugcagaaaau ugaugcugcc uuggcacagg 1380uugauacacu ucguucugac cugggugcgg uucagaaccg uuucaacucc gcuaucacca 1440accugggcaa uaccguaaau aaccugucuu cugcccguag ccguaucgaa gauuccgacu 1500acgcaaccga agucuccaac augucucgcg cgcagauucu gcagcaggcc gguaccuccg 1560uucuggcgca ggcgaaccag guuccgcaaa acguccucuc uuuacugcgu ugauaauagg 1620cuggagcccuc gguggccaug cuucuugccc cuugggccuc cccccagccc cucucccccu 1680uccugcaccc guacccccgu ggucuuugaa uaaagucuga gugggcggc 1729821518RNAArtificial SequenceSynthetic Polynucleotide 82auggcacaag ucauuaauac aaacagccug ucgcuguuga cccagaauaa ccugaacaaa 60ucccaguccg cacugggcac ugcuaucgag cguuugucuu ccggucugcg uaucaacagc 120gcgaaagacg augcggcagg acaggcgauu gcuaaccguu uuaccgcgaa caucaaaggu 180cugacucagg cuucccguaa cgcuaacgac gguaucucca uugcgcagac cacugaaggc 240gcgcugaacg aaaucaacaa caaccugcag cgugugcgug aacuggcggu ucagucugcg 300aaugguacua acucccaguc ugaccucgac uccauccagg cugaaaucac ccagcgccug 360aacgaaaucg accguguauc cggccagacu caguucaacg gcgugaaagu ccuggcgcag 420gacaacaccc ugaccaucca gguuggugcc aacgacggug aaacuaucga uauugauuua 480aaagaaauca gcucuaaaac acugggacuu gauaagcuua auguccaaga ugccuacacc 540ccgaaagaaa cugcuguaac cguugauaaa acuaccuaua aaaaugguac agauccuauu 600acagcccaga gcaauacuga uauccaaacu gcaauuggcg guggugcaac gggggguuacu 660ggggcugaua ucaaauuuaa agauggucaa uacuauuuag auguuaaagg cggugcuucu 720gcugguguuu auaaagccac uuaugaugaa acuacaaaga aaguuaauau ugauacgacu 780gauaaaacuc cguuggcaac ugcggaagcu acagcuauuc ggggaacggc cacuauaacc 840cacaaccaaa uugcugaagu aacaaaagag gguguugaua cgaccacagu ugcggcucaa 900cuugcugcag caggggguuac uggcgccgau aaggacaaua cuagccuugu aaaacuaucg 960uuugaggaua aaaacgguaa gguuauugau gguggcuaug cagugaaaau gggcgacgau 1020uucuaugccg cuacauauga ugagaaaaca ggugcaauua cugcuaaaac cacuacuuau 1080acagauggua cuggcguugc ucaaacugga gcugugaaau uugguggcgc aaaugguaaa 1140ucugaaguug uuacugcuac cgaugguaag acuuacuuag caagcgaccu ugacaaacau 1200aacuucagaa caggcgguga gcuuaaagag guuaauacag auaagacuga aaacccacug 1260cagaaaauug augcugccuu ggcacagguu gauacacuuc guucugaccu gggugcgguu 1320cagaaccguu ucaacuccgc uaucaccaac cugggcaaua ccguaaauaa ccugucuucu 1380gcccguagcc guaucgaaga uuccgacuac gcaaccgaag ucuccaacau gucucgcgcg 1440cagauucugc agcaggccgg uaccuccguu cuggcgcagg cgaaccaggu uccgcaaaac 1500guccucucuu uacugcgu 1518831790RNAArtificial SequenceSynthetic Polynucleotide 83ggggaaauaa gagagaaaag aagaguaaga agaaauauaa gagccaccau ggcacaaguc 60auuaauacaa acagccuguc gcuguugacc cagaauaacc ugaacaaauc ccaguccgca 120cugggcacug cuaucgagcg uuugucuucc ggucugcgua ucaacagcgc gaaagacgau 180gcggcaggac aggcgauugc uaaccguuuu accgcgaaca ucaaaggucu gacucaggcu 240ucccguaacg cuaacgacgg uaucuccauu gcgcagacca cugaaggcgc gcugaacgaa 300aucaacaaca accugcagcg ugugcgugaa cuggcgguuc agucugcgaa ugguacuaac 360ucccagucug accucgacuc cauccaggcu gaaaucaccc agcgccugaa cgaaaucgac 420cguguauccg gccagacuca guucaacggc gugaaagucc uggcgcagga caacacccug 480accauccagg uuggugccaa cgacggugaa acuaucgaua uugauuuaaa agaaaucagc 540ucuaaaacac ugggacuuga uaagcuuaau guccaagaug ccuacacccc gaaagaaacu 600gcuguaaccg uugauaaaac uaccuauaaa aaugguacag auccuauuac agcccagagc 660aauacugaua uccaaacugc aauuggcggu ggugcaacgg ggguuacugg ggcugauauc 720aaauuuaaag auggucaaua cuauuuagau guuaaaggcg gugcuucugc ugguguuuau 780aaagccacuu augaugaaac uacaaagaaa guuaauauug auacgacuga uaaaacuccg 840uuggcaacug cggaagcuac agcuauucgg ggaacggcca cuauaaccca caaccaaauu 900gcugaaguaa caaaagaggg uguugauacg accacaguug cggcucaacu ugcugcagca 960gggguuacug gcgccgauaa ggacaauacu agccuuguaa aacuaucguu ugaggauaaa 1020aacgguaagg uuauugaugg uggcuaugca gugaaaaugg gcgacgauuu cuaugccgcu 1080acauaugaug agaaaacagg ugcaauuacu gcuaaaacca cuacuuauac agaugguacu 1140ggcguugcuc aaacuggagc ugugaaauuu gguggcgcaa augguaaauc ugaaguuguu 1200acugcuaccg augguaagac uuacuuagca agcgaccuug acaaacauaa cuucagaaca 1260ggcggugagc uuaaagaggu uaauacagau aagacugaaa acccacugca gaaaauugau 1320gcugccuugg cacagguuga uacacuucgu ucugaccugg gugcgguuca gaaccguuuc 1380aacuccgcua ucaccaaccu gggcaauacc guaaauaacc ugucuucugc ccguagccgu 1440aucgaagauu ccgacuacgc aaccgaaguc uccaacaugu cucgcgcgca gauucugcag 1500caggccggua ccuccguucu ggcgcaggcg aaccagguuc cgcaaaacgu ccucucuuua 1560cugcguugau aauaggcugg agccucggug gccaugcuuc uugccccuug ggccuccccc 1620cagccccucc uccccuuccu gcacccguac ccccgugguc uuugaauaaa gucugagugg 1680gcggcaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1740aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaucuag

