

Exhibit 49

United States Patent Application 20190216917

US PATENT & TRADEMARK OFFICE

PATENT APPLICATION FULL TEXT AND IMAGE DATABASE



(5 of 21)

United States Patent Application	20190216917
Kind Code	A1
Ciaramella; Giuseppe ; et al.	July 18, 2019

HMPV RNA VACCINES

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.: **16/368099**

Filed: **March 28, 2019**

Related U.S. Patent Documents

<u>Application Number</u>	<u>Filing Date</u>	<u>Patent Number</u>
16040981	Jul 20, 2018	10272150
16368099		
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:

A61K 39/155 20130101; C07K 16/10 20130101; A61K 2039/55511 20130101; A61K 2039/70 20130101; C12N 2760/18534 20130101; A61K 39/12 20130101; Y02A 50/30 20180101; C12N 2760/18034 20130101; A61K 39/215 20130101; C12N 2760/18634 20130101; A61P 11/00 20180101; C12N 2760/18434 20130101; A61K 2039/55555 20130101; C07K 2317/76 20130101; A61K 2039/53 20130101; C12N 2760/18334 20130101; A61K 2039/6018 20130101; C12N 2770/20034 20130101; C07K 16/1027 20130101

International Class:

A61K 39/155 20060101 A61K039/155; C07K 16/10 20060101 C07K016/10; A61K 39/12 20060101 A61K039/12

Claims

1.-2. (canceled)

3. A human metapneumovirus (hMPV) vaccine, comprising: an isolated ribonucleic acid (RNA) polynucleotide comprising an open reading frame encoding an antigenic hMPV Fusion (F) protein formulated in a lipid nanoparticle that comprises a molar ratio of 20-60% ionizable cationic lipid, 5-25% non-cationic lipid, 25-55% sterol, and 0.5-15% PEG-modified lipid, wherein the isolated mRNA polynucleotide is not self-replicating RNA.

4.-95. (canceled)

96. A method of inducing an antigen-specific immune response in a subject, the method comprising administering to the subject the vaccine of claim 3 in an amount effective to produce an antigen-specific immune response in the subject.

97.-135. (canceled)

136. The hMPV vaccine of claim 3, wherein the isolated mRNA polynucleotide further encodes a 5' terminal cap, 7mG(5')ppp(5')NlmpNp.

137. The hMPV vaccine of claim 3, wherein at least 80% of the uracil in the open reading frame comprises a chemical modification selected from N1-methyl-pseudouridine and N1-ethyl-pseudouridine.

138. The hMPV vaccine of claim 3, wherein the chemical modification is in the 5-position of the uracil.

139. The hMPV vaccine of claim 3, wherein the open reading frame encoding an antigenic hMPV F protein comprises a RNA sequence that has at least 90% identity to the RNA sequence set forth in SEQ ID NO: 57.

140. The hMPV vaccine of claim 139, wherein the open reading frame encoding an antigenic hMPV F protein

comprises a RNA sequence set forth as SEQ ID NO: 57.

141. The hMPV vaccine of claim 3, wherein the antigenic hMPV F protein comprises an amino acid sequence that has at least 90% identity to the amino acid sequence set forth as SEQ ID NO: 5.

142. The hMPV vaccine of claim 141, wherein the antigenic hMPV F protein comprises an amino acid sequence set forth as SEQ ID NO: 5.

143. The hMPV vaccine of claim 3, formulated in an effective amount, wherein the effective amount is a total dose of 25 .mu.g-200 .mu.g.

144. The hMPV vaccine of claim 3, wherein the isolated RNA polynucleotide further comprises 5' terminal cap, a 5' UTR, a 3' UTR, and a polyA tail.

145. The hMPV vaccine of claim 144, wherein the open reading frame encoding an antigenic hMPV F protein comprises a RNA sequence that has at least 90% identity to the RNA sequence set forth in SEQ ID NO: 57.

146. The hMPV vaccine of claim 145, wherein the open reading frame encoding an antigenic hMPV F protein comprises a RNA sequence set forth as SEQ ID NO: 57.

147. The hMPV vaccine of claim 3, wherein the efficacy of the vaccine in vaccinated subjects is at least 60%, relative to unvaccinated subjects, following a single dose of the vaccine.

148. The hMPV vaccine of claim 3, wherein a single dose of the vaccine administered to a subject is sufficient to produce detectable levels of hMPV F protein as measured in serum of a subject vaccinated with at least one dose of the vaccine at 1-72 hours post administration.

149. The hMPV vaccine of claim 3, wherein a single dose of the vaccine administered to a subject is sufficient to produce a 1,000-10,000 neutralization titer produced by neutralizing antibody against the antigenic hMPV F protein as measured in serum of a subject vaccinated with at least one dose of the vaccine at 1-72 hours post administration.

150. The hMPV vaccine of claim 149, wherein the 1,000-10,000 neutralization titer is produced in the absence of antibody-dependent enhancement (ADE) of a hMPV-associated disease.

151. The hMPV vaccine of claim 150, wherein the hMPV-associated disease is alevolitis interstitial pneumonia.

152. The hMPV vaccine of claim 3, wherein an anti-hMPV F protein antibody titer produced in a subject vaccinated with at least one dose of the vaccine is increased by at least 1 log relative to a control, wherein the control is an anti-hMPV F protein antibody titer produced in a subject who has not been administered a vaccine against hMPV.

153. The hMPV vaccine of claim 3, wherein an anti-hMPV F protein antibody titer produced in a subject vaccinated with at least one dose of the vaccine is increased at least 2 times relative to a control, wherein the control is an anti-hMPV F protein antibody titer produced in a subject who has not been administered a vaccine against hMPV.

154. The hMPV vaccine of claim 3, wherein the ionizable cationic lipid comprises the following compound:
##STR00052##

155. The hMPV vaccine of claim 3, wherein the noncationic lipid is DSPC (1,2-Distearoyl-sn-glycero-3-phosphocholine).

156. The hMPV vaccine of claim 3, wherein the PEG-modified lipid is DMG-PEG (1,2-dimyristoyl-racglycero-

3-methoxypolyethylene glycol-2000).

157. The method of claim 3, wherein the lipid nanoparticle comprises 40-50% ionizable cationic lipid, 5-15% DSPC, 25-40% cholesterol, and 1-3.5% DMG-PEG.

158. The method of claim 157, wherein the lipid nanoparticle comprises 50% ionizable cationic lipid, 10% DSPC, 38.5% cholesterol, and 1.5% DMG-PEG.

Description

RELATED APPLICATIONS

[0001] This application is a continuation of U.S. application Ser. No. 16/040,981, filed Jul. 20, 2018, which is a continuation of U.S. application Ser. No. 15/674,599, now U.S. Pat. No. 10,064,934, filed Aug. 11, 2017, which is a continuation of international application number PCT/US2016/058327, 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. hMPV 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 addition 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 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 protein1 (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 51 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 51 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 51 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.

[0064] 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.

[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). 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).

[0066] 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.

[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 attaches to cell receptors.

[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 causes fusion of viral and cellular membranes.

[0069] 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.

[0070] 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.

[0071] In some embodiments, a 5' terminal cap is 7mG(5')ppp(5')NlmpNp.

[0072] 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.

[0073] 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).

[0074] In some embodiments, the lipid is

##STR00001##

[0075] In some embodiments, the lipid is

##STR00002##

[0076] In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), discussed below.

[0077] 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.

[0078] 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).

[0079] 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.

[0080] 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.

[0081] 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.

[0082] 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 (MLGSNSGQRVVFITILLVAPAYS; SEQ ID NO: 17), VSVg protein signal sequence (MKCLLYLAFLFIGVNCA; SEQ ID NO: 18) and Japanese encephalitis JEV signal sequence (MWLVSLAIVTACAGA; SEQ ID NO: 19).

[0083] 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.

[0084] 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.

[0085] 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).

[0086] 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).

[0087] In some embodiments, a lipid nanoparticle comprises compounds of Formula (I) and/or Formula (II), as discussed below.

[0088] In some embodiments, a lipid nanoparticle comprises Compounds 3, 18, 20, 25, 26, 29, 30, 60, 108-112, or 122, as discussed below.

[0089] 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).

[0090] In some embodiments, the nanoparticle has a net neutral charge at a neutral pH value.

[0091] In some embodiments, the respiratory virus vaccine is multivalent.

[0092] 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.

[0093] In some embodiments, an antigen-specific immune response comprises a T cell response or a B cell response.

[0094] 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.

[0095] 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.

[0096] 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.

[0097] In some embodiments, a RNA (e.g., mRNA) vaccine is administered to a subject by intradermal or intramuscular injection.

[0098] 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.

[0099] 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.

[0100] 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).

[0101] 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.

[0102] 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.

[0103] 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.

[0104] 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.

[0105] 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.

[0106] 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:

$$\text{Efficacy} = (\text{ARU} - \text{ARV}) / \text{ARU} \times 100; \text{ and}$$

$$\text{Efficacy} = (1 - \text{RR}) \times 100.$$

[0107] 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.

[0108] 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%.

[0109] 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.

[0110] 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.

[0111] 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.

[0112] 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.

[0113] 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).

[0114] 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).

[0115] 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.

[0116] 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.

[0117] In some embodiments, the subject is immunocompromised (has an impaired immune system, e.g., has an immune disorder or autoimmune disorder).

[0118] In some embodiments the nucleic acid vaccines described herein are chemically modified. In other embodiments the nucleic acid vaccines are unmodified.

[0119] 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.

[0120] 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.

[0121] 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.

[0122] 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.

[0123] 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, 2,000-10,000, 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.

[0124] 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.

[0125] 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.

[0126] 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.

[0127] 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.

[0128] 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.

[0129] 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.

[0130] 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.

[0131] 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.

[0132] 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.

[0133] 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.

[0134] 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.

[0135] 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.

[0136] 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.

[0137] 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.

[0138] 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 produced in a 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.

[0139] In exemplary embodiments of the invention, an efficacious vaccine produces an antibody titer of greater than 1:40, greater than 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.)

[0140] In exemplary aspects of the invention, antigen-specific antibodies are measured in units of $\mu\text{g/ml}$ 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 $>0.5 \mu\text{g/ml}$, $>0.1 \mu\text{g/ml}$, $>0.2 \mu\text{g/ml}$, $>0.35 \mu\text{g/ml}$, $>0.5 \mu\text{g/ml}$, $>1 \mu\text{g/ml}$, $>2 \mu\text{g/ml}$, $>5 \mu\text{g/ml}$ or $>10 \mu\text{g/ml}$. In exemplary embodiments of the invention, an efficacious vaccine produces $>10 \text{ mIU/ml}$, $>20 \text{ mIU/ml}$, $>50 \text{ mIU/ml}$, $>100 \text{ mIU/ml}$, $>200 \text{ mIU/ml}$, $>500 \text{ mIU/ml}$ or $>1000 \text{ mIU/ml}$. 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.

[0141] 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

[0142] 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.

[0143] 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).

[0144] 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.

[0145] 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.

[0146] 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.

[0147] 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).

[0148] 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).

[0149] 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).

[0150] 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).

[0151] 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 .about.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.

[0152] 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.

[0153] 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.

[0154] 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.

[0155] 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.

[0156] 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.

[0157] 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.

[0158] 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.

[0159] 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.

[0160] 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.

[0161] 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.

[0162] 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.

[0163] 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

[0164] 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.

[0165] 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.

[0166] The entire contents of International Application No. PCT/US2015/02740 is incorporated herein by reference.

Human Metapneumovirus (hMPV)

[0167] 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.

[0168] 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).

[0169] 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.

[0170] 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.

[0171] 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.

[0172] 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.

[0173] 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).

[0174] 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).

[0175] 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).

[0176] 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).

[0177] 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.

[0178] 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).

[0179] 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.

[0180] 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)

[0181] 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: Respirivirus (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).

[0182] 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.

[0183] 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.

[0184] 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.

[0185] 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.

[0186] PIV3 V is a non-structural protein that blocks IFN signaling in the infected cell, therefore acting as a virulence factor.

[0187] 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.

[0188] 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).

[0189] 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.

[0190] 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.

[0191] 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.

[0192] 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.

[0193] 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).

[0194] 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).

[0195] 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.

[0196] 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.

[0197] 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.

[0198] 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.

[0199] 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)

[0200] 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.

[0201] 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)).

[0202] 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.

[0203] 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.

[0204] 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.

[0205] 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.

[0206] 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.

[0207] 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.

[0208] 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.

[0209] 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.

[0210] 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)

[0211] 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).

[0212] 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).

[0213] 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.

[0214] 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.

[0215] 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.

[0216] In 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.

[0217] 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.

[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 HA protein and having MeV HA protein activity.

[0219] 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.

[0220] 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.

[0221] 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).

[0222] 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).

[0223] 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).

[0224] 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.

[0225] 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)

[0226] MERS-Co V.

[0227] MERS-CoV is a positive-sense, single-stranded RNA virus of the genus Betacoronavirus. The genomes are phylogenetically classified into two clades, Glade A and Glade 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.

[0228] 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. M Bio 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. M Bio 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. M Bio 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).

[0229] 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.

[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, N protein and M protein.

[0231] 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.

[0232] 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.

[0233] 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).

[0234] 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).

[0235] 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.

[0236] **SARS**-CoV.

[0237] 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.

[0238] 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.

[0239] 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.

[0240] 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.

[0241] 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).

[0242] 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.

[0243] HCoV-OC43.

[0244] 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.

[0245] HCoV-HKU1.

[0246] 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.

[0247] HCoV-NL63.

[0248] 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.

[0249] HCoV-229E.

[0250] 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

[0251] 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).

[0252] 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).

[0253] 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.

[0254] 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.

[0255] 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.

[0256] 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.

[0257] 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.

[0258] 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.

[0259] 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).

[0260] 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.

[0261] 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).

[0262] 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).

[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, a RSV antigenic polypeptide and a MeV antigenic polypeptide.

[0264] 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).

[0265] 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).

[0266] 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).

[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, 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).

[0268] 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.

[0269] 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.

[0270] 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).

[0271] 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.

[0272] 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).

[0273] 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).

[0274] 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.

[0275] 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).

[0276] 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).

[0277] Other combination respiratory virus RNA (e.g., mRNA) vaccines are encompassed by the present disclosure.

[0278] 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.

[0279] 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.

[0280] 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.

[0281] 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.

[0282] 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).

[0283] 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.

[0284] 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

[0285] 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.

[0286] 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.

[0287] 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."

[0288] 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.

[0289] 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.

[0290] 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.

[0291] 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)).

[0292] 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)).

[0293] 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

[0294] 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.

[0295] 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.

[0296] 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 phospho-threonine and/or phospho-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.

[0297] "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.

[0298] "Analog" 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.

[0299] 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.

[0300] 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.

[0301] "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.

[0302] 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.

[0303] "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.

[0304] 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).

[0305] 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.

[0306] 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.

[0307] 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.

[0308] 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.

[0309] 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.

[0310] 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.

[0311] 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

[0312] 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.

[0313] 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.

[0314] 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

[0315] 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.

[0316] 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.

[0317] 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 METPAQLLFLLLLWLPD TTG (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).

[0318] 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.

[0319] 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.

[0320] A signal peptide is typically cleaved from the nascent polypeptide at the cleavage junction during ER processing. The mature antigenic polypeptide produced by a respiratory virus RNA (e.g., mRNA) vaccine of the present disclosure typically does not comprise a signal peptide.

Chemical Modifications

[0321] 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.

[0322] 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 deoxyribonucleosides 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" if they contain amino acid substitutions, insertions or a combination of substitutions and insertions.

[0323] 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).

[0324] 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).

[0325] 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 linkage, 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.

[0326] 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 be 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 phosphodiester linkages, in which case the polynucleotides would comprise regions of nucleotides.

[0327] 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.

[0328] 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-glycinylicarbamoyladenosine; N6-isopentenyladenosine; N6-methyladenosine; N6-threonylicarbamoyladenosine; 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-threonylicarbamoyladenosine; 2-methyladenosine; 2-methylthio-N6-isopentenyladenosine; 7-deaza-adenosine; N1-methyladenosine; 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'-.alpha.-aminoadenosine TP; 2'-Deoxy-2'-.alpha.-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-adenosine; 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'-.alpha.-Ethylnyladenosine TP; 2-aminoadenine; 2-Aminoadenosine TP; 2-Amino-ATP; 2'-.alpha.-Trifluoromethyladenosine TP; 2-Azidoadenosine TP; 2'-b-Ethylnyladenosine 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'-Ethylnyladenosine 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-mercaptopcytidine 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-mercaptopcytidine 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)aracytidine 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; Methylwyosine; 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)guanaine; 2-(alkyl)guanaine; 2'-Amino-2'-deoxy-GTP; 2'-Azido-2'-deoxy-GTP; 2'-Deoxy-2'-a-aminoguanosine TP; 2'-Deoxy-2'-a-azidoguanosine TP; 6 (methyl)guanaine; 6-(alkyl)guanaine; 6-(methyl)guanaine; 6-methyl-guanosine; 7 (alkyl)guanaine; 7 (deaza)guanaine; 7 (methyl)guanaine; 7-(alkyl)guanaine; 7-(deaza)guanaine; 7-(methyl)guanaine; 8 (alkyl)guanaine; 8 (alkynyl)guanaine; 8 (halo)guanaine; 8 (thioalkyl)guanaine; 8-(alkenyl)guanaine; 8-(alkyl)guanaine; 8-(alkynyl)guanaine; 8-(amino)guanaine; 8-(halo)guanaine; 8-(hydroxyl)guanaine; 8-(thioalkyl)guanaine; 8-(thiol)guanaine; aza guanaine; deaza guanaine; N (methyl)guanaine; N-(methyl)guanaine; 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-Ethynylguanosine TP; 2'-b-Trifluoromethylguanosine TP; 2'-Deoxy-2',2'-difluoroguanosine TP; 2'-Deoxy-2'-a-mercaptopguanosine 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-mercaptopguanosine 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-methylpseudouridine; 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-(aminoalkylaminocarbonylethylenyl)-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)pseudouracil; 2' methyl, 2' amino, 2' azido, 2' fluoro-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; allylamino-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-Methoxybenzyl)pseudo-UTP; 1-(4-Methoxy-phenyl)pseudo-UTP; 1-(4-Methylbenzyl)pseudouridine TP; 1-(4-Methylbenzyl)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]pseudouridine TP; 1-{3-[2-(2-Aminoethoxy)-ethoxy]-propionyl} pseudouridine TP; 1-

Acetylpsseudouridine 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-Allylpsseudouridine TP; 1-Aminomethyl-pseudo-UTP; 1-Benzoylpsseudouridine TP; 1-Benzyloxymethylpsseudouridine TP; 1-Benzyl-pseudo-UTP; 1-Biotinyl-PEG2-psseudouridine TP; 1-Biotinylpsseudouridine TP; 1-Butyl-pseudo-UTP; 1-Cyanomethylpsseudouridine 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-Homoallylpsseudouridine TP; 1-Hydroxymethylpsseudouridine 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-Methanesulfonylmethylpsseudouridine TP; 1-Methoxymethylpsseudouridine 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-Morpholinomethylpsseudouridine TP; 1-Pentyl-pseudo-UTP; 1-Phenyl-pseudo-UTP; 1-Pivaloylpsseudouridine TP; 1-Propargylpsseudouridine TP; 1-Propyl-pseudo-UTP; 1-propynyl-psseudouridine; 1-p-tolyl-pseudo-UTP; 1-tert-Butyl-pseudo-UTP; 1-Thiomethoxymethylpsseudouridine TP; 1-Thiomorpholinomethylpsseudouridine TP; 1-Trifluoroacetylpsseudouridine TP; 1-Trifluoromethyl-pseudo-UTP; 1-Vinylpsseudouridine 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-mercaptopuridine 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-mercaptopuridine 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-(diaz)-2-(oxo)-phenthiazin-1-yl; 1,3-(diaz)-2-(oxo)-phenoxazin-1-yl; 1,3,5-(triaz)-2,6-(diox)-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)isocarbostyrylyl; 3-(methyl)isocarbostyrylyl; 4-(fluoro)-6-(methyl)benzimidazole; 4-(methyl)benzimidazole; 4-(methyl)indolyl; 4,6-(dimethyl)indolyl; 5 nitroindole; 5 substituted pyrimidines; 5-(methyl)isocarbostyrylyl; 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-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(aminoalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(aza)indolyl; 7-(guanidiniumalkylhydroxy)-1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-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-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(guanidiniumalkylhydroxy)-1,3-(diazia)-2-(oxo)-phenoxazin-1-yl; 7-(propynyl)isocarbostyrylyl; 7-(propynyl)isocarbostyrylyl, propynyl-7-(aza)indolyl; 7-deaza-inosinyl; 7-substituted 1-(aza)-2-(thio)-3-(aza)-phenoxazin-1-yl; 7-substituted 1,3-(diazia)-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; Isocarbostyrylyl; Isoguanisine; N2-substituted purines; N6-methyl-2-amino-purine; N6-substituted purines; N-alkylated derivative; Napthalenyl; Nitrobenzimidazolyl; Nitroimidazolyl; Nitroindazolyl; Nitropyrazolyl; Nubularine; O6-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-aminopyridopyrimidin-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-Aminopentaaxanonadecyl)adenosine TP.

[0329] 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.

[0330] 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.

[0331] 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.

[0332] In some embodiments, polynucleotides (e.g., RNA polynucleotides, such as mRNA polynucleotides) comprise pseudouridine (w) 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).

[0333] 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.

[0334] 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.

[0335] 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.

[0336] 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).

[0337] 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 (preQO), 7-aminomethyl-7-deaza-guanosine (preQ1), 7-methyl-guanosine (m7G), 1-methyl-guanosine (m1G), 8-oxo-guanosine, 7-methyl-8-oxo-guanosine.

[0338] 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.

[0339] 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.

[0340] 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). 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 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).

[0341] 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.

[0342] In some embodiments, the modified nucleobase is a modified uracil. Exemplary nucleobases and nucleosides having a modified uracil include pseudouridine (w), 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-uridine or 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.s.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 (Um), 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'-OH-ara-uridine, 5-(2-carbomethoxyvinyl) uridine, and 5-[3-(1-E-propenylamino)]uridine.

[0343] 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-formylcytidine (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.2Cm), 1-thio-cytidine, 2'-F-ara-cytidine, 2'-F-cytidine, and 2'-OH-ara-cytidine.

[0344] 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-glycylcarbamoyl-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.2A), 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.2Am), 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'-OH-ara-adenosine, and N6-(19-amino-pentaoxonadecyl)-adenosine.

[0345] 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 (o.sub.2yW), 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.sup.+), 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.2G), N2,7-dimethyl-guanosine (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.2Gm), 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, O6-methyl-guanosine, 2'-F-ara-guanosine, and 2'-F-guanosine.

N-Linked Glycosylation Site Mutants

[0346] 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)

[0347] 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.

[0348] 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.

[0349] 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.

[0350] 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.

[0351] 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.

[0352] 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

[0353] 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.

[0354] 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. burgdorferi*, *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.

[0355] A flagellin polypeptide, as used herein, refers to a full length flagellin protein, immunogenic fragments thereof, and peptides having at least 50% sequence identity 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 identity to a flagellin protein or immunogenic fragments thereof.

[0356] 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.

[0357] 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).

[0358] 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."

[0359] 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.

[0360] 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

[0361] 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

[0362] 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.

[0363] 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.

[0364] 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).

[0365] 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).

[0366] 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).

[0367] 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).

[0368] 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.

[0369] 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.

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.

[0370] In some embodiments the immune response is assessed by determining [protein] antibody titer in the subject.

[0371] 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.

[0372] 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.

[0373] 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.

[0374] 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

[0375] 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 for 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.

[0376] 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.

[0377] 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.

[0378] An "effective amount" of a 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.

[0379] 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).

[0380] 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.

[0381] Respiratory virus RNA (e.g. mRNA) vaccines may be administered 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.

[0382] 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.

[0383] 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.

[0384] 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.

[0385] 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

[0386] RNA (e.g., mRNA) vaccines (vaccine compositions) may comprise other components including, but not limited to, adjuvants.

[0387] In some embodiments, respiratory virus (e.g. mRNA) vaccines do not include an adjuvant (they are adjuvant free).

[0388] 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).

[0389] 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.

[0390] 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.

[0391] 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.

[0392] 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

[0393] 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.

[0394] 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.

[0395] 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)).

[0396] 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.

[0397] 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.

[0398] In some embodiments, the RNA (e.g., mRNA) vaccine may or may not contain an 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.

[0399] 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

[0400] 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).

[0401] 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).

[0402] 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.

[0403] 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-dimyristyl-oxypopyl-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.

[0404] 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- 1]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.

[0405] 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.

[0406] 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.

[0407] 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.

[0408] 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).

[0409] 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.

[0410] 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.

[0411] 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.

[0412] 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.

[0413] 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.

[0414] 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.

[0415] 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.

[0416] 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.

[0417] 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.

[0418] 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.

[0419] 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), 57.2/7.1/34.3/1.4 (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).

[0420] 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).

[0421] 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.

[0422] 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.

[0423] 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.

[0424] 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.

[0425] 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.

[0426] 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

[0427] 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.

[0428] 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.