17908413PRTSalmonella typhimurium 84Leu Gln Arg Val Arg Glu Leu Ala Val Gln Ser Ala Asn1 5 1085539PRTArtificial SequenceSynthetic Polypeptide 85Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Cys Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Phe145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Leu Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Cys Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Asn Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53586539PRTArtificial SequenceSynthetic Polypeptide 86Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Cys Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Cys Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu His Gln Trp His Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53587539PRTArtificial SequenceSynthetic Polypeptide 87Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu

Asp Leu Leu Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg

Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53588539PRTArtificial SequenceSynthetic Polypeptide 88Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53589539PRTArtificial SequenceSynthetic Polypeptide 89Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val

Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53590539PRTArtificial SequenceSynthetic Polypeptide 90Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53591539PRTArtificial SequenceSynthetic Polypeptide 91Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Pro Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn

Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440

445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53592539PRTArtificial SequenceSynthetic Polypeptide 92Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Pro Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53593539PRTArtificial SequenceSynthetic Polypeptide 93Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu

Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53594539PRTArtificial SequenceSynthetic Polypeptide 94Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Leu Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53595539PRTArtificial SequenceSynthetic Polypeptide 95Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln

Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53596539PRTArtificial SequenceSynthetic Polypeptide 96Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Trp Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln

Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53597539PRTArtificial SequenceSynthetic Polypeptide 97Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Leu Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Leu Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Leu Lys Asn Leu Trp Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg

Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53598539PRTArtificial SequenceSynthetic Polypeptide 98Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Pro Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 53599539PRTArtificial SequenceSynthetic Polypeptide 99Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Pro Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 535100539PRTArtificial SequenceSynthetic Polypeptide 100Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25

30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Pro Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val

Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 535101539PRTArtificial SequenceSynthetic Polypeptide 101Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Pro Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 535102539PRTArtificial SequenceSynthetic Polypeptide 102Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln

Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Pro Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 535103539PRTArtificial SequenceSynthetic Polypeptide 103Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asn Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 535104539PRTArtificial SequenceSynthetic Polypeptide 104Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Phe

Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245 250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Gln Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 535105539PRTArtificial SequenceSynthetic Polypeptide 105Met Ser Trp Lys Val Val Ile Ile Phe Ser Leu Leu Ile Thr Pro Gln1 5 10 15His Gly Leu Lys Glu Ser Tyr Leu Glu Glu Ser Cys Ser Thr Ile Thr 20 25 30Glu Gly Tyr Leu Ser Val Leu Arg Thr Gly Trp Tyr Thr Asn Val Phe 35 40 45Thr Leu Glu Val Gly Asp Val Glu Asn Leu Thr Cys Ser Asp Gly Pro 50 55 60Ser Leu Ile Lys Thr Glu Leu Asp Leu Thr Lys Ser Ala Leu Arg Glu65 70 75 80Leu Lys Thr Val Ser Ala Asp Gln Leu Ala Arg Glu Glu Gln Ile Glu 85 90 95Asn Pro Gly Ser Gly Ser Phe Val Leu Gly Ala Ile Ala Leu Gly Val 100 105 110Ala Ala Ala Ala Ala Val Thr Ala Gly Val Ala Ile Ala Lys Thr Ile 115 120 125Arg Leu Glu Ser Glu Val Thr Ala Ile Asn Asn Ala Leu Lys Lys Thr 130 135 140Asn Glu Ala Val Ser Thr Leu Gly Asn Gly Val Arg Val Leu Ala Thr145 150 155 160Ala Val Arg Glu Leu Lys Asp Phe Val Ser Lys Asn Leu Thr Arg Ala 165 170 175Ile Asn Lys Asn Lys Cys Asp Ile Asp Asp Leu Lys Met Ala Val Ser 180 185 190Phe Ser Gln Trp Asn Arg Arg Phe Leu Asn Val Val Arg Gln Phe Ser 195 200 205Asp Asn Ala Gly Ile Thr Pro Ala Ile Ser Leu Asp Leu Met Thr Asp 210 215 220Ala Glu Leu Ala Arg Ala Val Pro Asn Met Pro Thr Ser Ala Gly Gln225 230 235 240Ile Lys Leu Met Leu Glu Asn Arg Ala Met Val Arg Arg Lys Gly Phe 245

250 255Gly Ile Leu Ile Gly Val Tyr Gly Ser Ser Val Ile Tyr Met Val Gln 260 265 270Leu Pro Ile Phe Gly Val Ile Asp Thr Pro Cys Trp Ile Val Lys Ala 275 280 285Ala Pro Ser Cys Ser Glu Lys Lys Gly Asn Tyr Ala Cys Leu Leu Arg 290 295 300Glu Asp Gln Gly Trp Tyr Cys Gln Asn Ala Gly Ser Thr Val Tyr Tyr305 310 315 320Pro Asn Glu Lys Asp Cys Glu Thr Arg Gly Asp His Val Phe Cys Asp 325 330 335Thr Ala Ala Gly Ile Asn Val Ala Glu Gln Ser Lys Glu Cys Asn Ile 340 345 350Asn Ile Ser Thr Thr Asn Tyr Pro Cys Lys Val Ser Thr Gly Arg His 355 360 365Pro Ile Ser Met Val Ala Leu Ser Pro Leu Gly Ala Leu Val Ala Cys 370 375 380Tyr Lys Gly Val Ser Cys Ser Ile Gly Ser Asn Arg Val Gly Ile Ile385 390 395 400Lys Gln Leu Asn Lys Gly Cys Ser Tyr Ile Thr Asn Gln Asp Ala Asp 405 410 415Thr Val Thr Ile Asp Asn Thr Val Tyr Gln Leu Ser Lys Val Glu Gly 420 425 430Glu Gln His Val Ile Lys Gly Arg Pro Val Ser Ser Ser Phe Asp Pro 435 440 445Ile Lys Phe Pro Glu Asp Gln Phe Gln Val Ala Leu Asp Gln Val Phe 450 455 460Glu Asn Ile Glu Asn Ser Gln Ala Leu Val Asp Gln Ser Asn Arg Ile465 470 475 480Leu Ser Ser Ala Glu Lys Gly Asn Thr Gly Phe Ile Ile Val Ile Ile 485 490 495Leu Ile Ala Val Leu Gly Ser Ser Met Ile Leu Val Ser Ile Phe Ile 500 505 510Ile Ile Lys Lys Thr Lys Lys Pro Thr Gly Ala Pro Pro Glu Leu Ser 515 520 525Gly Val Thr Asn Asn Gly Phe Ile Pro His Asn 530 5351061617DNAArtificial SequenceSynthetic Polynucleotide 106atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tctgcaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccttt 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccct gaacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgtgt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc

aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcaa cgtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171071617DNAArtificial SequenceSynthetic Polynucleotide 107atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tctgcaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgtgt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagc accagtggca tgtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171081617DNAArtificial SequenceSynthetic Polynucleotide 108atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tccctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171091617DNAArtificial SequenceSynthetic Polynucleotide 109atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tccctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgaga accagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171101617DNAArtificial SequenceSynthetic Polynucleotide 110atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgctt aagaacctga cacgggccat taacaagaac 540aagtgcgaca tccctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171111617DNAArtificial SequenceSynthetic Polynucleotide 111atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgctt aagaacctga cacgggccat taacaagaac 540aagtgcgaca tccctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgaga accagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171121617DNAArtificial SequenceSynthetic Polynucleotide 112atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg cctgtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171131617DNAArtificial SequenceSynthetic Polynucleotide 113atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg cctgtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgaga accagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct

ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171141617DNAArtificial SequenceSynthetic Polynucleotide 114atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171151617DNAArtificial SequenceSynthetic Polynucleotide 115atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acctcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc

420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171161617DNAArtificial SequenceSynthetic Polynucleotide 116atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgctt aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171171617DNAArtificial SequenceSynthetic Polynucleotide 117atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctgt ggcgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171181617DNAArtificial SequenceSynthetic Polynucleotide 118atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acctcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgctt aagaacctgt ggcgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171191617DNAArtificial SequenceSynthetic Polynucleotide 119atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg cctgtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171201617DNAArtificial SequenceSynthetic Polynucleotide 120atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tccctgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171211617DNAArtificial SequenceSynthetic Polynucleotide 121atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcccta tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171221617DNAArtificial SequenceSynthetic Polynucleotide 122atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg cctagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg

ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171231617DNAArtificial SequenceSynthetic Polynucleotide 123atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttccc acctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171241617DNAArtificial SequenceSynthetic Polynucleotide 124atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctgaga accagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171251617DNAArtificial SequenceSynthetic Polynucleotide 125atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcga ccctatcaag ttccctcagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171261617DNAArtificial SequenceSynthetic Polynucleotide 126atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgtc tgtgctgaga 120accggctggt acaccaacgt gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcctggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgccat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagtggaa ccggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgcctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcctgctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcatc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga

1320cctgtgtcca gcagcttcga ccctatcaag ttccctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gcttcatccc tcacaac 16171271617RNAArtificial SequenceSynthetic Polynucleotide 127augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucugcaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccuuu 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggcccu gaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugugu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucaa cguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171281617RNAArtificial SequenceSynthetic Polynucleotide 128augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucugcaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugugu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagc accaguggca uguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171291617RNAArtificial SequenceSynthetic Polynucleotide 129augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucccugaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu ggugucca uc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171301617RNAArtificial SequenceSynthetic Polynucleotide 130augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucccugaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugaga accaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171311617RNAArtificial SequenceSynthetic Polynucleotide 131augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugcuu aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucccugaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu

ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171321617RNAArtificial SequenceSynthetic Polynucleotide 132augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugcuu aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucccugaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugaga accaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171331617RNAArtificial SequenceSynthetic Polynucleotide 133augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug ccugugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171341617RNAArtificial SequenceSynthetic Polynucleotide 134augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug ccugugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugaga accaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171351617RNAArtificial SequenceSynthetic Polynucleotide 135augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171361617RNAArtificial SequenceSynthetic Polynucleotide 136augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg accucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171371617RNAArtificial SequenceSynthetic Polynucleotide 137augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugcuu aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171381617RNAArtificial SequenceSynthetic Polynucleotide 138augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccugu ggcgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171391617RNAArtificial SequenceSynthetic Polynucleotide 139augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg accucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugcuu aagaaccugu ggcgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171401617RNAArtificial SequenceSynthetic Polynucleotide 140augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug ccugugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca

gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171411617RNAArtificial SequenceSynthetic Polynucleotide 141augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucccugaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171421617RNAArtificial SequenceSynthetic Polynucleotide 142augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc

420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcccua ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171431617RNAArtificial SequenceSynthetic Polynucleotide 143augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug ccuagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171441617RNAArtificial SequenceSynthetic Polynucleotide 144augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuuccc accuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu ggguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171451617RNAArtificial SequenceSynthetic Polynucleotide 145augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugaga accaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu ggguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171461617RNAArtificial SequenceSynthetic Polynucleotide 146augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccucagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu ggguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 16171471617RNAArtificial SequenceSynthetic Polynucleotide 147augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguggaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuaucuucgg cgugaucgac 840acacccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcacccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga cccuaucaag uucccugagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaaug gcuucauccc ucacaac 1617

* * * * *