[0429] In some embodiments, pharmaceutical compositions described herein may include, without limitation, liposomes such as those formed from 1,2-dioleoyloxy-N,N-dimethylaminopropane (DODMA) liposomes, DiLa2 liposomes from Marina Biotech (Bothell, Wash.), 1,2-dilinoleoyloxy-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.).

[0430] 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 entirety). 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% distearylphosphatidyl choline (DSPC), 10% PEG-S-DSG, and 15% 1,2-dioleoyloxy-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.

[0431] 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.

[0432] 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).

[0433] 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.

[0434] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid vesicle, which may have crosslinks between functionalized lipid bilayers.

[0435] 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).

[0436] 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)carbomoyl]-1,2-dimyristyl-oxypopyl-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.

[0437] In some embodiments, the RNA (e.g., mRNA) vaccines may be formulated in a lipid nanoparticle.

[0438] 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]methyl}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.

[0439] 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.

[0440] 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.

[0441] 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.

[0442] 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)

[0443] 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.

[0444] 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.

[0445] 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.

[0446] 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.

[0447] 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.

[0448] 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.

[0449] 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.

[0450] 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.

[0451] 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.

[0452] 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.

[0453] 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).

[0454] 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).

[0455] 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.

[0456] 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.

[0457] 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.

[0458] As a non-limiting example, the cationic lipid may be selected from (20Z,23Z)--N,N-dimethylnonacos-20,23-dien-10-amine, (17Z,20Z)--N,N-dimethylhexacos-17,20-dien-9-amine, (1Z,19Z)--N,N-dimethylpentacos-16,19-dien-8-amine, (13Z,16Z)--N,N-dimethyldocos-13,16-dien-5-amine, (12Z,15Z)--N,N-dimethylhenicos-12,15-dien-4-amine, (14Z,17Z)--N,N-dimethyltricos-14,17-dien-6-amine, (15Z,18Z)--N,N-dimethyltetracos-15,18-dien-7-amine, (18Z,21Z)--N,N-dimethylheptacos-18,21-dien-10-amine, (15Z,18Z)--N,N-dimethyltetracos-15,18-dien-5-amine, (14Z,17Z)--N,N-dimethyltricos-14,17-dien-4-amine, (19Z,22Z)--N,N-dimethyloctacos-19,22-dien-9-amine, (18Z,21Z)--N,N-dimethylheptacos-18,21-dien-8-amine, (17Z,20Z)--N,N-dimethylhexacos-17,20-dien-7-amine, (16Z,19Z)--N,N-dimethylpentacos-16,19-dien-6-amine, (22Z,25Z)--N,N-dimethylhentriaconta-22,25-dien-10-amine, (21Z,24Z)--N,N-dimethyltriaconta-21,24-dien-9-amine, (18Z)--N,N-dimethylheptacos-18-en-10-amine, (17Z)--N,N-dimethylhexacos-17-en-9-amine, (19Z,22Z)--N,N-dimethyloctacos-19,22-dien-7-amine, N,N-dimethylheptacos-10-amine, (20Z,23Z)--N-ethyl-N-methylnonacos-20,23-dien-10-amine, 1-[(11Z,14Z)-1-nonylicos-11,14-dien-1-yl]pyrrolidine, (20Z)--N,N-dimethylheptacos-20-en-10-amine, (15Z)--N,N-dimethyleptacos-15-en-10-amine, (14Z)--N,N-dimethylnonacos-14-en-10-amine, (17Z)--N,N-dimethylnonacos-17-en-10-amine, (24Z)--N,N-dimethyltriacont-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-nonylhenicos-12,15-dien-1-amine, (13Z,16Z)--N,N-dimethyl-3-nonyldocos-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-[(1R,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-pentylcyclopropyl]methyl]cyclopropyl]nonadecan-10-amine, N,N-dimethyl-1-[(1S,2R)-2-octylcyclopropyl]hexadecan-8-amine, N,N-dimethyl-[(1R,2S)-2-undecylcyclopropyl]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-[(1S,2R)-2-octylcyclopropyl]pentadecan-8-amine, R--N,N-dimethyl-1-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-3-(octyloxy)propan-2-amine, S--N,N-dimethyl-1-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-3-(octyloxy)propan-2-amine, 1-{2-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]-1-[(octyloxy)methyl]ethyl}pyrrolidine, (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}azetidide, (2S)-1-(hexyloxy)-N,N-dimethyl-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, (2S)-1-(heptyloxy)-N,N-dimethyl-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, N,N-dimethyl-1-(nonyloxy)-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, N,N-dimethyl-1-[(9Z)-octadec-9-en-1-yloxy]-3-(octyloxy)propan-2-amine; (2S)--N,N-dimethyl-1-[(6Z,9Z,12Z)-octadeca-6,9,12-trien-1-yloxy]-3-(octyloxy)propan-2-amine, (2S)-1-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,N-dimethyl-3-(pentyloxy)propan-2-amine, (2S)-1-(hexyloxy)-3-[(11Z,14Z)-icosa-11,14-dien-1-yloxy]-N,N-dimethylpropan-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)propan-2-amine, (2S)-1-[(13Z,16Z)-docosa-13,16-dien-1-yloxy]-3-(hexyloxy)-N,N-dimethylpropan-2-amine, (2S)-1-[(13Z)-docos-13-en-1-yloxy]-3-(hexyloxy)-N,N-dimethylpropan-2-amine, 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)oxyl-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, (2R)-1-[(3,7-dimethyloctyl)oxy]-N,N-dimethyl-3-[(9Z,12Z)-octadeca-9,12-dien-1-yloxy]propan-2-amine, N,N-dimethyl-1-(octyloxy)-3-[(8-[(1S,2S)-2-[(1R,2R)-2-pentylcyclopropyl]methyl]cyclopropyl]octyl)oxy]propan-2-amine, N,N-dimethyl-1-[[8-(2-octylcyclopropyl)octyl]oxyl]-3-(octyloxy)propan-2-amine and (11E,20Z,23Z)--N,N-dimethylnonacos-11,20,23-trien-10-amine or a pharmaceutically acceptable salt or stereoisomer thereof.

[0459] 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.

[0460] 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.

[0461] In some embodiments, the LNP formulation may contain PEG-DMG 2000 (1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine-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).

[0462] The lipid nanoparticles described herein may be made in a sterile environment.

[0463] 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.

[0464] 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.

[0465] 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.

[0466] 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.

[0467] 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.

[0468] 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.

[0469] 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.

[0470] 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, phytoglycogen 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).

[0471] 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.

[0472] 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.

[0473] In some embodiments, the lipid nanoparticles of the present disclosure may be hydrophobic polymer particles.

[0474] 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.

[0475] In some embodiments, the internal ester linkage may be located on either side of the saturated carbon.

[0476] 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.

[0477] 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.

[0478] 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, polyethyleneimines, 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 cyanoacrylate, 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).

[0479] 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).

[0480] 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 dimethyldioctadecylammonium 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, carbocysteine, eprazinone, mesna, ambroxol, sobrerol, domiodol, letosteine, stepronin, tiopronin, gelsolin, thymosin (34 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).

[0481] 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.

[0482] In some embodiments, the mucus penetrating lipid nanoparticles may be a hypotonic formulation comprising a mucosal penetration enhancing coating. The formulation may be hypotonic 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.

[0483] 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 muco-inert 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).

[0484] 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 (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).

[0485] 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).

[0486] 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.

[0487] 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.

[0488] 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.

[0489] 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 WO2012131106, the contents of each of which are incorporated herein by reference in their entirety).

[0490] 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.).

[0491] 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.

[0492] 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.).

[0493] 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.

[0494] 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.

[0495] 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.

[0496] 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.

[0497] 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).

[0498] 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.

[0499] 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.

[0500] 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.

[0501] 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.

[0502] 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).

[0503] 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.

[0504] 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).

[0505] 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).

[0506] 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.

[0507] 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.

[0508] 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).

[0509] In some embodiments, the therapeutic nanoparticles may comprise at least one cationic polymer described herein and/or known in the art.

[0510] 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.

[0511] 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.

[0512] In some embodiments, the therapeutic nanoparticles 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.

[0513] 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).

[0514] 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 entirety).

[0515] 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.

[0516] 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.

[0517] 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).

[0518] 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.

[0519] 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.

[0520] 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).

[0521] 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.

[0522] 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.

[0523] 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.

[0524] 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.

[0525] In some embodiments, RNA (e.g., mRNA) vaccine may be delivered using smaller LNPs. Such particles may comprise a diameter from below 0.1 μm up to 100 nm such as, but not limited to, less than 0.1 μm , less than 1.0 μm , less than 5 μm , less than 10 μm , less than 15 μm , less than 20 μm , less than 25 μm , less than 30 μm , less than 35 μm , less than 40 μm , less than 50 μm , less than 55 μm , less than 60 μm , less than 65 μm , less than 70 μm , less than 75 μm , less than 80 μm , less than 85 μm , less than 90 μm , less than 95 μm , less than 100 μm , less than 125 μm , less than 150 μm , less than 175 μm , less than 200 μm , less than 225 μm , less than 250 μm , less than 275 μm , less than 300 μm , less than 325 μm , less than 350 μm , less than 375 μm , less than 400 μm , less than 425 μm , less than 450 μm , less than 475 μm , less than 500 μm , less than 525 μm , less than 550 μm , less than 575 μm , less than 600 μm , less than 625 μm , less than 650 μm , less than 675 μm , less than 700 μm , less than 725 μm , less than 750 μm , less than 775 μm , less than 800 μm , less than 825 μm , less than 850 μm , less than 875 μm , less than 900 μm , less than 925 μm , less than 950 μm , less than 975 μm , or less than 1000 μm .

[0526] 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.

[0527] 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.

[0528] 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 für Mikrotechnik Mainz GmbH, Mainz Germany).

[0529] 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).

[0530] 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.

[0531] 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).

[0532] 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.

[0533] In some embodiments, the lipid nanoparticles may have a diameter from about 10 to 500 nm.

[0534] 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.

[0535] 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 diacylphosphatidylcholine, 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.

[0536] 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.

[0537] 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.

[0538] 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.

[0539] 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.

[0540] 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.

[0541] 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)-{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).

[0542] 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.

[0543] 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.

[0544] 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).

[0545] 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.

[0546] 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 incorporate 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.

[0547] 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.

[0548] 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.

[0549] 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.

[0550] 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.

[0551] 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 be 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.

[0552] At least one of the nanoparticles of the present disclosure may be embedded 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.

[0553] 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, pIsl, 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: Dioleoyl phosphatidylethanol-amine, DOSPA, DODAB, DOIC, DMEPC, DOGS: Dioctadecylamidoglycylspermin, DIMRI: Dimyristoxypropyl 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]-trimethylammonium, 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.

[0554] In other embodiments the RNA (e.g., mRNA) vaccine is not associated with a cationic or polycationic compounds.

[0555] In some embodiments, a nanoparticle comprises compounds of Formula (I):

##STR00003##

[0556] or a salt or isomer thereof, wherein:

[0557] 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';

[0558] 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;

[0559] 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,

[0560] --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)OR, and --C(R)N(R).sub.2C(O)OR, and each n is independently selected from 1, 2, 3, 4, and 5;

[0561] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0562] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0563] M and M' are independently selected from --C(O)O--, --OC(O)--, --C(O)N(R)--,

[0564] --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;

[0565] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0566] R.sub.8 is selected from the group consisting of C.sub.3-6 carbocycle and heterocycle;

[0567] 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; [0568] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0569] 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;

[0570] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0571] each R* is independently selected from the group consisting of C1-12 alkyl and C.sub.2-12 alkenyl;

[0572] each Y is independently a C3-6 carbocycle;

[0573] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0574] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13.

[0575] 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.

[0576] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0577] 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';

[0578] 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;

[0579] 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)OR, 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;

[0580] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0581] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0582] 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;

[0583] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0584] R.sub.8 is selected from the group consisting of C.sub.3-6 carbocycle and heterocycle;

[0585] 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;

[0586] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0587] 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;

[0588] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0589] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.2-12 alkenyl;

[0590] each Y is independently a C.sub.3-6 carbocycle;

[0591] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0592] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13, or salts or isomers thereof.

[0593] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0594] 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';

[0595] 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;

[0596] 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;

[0597] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0598] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0599] 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;

[0600] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0601] R.sub.8 is selected from the group consisting of C.sub.3-6 carbocycle and heterocycle;

[0602] 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;

[0603] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0604] 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;

[0605] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0606] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.2-12 alkenyl;

[0607] each Y is independently a C.sub.3-6 carbocycle;

[0608] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0609] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0610] or salts or isomers thereof.

[0611] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0612] 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';

[0613] 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;

[0614] 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;

[0615] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0616] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0617] 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;

[0618] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0619] R.sub.8 is selected from the group consisting of C.sub.3-6 carbocycle and heterocycle;

[0620] 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;

[0621] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0622] 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;

[0623] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0624] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.2-12 alkenyl;

[0625] each Y is independently a C.sub.3-6 carbocycle;

[0626] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0627] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13, or salts or isomers thereof.

[0628] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0629] 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';

[0630] 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;

[0631] 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;

[0632] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0633] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0634] 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;

[0635] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0636] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0637] 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;

[0638] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0639] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.1-12 alkenyl;

[0640] each Y is independently a C.sub.3-6 carbocycle;

[0641] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0642] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0643] or salts or isomers thereof.

[0644] In some embodiments, another subset of compounds of Formula (I) includes those in which

[0645] 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';

[0646] 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;

[0647] 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;

[0648] each R.sub.5 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0649] each R.sub.6 is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0650] 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;

[0651] R.sub.7 is selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0652] each R is independently selected from the group consisting of C.sub.1-3 alkyl, C.sub.2-3 alkenyl, and H;

[0653] 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;

[0654] each R" is independently selected from the group consisting of C.sub.3-14 alkyl and C.sub.3-14 alkenyl;

[0655] each R* is independently selected from the group consisting of C.sub.1-12 alkyl and C.sub.1-12 alkenyl;

[0656] each Y is independently a C.sub.3-6 carbocycle;

[0657] each X is independently selected from the group consisting of F, Cl, Br, and I; and

[0658] m is selected from 5, 6, 7, 8, 9, 10, 11, 12, and 13,

[0659] or salts or isomers thereof.

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

##STR00004##

[0661] 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.

[0662] 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.

[0663] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (IIE):

##STR00006##

[0664] or a salt or isomer thereof, wherein R.sub.4 is as described herein.

[0665] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIId):

##STR00007##

[0666] 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.

[0667] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIa), (IIb), (IIc), or (IIE):

##STR00008##

[0668] or a salt or isomer thereof, wherein R.sub.4 is as described herein.

[0669] In some embodiments, a subset of compounds of Formula (I) includes those of Formula (IIId):

##STR00009##

[0670] 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.

[0671] In some embodiments, the compound of Formula (I) is selected from the group consisting of:

##STR00010## ##STR00011## ##STR00012## ##STR00013## ##STR00014## ##STR00015##
##STR00016## ##STR00017## ##STR00018## ##STR00019##

[0672] In further embodiments, the compound of Formula (I) is selected from the group consisting of:

##STR00020##

[0673] In some embodiments, the compound of Formula (I) is selected from the group consisting of:

##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## ##STR00048## ##STR00049## ##STR00050##

and salts and isomers thereof.

[0674] In some embodiments, a nanoparticle comprises the following compound:

##STR00051##

or salts and isomers thereof.

[0675] 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)).

[0676] 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.

[0677] 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 (IIE) 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.

[0678] 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.

[0679] 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.

[0680] 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).

[0681] 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.

[0682] 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.

[0683] 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

[0684] 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.

[0685] 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) vaccine 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.

[0686] 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.

[0687] 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.

[0688] 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.

[0689] 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.

[0690] 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

[0691] 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.

[0692] 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.

[0693] 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.

[0694] 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.

[0695] 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.

[0696] 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).

[0697] 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.

[0698] 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.

[0699] 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.

[0700] 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.

[0701] 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, 600-800, 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

[0702] 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:

[0703] 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

[0704] 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:

[0705] 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

[0706] 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:

[0707] 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

[0708] 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:

[0709] 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

[0710] 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:

[0711] 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

[0712] 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:

[0713] 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

[0714] 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:

[0715] at least one RNA polynucleotide having an open reading frame encoding a PIV3 antigenic polypeptide or an immunogenic fragment thereof and a BetaCoV antigenic polypeptide or an immunogenic fragment thereof; or

[0716] 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:

[0717] 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

[0718] 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:

[0719] 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

[0720] 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:

[0721] 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

[0722] 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:

[0723] 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

[0724] 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:

[0725] 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

[0726] 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:

[0727] 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

[0728] 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:

[0729] 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

[0730] 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:

[0731] 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

[0732] 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:

[0733] 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

[0734] 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:

[0735] 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

[0736] 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:

[0737] 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

[0738] 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:

[0739] 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

[0740] 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:

[0741] 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

[0742] 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:

[0743] 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

[0744] 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:

[0745] 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

[0746] 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:

[0747] 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

[0748] 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:

[0749] 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

[0750] 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:

[0751] 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

[0752] 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:

[0753] 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

[0754] 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')NImpNp. 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 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

[0755] (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

[0756] (b) comprising a compound of Formula (I) and/or Formula (II),

[0757] 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

[0758] (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

[0759] (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 antigenic 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 antigenic 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 antigenic polypeptides. 86. The respiratory virus vaccine of any one of paragraphs 81-85, wherein the at least one antigenic polypeptide is selected from MeV antigenic 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 antigenic polypeptides (e.g., SEQ ID NO: 24-34). 88. The respiratory virus vaccine of paragraph 87, wherein the BetaCoV antigenic polypeptides are MERS antigenic polypeptides. 89. The respiratory virus vaccine of paragraph 87, wherein the BetaCoV antigenic polypeptides are **SARS** antigenic 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:

[0760] 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')NlmpNp. 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:

[0761] at least one messenger ribonucleic acid (mRNA) polynucleotide having a 5' terminal cap 7mG(5')ppp(5')NlmpNp, 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.

[0762] 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

[0763] 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.

[0764] 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.

[0765] 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.

[0766] 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

[0767] 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.

[0768] 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.

[0769] Monophosphate protecting groups may be selected from any of those known in the art.

[0770] 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.

[0771] For ligation methods, ligation with DNA T4 ligase, followed by treatment with DNase should readily avoid concatenation.

[0772] 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.

[0773] Ligation is then performed using any known click chemistry, orthoclick chemistry, solulink, or other bioconjugate chemistries known to those in the art.

[0774] Synthetic Route

[0775] The chimeric polynucleotide may be made using a series of starting segments. Such segments include:

[0776] (a) a capped and protected 5' segment comprising a normal 3'OH (SEG. 1)

[0777] (b) a 5' triphosphate segment, which may include the coding region of a polypeptide and a normal 3'OH (SEG. 2)

[0778] (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)

[0779] After synthesis (chemical or IVT), segment 3 (SEG. 3) may be treated with cordycepin and then with pyrophosphatase to create the 5' monophosphate.

[0780] 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.

[0781] 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).

[0782] The yields of each step may be as much as 90-95%.

Example 3: PCR for cDNA Production

[0783] 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.

[0784] 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)

[0785] 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.

[0786] 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.

[0787] 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

[0788] 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.

[0789] 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.

[0790] 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

[0791] 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 MgCl₂) (12.0 μ l); 20 mM ATP (6.0 μ l); Poly-A Polymerase (20 U); dH₂O up to 123.5 μ l and incubation at 37°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 MEGACLEARTM kit (Austin, Tex.) (up to 500 μ g). Poly-A Polymerase may be a recombinant enzyme expressed in yeast.

[0792] 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

[0793] 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.

[0794] 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

[0795] 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

[0796] 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

[0797] 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- α and IFN- β , 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

[0798] 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

[0799] 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

[0800] 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

[0801] 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

[0802] 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.

[0803] 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

[0804] 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.

[0805] 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.

[0806] 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

[0807] 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).

[0808] 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.

[0809] 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

[0810] 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.

[0811] 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.

[0812] 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

[0813] 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.

[0814] 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.

[0815] 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

[0816] 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.

[0817] 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

[0818] 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.

[0819] 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.

[0820] 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

[0821] 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.

[0822] 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.

[0823] 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.

[0824] 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.

[0825] 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).

[0826] 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

[0827] 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 Si 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).

[0828] 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).

[0829] 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

[0830] 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).

[0831] 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

[0832] 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, S1 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

[0833] 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.

[0834] 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.

[0835] 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

[0836] 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.

[0837] 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).

[0838] 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).

[0839] 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

[0840] 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.

[0841] 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

[0842] 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).

[0843] 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.

[0844] 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 PBS Pre- Prime Bleeds Bleeds Bleeds/ Bleeds Bleeds Harvest 1 (n = 8) (IM) Bleed Boost Splens/ 10 .mu.g Group 10 .mu.g Terminal Dose 2 (n = 8) (IM) Bleeds 2 .mu.g Group 2 .mu.g Dose 3 (n = 8) (IM) Total n = 24

[0845] 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|E ATGAGCTGGAAGGTGGTATTATCTTCAGCCTGCTGATTA 1 F051124.1| Human
CACCTCAACACGGCCTGAAGGAGAGCTACCTGGAAGAGA metapneumovirus
GCTGCTCCACCATCACCGAGGGCTACCTGAGCGTGCTGC isolate TN/92-4
GGACCGGCTGGTACACCAACGTGTTACCCCTGGAGGTGG fusion protein gene,
GCGACGTGGAGAACCTGACCTGCAGCGACGGCCCTAGCC complete genome
TGATCAAGACCGAGCTGGACCTGACCAAGAGCGCTCTGA
GAGAGCTGAAGACCGTGTCCGCCGACCAGCTGGCCAGAG
AGGAACAGATCGAGAACCCTCGGCAGAGCAGATTTCGTGC
TGGGCGCCATCGCTCTGGGAGTCGCCGCTGCCGCTGCAG
TGACAGCTGGAGTGGCCATTGCTAAGACCATCAGACTGG
AAAGCGAGGTGACAGCCATCAACAATGCCCTGAAGAAG
ACCAACGAGGCCGTGAGCACCCCTGGGCAATGGAGTGAGA
GTGCTGGCCACAGCCGTGCGGGAGCTGAAGGACTTCGTG
AGCAAGAACCTGACCAGAGCCATCAACAAGAACAAGTG
CGACATCGATGACCTGAAGATGGCCGTGAGCTTCTCCA
GTTCAACAGACGGTTCCTGAACGTGGTGAGACAGTTCTC
CGACAACGCTGGAATCACACCTGCCATTAGCCTGGACCT
GATGACCGACGCCGAGCTGGCTAGAGCCGTGCCAACAT
GCCACCGAGCGCTGGCCAGATCAAGCTGATGCTGGAGAA
CAGAGCCATGGTGCAGGAGAAAGGGCTTCGGCATCCTGAT
TGGGGTGTATGGAAGCTCCGTGATCTACATGGTGCAGCT
GCCCATCTTCGGCGTGATCGACACACCCTGCTGGATCGTG
AAGGCCGCTCCTAGCTGCTCCGAGAAGAAAGGAAACTAT
GCCTGTCTGCTGAGAGAGGACCAGGGCTGGTACTGCCAG
AACGCCGGAAGCACAGTGTACTATCCCAACGAGAAGGAC
TGCGAGACCAGAGGCGACCACGTGTTCTGCGACACCGCT
GCCGGAATCAACGTGGCCGAGCAGAGCAAGGAGTGCAA
CATCAACATCAGCACAACTACCCCTGCAAGGTGAG
CACCGGACGGCACCCCATCAGCATGGTGGCTCTGAGCCC
TCTGGGCGCTCTGGTGGCCTGCTATAAGGGCGTGTCTCTGT
AGCATCGGCAGCAATCGGGTGGGCATCATCAAGCAGCTG
AACAAGGGATGCTCCTACATACCAACCAGGACGCCGAC
ACCGTGACCATCGACAACACCGTGTACCAGCTGAGCAAG
GTGGAGGGCGAGCAGCACGTGATCAAGGGCAGACCCGT
GAGCTCCAGCTTCGACCCCATCAAGTTCCTGAGGACCA
GTTCAACGTGGCCCTGGACCAGGTGTTTGAGAACATCGA
GAACAGCCAGGCCCTGGTGGACCAGAGCAACAGAATCCT
GTCCAGCGCTGAGAAGGGCAACACCGGCTTCATCATTGT
GATCATTCTGATCGCCGTGCTGGGCAGCTCCATGATCCTG

GTGAGCATCTTCATCATTATCAAGAAGACCAAGAAACCC
ACCGGAGCCCCTCCTGAGCTGAGCGGCGTGACCAACAAT GGCTTCATTCCCCACAACCTGA
gb|AY525843.1|:30 ATGTCTTGAAAGTGATGATCATCATTTCGTTACTCATAA 2 65-4684 Human
CACCCCAGCACGGGCTAAAGGAGAGTTATTTGGAAGAAT metapneumovirus
CATGTAGTACTATAACTGAGGGATACCTCAGTGTTTTAAG isolate NL/1/99,
AACAGGCTGGTACACTAATGTCTTCACATTAGAAGTTGGT complete genome
GATGTTGAAAATCTTACATGTAAGTGGACCTAGCTTAA
TCAAAACAGAACTTGATCTAACAAAAAGTGCTTTAAGGG
AACTCAAAACAGTCTCTGCTGATCAGTTGGCGAGAGAGG
AGCAAATTGAAAATCCCAGACAATCAAGATTTGTCTTAG
GTGCGATAGCTCTCGGAGTTGCTACAGCAGCAGCAGTCA
CAGCAGGCATTGCAATAGCCAAAACCATAAGGCTTGAGA
GTGAGGTGAATGCAATTAAGGTGCTCTCAAACAACTA
ATGAAGCAGTATCCACATTAGGGAATGGTGTGCGGGTCC
TAGCCACTGCAGTGAGAGAGCTAAAAGAATTTGTGAGCA
AAAACCTGACTAGTGCAATCAACAGGAACAAATGTGACA
TTGCTGATCTGAAGATGGCTGTCAGCTTCAGTCAATTCAA
CAGAAGATTTCTAAATGTTGTGCGGCAGTTTTTCAGACAAT
GCAGGGATAACACCAGCAATATCATTGGACCTGATGACT
GATGCTGAGTTGGCCAGAGCTGTATCATAATGCCAACA
TCTGCAGGGCAGATAAAACTGATGTTGGAGAACCGCGCA
ATGGTAAGGAGAAAAGGATTTGGAATCCTGATAGGGGTC
TACGGAAGCTCTGTGATTTACATGGTTCAATTGCCGATCT
TTGGTGTGATAGATACACCTTGTGGATCATCAAGGCAGC
TCCCTCTTGCTCAGAAAAAACGGGAATTATGCTTGCCTC
CTAAGAGAGGATCAAGGGTGGTATTGTAAAAATGCAGGA
TCTACTGTTTACTACCCAAATGAAAAAGACTGCGAAACA
AGAGGTGATCATGTTTTTTGTGACACAGCAGCAGGGATC
AATGTTGCTGAGCAATCAAGAGAATGCAACATCAACATA
TCTACTACCAACTACCCATGCAAAGTCAGCACAGGAAGA
CACCTATAAGCATGGTTGCACTATCACCTCTCGGTGCTT
TGGTGGCTTGCTATAAAGGGGTAAGCTGCTCGATTGGCA GCAATTGGGT
TGGAATCATCAAACAATTACCCAAAGGCTGCTCATAAT
AACCAACCAGGATGCAGACACTGTAACAATTGACAATAC
CGTGTATCAACTAAGCAAAGTTGAAGGTGAACAGCATGT
ATAAAAGGGAGACCAGTTTCAAGCAGTTTTTGATCCAAT
CAAGTTTCTGAGGATCAGTTCAATGTTGCGCTTGATCAA
GTCTTCGAAAGCATTGAGAACAGTCAGGCACTAGTGGAC
CAGTCAAACAAAATTCTAACAGTGCAGAAAAAGGAAA
CACTGGTTTCATTATCGTAGTAATTTTGGTTGCTGTTCTTG
GTCTAACCATGATTTCAAGTGAAGCATCATCATAATCAA
GAAAACAAGGAAGCCACAGGAGCACCTCCAGAGCTGA
ATGGTGTACCAACGGCGGTTTCATACCACATAGTTA gb|KJ627414.1|:30
ATGTCTTGAAAGTGATGATTATCATTTCGTTACTCATAA 3 15-4634 Human
CACCTCAGCATGGACTAAAAGAAAGTTATTTAGAAGAAT metapneumovirus
CATGTAGTACTATAACTGAAGGATATCTCAGTGTTTTAAG strain hMPV/Homo
AACAGGTTGGTACACCAATGTCTTTACATTAGAAGTTGGT sapiens/PER/CFI04
GATGTTGAAAATCTTACATGTAAGTGGACCTAGCTTAA 97/2010/B,
TCAAAACAGAACTTGACCTAACCAAAAAGTGCTTTAAGAG complete genome
AACTCAAAACAGTTTCTGCTGATCAGTTAGCGAGAGAAG
AACAAATTGAAAATCCCAGACAATCAAGGTTTGTCTTAG
GTGCAATAGCTCTTGGAGTTGCCACAGCAGCAGCAGTCA
CAGCAGGCATTGCAATAGCCAAAACCTATAAGGCTTGAGA
GTGAAGTGAATGCAATCAAAGGTGCTCTCAAACAACCA

ATGAGGCAGTATCAACACTAGGAAATGGAGTGC GGGTCC
TAGCCACTGCAGTAAGAGAGCTGAAAGAATTTGTGAGCA
AAAACCTGACTAGTGCATCAACAAGAACAAGTGTGACA
TTGCTGATTTGAAGATGGCTGTCAGCTTCAGTCAGTTCAA
CAGAAGATTCCTAAATGTTGTGCGGCAGTTTTTCAGACAAT
GCAGGGATAACACCAGCAATATCATTGGACCTGATGAAT
GATGCTGAGCTGGCCAGAGCTGTATCATACATGCCAACA
TCTGCAGGACAGATAAAACTAATGTTAGAGAACCGTGCA
ATGGTGAGGAGAAAAGGATTTGGAATCTTGATAGGGGTC
TACGGAAGCTCTGTGATTTACATGGTCCAGCTGCCGATCT
TTGGTGTCATAAATACACCTTGTTGGATAATCAAGGCAGC
TCCCTCTTGTTGAGAAAAGATGGAAATTATGCTTGCCTC
CTAAGAGAGGATCAAGGGTGGTATTGTAAAAATGCAGGA
TCCACTGTTTACTACCAAATGAAAAAGACTGCGAAACA
AGAGGTGATCATGTTTTTTGTGACACAGCAGCAGGGATC
AATGTTGCTGAGCAATCAAGAGAATGCAACATCAACATA
TCTACCACCAACTACCCATGCAAAGTCAGCACAGGAAGA
CACCTATCAGCATGGTTGCACTATCACCTCTCGGTGCTT
TGGTAGCTTGCTACAAAGGGGTTAGCTGCTCGACTGGCA
GTAATCAGGTTGGAATAATCAAACA ACTACCTAAAGGCT
GCTCATACTAACTAACCAGGACGCAGACACTGTAACAA
TTGACAACACTGTGTATCAACTAAGCAAAGTTGAGGGTG
AACAGCATGTAATAAAAGGGAGACCAGTTTCAAGCAGTT
TTGATCCAATCAGGTTTCCTGAGGATCAGTTCAATGTTGC
GCTTGATCAAGTCTTTGAAAGCATTGAAAACAGTCAAGC
ACTAGTGGACCAGTCAAACAAAATTCTGAACAGTGCAGA AAAAGGAAACACTGGT
TTCATTATTGTAATAATTTTGATTGCTGTTCTTGGGTTAAC
CATGATTCAGTGAGCATCATCATATAATCAAAAAAAC
AAGGAAGCCCACAGGGGCACCTCCGGAGCTGAATGGTGT
TACCAACGGCGGTTTCATACCGCATAGTTAG gb|KJ723483.1|:55
ATGGAGTTGCCAATCCTCAAACAAATGCAATTACCACA 4 86-7310 Human
ATCCTTGCTGCAGTCACACTCTGTTTCGCTTCCAGTCAA respiratory
ACATCACTGAAGAATTTTATCAATCAACATGCAGTGCAG syncytial virus
TTAGCAAAGGCTATCTTAGTGCTCTAAGAACTGGTTGGTA strain RSV A/Homo
TACTAGTGTATAACTATAGAATTAAGTAATATCAAGGA sapiens/USA/84I-
AAATAAGTGTAATGGAACAGATGCTAAGGTAAAATTGAT 215A-01/1984,
AAAACAAGAATTAGATAAATATAAAAATGCTGTAACAGA complete genome
ATTGCAGTTGCTCATGCAAAGCACACCAGCAGCCAACAA
TCGAGCCAGAAGAGA ACTACCAAGGTTTATGAATTATAC
ACTCAATAATACCAAAAATACCAATGTAACATTAAGCAA
GAAAAGGAAAAGAAGATTTCTTGGCTTTTTGTTAGGTGTT
GGATCTGCAATCGCCAGTGGCATTGCTGTATCTAAGGTCC
TGCACCTAGAAGGGGAAGTGAACAAAATCAAAGTGCTC
TACTATCCACAAACAAGGCTGTAGTCAGCTTATCAAATG
GAGTTAGTGTCTTAACCAGCAAAGTGTTAGACCTCAAAA
ACTATATAGATAAACAGTTGTTACCTATTGTGAACAAGC
AAAGCTGCAGCATATCAAACATTGAAACTGTGATAGAGT
TCCAACAAAAGAACAACAGACTACTAGAGATTACCAGGG
AATTTAGTGTTAATGCAGGTGTA ACTACACCTGTAAGCAC
TTATATGTTAACTAATAGTGAATTATTATCATTAATCAAT
GATATGCCTATAACAAATGATCAGAAAAAGTTAATGTCC
AACAATGTTCAAATAGTTAGACAGCAAAGTTACTCTATC
ATGTCCATAATAAAGGAGGAAGTCTTAGCATATGTAGTA
CAATTACCACTATATGGTGTAATAGATACACCTGTTGGA

AACTGCACACATCCCCTCTATGTACAACCAACACAAAGG
AAGGGTCCAACATCTGCTTAACAAGAACCGACAGAGGAT
GGTATTGTGACAATGCAGGATCAGTATCTTTCTTCCCACA
AGCTGAAACATGTAAAGTTCAATCGAATCGGGTATTTTGT
GACACAATGAACAGTTTAAACATTACCAAGTGAAGTAAAT
CTCTGCAACATTGACATATTCAACCCCAAATATGATTGCA
AAATTATGACTTCAAAAACAGATGTAAGCAGCTCCGTTA
TCACATCTCTAGGAGCCATTGTGTCATGCTATGGCAAAC
TAAATGTACAGCATCCAATAAAAATCGTGGGATCATAAA
GACATTTTCTAACGGGTGTGATTATGTATCAAATAAGGG
GGTGGATACTGTGTCTGTAGGTAATACATTATATTATGTA
ATAAGCAAGAAGGCCAAAAGTCTCTATGTAAAAGGTGAA
CCAATAATAAATTTCTATGACCCATTAGTGTTCCCCTCTG
ATGAATTTGATGCATCAATATCTCAAGTCAATGAGAAGA
TTAACCAGAGCCTAGCATTATTCGTAAATCCGATGAATT
ATTACATAATGTAAATGCTGGTAAATCCACCACAAATAT
CATGATAACTACTATAATTATAGTGATTATAGTAATATTG
TTATCATTAATTGCAGTTGGACTGCTCCTATACTGCAAGG
CCAGAAGCACACCAGTCACACTAAGTAAGGATCAACTGA
GTGGTATAAATAATATTGCATTTAGTAACTGA hMPV mRNA Sequences gi|122891979|gb|E
AUGAGCUGGAAGGUGGUGAUUAUCUUCAGCCUGCUGAU 57 F051124.1| Human
UACACCUCAACACGGCCUGAAGGAGAGCUACCUGGAAG metapneumovirus
AGAGCUGCUCCACCAUCACCGAGGGCUACCUGAGCGUG isolate TN/92-4
CUGCGGACCGGCUGGUACACCAACGUGUUCACCCUGGA fusion protein gene,
GGUGGGCGACGUGGAGAACCUGACCUGCAGCGACGGCC complete genome
CUAGCCUGAUCAAGACCGAGCUGGACCUGACCAAGAGC
GCUCUGAGAGAGCUGAAGACCGUGUCCGCCGACCAGCU
GGCCAGAGAGGAACAGAUCGAGAACCUCGGCAGAGCA
GAUUCGUGCUGGGCGCAUCGCUCUGGGAGUCGCCGCU
GCCGCUGCAGUGACAGCUGGAGUGGCCAUUGCUAAGAC
CAUCAGACUGGAAAGCGAGGUGACAGCCAUCAACAAUG
CCUGAAGAAGACCAACGAGGCCGUGAGCACCCUGGGC
AAUGGAGUGAGAGUGCUGGCCACAGCCGUGCGGGAGCU
GAAGGACUUCGUGAGCAAGAACCUGACCAGAGCCAUCA
ACAAGAACAAGUGCGACAUCGAUGACCUGAAGAUGGCC
GUGAGCUUCUCCAGUUCAACAGACGGUUCUGAACGU
GGUGAGACAGUUCUCCGACAACGCUGGAAUCACACCUG
CCAUUAGCCUGGACCUGAUGACCGACGCCGAGCUGGCU
AGAGCCGUGCCCAACAUGCCCACCAGCGCUGGCCAGAU
CAAGCUGAUGCUGGAGAACAGAGCCAUGGUGCGGAGAA
AGGGCUUCGGCAUCCUGAUUGGGGUGUAUGGAAGCUCC
GUGAUCUACAUGGUGCAGCUGCCAUCUUCGGCGUGAU
CGACACACCCUGCUGGAUCGUGAAGGCCGCUCCUAGCU
GCUCCGAGAAGAAAGGAAACUAUGCCUGUCUGCUGAGA
GAGGACCAGGGCUGGUACUGCCAGAACGCCGGAAGCAC
AGUGUACUAUCCCAACGAGAAGGACUGCGAGACCAGAG
GCGACCACGUGUUCUGCGACACCGCUGCCGGAUCAAC
GUGGCCGAGCAGAGCAAGGAGUGCAACAUCAACAUCAG
CACAACCAACUACCCUGCAAGGUGAGCACCGGACGGC
ACCCAUACAGCAUGGUGGCUCUGAGCCCUCUGGGCGCU
CUGGUGGCCUGCUAUAAGGGCGUGUCCUGUAGCAUCGG
CAGCAAUCGGGUGGGCAUCAUCAAGCAGCUGAACAAGG
GAUGCUCUACAUCACCAACCAGGACGCCGACCCGUG
ACCAUCGACAACACCGUGUACCAGCUGAGCAAGGUGGA

GGGCGAGCAGCACGUGAUC AAGGGCAGACCCGUGAGCU
CCAGCUUCGACCCCAUCAAGU UCCCUGAGGACCAGUUC
AACGUGGCCUGGACCAGGUGUUUGAGAACAUCGAGAA
CAGCCAGGCCUGGUGGACCAGAGCAACAGAAUCCUGU
CCAGCGCUGAGAAGGGCAACACCGGCUUCAUCAUUGUG
AUCAUUCUGAUCGCCGUGCUGGGCAGCUCCAUGAUCCU
GGUGAGCAUCUUCAUCAUUAUCAAGAAGACCAAGAAAC
CCACCGGAGCCCCUCCUGAGCUGAGCGGCGUGACCAAC AAUGGCUUCAU UCCCCACAACUGA
gb|AY525843.1|:30 AUGUCUUGGAAAGUGAUGAUCAUCAUUUCGUUACUCAU 58 65-4684 Human
AACACCCCAGCACGGGCUAAAGGAGAGUUAUUUGGAAG metapneumovirus
AAUCAUGUAGUACUAUAACUGAGGGAUACCUCAGUGUU isolate NL/1/99,
UUAAGAACAGGCUGGUACACUAAUGUCUUCACAUAUAGA complete genome
AGUUGGUGAUGUUGAAAAUCUUAUGUACUGAUGGA
CCUAGCUUAAUCAAAAACAGAACUUGAUCUAAACAAAAG
UGCUIUAAGGGAACUAAAACAGUCUCUGCUGAUCAGU
UGGCGAGAGAGGAGCAAAUUGAAAAUCCAGACAAUCA
AGAUUUGUCUUAGGUGCGAUAGCUCUCGGAGUUGCUAC
AGCAGCAGCAGUCACAGCAGGCAUUGCAAUAGCCAAA
CCAUAAGGCUUGAGAGUGAGGUGAAUGCAAUUAAGG
UGCUCUCAAAACAAACUAAUGAAGCAGUAUCCACAUAUAG
GGAAUGGUGUGCGGGUCCUAGCCACUGCAGUGAGAGAG
CUAAAAGAAUUUGUGAGCAAAAACCUAGCUAGUGCAAU
CAACAGGAACAAUUGUGACAUUGCUGAUCUGAAGAUGG
CUGUCAGCUUCAGUCAAUUCAACAGAAGAUUUCUAAA
GUUGUGCGGCAGUUUCAGACAAUGCAGGGUAACACC
AGCAAUAUCAUUGGACCUGAUGACUGAUGCUGAGUUGG
CCAGAGCUGUAUCAUCAUGCCAACAUCUGCAGGGCAG
AUAAAACUGAUGUUGGAGAACC GCGCAAUGGUAAGGAG
AAAAGGAUUUGGAAUCCUGAUAGGGGUCUACGGAAGCU
CUGUGAUUUACAUGGUUCAAUUGCCGAUCUUUGGUGUC
AUAGAUACACCUUGUUGGAUCAUCAAGGCAGCUCCCUC

UUGCUCAGAAAAAACGGGAAUUAUGCUUGCCUCCUAA
UACUGUUUACUACCCAAAUGAAAAAGACUGCGAAACAA
GAGGUGAUCAUGUUUUUGUGACACAGCAGCAGGGAU
AAUGUUGCUGAGCAAUCAAGAGAAUGCAACAUCAACAU
AUCUACUACCAACUACCCAUGCAAAGUCAGCACAGGAA
GACACCCUAUAAGCAUGGUUGCACUAUCACCUCUCGGU
GCUUUGGUGGCUUGCUAUAAAGGGGUAAGCUGCUCGAU UGGCAGCAAUUGGGU
UGGAAUCAUCAAAACAAUUAACCCAAAGGCUGCUCAUACA
UAACCAACCAGGAUGCAGACACUGUAACAAUUGACAAU
ACCGUGUAUCAACUAAGCAAAGUUGAAGGUGAACAGCA
UGUAAUAAAAGGGAGACCAGUUUCAAGCAGUUUUGAUC
CAAUCAAGUUCCUGAGGAUCAGUUCAAUGUUGCGCUU
GAUCAAGUCUUCGAAAGCAUUGAGAACAGUCAGGCACU
AGUGGACCAGUCAAAACAAAUUCUAAACAGUGCAGAAA
AAGGAAACACUGGUUCAUUAUCGUAGUAAUUUUGGU
UGCUGUUCUUGGUCUAACCAUGAUUUCAGUGAGCAUCA
UCAUCAUAAUCAAGAAAACAAGGAAGCCCACAGGAGCA
CCUCCAGAGCUGAAUGGUGUCACCAACGGCGGUUCAU ACCACAUAGUUAG gb|KJ627414.1|:30
AUGUCUUGGAAAGUGAUGAUUAUCAUUUCGUUACUCAU 59 15-4634 Human
AACACCUCAGCAUGGACUAAAAGAAAGUUAUUUAGAAG metapneumovirus
AAUCAUGUAGUACUAUAACUGAAGGAUAUCUCAGUGUU strain hMPV/Homo
UUAAGAACAGGUUGGUACACCAAUGUCUUUCAUAUAGA sapiens/PER/CFI04

AGUUGGUGAUGUUGAAAAUCUACAUGUACUGAUGGA 97/2010/B,
CCUAGCUUAAUCAAACAGAACUUGACCUAACCAAAAAG complete genome
UGCUIUAAGAGAACUCAAAAACAGUUUCUGCUGAUCAGU
UAGCGAGAGAAGAACAUAUUGAAAAUCCAGACAAUCA
AGGUUUGUCCUAGGUGCAAUAGCUCUUGGAGUUGCCAC
AGCAGCAGCAGUCACAGCAGGCAUUGCAAUAGCCAAAA
CUAUAAGGCUUGAGAGUGAAGUGAAUGCAAUCAAAGG
UGCUCUCAAAAACAACCAUUGAGGCAGUAUCAACACUAG
GAAAUGGAGUGCGGGUCCUAGCCACUGCAGUAAGAGAG
CUGAAAGAAUUUGUGAGCAAAAACCUAGACUAGUGCGAU
CAACAAGAACAAGUGUGACAUUGCUGAUUUGAAGAUGG
CUGUCAGCUUCAGUCAGUUCAACAGAAGAUUCCUAAA
GUUGUGCGGCAGUUUUCAGACAAUGCAGGGUAACACC
AGCAAUAUCAUUGGACCUGAUGAAUGAUGCUGAGCUGG
CCAGAGCUGUAUCAUACAUGCCAACAUCUGCAGGACAG
AUAAAACUAAUGUUAGAGAACCGUGCAAUGGUGAGGA
GAAAAGGAUUUGGAAUCUUGAUAGGGGUCUACGGAAG
CUCUGUGAUUUACAUGGUCCAGCUGCCGAUCUUUGGUG
UCAUAAAACACCUUGUUGGAUAAUCAAGGCAGCUC
UCUUGUUCAGAAAAAGAUGGAAAUUAUGCUUGCCUCCU
AAGAGAGGAUCAAGGGUGGUUUGUAAAAAUGCAGGA
UCCACUGUUUACUACCCAAAUGAAAAAGACUGCGAAAC
AAGAGGUGAUCAUGUUUUUUGUGACACAGCAGCAGGGA
UCAAUGUUGCUGAGCAAUCAAGAGAAUGCAACAUCAAC
AUUUCUACCACCAACUACCCAUGCAAAGUCAGCACAGG
AAGACACCCUAUCAGCAUGGUUGCACUAUCACCUCUCG
GUGCUUUGGUAGCUUGCUACAAAGGGGUUAGCUGCUCG
ACUGGCAGUAAUCAGGUUGGAAUAAUCAAAACUACC
UAAAGGCUGCUCAUACAUAACUAACCAGGACGCAGACA
CUGUAACAAUUGACAACACUGUGUAUCAACUAAAGCAA
GUUGAGGGUGAACAGCAUGUAAUAAAAGGGAGACCAG
UUUCAAGCAGUUUUGAUCCAUCAGGUUUCUGAGGAU
CAGUUCAAUGUUGCGCUUGAUCAAGUCUUUGAAAGCAU
UGAAAACAGUCAAGCACUAGUGGACCAGUCAAAACAAA
UUCUGAACAGUGCAGAAAAAGGAAACACUGGU
UUCAUUAUUGUAAUAAUUUUGAUUGCUGUUCUUGGGU
UAACCAUGAUUUCAGUGAGCAUCAUCAUAAUCAA
AAAACAAGGAAGCCCACAGGGGCACCUCCGGAGCUGAA
UGGUGUUACCAACGGCGGUUCAUACCGCAUAGUUAG gb|KJ723483.1|:55
AUGGAGUUGCCAAUCCUCAAAAACAAAUGCAAUACCAC 60 86-7310 Human
AAUCCUUGCUGCAGUCACACUCUGUUUCGCUUCCAGUC respiratory
AAAACAUCACUGAAGAAUUUUAUCAUCAACAUGCAGU syncytial virus
GCAGUUAGCAAAGGCUAUCUUAGUGCUCUAAGAACUGG strain RSV A/Homo
UUGGUUAUCUAGUGUUUAUAACUAUAGAAUUAAGUAAU sapiens/USA/84I-
AUCAAGGAAAAUAGUGUAAUGGAACAGAUGCUAAGG 215A-01/1984,
UAAAAUUGAUAAAACAAGAAUUAAGAUAAAUAUAAAA complete genome
UGCUGUAACAGAAUUGCAGUUGCUCUUGCAAAGCACAC
CAGCAGCCAACAUCGAGCCAGAAGAGAACUACCAAGG
UUUAUGAAUUAUACACUCAUAAUACCAAAAAUACCAA
UGUAACAUAUAGCAAGAAAAGGAAAAGAAGAUUUCU
GGCUUUUUGUUAGGUGUUGGAUCUGCAAUCGCCAGUGG
CAUUGCUGUAUCUAAAGGUCCUGCACCUAGAAGGGGAAG
UGAACAAAAUCAAAAGUGCUCUACUAUCCACAAACAAG
GCUGUAGUCAGCUUAUCAAAUGGAGUUAGUGUCUUAAC

CAGCAAAGUGUUAGACCUCAAAAACUAUAUAGAUAAAC
AGUUGUUACCUAUUGUGAACAAAGCAAAGCUGCAGCAUA
UCAAAACAUUGAAACUGUGAUAGAGUCCAACAAAAGAA
CAACAGACUACUAGAGAUUACCAGGGAAUUUAGUGUUA
AUGCAGGUGUAACUACACCUGUAAGCACUUAUAUGUUA
ACUAAUAGUGAAUUAUUAUCAUUAUCAAUGAUUAGCC
UAUAACAAAUGAUCAGAAAAAGUUAUUGUCCAACAAUG
UUCAAAUAGUUAGACAGCAAAGUUACUCUAUCAUGUCC
AUAUAAAGGAGGAAGUCUUAGCAUAUGUAGUACAAU
UACCACUAUAUGGUGUAAUAGAUACACCCUGUUGGAAA
CUGCACACAUCCCCUCUAUGUACAACCAACACAAAGGA
AGGGUCCAACAUCUGCUUAAACAAGAACCGACAGAGGAU
GGUAUUGUGACAAUGCAGGAUCAGUAUCUUUCUCCCA
CAAGCUGAAACAUGUAAAGUUCAAUCGAAUCGGGUAAU
UUGUGACACAAUGAACAGUUUAACAUAUACCAAGUGAAG
UAAAUCUCUGCAACAUAUGACAUAUUAACCCCAAUAU
GAUUGCAAAAUAUGACUUCAAAAACAGAUGUAAGCAG
CUCGUAUACACAUCUCUAGGAGCCAUUGUGUCAUGCU
AUGGCAAAACUAAAUGUACAGCAUCCAUAUAAAAUCGU
GGGAUCAUAAAGACAUAUUUCUAACGGGUGUGAUUAUG
UAUCAAAUAAGGGGGUGGAUACUGUGUCUGUAGGUAA
UACAUUAUAUUAUGUAAAUAAGCAAGAAGGCAAAAGU
CUCUAUGUAAAAGGUGAACCAUAUAAUAAUUAUUGA
CCAUUAGUGUUCCCCUCUGAUGAAUUUGAUGCAUCA
UAUCUCAAGUCAUUGAGAAGAUUAACCAGAGCCUAGCA
UUUAUUCGUAAAUCCGAUGAAUUAUUAUUAUUGUAA
AUGCUGGUAUUCCACCACAAUAUCAUGAUAAUCUACU
AUAAUUAUAGUGAUUAUAGUAAUAUUGUUAUCAUUA
UUGCAGUUGGACUGCUCUUAUACUGCAAGGCCAGAAGC
ACACCAGUCACACUAAGUAAGGAUCAACUGAGUGGUAAU AAAUAAUUAUUGCAUUUAGUAACUGA

TABLE-US-00004 TABLE 3 hMPV Amino Acid Sequences SEQ ID Description Sequence NO:
gi|122891979|gb|E MSWKVVIIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGW 5 F051124.1| Human
YTNVFTLEVGDVENLTCS DGPSLIKTELDLTKSALRELKTVS metapneumovirus
ADQLAREEQIENPRQSRFVLGAIALGVAAAAVTAGVAIAK isolate TN/92-4
TIRLESEVTAINNALKKTNEAVSTLGNGVRVLATAVRELKD fusion protein gene,
FVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS complete cds
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRA
MVRKGFILIGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPS
CSEKKGNYACLLREDQGWYCNAGSTVYYPNEKDCETR
DHFVCDTAAGINVAEQSKECNINISTTNYPCKVSTGRHPISM
VALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQF
NVALDQVFENIENSQALVDQSNRILSSAEKGNTGFIIVILIAV
LGSSMILVSIFIIKKTKKPTGAPPELSTNNGFIPHN gb|AY525843.1|:30
MSWKVMIIISLITPQHGLKESYLEESCSTITEGYLSVLRTGW 6 65-4684 Human
YTNVFTLEVGDVENLTCTDGPSLIKTELDLTKSALRELKTVS metapneumovirus
ADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGIAIAKT isolate NL/1/99,
IRLESEVNAIKGALKQTNEAVSTLGNGVRVLATAVRELKEF complete cds
VSKNLTSAINRNKCDIADLKMAVSFSQFNRRFLNVVRQFSD
NAGITPAISLDLMTDAELARAVSYMPTSAGQIKLMLLENRAM
VRRKGFILIGVYGSSVIYMVQLPIFGVIDTPCWIKAAPSCS
EKNNGNYACLLREDQGWYCKNAGSTVYYPNEKDCETRGDH
VFCDTAAGINVAEQSRECNINISTTNYPCKVSTGRHPISMVA

LSPLGALVACYKGVSCSIGSNWVGIIKQLPKGCSYITNQDAD
 TVTIDNTVYQLSKVEGEQHVIKGRPVSFFDPIKFPEDQFNV
 ALDQVFESIENSQALVDQSNKILNSAEKGNTGFIIVVILVAVL
 GLTMISVSIIIIKKTRKPTGAPPELNGVTNGGFIPHS gb|KJ627414.1|:30
 MSWKVMIIISLLITPQHGLKESYLEESCSTITEGYLSVLRTGW 7 15-4634 Human
 YTNVFTLEVGDVENLTCTDGPLIKTELDTLSALRELKTVS metapneumovirus
 ADQLAREEQIENPRQSRFVLGAIALGVATAAAVTAGIAIAKT strain hMPV/Homo
 IRLESEVNAIKGALKTTNEAVSTLGNVVRVLATAVRELKEF sapiens/PER/CFI04
 VSKNLTSAINKNKCDIADLKMAVSFSQFNRRFLNVVRQFSD 97/2010/B,
 NAGITPAISLDMNDAELARAVSYMPTSAGQIKLMLENRAM complete cds
 VRRKGFGLIGVYGSSVIYMQVLPFGVINTPCWIIKAAPSCS
 EKDGNYA CLLREDQGWYCKNAGSTVYYPNEKDCETRGDH
 VFCDTAAGINVAEQSRECNINISTTNYPCVKVSTGRHPISMVA
 LSPLGALVACYKGVSCSTGSNQVGIKQLPKGCSYITNQDAD
 TVTIDNTVYQLSKVEGEQHVIKGRPVSFFDPIRFPEDQFNV
 ALDQVFESIENSQALVDQSNKILNSAEKGNTGFIIVILIAVLG
 LTMISVSIIIIKKTRKPTGAPPELNGVTNGGFIPHS gb|KJ723483.1|:55
 MELPILKTNAITTLAAVTLCFASSQNITEEFYQSTCSAVSKG 8 86-7310 Human
 YLSALRTGWYTSVITIELSNIKENKNGTDAKVKLIKQELDK respiratory
 YKNAVTELQLLMQSTPAANNRARELPRFMNYTLNNTKNT syncytial virus
 NVTLSKRRRRLGFLGVSIAIASGIAVSKVLHLEGEVNI strain RSV A/Homo
 KSALLSTNKAVVSLNGVSVLTSKVLDLKNYIDKQLLPVN sapiens/USA/84I-
 KQSCSISNIETVIEFQQKNNRLEITREFSVNAGVTTPVSTYM 215A-01/1984,
 LTNSELLSLINDMPITNDQKKLMSNNVQIVRQQSYSIMSIIKE complete cds
 EVLAYVVQLPLYGVIDTPCWKLHTSPLCTTNTKEGSNICLTR
 TDRGWYCDNAGSVSFFPQAETCKVQSNRVFCDTMNSLTLP
 SEVNLCNIDIFNPKYDCKIMTSKTDVSSSVITSLGAIVSCYGK
 TKCTASNKNRGIKTFNSGCDYVSNKGVDTVSVGNTLYYVN
 KQEGKSLYVKGEPIINFYDPLVFPDEFDASISQVNEKINQSL
 AFIRKSDELLHNVNAGKSTTNIMITIIIIVIIILLSLIAVGLLL 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|:4 ATGCCAATTTCAATACTGTTAATTATTACAACCATGATC 9 990-6609 Human
 ATGGCATCACACTGCCAAATAGACATCACA AACTACA parainfluenza
 GCATGTAGGTGTATTGGTCAACAGTCCCAAAGGGATGA virus 3 strain
 AGATATCACA AACTTCGAAACAAGATATCTAATCCTGA HPIV3/Homo
 GTCTCATACCA A AATAGAAGATTCTA ACTCTTGTGGTG sapiens/PER/FLA4
 ACCAACAGATCAAGCAATACAAGAGGTTATTGGATAGA 815/2008[fusion
 CTGATCATTCTTTATATGATGGACTAAGATTACAGAAG glycoprotein F0]
 GATGTGATAGTACTAATCAAGAATCCAATGAAAACAC

TGATCCCAGAACAGAACGATTCTTTGGAGGGGTAATTGG
AACTATTGCTCTAGGAGTAGCAACCTCAGCACAAATTAC
AGCAGCAGTTGCTCTGGTTGAAGCCAAGCAGGCAAGAT
CAGACATTGAAAACTCAAGGAAGCAATCAGGGACACA
AATAAAGCAGTGCAGTCAGTTCAGAGCTCTGTAGGAAA
TTTGATAGTAGCAATTAATCAGTCCAGGATTATGTCAA
CAAAGAAATCGTGCCATCGATTGCGAGACTAGGTTGTG
AAGCAGCAGGACTTCAGTTAGGGATTGCATTAACACAG
CATTACTCAGAATTAACAAATATATTTGGTGATAACATA
GGATCGTTACAAGAAAAAGGAATAAAATTACAAGGTAT
AGCATCATTATACCGTACAAATATCACAGAAATATTCAC
AACATCAACAGTTGACAAATATGATATTTATGATCTATT
ATTTACAGAATCAATAAAGGTGAGAGTTATAGATGTTGA
TTTGAATGATTACTCAATAACCCTCCAAGTCAGACTCCC
TTTATTGACCAGACTGCTGAACACTCAAATCTACAAAGT
AGATTCCATATCATAACAATATCCAAAATAGAGAATGGTA
TATCCCTCTTCCCAGCCATATCATGACGAAAGGGGCATT
TCTAGGTGGAGCAGATGTCAAAGAATGCATAGAAGCAT
TCAGCAGTTATATATGCCCTTCTGATCCAGGATTTGTA
AAACCATGAAATGGAGAGCTGTCTATCAGGAAACATAT
CCCAATGTCCAAGAACCACAGTCACATCAGACATAGTTC
CTAGGTATGCATTTGTCAATGGAGGAGTGGTTGCGAATT
GTATAACAACACTACATGTACATGCAATGGTATCGGTAATA
GAATCAACCAACCACCTGATCAAGGAGTCAAATTATA
ACACATAAAGAATGTAATACAATAGGTATCAACGGAAT
GCTATTCAACACAACAAGAAGGAACTCTTGCATTCTA
CACACCAGACGACATAACATTAACAATTCTGTTGCACT
TGATCCGATTGACATATCAATCGAGCTCAACAAGGCCAA
ATCAGATCTTGAGGAATCAAAGAATGGATAAGAAGGT
CAAATCAAAGCTAGATTCTATTGGAAGTTGGCATCAAT
CTAGCACTACAATCATAGTTATTTTGATAATGATGATTA
TATTGTTTATAATTAATAACAATAATTACAATTGCAA
TTAAGTATTACAGAATTCAAAGAGAAATCGAGTGGAT
CAAATGATAAGCCGTATGTATTAACAACAAG gi|612507167|gb|A
ATGGAATACTGGAAGCACACCAACCACGGAAAGGATGC 10 HX22430.1|
TGTAATGAGCTGGAGACATCCACAGCCACTCATGGCA hemagglutinin-
ACAAGCTACCAACAAGATAACATATATATTGTGGACG neuraminidase
ATAACCCTGGTGTATTATCAATAGTCTTCATCATAGTG [Human
CTAACTAATTCCATCAAAGTGAAAAGGCCCGCGAATC parainfluenza
ATTGCTACAAGACATAAATAATGAGTTTATGGAAGTTAC virus 3]
AGAAAAGATCCAAGTGGCATCGGATAATACTAATGATC
TAATACAGTCAGGAGTGAATACAAGGCTTCTTACAATTC
AGAGTCATGTCCAGAATTATATACCAATATCATTGACAC
AACAAATATCGGATCTTAGGAAATTCATTAGTGAAATTA
CAATTAGAAATGATAATCAAGAAGTGCCACCACAAAGA
ATAACACATGATGTGGGTATAAAACCTTTAAATCCAGAT
GATTTCTGGAGATGCACGTCTGGTCTTCCATCTTTGATG
AAAACCTCAAAAATAAGATTAATGCCGGGACCAGGATT
ATTAGCTATGCCAACGACTGTTGATGGCTGTGTCAGAAC
CCCGTCCTTAGTGATAAATGATCTGATTTATGCTTACAC
CTCAAATCTAATTACTCGAGGTTGCCAGGATATAGGGAA
ATCATATCAAGTATTACAGATAGGGATAATAACTGTAAA
CTCAGACTTGGTACCTGACTTAAATCCTAGGATCTCTCA
TACCTTCAACATAAATGACAATAGAAAGTCATGTTCTCT

AGCACTCCTAAATACAGATGTATATCAACTGTGTTCAAC
CCCAAAAGTTGATGAAAGATCAGATTATGCATCATCAG
GCATAGAAGATATTGTACTIONGATATTGTCAATTATGATG
GCTCAATCTCGACAACAAGATTTAAGAATAATAATATAA
GTTTTGATCAACCATATGCGGCATTATACCCATCTGTTG
GACCAGGGATATACTACAAAGGCAAAATAATTTTCTC
GGGTATGGAGGTCTTGAACATCCAATAAATGAGAATGC
AATCTGCAACACAACCTGGGTGTCCTGGGAAAACACAGA
GAGACTGTAATCAAGCATCTCATAGTCCATGGTTTTTCAG
ATAGAAGGATGGTCAACTCTATAATTGTTGTTGACAAGG
GCTTGAACCTCAGTTCCAAAATTGAAGGTATGGACGATAT
CTATGAGACAAAATTACTGGGGGTCAGAAGGAAGATTA
CTTCTACTAGGTAACAAGATCTACATATACACAAGATCT
ACAAGTTGGCACAGCAAGTTACAATTAGGAATAATTGA
CATTACTGACTACAGTGATATAAGGATAAAATGGACAT
GGCATAATGTGCTATCAAGACCAGGAAACAATGAATGT
CCATGGGGACATTCATGTCCGGATGGATGTATAACGGG
AGTATATACCGATGCATATCCACTCAATCCCACAGGAAG
CATTGTATCATCTGTATATTGGACTCACAAAATCGAG
AGTCAACCCAGTCATAACTTACTCAACAGCAACCGAAA
GGGTAAACGAGCTGGCTATCCGAAACAAAACACTCTCA
GCTGGGTACACAACAACAAGCTGCATTACACACTATAA
CAAAGGGTATTGTTTTTCATATAGTAGAAATAAATCATAA
AAGCTTAAACACATTTCAACCCATGTTGTTCAAACAGA GATTCCAAAAGCTGCAGT
HPIV3_HN_Codon ATGGAATACTGGAAGCACACCAACCACGGCAAGGACGC 11 Optimized
CGGCAACGAGCTGGAAACCAGCACAGCCACACACGGCA
ACAAGCTGACCAACAAGATCACCTACATCCTGTGGACC
ATCACCCCTGGTGCTGCTGAGCATCGTGTTTCATCATCGTG
CTGACCAATAGCATCAAGAGCGAGAAGGCCAGAGAGAG
CCTGCTGCAGGACATCAACAACGAGTTCATGGAAGTGA
CCGAGAAGATCCAGGTGGCCAGCGACAACACCAACGAC
CTGATCCAGAGCGGCGTGAACACCCGGCTGCTGACCATC
CAGAGCCACGTGCAGAACTACATCCCCATCAGCCTGACC
CAGCAGATCAGCGACCTGCGGAAGTTCATCAGCGAGAT
CACCATCCGGAACGACAACCAGGAAGTGCCCCCCCAGA
GAATCACCCACGACGTGGGCATCAAGCCCCTGAACCCC
GACGATTTCTGGCGGTGTACAAGCGGCCTGCCAGCCTG
ATGAAGACCCCCAAGATCCGGCTGATGCCTGGCCCTGG
ACTGCTGGCCATGCCTACCACAGTGGATGGCTGTGTGCG
GACCCCCAGCCTCGTGATCAACGATCTGATCTACGCCTA
CACCAGCAACCTGATCACCCGGGGCTGCCAGGATATCG
GCAAGAGCTACCAGGTGCTGCAGATCGGCATCATCACC
GTGAACTCCGACCTGGTGCCCGACCTGAACCCCTCGGATC
AGCCACACCTTCAACATCAACGACAACAGAAAGAGCTG
CAGCCTGGCTCTGCTGAACACCGACGTGTACCAGCTGTG
CAGCACCCCCAAGGTGGACGAGAGAAGCGACTACGCCA
GCAGCGGCATCGAGGATATCGTGCTGGACATCGTGAAC
TACGACGGCAGCATCAGCACCAACCCGGTTCAAGAACA
CAACATCAGCTTCGACCAGCCCTACGCCGCCCTGTACCC
TTCTGTGGGCCCTGGCATCTACTACAAGGGCAAGATCAT
CTTCCCTGGGCTACGGCGGCCTGGAACACCCCATCAACGA
GAACGCCATCTGCAACACCACCGGCTGCCCTGGCAAGA
CCCAGAGAGACTGCAATCAGGCCAGCCACAGCCCCTGG
TTCAGCGACCGCAGAATGGTCAACTCTATCATCGTGGTG

GACAAGGGCCTGAACAGCGTGCCCAAGCTGAAAGTGTG
GACAATCAGCATGCGCCAGA ACTACTGGGGCAGCGAGG
GCAGACTTCTGCTGCTGGGAAACAAGATCTACATCTACA
CCCGGTCCACCAGCTGGCACAGCAA ACTGCAGCTGGGA
ATCATCGACATCACCGACTACAGCGACATCCGGATCAA
GTGGACCTGGCACAACGTGCTGAGCAGACCCGGCAACA
ATGAGTGCCCTTGGGGCCACAGCTGCCCCGATGGATGTA
TCACCGGCGTGTACACCGACGCCTACCCCCTGAATCCTA
CCGGCTCCATCGTGTCCAGCGTGATCCTGGACAGCCAGA
AAAGCAGAGTGAACCCCGTGATCACATACAGCACCGCC
ACCGAGAGAGTGAACGAACTGGCCATCAGAAACAAGAC
CCTGAGCGCCGGCTACACCACCACAAGCTGCATCACAC
ACTACAACAAGGGTACTGCTTCCACATCGTGGAATCA
ACCACAAGTCCCTGAACACCTTCCAGCCCATGCTGTTCA AGACCGAGATCCCCAAGAGCTGCTCC
HPIV3_F_Codon ATGCCCATCAGCATCCTGCTGATCATCACCACAATGATC 12 Optimized
ATGGCCAGCCACTGCCAGATCGACATCACC AAGCTGCA
GCACGTGGGCGTGCTCGTGAACAGCCCCAAGGGCATGA
AGATCAGCCAGAACTTCGAGACACGCTACCTGATCCTGA
GCCTGATCCCCAAGATCGAGGACAGCAACAGCTGCGGC
GACCAGCAGATCAAGCAGTACAAGCGGCTGCTGGACAG
ACTGATCATCCCCCTGTACGACGGCCTGCGGCTGCAGAA
AGACGTGATCGTGACCAACCAGGAAAGCAACGAGAACA
CCGACCCCCGGACCGAGAGATTCTTCGGCGGCGTGATCG
GCACAATCGCCCTGGGAGTGGCCACAAGCGCCCAGATT
ACAGCCGCTGTGGCCCTGGTGG AAGCCAAGCAGGCCAG
AAGCGACATCGAGAAGCTGAAAGAGGCCATCCGGGACA
CCAACAAGGCCGTGCAGAGCGTG CAGTCCAGCGTGGGC
AATCTGATCGTGGCCATCAAGTCCGTGCAGGACTACGTG
AACAAAGAAATCGTGCCCTCTATCGCCCGGCTGGGCTGT
GAAGCTGCCGGACTGCAGCTGGGCATTGCCCTGACACA
GCACTACAGCGAGCTGACCAACATCTTCGGCGACAACA
TCGGCAGCCTGCAGGAAAAGGGCATT AAGCTGCAGGGA
ATCGCCAGCCTGTACCGCACCAACATCACCGAGATCTTC
ACCACCAGCACCGTGGATAAGTACGACATCTACGACCT
GCTGTTACCGAGAGCATCAAAGTGCGCGTGATCGACGT
GGACCTGAACGACTACAGCATCACCTGCAAGTGCGGC
TGCCCCTGCTGACCAGACTGCTGAACACCCAGATCTACA
AGGTGGACAGCATCTCCTACAACATCCAGA ACCGCGAG
TGGTACATCCCTCTGCCAGCCACATTATGACCAAGGGC
GCCTTTCTGGGCGGAGCCGACGTGAAAGAGTGCATCGA
GGCCTTCAGCAGCTACATCTGCCCCAGCGACCCTGGCTT
CGTGCTGAACCACGAGATGGAAAGCTGCCTGAGCGGCA
ACATCAGCCAGTGCCCCAGAACCACCGTGACCTCCGAC
ATCGTGCCAGATA CGCCTTCGTGAATGGCGGCGTGGTG
GCCAACTGCATCACACCACCTGTACCTGCAACGGCATC
GGCAACCGGATCAACCAGCCTCCCGATCAGGGCGTGAA
GATTATCACCCACAAAGAGTGTAACACCATCGGCATCA
ACGGCATGCTGTTCAATACCAACA AAGAGGGCACCCCTG
GCCTTCTACACCCCCGACGATATCACCTGAACA ACTCC
GTGGCTCTGGACCCCATCGACATCTCCATCGAGCTGAAC
AAGGCCAAGAGCGACCTGGAAGAGTCCAAAGAGTGGAT
CCGGCGGAGCAACCAGAAGCTGGACTCTATCGGCAGCT
GGCACCAAGAGCAGCACCACCATCATCGTGATCCTGATTA
TGATGATTATCCTGTT CATCATCAACATTACCATCATCAC

TATCGCCATTAAGTACTACCGGATCCAGAAACGGAACC
GGGTGGACCAGAATGACAAGCCCTACGTGCTGACAAAC AAG PIV3 mRNA Sequences
>gb|KJ672601.1|:4 AUGCCAAUUUCAUACUGUAAUUUAUACAACCAUGA 61 990-6609 Human
UCAUGGCAUCACACUGCCAAAUAGACAUCACAAAACU parainfluenza
ACAGCAUGUAGGUGUAUUGGUCAACAGUCCCAAAGGG virus 3 strain
AUGAAGAUUCACAAAACUUCGAAACAAGAUUCUAA HPIV3/Homo
UCCUGAGUCUCAUACCAAAAAUAGAAGAUUCUAACUC sapiens/PER/FLA4
UUGUGGUGACCAACAGAUCAAGCAAUACAAGAGGUUA 815/2008[fusion
UUGGAUAGACUGAUCAUCCUUUAUAUGAUGGACUAA glycoprotein F0]
GAUUACAGAAGGAUGUGAUAGUGACUAAUCAAGAAUC
CAAUGAAAACACUGAUCCCAGAACAGAACGAUUCUUU
GGAGGGGUAUUUGGAACUUAUUGCUCUAGGAGUAGCAA
CCUCAGCACAAAUAACAGCAGCAGUUGCUCUGGUUGA
AGCCAAGCAGGCAAGAUCAAGACAUUGAAAAACUCAAG
GAAGCAAUCAGGGACACAAUAAAGCAGUGCAGUCAG
UUCAGAGCUCUGUAGGAAAUUUGAUAGUAGCAAUUA
AUCAGUCCAGGAUUUGUCAACAAAGAAAUCGUGCCA
UCGAUUGCGAGACUAGGUUGUGAAGCAGCAGGACUUC
AGUUAGGGAUUGCAUUAACACAGCAUACUCAGAAUU
AACAAAUAUAUUUGGUGAUACAUAAGGAUCGUUACAA
GAAAAGGAAUAAAUAACAAGGUUAUAGCAUCAUUUA
ACCGUACAAAUAUCACAGAAAUAUUCACAACAUAAC
AGUUGACAAAUAUGAUUUUAUGAUCUUAUUUUACA
GAAUCAUAAAGGUGAGAGUUAUAGAUGUUGAUUUUGA
AUGAUUACUCAUAACCCUCCAAGUCAGACUCCCUUU
AUUGACCAGACUGCUGAACACUCAAAUCUACAAAGUA
GAUCCAUUAUCAUAUAUCCAAAAUAGAGAAUGGU
AUAUCCCUUCUCCAGCCAUUAUCAUGACGAAAGGGGC
AUUUCUAGGUGGAGCAGAUGUCAAGAAUGCAUAGAA
GCAUUCAGCAGUUAUAUUGCCCUUCUGAUCCAGGAU
UUGUACUAAACCAUGAAAUGGAGAGCUGUCUAUCAGG
AAACAUAUCCCAAUGUCCAAGAACCACAGUCACAUCA
GACAUAGUCCUAGGUUAUGCAUUUGUCAUUGGAGGAG
UGGUUGCGAAUUGUAUAACAACUACAUGUACAUGCAA
UGGUAUCGGUAAUAGAAUCAACCAACCACUGAUCAA
GGAGUCAAAAUAUAACACAUAAGAAUGUAAUACAA
UAGGUUAUCAACGGAAUGCUAUUCAACACAAACAAGA
AGGAACUCUUGCAUUCUACACACCAGACGACAUACA
UUAAACAUAUCUGUUGCACUUGAUCCGAUUGACAUAU
CAAUCGAGCUCAACAAGGCCAAAUCAGAUUCUUGAGGA
AUCAAAAGAAUGGAUAAGAAGGUCAAAUCAAAAGCUA
GAUUCUAUUGGAAGUUGGCAUCAUUCUAGCACUACAA
UCAUAGUUAUUUGAUAAUGAUGAUUAUAUUGUUUAU
AAUUAUAUAACAAUAUAUAACAUAUUGCAAUAAGUAU
UACAGAAUUCAAAAGAGAAAUCGAGUGGAUCAAAAUG
AUAAGCCGUUAUGUAUUAACAAACAAG gi|612507167|gb|A
AUGGAAUACUGGAAGCACACCAACCACGGAAAGGAUG 62 HX22430.1|
CUGGUAAUGAGCUGGAGACAUCCACAGCCACUCAUGG hemagglutinin-
CAACAAGCUCACCAACAAGAUACAUAUAUAUUGUGG neuraminidase
ACGAUAACCCUGGUGUUAUUAUCAAUAGUCUUCAUCA [Human
UAGUGCUAACUAAUCCAUCAAAAAGUGAAAAGGCCCG parainfluenza
CGAAUCAUUGCACAAGACAUAUAAUAAUGAGUUUAUG virus 3]
GAAGUUACAGAAAAGAUCCAAGUGGCAUCGGAUAAUA
CUAAUGAUCUAAUACAGUCAGGAGUGAAUACAAGGCU

UCUUACAAUUCAGAGUCAUGUCCAGAAUUAUAUACCA
AUUAUCAUUGACACAACAAUUAUCGGAUCUUAGGAAAU
UCAUUAGUGAAAUUAACAAUUAAGAAAUGAUAUUAAGA
AGUGCCACCACAAAGAAUAACACAUGAUGUGGGUAUA
AAACCUUUAUUAUCCAGAUGAUUUCUGGAGAUGCACGU
CUGGUCUUCCAUCUUUGAUGAAAACUCCAAAAAUAAG
AUUAAUGCCGGGACCAGGAUUUAUUAAGCUAUGCCAACG
ACUGUUGAUGGCUGUGUCAGAACCCCGUCCUUAUGUGA
UAAAUGAUCUGAUUUAUGCUUACACCUCAAAUCUAAU

UACUCGAGGUUGCCAGGAUUAUAGGGAAAUCAUAUCAA
GUAUUACAGAUAGGGAUAAUAACUGUAAACUCAGACU
UGGUACCUGACUUAUUAUCCUAGGAUCUCUCAUACCUU
CAACAUAUUAUGACAUAUAGAAAGUCAUGUUCUCUAGCA
CUCCUAAAUAACAGAUGUAUAUCAACUGUGUUAACCC
CAAAGUUGAUGAAAGAUCAGAUUAUGCAUCAUCAGG
CAUAGAAGAUUAUUGUACUUGAUAUUGUCAAUUAUGAU
GGUCUAAUCUCGACAACAAGAUUUAAGAAUAAUAAUA
UAAGUUUUGAUAACCAUAUUGCGGCAUUUAUACCCAUC
UGUUGGACCAGGGAUUAUCUACAAAGGCAAAAUAUA
UUUCUCGGGUUAUGGAGGUCUUGAACAUCCAAUAAAUG
AGAAUGCAAUCUGCAACACAACUGGGUGUCCUGGGAA
AACACAGAGAGACUGUAAUCAAGCAUCUCAUAGUCCA
UGGUUUUCAGAUAGAAGGAUGGUCAACUCUAUAAUUG
UUGUUGACAAGGGCUUGAACUCAGUCCAAAAUUGAA
GGUAUGGACGAUAUCUAUGGAGACAAAUAUACUGGGGG
UCAGAAGGAAGAUUAUCUUCUACUAGGUAACAAGAUUCU
ACAUUAACACAAGAUCUACAAGUUGGCACAGCAAGUU
ACAAUUAAGGAAUAAUUGACAUUACUGACUACAGUGAU
AUAAGGAUAAAUAUGGACAUGGCAUAAUUGUCUAUCAA
GACCAGGAAACAUAUGAAUGUCCAUGGGGACAUUCAUG
UCCGGAUGGAUGUAUAACGGGAGUAUAUACCGAUGCA
UAUCCACUCAAUCCCACAGGAAGCAUUGUAUCAUCUG
UCAUAUUGGACUCACAAAAUUCGAGAGUCAACCCAGU
CAUAACUUAUCUACACAGCAACCCGAAAGGGUAAACGAG
CUGGCUAUCCGAAACAAAACACUCUCAGCUGGGUACA
CAACAACAAGCUGCAUUAACACACUAUAACAAAGGGUA
UUGUUUUCAUUAUAGUAGAAAUAUUAUAAAAGCUUA
AACACAUUUAACCCAUGUUGUUAUAAACAGAGAUUC

CAAAAAGCUGCAGU HPIV3_HN_Codon
AUGGAAUACUGGAAGCACACCAACCACGGCAAGGACG 63 Optimized

CCGGCAACGAGCUGGAAACCAGCACAGCCACACACGGC
AAACAAGCUGACCAACAAGAUCACCUACAUCUUGGGA
CCAUCACCCUGGUGCUGCUGAGCAUCGUGUUCAUCAUC
GUGCUGACCAAUAGCAUCAAGAGCGAGAAGGCCAGAG
AGAGCCUGCUGCAGGACAUCAACAACGAGUUCAUGGA
AGUGACCGAGAAGAUCAGGUGGCCAGCGACAACACC
AACGACCUGAUCCAGAGCGGGGUGAACACCCGGCUGCU
GACCAUCCAGAGCCACGUGCAGAACUACAUCCCAUCA
GCCUGACCCAGCAGAUCAGCGACCUGCGGAAGUUCAUC
AGCGAGAUCACCAUCCGGAACGACAACCAGGAAGUGC
CCCCCAGAGAAUCACCCACGACGUGGGCAUCAAGCCC
CUGAACCCCGACGAUUUCUGGCGGUGUACAAGCGGCC
UGCCCAGCCUGAUGAAGACCCCAAGAUCCGGCUGAUG
CCUGGCCUGGACUGCUGGCCAUGCCUACCACAGUGGA

UGGCUGUGUGCGGACCCCCAGCCUCGUGAUCAACGAUC
UGAUCUACGCCUACACCAGCAACCUGAUACCCGGGGC
UGCCAGGAUAUCGGCAAGAGCUACCAGGUGCUGCAGA
UCGGCAUCAUACCGUGAACUCCGACCUGGUGCCCGAC
CUGAACCCUCGGAUCAGCCACACCUUCAACAUCAACGA
CAACAGAAAGAGCUGCAGCCUGGCUCUGCUGAACACC
GACGUGUACCAGCUGUGCAGCACCCCAAGGUGGACG
AGAGAAGCGACUACGCCAGCAGCGGCAUCGAGGAUUAU
CGUGCUGGACAUCGUGAACUACGACGGCAGCAUCAGC
ACCACCCGGUUCAAGAAACAACAUCAGCUUCGACCA
GCCCUACGCCGCCUGUACCCUUCUGUGGGCCUGGCA
UCUACUACAAGGGCAAGAUAUCUUCUGGGCUACGG
CGGCCUGGAACCCCAUCAACGAGAACGCCAUCUGCA
ACACCACCGGCUGCCUGGCAAGACCCAGAGAGACUGC
AAUCAGGCCAGCCACAGCCCCUGGUUCAGCGACCGCAG
AAUGGUCAACUCUAUCAUCGUGGUGGACAAGGGCCUG
AACAGCGUGCCCAAGCUGAAAGUGUGGACAAUCAGCA
UGC GCCAGAACUACUGGGGCAGCGAGGGCAGACUUCU
GCUGCUGGGAAACAAGAUCUACAUCUACACCCGGUCC
ACCAGCUGGCACAGCAAACUGCAGCUGGGAAUCAUCG
ACAUCACCGACUACAGCGACAUCGGAUCAAGUGGACC
UGGCACAACGUGCUGAGCAGACCCGGCAACA AUGAGU
GCCCUUGGGGCCACAGCUGCCCCGAUGGAUGUAUCACC
GGCGUGUACACCGACGCCUACCCCCUGAAUCCUACCGG
CUCCAUCGUGUCCAGCGUGAUCCUGGACAGCCAGAAA
AGCAGAGUGAACCCCGUGAUCACAUACAGCACCGCCAC
CGAGAGAGUGAACGAACUGGCCAUCAGAAACAAGACC
CUGAGCGCCGGCUACACCACCACAAGCUGCAUCACACA
CUACAACAAGGGCUACUGCUUCCACAUCGUGGAAAUC
AACCACAAGUCCUGAACACCUUCCAGCCCAUGCUGUU
CAAGACCGAGA UCCCCAAGAGCUGCUC HPIV3_F_Codon
AUGCCCAUCAGCAUCCUGCUGAUCAUACCCACAAUGAU 64 Optimized mRNA
CAUGGCCAGCCACUGCCAGAU CGACAUCACCAAGCUGC sequence
AGCACGUGGGCGUGCUCGUGAACAGCCCCAAGGGCAU
GAAGAUCAGCCAGAACUUCGAGACACGCUACCUGAUC
CUGAGCCUGA UCCCCAAGAU CGAGGACAGCAACAGCU
GCGGCGACCAGCAGAUCAAGCAGUACAAGCGGCUGCU
GGACAGACUGAUCAUCCCCUGUACGACGGCCUGCGGC
UGCAGAAAGACGUGAUCGUGACCAACCAGGAAAGCAA
CGAGAACACCGACCCCGGACCGAGAGAUUCUUCGGCG
GCGUGAUCGGCACA AU CGCCUGGGAGUGGCCACAAG
CGCCAGAUUACAGCCGCUGUGGCCUUGGUGGAAGCCA
AGCAGGCCAGAAAGCGACAUCGAGAAGCUGAAAGAGGC
CAUCCGGGACACCAACAAGGCCGUGCAGAGCGUGCAG
UCCAGCGUGGGCAAUCUGAUCGUGGCCAUCAAGUCCG
UGCAGGACUACGUGAACAAAGAAAUCGUGCCCUCUAU
CGCCCGGCUGGGCUGUGAAGCUGCCGGACUGCAGCUG
GGCAUUGCCCUGACACAGCACUACAGCGAGCUGACCAA
CAUCUUCGGCGACAACAUCGGCAGCCUGCAGGAAAAG
GGCAUUAAGCUGCAGGGAAUCGCCAGCCUGUACCGCA
CCAACAUCACCGAGAUCUUCACCACCAGCACCGUGGAU
AAGUACGACAUCUACGACCUGCUGUUCACCGAGAGCA
UCAAAGUGCGCGUGAUCGACGUGGACCUGAACGACUA
CAGCAUCACCCUGCAAGUGCGGCUGCCCCUGCUGACCA

GACUGCUGAACACCCAGAUCUACAAGGUGGACAGCAU
CUCCUACAACAUCCAGAACCGCGAGUGGUACAUCCCUC
UGCCCAGCCACAUUAUGACCAAGGGCGCCUUCUGGGC
GGAGCCGACGUGAAAGAGUGCAUCGAGGCCUUCAGCA
GCUACAUCUGCCCCAGCGACCCUGGCUUCGUGCUGAAC
CACGAGAUGGAAAGCUGCCUGAGCGGCAACAUCAGCC
AGUGCCCCAGAACCACCGUGACCUCCGACAUCGUGCCC
AGAUAACGCCUUCGUGAAUGGGCGGCGUGGUGGCAACU
GCAUCACCACCACCUUGUACCUGCAACGGCAUCGGCAAC
CGGAUCAACCAGCCUCCC GAUCAGGGGCGUGAAGAUUA
UCACCCACAAAGAGUGUAACACCAUCGGCAUCAACGGC
AUGCUGUUCAAUACCAACAAAGAGGGGCACCCUGGCCU
UCUACACCCCCGACGAUAUCACCCUGAACAAACUCCGUG
GCUCUGGACCCCAUCGACAUCUCCAUCGAGCUGAACAA
GGCCAAGAGCGACCUUGGAAGAGUCCAAAGAGUGGAUC
CGGCGGAGCAACCAGAAGCUGGACUCUAUCGGCAGCU
GGCACCAGAGCAGCACCACCAUCAUCGUGAUCCUGAUU
AUGAUGAUUAUCCUGUUCAUCAUCAACAUUACCAUCA
UCACUAUCGCCAUUAAGUACUACCGGAUCCAGAAACG
GAACCGGGUGGACCAGAAUGACAAGCCCUACGUGCUG ACAACAAG

TABLE-US-00007 TABLE 6 PIV3 Amino Acid Sequences SEQ ID Description Sequence NO:
>gi|612507166|gb| MPISILLIITMIMASHCQIDITKLQHVGVLVNSPKGMKISQ 13 AHX22429.1|
NFETRYLILSLIPKIEDSNSCGDQQIKQYKRLLDRLIPLYDG fusion glycoprotein
LRLQKDVIVTNQESNENTDPRTERFFGGVIGTIALGVATSA F0 [Human
QITAAVALVEAKQARS DIEKLKEAIRDTNKAVQSVQSSVG parainfluenza virus
NLIVAIKSVQDYVNKEIVPSIARLGCEAAGLQLGIALTQHYS 3]
ELTNIFGDNIGSLQEKGIKLQGIASLYRTNITEIFTTSTVDKY
DIYDLLFTESIKVRVIDVDLNDYSITLQVRLPLLTRLLNTQIY
KVDSISYNIQNREWIPLPSHIMTKGAFLGGADVKECIEAFS
SYICPSDPGFVLNHEMESCLSGNISQCPRTT VTS DIVPRYAF
VNGGVVANCITTTCTCNGIGNRINQPPDQGVKIITHKECENTI
GINGMLFNTNKEGTLAFYTPDDITLNSVALDPIDISIELNK
AKSDLEESKEWIRRSNQKLDSIGSWHQSSTTIIVILIMMILFI
INITIITIAIKYYRIQKRNRVDQNDKPYVLTNK gi|612507167|gb|
MEYWKHTNHGKDAGNELETSTATHGNKLTNKITYILWTIT 14 AHX22430.1|
LVLLSIVFIIVLTNSIKSEKARESLLQDINNEFMVTEKIQVA hemagglutinin-
SDNTNDLIQSGVNTRLLTIQSHVQNYIPISLTQQISDLRKFIS neuraminidase
EITIRNDNQEVPPQRITHDVGIKPLNPPDFWRCTSGLP SLMK [Human
TPKIRLMPGPGLLAMPTTVDGCVRTPSLVINDLIYAYTSNLI parainfluenza virus
TRGCQDIGKSYQVLQIGIITVNSDLV PDLNPRISHTFNINDN 3]
RKSCSLALLNTDVYQLCSTPKVDERSDYASSGIEDIVLDIV
NYDGSISTTRFKNNNISFDQPYAALYPSVGPGIYYKGIIFL
GYGGLEHPINENAICNTTGCPGKTQRDCNQASHSPWFSDR
RMVNSIIVVDKGLNSVPKLVWTISMQRQNYWGSEGRLLLL
GNKIYIYTRSTSWHKLQLGIIDITDYSDIRIKWTWHNVLSR
PGNNECPWGHSCPDGCITGVYTDAYPLNPTGSIVSSVILDS
QKSRVNPVITYSTATERVNELAIRNKTLSAGYTTTSCITHY
NKG YCFHIVEINH KSLNTFQPMLFKTEIPKSCS

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 ID Description Sequence NO: HuIgG.sub.k signal
METPAQLLFLLLLWLPDPTTG 15 peptide IgE heavy chain MDWTWILFLVAAATRVHS 16 epsilon -1 signal
peptide Japanese MLGSNSGQRVVFILLLLVAPAYS 17 encephalitis PRM signal sequence VSVg protein
MKCLLYLAFLFIGVNCA 18 signal sequence Japanese MWLVSLAIVTACAGA 19 encephalitis JEV 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 Betacoronavirus Nucleic Acid Sequence SEQ ID Strain Nucleic Acid Sequence
NO: gb|KJ156934.1|:21 ATGATACTCAGTGTCTACTGATGTTCTTGTTAACACC 20 405-25466
Middle TACAGAAAGTTACGTTGATGTAGGGCCAGATTCTGTTAAG East respiratory
TCTGCTTGATTGAGGTTGATATACAACAGACCTTCTTTGA syndrome
TAAACTTGGCCTAGGCCAATTGATGTTTCTAAGGCTGAC coronavirus
GGTATTATATACCCTCAAGGCCGTACATATTCTAACATAA isolate
CTATCACTTATCAAGGTCTTTTTCCCTATCAGGGAGACCAT Riyadh_14_2013,
GGTGATATGTATGTTTACTCTGCAGGACATGCTACAGGCA spike protein
CAACTCCACAAAAGTTGTTTGTAGCTAACTATTCTCAGGA (nucleotide)
CGTCAAACAGTTTGCTAATGGGTTTGTCTCGTCCGTATAGGA
GCAGCTGCCAATTCCACTGGCACTGTTATTATTAGCCCATC
TACCAGCGCTACTATACGAAAAATTTACCCTGCTTTTATGC
TGGGTTCTTCAGTTGGTAATTTCTCAGATGGTAAAATGGG
CCGCTTCTTCAATCATACTCTAGTTCTTTTGCCCGATGGAT
GTGGCACTTTACTTAGAGCTTTTTATTGTATTCTAGAGCCT
CGCTCTGGAAATCATTGTCCTGCTGGCAATTCCTATACTTC

TTTTGCCACTTATCACACTCCTGCAACAGATTGTTCTGATG
GCAATTACAATCGTAATGCCAGTCTGAACTCTTTAAGGA
GTATTTAATTTACGTAACTGCACCTTTATGTACACTTATA
ACATTACCGAAGATGAGATTTTAGAGTGGTTTGGCATTAC
ACAACTGCTCAAGGTGTTACCTCTTCTCATCTCGGTATG
TTGATTTGTACGGCGGCAATATGTTTCAATTTGCCACCTTG
CCTGTTTATGATACTATTAAGTATTATTCTATCATTCTCA
CAGTATTCGTTCTATCCAAAGTGATAGAAAAGCTTGGGCT
GCCTTCTACGTATATAAACTTCAACCGTTAACTTTCCTGTT
GGATTTTCTGTTGATGGTTATATACGCAGAGCTATAGACT
GTGGTTTTAATGATTTGTCACAACTCCACTGCTCATATGAA
TCCTTCGATGTTGAATCTGGAGTTTATTCAGTTTCGTCTTT
CGAAGCAAACCTTCTGGCTCAGTTGTGGAACAGGCTGAA
GGTGTGGAATGTGATTTTTCACCTCTTCTGTCTGGCACACC
TCCTCAGGTTTATAATTTCAAGCGTTTGGTTTTTACCAATT
GCAATTATAATCTTACCAAATTGCTTTCACTTTTTTCTGTG
AATGATTTTACTTGTAGTCAAATATCTCCAGCAGCAATTGC
TAGCAACTGTTATTCTTCACTGATTTTGGATTATTTTCAT
ACCCACTTAGTATGAAATCCGATCTCAGTGTTAGTTCTGCT
GGTCCAATATCCCAGTTTAATTATAAACAGTCCTTTTCTAA
TCCCACATGTTTGATCTTAGCGACTGTTCCCTCATAACCTTA
CTACTATTACTAAGCCTCTTAAGTACAGCTATATTAACAA
GTGCTCTCGTCTTCTTTCTGATGATCGTACTGAAGTACCTC
AGTTAGTGAACGCTAATCAATACTCACCTGTGTATCCATT
GTCCCATCCACTGTGTGGGAAGACGGTGATTATTATAGGA
AACAACTATCTCCACTTGAAGGTGGTGGCTGGCTTGTGTC
TAGTGGCTCAACTGTTGCCATGACTGAGCAATTACAGATG
GGCTTTGGTATTACAGTTCAATATGGTACAGACACCAATA
GTGTTTGCCCCAAGCTTGAATTTGCTAATGACACAAAAT
TGCCTCTCAATTAGGCAATTGCGTGGAATATCCCTCTATG
GTGTTTCGGGCCGTGGTGTTTTTCAGAATTGCACAGCTGTA
GGTGTTCGACAGCAGCGCTTTGTTTATGATGCGTACCAGA
ATTTAGTTGGCTATTATTCTGATGATGGCAACTACTACTGT
CTGCGTGCTTGTGTTAGTGTTCCCTGTTTCTGTCATCTATGA
TAAAGAACTAAAACCCACGCTACTCTATTTGGTAGTGTT
GCATGTGAACACATTTCTTCTACCATGTCTCAATACTCCCG
TTCTACGCGATCAATGCTTAAACGGCGAGATTCTACATAT
GGCCCCCTTCAGACACCTGTTGGTTGTGTCCTAGGACTTGT
TAATTCCTCTTTGTTTCGTAGAGGACTGCAAGTTGCCTCTCG
GTCAATCTCTCTGTGCTCTTCCCTGACACACCTAGTACTCTC
ACACCTCGCAGTGTGCGCTCTGTGCCAGGTGAAATGCGCT
TGGCATCCATTGCTTTAATCATCCCATTCAGGTTGATCAA
CTTAATAGTAGTTATTTAAATTAAGTATACCCACTAATTT
TTCCTTTGGTGTGACTCAGGAGTACATTCAGACAACCATT
AGAAAGTTACTGTTGATTGTAAACAGTACGTTTGCAATGG
TTTCCAGAAGTGTGAGCAATTACTGCGCGAGTATGGCCAG
TTTTGTTCCAAAATAAACAGGCTCTCCATGGTGCCAATTT
ACGCCAGGATGATTCTGTACGTAATTTGTTTTCGAGCGTG
AAAAGCTCTCAATCATCTCCTATCATAACCAGGTTTTGGAG
GTGACTTTAATTTGACACTTCTAGAACCTGTTTCTATATCT
ACTGGCAGTCGTAGTGCACGTAGTGCTATTGAGGATTTGC
TATTTGACAAAGTCACTATAGCTGATCCTGGTTATATGCA
AGGTTACGATGATTGTATGCAGCAAGGTCCAGCATCAGCT
CGTGATCTTATTTGTGCTCAATATGTGGCTGGTTATAAAGT

ATTACCTCCTCTTATGGATGTTAATATGGAAGCCGCGTATA
CTTCATCTTTGCTTGGCAGCATAGCAGGTGTTGGCTGGACT
GCTGGCTTATCCTCCTTTGCTGCTATTCCATTTGCACAGAG
TATYTTTTATAGGTTAAACGGTGTGGCATTACTCAACAG
GTTCTTTCAGAGAACCAAAAGCTTATTGCCAATAAGTTTA
ATCAGGCTCTGGGAGCTATGCAAACAGGCTTCACTACAAC
TAATGAAGCTTTTCGGAAGGTTTCAGGATGCTGTGAACAAC
AATGCACAGGCTCTATCCAAATTAGCTAGCGAGCTATCTA
ATACTTTTGGTGCTATTTCCGCCTCTATTGGAGACATCATA
CAACGTCTTGATGTTCTCGAACAGGACGCCCAAATAGACA
GACTTATTAATGGCCGTTTGACAACACTAAATGCTTTTGTT
GCACAGCAGCTTGTTCTCGAATCAGCTGCTCTTTCCGC
TCAATTGGCTAAAGATAAAGTCAATGAGTGTGTCAAGGCA
CAATCCAAGCGTTCTGGATTTTGCGGTCAAGGCACACATA
TAGTGTCCCTTTGTTGAAATGCCCTAATGGCCTTTACTTT
ATGCATGTTGGTTATTACCCTAGCAACCACATTGAGGTTGT
TTCTGCTTATGGTCTTTGCGATGCAGCTAACCTACTAATT
GTATAGCCCTGTAAATGGCTACTTTATTAATAACTAATAAC
ACTAGGATTGTTGATGAGTGGTCATATACTGGCTCGTCCTT
CTATGCACCTGAGCCCATCACCTCTCTTAATACTAAGTATG
TTGCACCACAGGTGACATACCAAACATTTCTACTAACCT
CCCTCCTCCTCTTCTCGGCAATTCACCGGGATTGACTTCC
AAGATGAGTTGGATGAGTTTTTCAAAAATGTTAGCACCAG
TATACCTAATTTTGGTTCTCTAACACAGATTAATACTACAT
TACTCGATCTTACCTACGAGATGTTGTCTCTTCAACAAGTT
GTAAAGCCCTTAATGAGTCTTACATAGACCTTAAAGAGC
TTGGCAATTATACTTATTACAACAATGGCCGTGGTACAT
TTGGCTTGGTTTCATTGCTGGGCTTGTGTCCTTAGCTCTAT
GCGTCTTCTTCATACTGTGCTGCACTGGTTGTGGCACAAAC
TGTATGGGAAAACCTAAGTGTAATCGTTGTTGTGATAGAT
ACGAGGAATACGACCTCGAGCCGCATAAGGTTTCATGTTCA CTAA MERS S FL
ATGATACTCAGTGTTTCTACTGATGTTCTTGTTAACACC 21 SPIKE
TACAGAAAGTTACGTTGATGTAGGGCCAGATTCTGTTAAG 2cEMC/2012
TCTGCTTGATTGAGGTTGATATACAACAGACTTTCTTTGA (XbaI change (T to
TAAAACCTGGCCTAGGCCAATTGATGTTTCTAAGGCTGAC G)) (nucleotide)
GGTATTATATAACCCTCAAGGCCGTACATATTCTAACATAA
CTATCACTTATCAAGGTCTTTTTCCCTATCAGGGAGACCAT
GGTGATATGTATGTTTACTCTGCAGGACATGCTACAGGCA
CAACTCCACAAAAGTTGTTTGTAGCTAACTATTCTCAGGA
CGTCAAACAGTTTGCTAATGGGTTTGTCTCGTCCGTATAGGA
GCAGCTGCCAATTCCACTGGCACTGTTATTATTAGCCCATC
TACCAGCGCTACTATACGAAAATTTACCCTGCTTTTATGC
TGGGTTCTTCAGTTGGTAATTTCTCAGATGGTAAAATGGG
CCGCTTCTTCAATCATACTCTAGTTCTTTTGCCCGATGGAT
GTGGCACTTTACTTAGAGCTTTTTATTGTATTCTGGAGCCT
CGCTCTGGAAATCATTGTCCTGCTGGCAATTCCTATACTTC
TTTTGCCACTTATCACACTCCTGCAACAGATTGTTCTGATG
GCAATTACAATCGTAATGCCAGTCTGAACTCTTTTAAGGA
GTATTTAATTTACGTAACCTGCACCTTTATGTACACTTATA
ACATTACCGAAGATGAGATTTTAGAGTGGTTTGGCATTAC
ACAACTGCTCAAGGTGTTACCTCTTCTCATCTCGGTATG
TTGATTTGTACGGCGGCAATATGTTTCAATTTGCCACCTTG
CCTGTTTATGATACTATTAAGTATTATTCTATCATTCTCA
CAGTATTCGTTCTATCCAAAGTGATAGAAAAGCTTGGGCT

GCCTTCTACGTATATAAACTTCAACCGTTAACTTTCCTGTT
GGATTTTTCTGTTGATGGTTATATACGCAGAGCTATAGACT
GTGGTTTTAATGATTTGTCACAACCTCCACTGCTCATATGAA
TCCTTCGATGTTGAATCTGGAGTTTATTCAGTTTCGTCTTT
CGAAGCAAACCTTCTGGCTCAGTTGTGGAACAGGCTGAA
GGTGTGGAATGTGATTTTTACCTCTTCTGTCTGGCACACC
TCCTCAGGTTTATAATTTCAAGCGTTTGGTTTTTACCAATT
GCAATTATAATCTTACCAAATTGCTTTCACTTTTTTCTGTG
AATGATTTTACTTGTAGTCAAATATCTCCAGCAGCAATTGC
TAGCAACTGTTATTCTTCACTGATTTTGGATTACTTTTCAT
ACCCACTTAGTATGAAATCCGATCTCAGTGTTAGTTCTGCT
GGTCCAATATCCCAGTTTAATTATAAACAGTCCTTTTCTAA
TCCCACATGTTTGATTTTAGCGACTGTTCCCTCATAACCTTA
CTACTATTACTAAGCCTCTTAAGTACAGCTATATTAACAA
GTGCTCTCGTCTTCTTTCTGATGATCGTACTGAAGTACCTC
AGTTAGTGAACGCTAATCAATACTCACCTGTGTATCCATT
GTCCCATCCACTGTGTGGGAAGACGGTGATTATTATAGGA
AACAACTATCTCCACTTGAAGGTGGTGGCTGGCTTGTGTC
TAGTGGCTCAACTGTTGCCATGACTGAGCAATTACAGATG
GGCTTTGGTATTACAGTTCAATATGGTACAGACACCAATA
GTGTTTGCCCCAAGCTTGAATTTGCTAATGACACAAAAT
TGCCTCTCAATTAGGCAATTGCGTGGAATATCCCTCTATG
GTGTTTCGGGCCGTGGTGTTTTTCAGAATTGCACAGCTGTA
GGTGTTCGACAGCAGCGCTTTGTTTATGATGCGTACCAGA
ATTTAGTTGGCTATTATTCTGATGATGGCAACTACTACTGT
TTGCGTGCTTGTGTTAGTGTTCCCTGTTTCTGTCATCTATGAT
AAAGAACTAAAACCCACGCTACTCTATTTGGTAGTGTTG
CATGTGAACACATTTCTTCTACCATGTCTCAATACTCCCGT
TCTACGCGATCAATGCTTAAACGGCGAGATTCTACATATG
GCCCCCTTCAGACACCTGTTGGTGTGTCTTAGGACTTGTT
AATTCCTCTTTGTTCGTAGAGGACTGCAAGTTGCCTCTTGG
TCAATCTCTCTGTGCTCTTCCTGACACACCTAGTACTCTCA
CACCTCGCAGTGTGCGCTCTGTTCCAGGTGAAATGCGCTT
GGCATCCATTGCTTTTAAATCATCTATTTCAGGTTGATCAAC
TTAATAGTAGTTATTTTAAATTAAGTATACCCACTAATTTT
TCCTTTGGTGTGACTCAGGAGTACATTCAGACAACCATT
AGAAAGTTACTGTTGATTGTAAACAGTACGTTTGCAATGG
TTTCCAGAAGTGTGAGCAATTACTGCGCGAGTATGGCCAG
TTTTGTTCCAAAATAAACAGGCTCTCCATGGTGCCAATTT
ACGCCAGGATGATTCTGTACGTAATTTGTTTTCGAGCGTG
AAAAGCTCTCAATCATCTCCTATCATAACAGGTTTTGGAG
GTGACTTTAATTTGACACTTCTGGAACCTGTTTCTATATCT
ACTGGCAGTCGTAGTGCACGTAGTGCTATTGAGGATTTGC
TATTTGACAAAGTCACTATAGCTGATCCTGGTTATATGCA
AGGTTACGATGATTGCATGCAGCAAGGTCCAGCATCAGCT
CGTGATCTTATTTGTGCTCAATATGTGGCTGGTTACAAAGT
ATTACCTCCTCTTATGGATGTTAATATGGAAGCCGCGTATA
CTTCATCTTTGCTTGGCAGCATAGCAGGTGTTGGCTGGACT
GCTGGCTTATCCTCCTTTGCTGCTATTCCATTTGCACAGAG
TATCTTTTATAGGTTAAACGGTGTGGCATTACTCAACAGG
TTCTTTCAGAGAACCAAAAAGCTTATTGCCAATAAGTTTAA
TCAGGCTCTGGGAGCTATGCAAACAGGCTTCACTACAAC
AATGAAGCTTTTCAGAAGGTTTCAGGATGCTGTGAACAACA
ATGCACAGGCTCTATCCAAATTAGCTAGCGAGCTATCTAA

TACTTTTGGTGCTATTTCCGCCTCTATTGGAGACATCATA
AACGTCTTGATGTTCTCGAACAGGACGCCCAAATAGACAG
ACTTATTAATGGCCGTTTGACAACACTAAATGCTTTTGTG
CACAGCAGCTTGTTCGTTCCGAATCAGCTGCTCTTTCCGCT
CAATTGGCTAAAGATAAAGTCAATGAGTGTGTCAAGGCAC
AATCCAAGCGTTCTGGATTTTGCGGTCAAGGCACACATAT
AGTGCCTTTGTTGTAATGCCCTAATGGCCTTTACTTCA
TGCATGTTGGTTATTACCCTAGCAACCACATTGAGGTTGTT
TCTGCTTATGGTCTTTGCGATGCAGCTAACCCCTACTAATTG
TATAGCCCCTGTTAATGGCTACTTTATTAATAAATAACA
CTAGGATTGTTGATGAGTGGTCATATACTGGCTCGTCCTTC
TATGCACCTGAGCCATTACCTCCCTTAATACTAAGTATGT
TGCACCACAGGTGACATAACAAAACATTTCTACTAACCTC
CCTCCTCCTCTTCTCGGCAATTCCACCGGGATTGACTTCCA
AGATGAGTTGGATGAGTTTTTCAAAAATGTTAGCACCAGT
ATACCTAATTTTGGTTCCCTAACACAGATTAATACTACATT
ACTCGATCTTACCTACGAGATGTTGTCTCTTCAACAAGTTG
TTAAAGCCCTAATGAGTCTTACATAGACCTTAAAGAGCT
TGGCAATTATACTTATTACAACAATGGCCGTGGTACATT
TGGCTTGGTTTCATTGCTGGGCTTGTGCCTTAGCTCTATG
CGTCTTCTTCATACTGTGCTGCACTGGTTGTGGCACAAACT
GTATGGGAAAACCTAAGTGAATCGTTGTTGTGATAGATA
CGAGGAATACGACCTCGAGCCGCATAAGGTTTCATGTTTAC TAA Novel_MERS_S2_
ATGATCCACTCCGTGTTCCCTCCTCATGTTCCCTGTTGACCCC 22 subunit_trimeric
CACTGAGTCAGACTGCAAGCTCCCGCTGGGACAGTCCCTG vaccine
TGTGCGCTGCCTGACACTCCTAGCACTCTGACCCCACGCTC (nucleotide)
CGTGCAGTCCGCTGCCTGGCGAAATGCGGCTGGCCTCCATC
GCCTTCAATCACCCAATCCAAGTGGATCAGCTGAATAGCT
CGTATTTCAAGCTGTCCATCCCCACGAACTTCTCGTTCGGG
GTCACCCAGGAGTACATCCAGACCACAATTCAGAAGGTCA
CCGTCGATTGCAAGCAATACGTGTGCAACGGCTTCCAGAA
GTGCGAGCAGCTGCTGAGAGAATACGGGCAGTTTTTGCAGC
AAGATCAACCAGGCGCTGCATGGAGCTAACTTGCGCCAGG
ACGACTCCGTGCGCAACCTCTTTGCCTCTGTGAAGTCATCC
CAGTCCCTCCCAATCATCCCGGGATTCGGAGGGGACTTCA
ACCTGACCCTCCTGGAGCCCCTGTGTCGATCAGCACCGGTAG
CAGATCGGCGCGCTCAGCCATTGAAGATCTTCTGTTTCGAC
AAGGTACCATCGCCGATCCGGGCTACATGCAGGGATACG
ACGACTGTATGCAGCAGGGACCAGCCTCCGCGAGGGACCT
CATCTGCGCGCAATACGTGGCCGGGTACAAAGTGCTGCCT
CCTCTGATGGATGTGAACATGGAGGCCGCTTATACTTCGT
CCCTGCTCGGCTCTATCGCCGGCGTGGGGTGGACCGCCGG
CCTGTCCTCCTTCGCCGCTATCCCCTTTGCACAATCCATTT
TCTACCGGCTCAACGGCGTGGGCATTACTCAACAAGTCCT
GTCGGAGAACCAGAAGTTGATCGCAAACAAGTTCAATCA
GGCCCTGGGGGCCATGCAGACTGGATTCCTACTACGACTAAC
GAAGCGTTCCAGAAGGTCCAGGACGCTGTGAACAACAAC
GCCAGGCGCTCTCAAAGCTGGCCTCCGAACTCAGCAACA
CCTTCGGAGCCATCAGCGCATCGATCGGTGACATAATTCA
GCGGCTGGACGTGCTGGAGCAGGACGCCCAGATCGACCG
CCTCATCAACGGACGGCTGACCACCTTGAATGCCTTCGTG
GCACAACAGCTGGTCCGGAGCGAATCAGCGGCACTTTCCG
CCCAACTCGCCAAGGACAAAGTCAACGAATGCGTGAAGG
CCAGTCCAAGAGGTCCGGTTTCTGCGGTCAAGGAACCCA

TATTGTGTCCTTCGTCGTGAACGCGCCCAACGGTCTGTACT
TTATGCACGTCCGGCTACTACCCGAGCAATCATATCGAAGT
GGTGTCCGCCTACGGCCTGTGCGATGCCGCTAACCCCACT
AACTGTATTGCCCTGTGAACGGATATTTTATTAAGACCA
ACAACACCCGCATTGTGGACGAATGGTCATACACCGGTTC
GTCCTTCTACGCGCCCGAGCCCATCACTTCACTGAACACC
AAATACGTGGCTCCGCAAGTGACCTACCAGAACATCTCCA
CCAATTTGCCGCCGCCGCTGCTCGGAAACAGCACCGGAAT
TGATTTCCAAGATGAACTGGACGAATTCTTCAAGAACGTG

TCCACTTCCATTCCCAACTTCGGAAGCCTGACACAGATCA
ACACCACCCTTCTCGACCTGACCTACGAGATGCTGAGCCT
TCAACAAGTGGTCAAGGCCCTGAACGAGAGCTACATCGAC
CTGAAGGAGCTGGGCAACTATACTACTACAACAAGTGGC
CGGACAAGATTGAGGAGATTCTGTGCGAAAATCTACCACAT
TGAAAACGAGATCGCCAGAATCAAGAAGCTTATCGGCGA AGCC MERS_S0_Full-
ATGGAAACCCCTGCCAGCTGCTGTTCTGCTGCTGCTGTG 23 length Spike
GCTGCCTGATACCACCGGCAGCTATGTGGACGTGGGCCCC protein
GATAGCGTGAAGTCCGCCTGTATCGAAGTGGACATCCAGC (nucleotide, codon
AGACCTTTTTTCGACAAGACCTGGCCCAGACCCATCGACGT optimized)
GTCCAAGGCCGACGGCATCATCTATCCACAAGGCCGGACC
TACAGCAACATCACCATTACCTACCAGGGCCTGTTCCCAT
ATCAAGGCGACCACGGCGATATGTACGTGTACTCTGCCGG
CCACGCCACCGGCACCACACCCCAGAAACTGTTTCGTGGCC
AACTACAGCCAGGACGTGAAGCAGTTCGCCAACGGCTTCG
TCGTGCGGATTGGCGCCGCTGCCAATAGCACCGGCACAGT
GATCATCAGCCCCAGCACAGCGCCACCATCCGGAAGATC
TACCCCGCCTTCATGCTGGGCAGCTCCGTGGGCAATTTCA
GCGACGGCAAGATGGGCCGGTTCTTCAACCACACCCTGGT
GCTGCTGCCCGATGGCTGTGGCACACTGCTGAGAGCCTTC
TACTGCATCCTGGAACCCAGAAGCGGCAACCACTGCCCTG
CCGGCAATAGCTACACCAGCTTCGCCACCTACCACACACC
CGCCACCGATTGCTCCGACGGCAACTACAACCGGAACGCC
AGCCTGAACAGCTTCAAAGAGTACTTCAAACCTGCGGAACT
GCACCTTCATGTACACCTACAATATCACCGAGGACGAGAT
CCTGGAATGGTTCGGCATCACCCAGACCGCCCAGGGCGTG
CACCTGTTACGACGAGATACGTGGACCTGTACGGCGGCA
ACATGTTCCAGTTTGCCACCCTGCCCGTGTACGACACCATC
AAGTACTACAGCATCATCCCCACAGCATCCGGTCCATCC
AGAGCGACAGAAAAGCCTGGGCCGCCTTCTACGTGTACAA
GCTGCAGCCCCTGACCTTCTGCTGGACTTCAGCGTGGAC
GGCTACATCAGACGGGCCATCGACTGCGGCTTCAACGACC
TGAGCCAGCTGCACTGCTCCTACGAGAGCTTCGACGTGGA
AAGCGGCGTGTACAGCGTGTCCAGCTTCGAGGCCAAGCCT
AGCGGCAGCGTGGTGGAAACAGGCTGAGGGCGTGGAAATGC
GACTTCAGCCCTCTGCTGAGCGGCACCCCTCCCCAGGTGT
ACAACCTCAAGCGGCTGGTGTTCACCAACTGCAATTACAA
CCTGACCAAGCTGCTGAGCCTGTTCTCCGTGAACGACTTC
ACCTGTAGCCAGATCAGCCCTGCCGCCATTGCCAGCAACT
GCTACAGCAGCCTGATCCTGGACTACTTCAGCTACCCCT
GAGCATGAAGTCCGATCTGAGCGTGTCTCCGCCGGACCC
ATCAGCCAGTTCAAACATAAGCAGAGCTTCAGCAACCCTA
CCTGCCTGATTCTGGCCACCGTGCCCCACAATCTGACCAC
CATACCAAGCCCCTGAAGTACAGCTACATCAACAAGTGC

AGCAGACTGCTGTCCGACGACCGGACCGAAGTGCCCCAGC
TCGTGAACGCCAACCAGTACAGCCCCTGCGTGTCCATCGT
GCCCAGCACCGTGTGGGAGGACGGCGACTACTACAGAAA
GCAGCTGAGCCCCCTGGAAGGCGGCGGATGGCTGGTGGCT
TCTGGAAGCACAGTGGCCATGACCGAGCAGCTGCAGATG
GGCTTTGGCATCACCGTGCAGTACGGCACCGACACCAACA
GCGTGTGCCCAAGCTGGAATTCGCCAATGACACCAAGAT
CGCCAGCCAGCTGGGAAACTGCGTGGAATACTCCCTGTAT
GGCGTGTCCGGACGGGGCGTGTTCCAGAATTGCACAGCAG
TGGGAGTGCGGCAGCAGAGATTCGTGTACGATGCCTACCA
GAACCTCGTGGGCTACTACAGCGACGACGGCAATTACTAC
TGCCTGCGGGCCTGTGTGTCCGTGCCCGTGTCCGTGATCTA
CGACAAAGAGACAAAGACCCACGCCACACTGTTCCGGCTCC
GTGGCCTGCGAGCACATCAGCTCCACCATGAGCCAGTACT
CCCCTCCACCCGGTCCATGCTGAAGCGGAGAGATAGCAC
CTACGGCCCCCTGCAGACACCTGTGGGATGTGTGCTGGGC
CTCGTGAACAGCTCCCTGTTTGTGGAAGATTGCAAGCTGC
CCCTGGGCCAGAGCCTGTGTGCCCTGCCAGATACCCCTAG
CACCTGACCCCTAGAAGCGTGCCTCTGTGCCCGGCGAA
ATGCGGCTGGCCTCTATCGCCTTCAATCACCCCATCCAGGT
GGACCAGCTGAACTCCAGCTACTTCAAGCTGAGCATCCCC
ACCAACTTCAGCTTCGGCGTGACCCAGGAGTACATCCAGA
CCACAATCCAGAAAGTGACCGTGGACTGCAAGCAGTACGT
GTGCAACGGCTTTCAGAAGTGCGAACAGCTGCTGCGCGAG
TACGGCCAGTTCTGCAGCAAGATCAACCAGGCCCTGCACG
GCGCCAACCTGAGACAGGATGACAGCGTGCGGAACCTGTT
CGCCAGCGTGAAAAGCAGCCAGTCCAGCCCCATCATCCCT
GGCTTCGGCGGCGACTTTAACCTGACCCTGCTGGAACCTG
TGTCCATCAGCACCGGCTCCAGAAGCGCCAGATCCGCCAT
CGAGGACCTGCTGTTTCGACAAAGTGACCATTGCCGACCCC
GGCTACATGCAGGGCTACGACGATTGCATGCAGCAGGGCC
CAGCCAGCGCCAGGGATCTGATCTGTGCCCAGTATGTGGC
CGGCTACAAGGTGCTGCCCCCCTGATGGACGTGAACATG
GAAGCCGCCTACACCTCCAGCCTGCTGGGCTCTATTGCTG
GCGTGGGATGGACAGCCGGCCTGTCTAGCTTTGCCGCCAT
CCCTTTCGCCCAGAGCATCTTCTACCGGCTGAACGGCGTG
GGCATCACACAACAGGTGCTGAGCGAGAACCAGAAGCTG
ATCGCCAACAAGTTTAACCAGGCACTGGGCGCCATGCAGA
CCGGCTTACCACCACCAACGAGGCCTTCAGAAAGGTGCA
GGACGCCGTGAACAACAACGCCCAGGCTCTGAGCAAGCT
GGCCTCCGAGCTGAGCAATACCTTCGGCGCCATCAGCGCC
TCCATCGGCGACATCATCCAGCGGCTGGACGTGCTGGAAC
AGGACGCCCAGATCGACCGGCTGATCAACGGCAGACTGA
CCACCCTGAACGCCTTCGTGGCACAGCAGCTCGTGCGGAG
CGAATCTGCCGCTCTGTCTGCTCAGCTGGCCAAGGACAAA
GTGAACGAGTGCCTGAAGGCCCAGTCCAAGCGGAGCGGC
TTTTGTGGCCAGGGCACCCACATCGTGTCCCTTCGTCTGAA
TGCCCCCAACGGCCTGTACTTTATGCACGTGGGCTATTACC
CCAGCAACCACATCGAGGTGGTGTCCGCCTATGGCCTGTG
CGACGCCGCAATCCTACCAACTGTATCGCCCCCGTGAAC
GGCTACTTCATCAAGACCAACAACACCCGGATCGTGGACG
AGTGGTCTACACAGGCAGCAGCTTCTACGCCCCCGAGCC
CATCACCTCCCTGAACACCAATAACGTGGCCCCCAAGTG
ACATACCAGAACATCTCCACCAACCTGCCCCCTCCACTGC

TGGGAAATTCCACCGGCATCGACTTCCAGGACGAGCTGGA
CGAGTTCTTCAAGAACGTGTCCACCTCCATCCCCAACTTCG
GCAGCCTGACCCAGATCAACACCACTCTGCTGGACCTGAC
CTACGAGATGCTGTCCCTGCAACAGGTCGTGAAAGCCCTG
AACGAGAGCTACATCGACCTGAAAGAGCTGGGGAACTAC
ACCTACTACAACAAGTGGCCTTGGTACATTTGGCTGGGCT
TTATCGCCGGCCTGGTGGCCCTGGCCCTGTGCGTGTTCTTC
ATCCTGTGCTGCACCGGCTGCGGCACCAATTGCATGGGCA
AGCTGAAATGCAACCGGTGCTGCGACAGATACGAGGAAT
ACGACCTGGAACCTCACAAAGTGCATGTGCAC Betacoronavirus mRNA Sequences gb|KJ156934.1|:21
AUGAUACACUCAGUGUUUCUACUGAUGUUCUUGUUAAC 65 405-25466 Middle
ACCUACAGAAAGUUACGUUGAUGUAGGGCCAGAUUCUG East respiratory
UUAAGUCUGCUUGUAUUGAGGUUGAUUAACAACAGACC syndrome
UUCUUUGAUAAAACUUGGCCUAGGCCAAUUGAUGUUUC coronavirus
UAAGGCUGACGGUAUUUAUUAUACCCUCAAGGCCGUACAU isolate
AUUCUAACAUAACUAUCACUUAUCAAGGUCUUUUUCCCU Riyadh_14_2013,
AUCAGGGAGACCAUGGUGAUUUGUAUGUUUACUCUGCA spike protein
GGACAUGCUCACAGGCACAACUCCACAAAAGUUGUUUGU (nucleotide)
AGCUAACUAUUCUCAGGACGUCAAACAGUUUGC UAAUG
GGUUUGUCGUC CGUAUAGGAGCAGCUGCCAAUUCACUG
GCACUGUUAUUUAGCCCAUCUACCAGCGCUACUAUAC
GAAAAAUUUACCCUGCUUUUAUGCUGGGUUCUUCAGUU
GGUAAUUUCAGAUUGGUA AAAUUGGCCGCUUCUCAA
UCAUACUCUAGUUCUUUUGCCCGAUGGAUGUGGCACUU
UACUUAGAGCUUUUUAUUGUAUUCUAGAGCCUCGCUCU
GGAAUCAUUGUCCUGCUGGCAAUCCUAUACUUCUUU
UGCCACUUAUCACACUCCUGCAACAGAUUGUUCUGAUGG
CAAUUACAAUCGUA AUGCCAGUCUGAACUCUUUUAAGG
AGUAUUUUAUUUACGUAACUGCACCUUUUAUGUACACU
UAUAACAUAUACCGAAGAUGAGAUUUUAGAGUGGUUUGG
CAUUACACAAACUGCUC AAGGUGUACCCUCUUCUCAUC
UCGGUAUGUUGAUUUGUACGGCGGCAAUAUGUUCAAU
UUGCCACCUUGCCUGUUUAUGAUACUAUUAAGUAUUUAU
UCUAUCAUUCUCACAGUAUUCGUUCUAUCCAAAGUGAU
AGAAAAGCUUGGGCUGCCUUCUACGUAUAUAAACUUCA
ACCGUUAACUUUCUGUUGGAUUUUUCUGUUGAUGGUU
AUUAACGCAGAGCUAUAGACUGUGGUUUUAUGAUUUG
UCACAACUCCACUGCUCUAUUGAAUCCUUCGAUGUUGAA
UCUGGAGUUUAUUCAGUUUCGUCUUUCGAAGCAAACC
UUCUGGCUCAGUUGUGAACAGGCUGAAGGUGUUGAAU
GUGAUUUUUCACCUCUUCUGUCUGGCACACCUCUCAGG
UUUAUAAUUUCAAGCGUUUGGUUUUACCAAUUGCAAU
UAUAAUCUUACCAAUUGCUUCACUUUUUCUGUGAA
UGAUUUUACUUGUAGUCAAAUAUCUCCAGCAGCAAUUG
CUAGCAACUGUUAUUCUUCACUGAUUUUUGGAUUUUUU
UCAUACCCACUAGUAUGAAAUCCGAUCUCAGUGUUGAG
UUCUGCUGGUCAAUAUCCAGUUUAUUUAUAAACAGU
CCUUUUCUAAUCCACAUGUUUGAUCUUAGCGACUGUUC
CUCAUAACCUUACUACUAUUAACUAAGCCUCUUAAGUACA
GCUAUUAACAAGUGCUCUCGUCUUCUUUCUGAUGAU
CGUACUGAAGUACCUCAGUUAGUGAACGCUAAUCAUA
CUCACCCUGUGUAUCCAUUGUCCAUCCACUGUGUGGGA
AGACGGUGAUUAUUAUAGGAAACAACUAUCUCCACUUG
AAGGUGGUGGCUGGCUUGUUGCUAGUGGCUCAACUGUU

GCCAUGACUGAGCAAUUACAGAUGGGCUUUGGUUUUAC
AGUUCAAUAUGGUACAGACACCAAUAGUGUUUGCCCA
AGCUUGAAUUUGCUAAUGACACAAAAUUGCCUCUCA
UUAGGCAAUUGCGUGGAAUAUUCUUCUAUGGGUGUUUC
GGGCCGUGGUGUUUUUUCAGAAUUGCACAGCUGUAGGUG
UUCGACAGCAGCGCUUUGUUUAUGAUGCGUACCAGAAU
UUAGUUGGCUAUUAUUCUGAUGAUGGCAACUACUACUG
UCUGCGUGCUUGUGUUAGUGUUCUGUUUCUGUCAUCU
AUGAUAAAGAAACUAAAACCCACGCUACUCUAUUUGGU
AGUGUUGCAUGUGAACACAUUUCUUCUACCAUGUCUCA
AUACUCCCGUUCUACGCGAUCAAUGCUUAAACGGCGAGA
UUCUACAUAUGGCCCCCUUCAGACACCUGUUGGUUGUGU
CCUAGGACUUGUUAUUCUUCUUGUUCGUAGAGGACU
GCAAGUUGCCUCUCGGUCAUUCUCUCUGUGUCUUCUG
ACACACCUAGUACUCUCACACCUCGCAGUGUGCGCUCUG
UGCCAGGUGAAAUGCGCUUGGCAUCCAUUGCUUUUAAU
CAUCCCAUUCAGGUUGAUCACUAAUAGUAGUUAUUU
UAAAUAAGUAUACCCACUAAUUUUUCCUUUGGUGUGA
CUCAGGAGUACAUUCAGACAACCAUUCAGAAAGUUACU
GUUGAUUGUAAACAGUACGUUUGCAAUGGUUUCAGAA
GUGUGAGCAAUACUGCGCGAGUAUGGCCAGUUUUGU
CCAAAUAACAGGCUCUCAUGGUGCCAAUUUACGCC
AGGAUGAUUCUGUACGUAAUUUGUUUGCGAGCGUGAAA
AGCUCUCAAUCAUCUCCUAUCAUACCAGGUUUUGGAGGU
GACUUUAAUUUGACACUUCUAGAACCUGUUUCUAUAUC
UACUGGCAGUCGUAGUGCACGUAGUGCUAUUGAGGAUU
UGCUAUUUGACAAAGUCACUAUAGCUGAUCCUGGUUAU
AUGCAAGGUUACGAUGAUUGUAUGCAGCAAGGUCCAGC
AUCAGCUCGUGAUCUUAUUUGUGCUCAAUAUGUGGCUG
GUUAUAAAGUAUUACCUCCUCUUAUGGAUGUAAUAUG
GAAGCCGCGUAUACUUCUUCUUGCUUGGCAGCAUAGCA
GGUGUUGGCUGGACUGCUGGCCUUAUCCUCCUUUGCUGCU
AUUCCAUUUGCACAGAGUAUYUUUUUAUAGGUUAAACGG
UGUUGGCAUUAUCUACACAGGUUCUUUCAGAGAACCAA
AGCUUAUUGCCAAUAAGUUUAAUACAGGCUCUGGGAGCU
AUGCAAACAGGCUUCACUACAACUAAUGAAGCUUUUCG
GAAGGUUCAGGAUGCUGUGAACAACAUGCACAGGCUC
UAUCCAAAUAAGCUAGCGAGCUAUCUAAUACUUUUGGU
GCUAUUUCCGCCUCUAUUGGAGACAUCAUACAACGUCUU
GAUGUUCUCGAACAGGACGCCCAAUAGACAGACUUUAU
UAAUGGCCGUUUGACAACACUAAAUGCUUUUGUUGCAC
AGCAGCUUGUUCGUUCCGAAUCAGCUGCUCUUUCCGCUC
AAUUGGCUAAAGAUAAAGUCAUUGAGUGUGUCAAGGCA
CAAUCCAAGCGUUCUGGAUUUUGCGGUCAAGGCACACAU
AUAGUGUCCUUUGUUGUAAAUGCCCCUAAUGGCCUUUA
CUUUUAGCAUGUUGGUUAUUACCCUAGCAACCACAUUG
AGGUUGUUUCUGCUUAUGGUCUUUGCGAUGCAGCUAAC
CCUACUAAUUGUAUAGCCCCUGUUAUUGGCUACUUUAU
UAAAACUAAUAACACUAGGAUUGUUGAUGAGUGGUCAU
AUACUGGCUCGUCCUUCUUAUGCACCUGAGCCCAUCACCU
CUCUUAUACUAAGUAUGUUGCACCACAGGUGACAUAACC
AAAACAUUUCUACUAAACCUCCUCCUCCUCUUCUCGGCA
AUUCCACCGGGAUUGACUUCUCCAAGAUGAGUUGGAUGAG
UUUUUCAAAAAUGUUAGCACCAGUAUACCUAAUUUUGG

UUCUCUAACACAGAUUAAUACUACAUAUACUCGAUCUUAC
CUACGAGAUGUUGUCUCUUAACAAGUUGUAAAAGCCC
UUAAUGAGUCUUAACAUAGACCUUAAAGAGCUUGGCAAU
UAUACUUAUUACAACAAAUGGCCGUGGUACAUAUUGGCU
UGGUUUAUUGCUGGGCUUGUUGCCUAGCUCUAUGCG
UCUUCUUAUACUGUGCUGCACUGGUUGUGGCACAAACU
GUAUGGGAAAACUUAAGUGUAAUCGUUGUUGUGAUAGA
UACGAGGAAUACGACCUCGAGCCGCAUAAGGUUCAUGU UCACUAA MERS S FL
AUGAUACACUCAGUGUUUCUACUGAUGUUCUUGUUAAC 66 SPIKE
ACCUACAGAAAGUUACGUUGAUGUAGGGCCAGAUUCUG 2cEMC/2012
UUAAGUCUGCUUGUAUUGAGGUUGAUUAACAACAGACU (XBal change (U
UUCUUUGAUAAAACUUGGCCUAGGCCAAUUGAUGUUUC to G))
UAAGGCUGACGGUAUUUAUACCCUCAAGGCCGUACAU (nucleotide)
AUUCUAACAUAACUUAUCACUUAUCAAGGUCUUUUUCCCU
AUCAGGGAGACCAUGGUGAUUAUGUAUGUUUACUCUGCA
GGACAUGCUCACAGGCACAACUCCACAAAAGUUGUUUGU
AGCUAACUAUUCUCAGGACGUCAAACAGUUUGCUAAUG
GGUUUGUCGUCCGUUAUAGGAGCAGCUGCCAAUCCACUG
GCACUGUUAUUUAUAGCCCAUCUACCAGCGCUACUAUAC
GAAAAAUUUACCCUGCUUUUAUGCUGGGUUCUUCAGUU
GGUAAUUUCUCAGAUGGUAAAUGGGCCGCUUCUCAA
UCAUACUCUAGUUCUUUUGCCCAGUUGGAUGUGGCACUU
UACUUAGAGCUUUUUUAUUGUAUUCUGGAGCCUCGCUCU
GGAAUCAUUGUCCUGCUGGCAAUCCUAUACUUCUUU
UGCCACUUAUCACACUCCUGCAACAGAUUGUUCUGAUGG
CAAUUACAAUCGUAAUGCCAGUCUGAACUCUUUUAAAG
AGUAUUUUAAUUUACGUAAUCUGCACCUUUUAUGUACACU
UAUAACAUAUACCGAAGAUGAGAUUUUAGAGUGGUUUGG
CAUUACACAAACUGCUCUAAAGGUGUUCACCUCUUCUCAUC
UCGGUAUGUUGAUUUUGUACGGCGGCAAUAUGUUUCAAU
UUGCCACCUUGCCUGUUUAUGAUACUAUUAAGUAUUUAU
UCUAUCAUUCUCACAGUAUUCGUUCUAUCCAAGUGAU
AGAAAAGCUUGGGCUGCCUUCUACGUUAUUAACUUCA
ACCGUUAACUUCUGUUGGAUUUUUCUGUUGAUGGUU
AUUAACGCAGAGCUUAUAGACUGUGGUUUUAAUGAUUUG
UCACAACUCCACUGCUCUAUUGAAUCCUUCGAUGUUGAA
UCUGGAGUUUAUUCAGUUUCGUCUUUCGAAGCAAAC
UUCUGGCUCAGUUGUGGAACAGGCUGAAGGUGUUGAAU
GUGAUUUUUCACCUCUUCUGUCUGGCACACCUCUCAGG

UUUAUAAUUUCAAGCGUUUGGUUUUUACCAAUUGCAAU
UAUAAUCUUACCAAUUGCUUUCACUUUUUUCUGUGAA
UGAUUUUACUUGUAGUCAAAUAUCUCCAGCAGCAAUUG
CUAGCAACUGUUAUUCUUCACUGAUUUUUGGAUUACUUU
UCAUACCCACUUAAGUAUGAAAUCCGAUCUCAGUGUUG
UUCUGCUGGUCCAAUAUCCAGUUUAUUUAUAAAACAGU
CCUUUUCUAAUCCACAUGUUUGAUUUUAGCGACUGUUC
CUCUAACCUUACUACUAUUAACUAAGCCUCUUAAGUACA
GCUAUUAUACAAGUGCUCUCGUCUUCUUCUGAUGAU
CGUACUGAAGUACCUCAGUUAUGUGAACGCUAAUCAUA
CUCACCCUGUGUAUCCAUUGUCCAUCCACUGUGUGGGA
AGACGGUGAUUAUUUAUAGGAAACAACUAUCUCCACUUG
AAGGUGGUGGCUGGCUUGUUGCUAGUGGCUCAACUGUU
GCCAUGACUGAGCAAUUACAGAUGGGCUUUGGUUAUAC

AGUUCAUAUGGUACAGACACCAAUAGUGUUUGCCCCA
AGCUUGAAUUUGCUAAUGACACAAAAUUGCCUCUCA
UUAGGCAAUUGCGUGGAAUUAUCCCCUCAUGGGUGUUUC
GGGCCGUGGUGUUUUUCAGAAUUGCACAGCUGUAGGUG
UUCGACAGCAGCGCUUUGUUUAUGAUGCGUACCAGAAU
UUAGUUGGCUAUUAUUCUGAUGAUGGCAACUACUACUG
UUUGCGUGCUUGUGUUAGUGUUCUGUUUCUGUCAUCU
AUGAUAAAGAAACUAAAACCCACGCUACUCUAUUUGGU
AGUGUUGCAUGUGAACACAUUUCUUCUACCAUGUCUCA
AUACUCCCCGUUCUACGCGAUCAAUGCUUAAACGGCGAGA
UUCUACAUAUGGCCCCCUUCAGACACCUGUUGGUUGUGU
CCUAGGACUUGUUAAUUCUCUUCUUGUUCGUAGAGGACU
GCAAGUUGCCUCUUGGUCAAUCUCUCUGUGCUCUUCUG
ACACACCUAGUACUCUCACACCUCGCAGUGUGCGCUCUG
UUCAGGUGAAAUGCGCUUGGCAUCCAUGCUUUUAAU
CAUCCUAUUCAGGUUGAUC AACUAAUAGUAGUUUUU
UAAAUAAGUAUACCCACUAAUUUUUCCUUGGUGUGA
CUCAGGAGUACAUUCAGACAACCAUUCAGAAAGUUACU
GUUGAUUGUAAACAGUACGUUUGCAAUGGUUUCAGAA
GUGUGAGCAAUACUGCGCGAGUAUGGCCAGUUUUGUU
CCAAAUAACAGGCUCUCAUGGUGCCAAUUUACGCC
AGGAUGAUUCUGUACGUAAUUUGUUUGCGAGCGUGAAA
AGCUCUCAAUCAUCUCCUAUCAUACCAGGUUUUGGAGGU
GACUUUAAUUUGACACUUCUGGAACCGUUUCUAUAUC
UACUGGCAGUCGUAGUGCACGUAGUGCUAUUGAGGAUU
UGCUAUUUGACAAAGUCACUAUAGCUGAUCCUGGUUAU
AUGCAAGGUUACGAUGAUUGCAUGCAGCAAGGUCCAGC
AUCAGCUCGUGAUCUUAUUUGUGCUCAAUAUGUGGCUG
GUUACAAAGUAUUACCUCCUCUUAUGGAUGUAAUAUG
GAAGCCGCGUAUACUUCUUCUUGCUUGGCAGCAUAGCA
GGUGUUGGCUGGACUGCUGGCCUUAUCCUCCUUGCUGCU
AUCCAUUUGCACAGAGUAUCUUUUUAUAGGUUAAACGG
UGUUGGCAUUACUCAACAGGUUCUUCAGAGAACCAA
AGCUUAUUGCCAAUAAGUUUAAUCAGGCUCUGGGAGCU
AUGCAAACAGGCUUCACUACAACUAAUGAAGCUUUUCA
GAAGGUUCAGGAUGCUGUGAACAACA AUGCACAGGCUC
UAUCCAAAUAGCUAGCGAGCUAUCUAAUACUUUUGGU
GCUAUUUCCGCCUCUAUUGGAGACAUCAUACAACGUCUU
GAUGUUCUCGAACAGGACGCCCAAUAGACAGACUUUAU
UAAUGGCCGUUUGACAACACUAAAUGCUUUUGUUGCAC
AGCAGCUUGUUCGUUCCGAAUCAGCUGCUCUUCCGCUC
AAUUGGCUAAAGAUAAAGUCAUAGAGUGUGUCAAGGCA
CAAUCCAAGCGUUCUGGAUUUUGCGGUCAAGGCACACAU
AUAGUGUCCUUGUUGUAAAUGCCCCUAAUGGCCUUUA
CUUCAUGCAUGUUGGUUAUUACCCUAGCAACCACAUUGA
GGUUGUUUCUGCUUAUGGUCUUGCGAUGCAGCUAACC
CUACUAAUUGUAUAGCCCCUGUUAUUGGCUACUUUAU
AAAACUAAUAACACUAGGAUUGUUGAUGAGUGGUCAUA
UACUGGCUCGUCCUUCU AUGCACCUGAGCCCAUACCUC
CCUAAUACUAAGUAUGUUGCACCACAGGUGACAUACCA
AAACAUUUCUACUAAACUCCUCCUCCUUCUCUGGCAA
UUCACCGGGAUUGACUCCAAGAUGAGUUGGAUGAGU
UUUUCAAAAAUGUUAGCACCAGUAUACCUAAUUUUGGU
UCCCUAACACAGAUUAUACUACAUAUCUGAUCUACC

UACGAGAUGUUGUCUCUUCAACAAGUUGUUAAAGCCCU
UAAUGAGUCUUACAUAAGACCUUAAAGAGCUUGGCAAUU
AUACUUUUACAACAAUUGGCCGUGGUACAUUUGGCUU
GGUUUCAUUGCUGGGCUUGUUGCCUUAGCUCUAUGCGU
CUUCUUCAUACUGUGCUGCACUGGUUGUGGCACAAACUG
UAUGGGAAAACUUAAAGUGUAAUCGUUGUUGUGAUAGAU
ACGAGGAAUACGACCUCGAGCCGCAUAAGGUUCAUGUUC ACUAA Novel_MERS_S2_
AUGAUCCACUCCGUGUUCCUCCUCAUGUUCCUGUUGACC 67 subunit_trimeric
CCCACUGAGUCAGACUGCAAGCUCCCGCUGGGACAGUCC vaccine
CUGUGUGCGCUGCCUGACACUCCUAGCACUCUGACCCCA (nucleotide)
CGCUCGUGCGGUCGGUGCCUGGGCAAUUGCGGCUGGCC
UCCAUCGCCUUCAAUCACCCAAUCCAAGUGGAUCAGCUG
AAUAGCUCGUUUUCAAGCUGUCCAUCCCCACGAACUUC
UCGUUCGGGGUCACCCAGGAGUACAUCCAGACCACAAUU
CAGAAGGUCACCGUCGAUUGCAAGCAAUACGUGUGCAAC
GGCUUCCAGAAGUGCGAGCAGCUGCUGAGAGAAUACGG
GCAGUUUUGCAGCAAGAUAACCAGGCGCUGCAUGGAGC
UAACUUGCGCCAGGACGACUCCGUGCGCAACCUCUUUGC
CUCUGUGAAGUCAUCCAGUCCUCCCCAAUCAUCCCGGG
AUUCGGAGGGGACUUCAACCUGACCCUCCUGGAGCCCGU
GUCGAUCAGCACCGGUAGCAGAUCGGCGCGCUCAGCCAU
UGAAGAUCUUCUGUUCGACAAGGUCACCAUCGCCGAUCC
GGGCUACAUGCAGGGAUACGACGACUGUAUGCAGCAGG
GACCAGCCUCCGCGAGGGACCUCAUCUGCGCGCAAUACG
UGGCCGGGUACAAAGUGCUGCCUCCUCUGAUGGAUGUG
AACAUUGGAGGCCGCUUAUACUUCGUCCUUGCUCGGCUCU
AUCGCCGGCGUGGGGUGGACCGCCGGCCUGUCCUCCUUC
GCCGCUAUCCCCUUUGCACAAUCCAUUUUCUACCGGCUC
AACGGCGUGGGCAUUACUCAACAAGUCCUGUCGGAGAAC
CAGAAGUUGAUCGCAAACAAGUUCAAUCAGGCCUUGGG
GGCCAUGCAGACUGGAUUCACUACGACUAACGAAGCGUU
CCAGAAGGUCCAGGACGCUGUGAACAACAACGCCCAGGC
GCUCUCAAGCUGGCCUCCGAACUCAGCAACACCUUCGG
AGCCAUCAGCGCAUCGAUCGGUGACAUAUUUCAGCGGCU
GGACGUGCUGGAGCAGGACGCCCAGAUCGACCGCCUCAU
CAACGGACGGCUGACCACCUUGAAUGCCUUCGUGGCACA
ACAGCUGGUCCGGAGCGAAUCAGCGGCACUUUCCGCCCA
ACUCGCCAAGGACAAAGUCAACGAAUGCGUGAAGGCCCA
GUCCAAGAGGUCCGGUUUCUGCGGUAAGGAACCCAUAU
UGUGUCCUUCGUCGUGAACGCGCCCAACGGUCUGUACUU
UAUGCACGUCGGCUACUACCCGAGCAAUCAUAUCGAAGU
GGUGUCCGCCUACGGCCUGUGCGAUGCCGCUAACCCAC
UAACUGUAUUGCCCCUGUGAACGGAAUUUUUAUUAAGA
CCAACAACACCCGCAUUGUGGACGAAUGGUCAUACACCG
GUUCGUCCUUCUACGCGCCCGAGCCCAUCACUUCACUGA
ACACCAAUACGUGGCUCGCAAGUGACCUACCAGAACA
UCUCCACCAAUUUGCCGCCCGCCGUCUCGGAAACAGCA
CCGGAAUUGAUUUCCAAGAUGAACUGGACGAAUUCUUC
AAGAACGUGUCCACUCCAUUCCCAACUUCGGAAGCCUG
ACACAGAUCAACACCACCCUUCUCGACCUGACCUACGAG
AUGCUGAGCCUUAACAAGUGGUCAAGGCCUGAACGAG
AGCUACAUCGACCUGAAGGAGCUGGGCAACUAUACCUAC
UACAACAAGUGGCCGGACAAGAUUGAGGAGAUUCUGUC
GAAAUCUACCACAUUGAAAACGAGAUCGCCAGAAUCA AGAAGCUUAUCGGCGAAGCC

MERS_S0_Full- AUGGAAACCCUGCCCAGCUGCUGUUCUGCUGCUG 68 length Spike
UGGCUGCCUGAUACCACCGGCAGCUAUGUGGACGUGGGC protein
CCCGAUAGCGUGAAGUCCGCCUGUAUCGAAGUGGACAUC (nucleotide, codon
CAGCAGACCUUUUUCGACAAGACCUGGCCAGACCCAUC optimized)
GACGUGUCCAAGGCCGACGGCAUCAUCAUCCACAAGGC
CGGACCUACAGCAACAUCACCAUACCACCAGGGCCUG
UUCCCAUAUCAAGGCGACCACGGCGAUUUGUACGUGUAC
UCUGCCGGCCACGCCACCGGCACCACACCCCAGAAACUG
UUCGUGGCCAACUACAGCCAGGACGUGAAGCAGUUCGCC
AACGGCUUCGUCGUGCGGAUUGGGCGCCGCUGCCAAUAGC
ACCGGCACAGUGAUCAUCAGCCCCAGCACCAGCGCCACC
AUCCGGAAGAUCUACCCCGCCUUCAUGCUGGGCAGCUCC
GUGGGCAAUUUCAGCGACGGCAAGAUGGGCCGGUUCUU
CAACCACACCCUGGUGCUGCUGCCCAGUAGGCUGUGGCAC
ACUGCUGAGAGCCUUCUACUGCAUCCUGGAACCCAGAAG
CGGCAACCACUGCCCUGCCGGCAAUAGCUACACCAGCUU
CGCCACCUACCACACACCCGCCACCGAUUGCUCGACGG
CAACUACAACCGGAACGCCAGCCUGAACAGCUUCAAGA
GUACUUAACCGUGCGGAACUGCACCUUCAUGUACACCUA
CAAUAUCACCGAGGACGAGAUCUGGAAUGGUUCGGCA
UCACCAGACCGCCCAGGGCGUGCACCUGUUCAGCAGCA
GAUACGUGGACCUGUACGGCGGCAACAUGUUCAGUUU
GCCACCCUGCCCUGUACGACACCAUCAAGUACUACAGC
AUCAUCCCCACAGCAUCCGGUCCAUCAGAGCGACAGA
AAAGCCUGGGCCGCCUUCUACGUGUACAAGCUGCAGCCC
CUGACCUUCCUGCUGGACUUCAGCGUGGACGGCUACAUC
AGACGGGCCAUCGACUGCGGCUUCAACGACCUGAGCCAG
CUGCACUGCUCUACGAGAGCUUCGACGUGGAAAGCGGC
GUGUACAGCGUGUCCAGCUUCGAGGCCAAGCCUAGCGGC
AGCGUGGUGGAACAGGCUGAGGGCGUGGAAUGCGACUU
CAGCCCUCUGCUGAGCGGCACCCCUCCCCAGGUGUACAA
CUUCAAGCGGCUGGUGUUCACCAACUGCAAUACAACCU
GACCAAGCUGCUGAGCCUGUUCUCCGUGAACGACUUCAC
CUGUAGCCAGAUACAGCCCUGCCGCCAUUGCCAGCAACUG
CUACAGCAGCCUGAUCCUGGACUACUUCAGCUACCCCCU
GAGCAUGAAGUCCGAUCUGAGCGUGUCCUCCGCCGGACC
CAUCAGCCAGUUAACUACAAGCAGAGCUUCAGCAACCC
UACCUGCCUGAUUCUGGCCACCGUGCCCCACAAUCUGAC
CACCAUCACCAAGCCCCUGAAGUACAGCUACAUCAACAA
GUGCAGCAGACUGCUGUCCGACGACCGGACCGAAGUGCC
CCAGCUCGUGAACGCCAACCAGUACAGCCCCUGCGUGUC
CAUCGUGCCCAGCACCGUGUGGGAGGACGGCGACUACUA
CAGAAAGCAGCUGAGCCCCUGGAAGGCGGCGGAUGGCU
GGUGGCUUCUGGAAGCACAGUGGCCAUGACCGAGCAGCU
GCAGAUGGGCUUUGGCAUACCCGUGCAGUACGGCACCGA
CACCAACAGCGUGUGCCCCAAGCUGGAAUUCGCCAAUGA
CACCAAGAUCGCCAGCCAGCUGGGAAACUGCGUGGAAUA
CUCCCUGUAUGGCGUGUCCGGACGGGGCGUGUUCAGAA
UUGCACAGCAGUGGGAGUGCGGCAGCAGAGAUUCGUGU
ACGAUGCCUACCAGAACCUCGUGGGCUACUACAGCGACG
ACGGCAAUUACUACUGCCUGCGGGCCUGUGUGUCCGUGC
CCGUGUCCGUGAUCUACGACAAAGAGACAAAGACCCACG
CCACACUGUUCGGCUCCGUGGGCCUGCGAGCAUCAGCU
CCACCAUGAGCCAGUACUCCCGCUCCACCCGGUCCAUGC

UGAAGCGGAGAGAUAGCACCUACGGCCCCUGCAGACAC
CUGUGGGAUGUGUGCUGGGCCUCGUGAACAGCUCCCUGU
UUGUGGAAGAUUGCAAGCUGCCCCUGGGCCAGAGCCUGU
GUGCCCUGCCAGAUACCCCUAGCACCCUGACCCCUAGAA
GCGUGCGCUCUGUGCCCGGCGAAAUGCGGCUGGCCUCUA
UCGCCUUAUCACCCCAUCCAGGUGGACCAGCUGAACU
CCAGCUACUUAAGCUGAGCAUCCCCACCAACUUCAGCU
UCGGCGUGACCCAGGAGUACAUCCAGACCACAAUCCAGA
AAGUGACCGUGGACUGCAAGCAGUACGUGUGCAACGGC
UUUCAGAAGUGCGAACAGCUGCUGCGCGAGUACGGCCAG
UUCUGCAGCAAGAUCAACCAGGCCUGCACGGCGCCAAC
CUGAGACAGGAUGACAGCGUGCGGAACCUUGUUCGCCAGC
GUGAAAAGCAGCCAGUCCAGCCCCAUCAUCCCUGGCUUC
GGCGGCGACUUUAACCUGACCCUGCUGGAACCUGUGUCC
AUCAGCACCGGCUCCAGAAGCGCCAGAUCCGCCAUCGAG
GACCUGCUGUUCGACAAAGUGACCAUUGCCGACCCCGGC
UACAUGCAGGGCUACGACGAUUGCAUGCAGCAGGGCCCA
GCCAGCGCCAGGGAUCUGAUCUGUGCCCAGUAUGUGGCC
GGCUACAAGGUGCUGCCCCCCCUGAUGGACGUGAACAU
GAAGCCGCCUACACCUCAGCCUGCUGGGCUCUAUUGCU
GGCGUGGGAUGGACAGCCGGCCUGUCUAGCUUUGCCGCC
AUCCCUUUCGCCAGAGCAUCUUCUACCGGCUGAACGGC
GUGGGCAUCACACAACAGGUGCUGAGCGAGAACCAGAA
GCUGAUCGCCAACAAAGUUUAACCAGGCACUGGGCGCCA
GCAGACCGGCUUCACCACCACCAACGAGGCCUUCAGAAA
GGUGCAGGACGCCGUGAACAAACGCCCAGGCUCUGAG
CAAGCUGGCCUCCGAGCUGAGCAAUACCUUCGGCGCCA
CAGCGCCUCCAUCGGCGACAUCAUCCAGCGGCUGGACGU
GCUGGAACAGGACGCCAGAUCCGACCGGCUGAUCAACGG
CAGACUGACCACCCUGAACGCCUUCGUGGCACAGCAGCU
CGUGCGGAGCGAAUCUGCCGCUCUGUCUGCUCAGCUGGC
CAAGGACAAAGUGAACGAGUGCGUGAAGGCCCAGUCCA
AGCGGAGCGGCUUUUGUGGCCAGGGCACCCACAUCGUGU
CCUUCGUCGUGAAUGCCCCAACGGCCUGUACUUUAUGC
ACGUGGGCUAUUACCCAGCAACCACAUCGAGGUGGUGU
CCGCCUAUGGCCUGUGCGACGCCGCCAAUCCUACCAACU
GUAUCGCCCCCGUGAACGGCUACUUCAUCAAGACCAACA
ACACCCGGAUCGUGGACGAGUGGUCCUACACAGGCAGCA
GCUUCUACGCCCCCGAGCCAUCACCUCCUGAACACCA
AAUACGUGGGCCCCCAAGUGACAUACCAGAACAUCCCA
CCAACCUGCCCCUCCACUGCUGGGAAAUCCACCGGCA
UCGACUUCAGGACGAGCUGGACGAGUUCUUAAGAACG
UGUCCACCUCUACCCCAACUUCGGCAGCCUGACCCAGA
UCAACACCACUCUGCUGGACCUGACCUACGAGAUGCUGU
CCCUGCAACAGGUCGUGAAAGCCCUGAACGAGAGCUACA
UCGACCUGAAAGAGCUGGGGAACUACACCUACUACAACA
AGUGGCCUUGGUACA AUUUGGCUGGGCUUUAUCGCCGGCC
UGGUGGCCUUGGCCUGUGCGUGUUCUUAUCCUGUGCU
GCACCGGCUGCGGCACCAAUUGCAUGGGCAAGCUGAAAU
GCAACCGGUGCUGCGACAGAUACGAGGAAUACGACCUGG AACCUACAAAGUGCAUGUGCAC

TABLE-US-00012 TABLE 11 Betacoronavirus Amino Acid Sequences SEQ ID Strain Amino Acid Sequence
NO: gb|KJ156934.1|:21 MIHSVFLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFDFKT 24 405-25466
Middle WPRPIDVSKADGIIYPQGRITYSNITITYQGLFPYQGDHGDY East respiratory

VYSAGHATGTTpQKLFVANYSQDVKQFANGFVVRIGAAANS syndrome
TGTVIIISPSTSATIRKIYPAMFLGSSVGNFSDGKMGRFFNHTL coronavirus
VLLPDGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTPA isolate
TDCSDGNYNRNASLNSFKEYFNLRNCTFMYTYNITEDEILEW Riyadh_14_2013,
FGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYSII spike protein
PHSIRSIQSDRKAWAAFYVYKQLQPLTFLLDVSDGYIRRAIDC (amino acid)
GFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQAEGV
ECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSVNDFT
CSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAGPISQFN
YKQSFNPTCLILATVPHNLTTITKPLKYSYINKCSRLLSDDRT
EVPQLVNANQYSPCVSIVPSTVWEDGDYRQKQLSPLEGGGW
LVASGSTVAMTEQLQMFGITVQYGTDTNSVCPKLEFANDT
KIASQLGNCVEYSLYGVSGRGVFQNCTAVGVRQQRFFVYDA
YQNLVGYYSDDGNYCLRACVSVPSVVIYDKETKTHATLFG
SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL
VNSSLFVEDCKLPLGQSLCALPDTPTSTLTPRSVRSVPGEMRLA
SIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTTIQKVTV
DCKQYVCNGFQKCEQLLREYGGQFCSKINqALHGANLRQDDS
VRNLFASVKSSQSSPIIPGFGGDFNLTLLPVSISTGSRARSASAI
EDLLFDKVTIADPGYMQGYDDCMQQGPASARDLICAQYVA
GYKVLPLMDVNMEAAYTSSLLGSIAGVGWTAGLSSFAAIPF
AQSFYRLNGVGITQQVLSNQKLIANKFNQALGAMQTGFTT
TNEAFrKVQDAVNNNAQALSKLASELSNTFGAISASIGDIIQR
LDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESAALSAQLA
KDKVNECVKAQSKRSGFCGQGHIVSFVFNAPNGLYFMHV
GYPSNHIEVVSAYGLCDAANPTNCIAPVNGYFIKTNTRIV
DEWSYTGSSFYAPEPITSLNTKYVAPQVTYQNISTNLPPPLLG
NSTGIDFQDELDEFFKNVSTSIPTNFGSLTQINTTLLDLTYEMLS
LQQVVKALNESYIDLKELGNYTYYNKWPWYIWLGFIAGLVA
LALCVFFILCCTGCGTNCMGKLCNRCCDRYEEYDLEPHKV HVH MERS S FL
MIHSVFLMFLPTESYVDVGPDSVKSACIEVDIQQTFDFKT 25 SPIKE
WPRPIDVSKADGIIPQGRYSNITITYQGLFPYQGDHGDYMY 2cEMC/2012
VYSAGHATGTTpQKLFVANYSQDVKQFANGFVVRIGAAANS (XbaI change (T to
TGTVIIISPSTSATIRKIYPAMFLGSSVGNFSDGKMGRFFNHTL G)) (amino acid)
VLLPDGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTPA
TDCSDGNYNRNASLNSFKEYFNLRNCTFMYTYNITEDEILEW
FGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYSII
PHSIRSIQSDRKAWAAFYVYKQLQPLTFLLDVSDGYIRRAIDC
GFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQAEGV
ECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSVNDFT
CSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAGPISQFN
YKQSFNPTCLILATVPHNLTTITKPLKYSYINKCSRLLSDDRT
EVPQLVNANQYSPCVSIVPSTVWEDGDYRQKQLSPLEGGGW
LVASGSTVAMTEQLQMFGITVQYGTDTNSVCPKLEFANDT
KIASQLGNCVEYSLYGVSGRGVFQNCTAVGVRQQRFFVYDA
YQNLVGYYSDDGNYCLRACVSVPSVVIYDKETKTHATLFG
SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL
VNSSLFVEDCKLPLGQSLCALPDTPTSTLTPRSVRSVPGEMRLA
SIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTTIQKVTV
DCKQYVCNGFQKCEQLLREYGGQFCSKINQALHGANLRQDDS
VRNLFASVKSSQSSPIIPGFGGDFNLTLLPVSISTGSRARSASAI
EDLLFDKVTIADPGYMQGYDDCMQQGPASARDLICAQYVA
GYKVLPLMDVNMEAAYTSSLLGSIAGVGWTAGLSSFAAIPF
AQSFYRLNGVGITQQVLSNQKLIANKFNQALGAMQTGFTT

TNEAFQKVQDAVNNNAQALSKLASELSNTFGAISASIGDIIQR
LDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESAALSAQLA
KDKVNECVKAQSKRSGFCGQGTHIVSFVVNAPNGLYFMHV
GYPSNHIEVVSAYGLCDAANPTNCIAPVNGYFIKTNTRIV
DEWSYTGSSFYAPEPITSLNTKYVAPQVTYQNI
STNLPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTLLDLTYEMLS
LQQVVKALNESYIDLKELGNYTYYNKWPWYIWLGFIAGLVA
LALCVFFILCCTGCGTNCMGKLCNRCCDRYEEYDLEPHKV HVH Novel_MERS_S2_
MIHSVFLLMFLLTPTESDCKLPLGQSLCALPDTPTSTLTPRSVR 26 subunit trimeric
SVPGEMRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYI vaccine (amino
QTTIQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINQALH acid)
GANLRQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLLEPVSIS
TGSRARSARSAIEDLLFDKVTIADPGYMQGYDDCMQOGPASAR
DLICAQYVAGYKVLPLMDVNMEAAYTSSLLGSIAGVGWTA
GLSSFAAIPFAQSIFYRLNGVGITQQVLSNQKLIANKFNQAL
GAMQTGFTTTNEAFQKVQDAVNNNAQALSKLASELSNTFG
AISASIGDIIQR
LDVLEQDAQIDRLINGRLTTLNAFVAQQLVRS
ESAALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVVNA
PNGLYFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNGY
FIKTNTRIVDEWSYTGSSFYAPEPITSLNTKYVAPQVTYQNI
STNLPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTLL
DLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWPDKIE EILSKIYHIENEIARIKKLIGEA Isolate
A1- MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKT 27 Hasa_1_2013
WPRPIDVSKADGIIPQGRITYSNITITYQGLFPYQGDHGDYMY (NCBI accession
VYSAGHATGTTTPQKLFVANYSQDVKQFANGFVVRIGAAANS #AGN70962)
TGTVIIISPSTSATIRKIYPAFMLGSSVGNFSDGKMGRFFNHTL
VLLPDGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTPA
TDCSDGNYNRNASLNSFKEYFNLRNCTFMYTYNITEDEILEW
FGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYSII
PHSIRSIQSDRKAWAAFYVYKQLQPLTFLLDVSDGYIRRAIDC
GFNDLSQLHCSYESFDVESGVYSVSSFEAKPSGSVVEQAEGV
ECDFSPLLSGTPPQVYNFKRLVFTNCNYNLTKLLSLFSVNDFT
CSQISPAAIASNCYSSLILDYFSYPLSMKSDLSVSSAGPISQFN
YKQSFNPTCLILATVPHNLTTITKPLKYSYINKCSRLLSDDRT
EVPQLVNANQYSPCVSIVPSTVWEDGDYRQKQLSPLEGGGW
LVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT
KIASQLGNCVEYSLYGVSGRGVFNCTAVGVRQRFVYDA
YQNLVGYYSDDGNYCLRACVSVPSVIYDKETKTHATLFG
SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL
VNSSLFVEDCKLPLGQSLCALPDTPTSTLTPRSVRSVPGEMRLA
SIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTTIQKVTV
DCKQYVCNGFQKCEQLLREYGQFCSKINQALHGANLRQDDSV
VRNLFASVKSSQSSPIIPGFGGDFNLTLLLEPVSISTGSRARSAR
SAIEDLLFDKVTIADPGYMQGYDDCMQOGPASARDLICAQYVA
GYKVLPLMDVNMEAAYTSSLLGSIAGVGWTAGLSSFAAIPF
AQSIFYRLNGVGITQQVLSNQKLIANKFNQALGAMQTGFTT
TNEAFRQKVQDAVNNNAQALSKLASELSNTFGAISASIGDIIQR
LDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESAALSAQLA
KDKVNECVKAQSKRSGFCGQGTHIVSFVVNAPNGLYFMHV
GYPSNHIEVVSAYGLCDAANPTNCIAPVNGYFIKTNTRIV
DEWSYTGSSFYAPEPITSLNTKYVAPHVITYQNI
STNLPPLLGNSTGIDFQDELDEFFKNVSTSIPNFGSLTQINTTLLDLTYEMLS
LQQVVKALNESYIDLKELGNYTYYNKWPWYIWLGFIAGLVA
LALCVFFILCCTGCGTNCMGKLCNRCCDRYEEYDLEPHKV HVH Middle East

MIHSVFLLMFLLTPTESYVDVGPDSVKSACIEVDIQQTFFDKT 28 respiratory
WPRPIDVSKADGIIYPQGRYTSNITITYQGLFPYQGDHGDYMY syndrome
VYSAGHATGTPQKLFVANYSQDVKQFANGFVVRIGAAANS coronavirus S
TGTVIIISPSTSATIRKIYPFMLGSSVGNFSDGKMGRFFNHTL protein
VLLPDGCGTLLRAFYCILEPRSGNHCPAGNSYTSFATYHTPA UniProtKB-
TDCSDGNYNRNASLNSFKEYFNLRNCTFMITYNITEDEILEW R9UQ53
FGITQTAQGVHLFSSRYVDLYGGNMFQFATLPVYDTIKYYSII
PHSIRSIQSDRKAWAAFYVYKQLPLTFLLDVSDGYIRRAIDC
GFNDLSQLHCSYESFDVESGVVSVSSFEAKPSGSVVEQAEGV
ECDFSPLLSGTPPVYNFKRLVFTNCNYNLTKLLSLFSVNDFT
CSQISPAAIASNCYSSLILDYFSYPLSMKSDLVSSAGPISQFN
YKQSFNPTCLILATVPHNLTTITKPLKYSYINKCSRLSDDRT
EVPQLVNANQYSPCVSIVPSTVWEDGDYRQKQLSPLEGGGW
LVASGSTVAMTEQLQMGFGITVQYGTDTNSVCPKLEFANDT
KIASQLGNCVEYSLYGVSGRGVFQNTAVGVRQRFVYDA
YQNLVGYYSDDGNYYCLRACVSVVSVIYDKETKTHATLFG
SVACEHISSTMSQYSRSTRSMLKRRDSTYGPLQTPVGCVLGL
VNSSLFVEDCKLPLGQSLCALPDTPTSTLTPRSVRSVPGEMRLA
SIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYIQTTIQKVTV
DCKQYVCNGFQKCEQLLREYGFQFCSKINQALHGANLRQDDS
VRNLFASVKSSQSSPIIPGFGGDFNLTLEPVSISTGSRARSASAI
EDLLFDKVTIADPGYMQGYDDCMQQGPASARDLICAQYVA
GYKVLPLMDVNMEAAYTSSLLGSIAGVGWTAGLSSFAAIPF
AQSFYRLNGVGITQQVLSNQKLIANKFNQALGAMQTGFTT
TNEAFRKVQDAVNNNAQALSKLASELSNTFGAISASIGDIIQR
LDVLEQDAQIDRLINGRLTTLNAFVAQQLVRSESAALSAQLA
KDKVNECVKAQSKRSGFCGQGTHIVSFVFNAPNGLYFMHV
GYPSNHIEVVSAAYGLCDAANPTNCIAPVNGYFIKTNTRIV
DEWSYTGSSFYAPEPITSLNTKYVAPHVTYQNISTNLPPLLG
NSTGIDFQDELDEFFKNVSTSIPTNFGSLTQINTTLLDLTYEMLS
LQQVVKALNESYIDLKELGNYYNKWPWYIWLGFIAGLVA
LALCVFFILCCTGCGTNCMGKLCNRCCDRYEEYDLEPHKV HVH Human **SARS**
MFIFLLFLTSTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYY 29 coronavirus
PDEIFRSDTLYLTQDLFLPFYSNVTGFHTINHTFGNPVIPFKDG (**SARS-CoV**)
IYFAATEKSNVVRGWVFGSTMNKSQSIVIIINNSTNVVIRAC (Severe acute
NFELCDNPFPAVSKPMGTQHTMIFDNFNCTFEYISDAFSLD respiratory
VSEKSGNFKHLREFVFKNKDGLYVYKGYQPIDVVRDLPSGF syndrome
NTLKPIFKLPLGINITNFRAILTAFSPAQDIWGTSAAYFVGYL coronavirus)
KPTTFMLKYDENGITDAVDCSQNPLAELKCSVKSFEIDKGI Spike
YQTSNFRVVPVSGDVVRFPNITNLCPFGEVFNATKFPVYAWE glycoprotein
RKKISNCVADYSVLYNSTFFSTFKCYGVSATKLNLDLCSNVY UniProtKB-
ADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVLAW P59594
NTRNIDATSTGNYNKYRYLRHGKLRPFERDISNVPFSPDGK
PCTPPALNCYWPLNDYGFYTTTGIGYQPYRVVLSFELLNAP
ATVCGPKLSTDLIKNQCVNFNGLTGTGVLTPSSKRFQPFQ
QFGRDVSDFDTSVRDPKTSEILDISPCSFGGVSVITPGTNASSE
VAVLYQDVNCTDVSTAIHADQLTPAWRIYSTGNNVFQTQAG
CLIGAEHVDTSYECDIPIGAGICASYHTVSLLRSTSQKSIVAYT
MSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMAKTSVDCN
MYICGDSTECANLLLQYGSFCTQLNRALSGIAAEQDRNTREV
FAQVKQMYKTPTLKYFGGFNFSQILPDPLKPTKRSFIEDLLFN
KVTLADAGFMKQYGECLGDINARDLICAQKFNGLTVLPPLL
TDDMIAAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYR
FNGIGVTQNVLYENQKQIANQFNKAISQIQESLTTTSTALGKL

QDVVNQNAQALNTLVKQLSSNFGAISSVLNDILSRDKVEAE
VQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSEC
VLGQSKRVDFCGKGYHLMSFPQAAPHGVVFLHVTVYVPSQER
NFTTAPAICHEGKAYFPREGVVFVNGTSWFITQRNFFSPQIIT
DNTFVSGNCDVVIGIINNTVYDPLQPELDSFKEELDKYFKNH
TSPDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQE
LGKYEQYIKWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCL
KGACSCGSCCKFDEDDSEPVLKGVKLHYT Human
MFLILLISLPTAFVIGDLKCTSDNINDKDTGPPPISDTVDVT 30 coronavirus OC43
NGLGTYYVLDRVYLNNTLFLNGYYPTSGSTYRNMALKGSVL (HCoV-OC43)
LSRLWFKPPFLSDFINGIFAKVKNTKVIKDRVMYSEFPAITIGS Spike
TFVNTSYSVVVQPRINSTQDGDNKLQGLLEVSVQCQYNMCE glycoprotein
YPQTICHPNLGNHRKELWHLDTGVVSCLYKRNFTYDVNAD UniProtKB-
YLYFHFYQEGGTFYAYFTDTGVVTKFLFNVYLGMAISHYYV P36334
MPLTCNSKLTLEYWVTPLTSRQYLLAFNQDGIIFNAEDCMSD
FMSEIKCKTQSIAPPTGVYELNGYTVQPIADVYRRKPNLPC
NIEAWLNDKSVPSPLNWERKTFSNCFNMSSLMSFIQADSFT
CNNIDAAKIYGMCFSSITIDKFAIPNGRKVDLQLGNLGYLQSF
NYRIDTTATSCQLYYNLPAAVSVSRFNPSTWKNRFGFIEDS
VFKPRPAGVLTNHADVYAQHCFKAPKNFCPCKLNGSCVGS
PGKNNIGITCPAGTNYLTCNDLCTPDPITFTGTYKCPQTKSL
VGIGEHCGLAVKSDYCGGNSCTCRPQAFLGWSADSCLOGD
KCNIFANFILHDVNSGLTCSTDLQKANTDIIILGVCVNYDLYGI
LGQGIFVEVNATYYNSWQNLLYDSNGNLYGFRDYIINRTFMI
RSCYSGRVSAAFHANSSEPALLFRNIKCNYVFNNLSLTRLQPI
NYFDSYLGCVVNAYNSTAISVQTCDLTVGSGYCVDYSKNRR
SRGAIITGYRFTNFEPFTVNSVNDLSLEPVGGLYEIQIPSEFTIG
NMVEFIQTSSPKVTIDCAAFVCGDYAACKSQLVEYGSFCDNI
NAILTEVNELLDTTQLQVANSLMNGVTLSTKLKDGVNFNVD
DINFSPVLGCLGSECSKASSRSAIEDLLFDKVKLSDVGFVEAY
NNCTGGAEIRDLCVQSYKGIKVLPLLENQISGYTLAATSA
SLFPPWTAAGVPFYLVNQQYRINGLGVTMDVLSQNQKLIAN
AFNNALYAIQEGFDATNSALVKIQAVVNANAEALNLLQQL
SNRFGAISASLQEILSRLEAEAEQIDRLINGRLTALNAYVS
QQLSDSTLVKFSAAQAMEKVNECVKSQSSRINFCGNGNHIIS
LVQNAPYGLYFIHFSYVPTKYVTARVSPGLCIAGDRGIAPKS
GYFVNVNNTWMYTGSYYYPEPITENNVVMSTCAVNYTK
APYVMLNTSIPNLPDFKEELDQWFKNQTSVAPDLSLDYINVT
FLDLQVEMNRLQEAIKVLNQSYINLKDIDGTYEYYVKWPWYV
WLLICLAGVAMLVLLFFICCTGCGTSCFKKCGGCCDDYTG YQELVIKTSHDD Human
MFLIIFILPTTLAVIGDFNCTNSFINDYNKTIPRISEDVVDVSLG 31 coronavirus
LGTYYVLNRVYLNNTLLFTGYFPKSGANFRDLALKGSIYLSL HKU1 (isolate
LWYKPPFLSDFNNGIFSKVKNTKLYVNNPLYSEFSTIVIGSVF N5) (HCoV-
VNTSYTIVVQPHNGILEITACQYTMCEYPHTVCKSKGSIRNES HKU1) Spike
WHIDSSEPLCLFKKNFTYNVSADWLYFHFYQERGVFYAYYA glycoprotein
DVGMPPTTFLSFLYLGTLISHYYVMPLTCNAISSNTDNETLEY UniProtKB-
WVTPLSRRQYLLNFDEHGVITNAVDCSSSFLSEIQCKTQSFAP Q0ZME7
NTGVYDLSGFTVKPVATVYRRIPNLPDCDIDNWLNNVSVPS
LNWERRIFSNCNFNLSLRLVHVDSFSCNNLDKSKIFGSCFN
SITVDKFAIPNRRRDDLQLGSSGFLQSSNYKIDISSSSCQLYYS
LPLVNVNTINNFNPSSWNRRYGFGSFNLSSYDVVYSDHCFVN
SDFCPCADPSVVNSCAKSKPPSAICPAGTKYRHCDLDTTLYV
KNWCRCSCLPDPISTYSPNTCPQKVVVVGIGEHCPLGINEE
KCGTQLNHSSCFCSPDAFLGWSFDCISNNRCNIFSNFINGIN

SGTTCNDLLYSNTEISTGVCVNYDLYGITGQGIFKEVSAAY
YNNWQNLLYDSNGNIIGFKDFLTNKTITILPCYSGRVSAAFY
QNSSSPALLYRNLCASYVLNNISFISQPFYFDSYLGCVLNAVN
LTSYSVSSCDLRMGSGFCIDYALPSSRRKRRGISSPYRFVTFEP
FNVSFVNDVETVGGVLEIPIQIPNFTIAGHEEFIQTSSPKVTIDC
SAFVCSNYAACHDLLSEYGTFCDNINSILNEVNDLLDITQLQV
ANALMQGVTLSSNLNTNLHSDVDNIDFKSLLGCLGSQCGSSS
RSLLEDLLFNKVKLSVDVGFVEAYNNCTGGSEIRDLLCVQSFN
GIKVLPPILSETQISGYTTAATVAAMFPPWSAAAGVPFSLNVQ
YRINGLGVTMDVLNKNQKLIANAFNKALLSIQNGFTATNSAL
AKIQSVVNANAQALNSLLQQLFNKFGAISSSLQEILSRLDNLE
AQVQIDRLINGRLTALNAYVSQQLSDITLIKAGASRAIEKVNE
CVKSQSPRINFCGNGNHILSLVQNAPYGLLFIHFSYKPTSFKT

VLVSPGLCLSGDRGIAPKQGYFIKQNDSWMFTGSSYYYPEPIS
DKNVVMNSCSVNFTKAPFIYLNNSIPNLSDFEAELSLWFKN
HTSIAPNLTFNSHINATFLDLYEMNVIQESIKSLNSSFINLKEI
GTYEMYVKWPWYIWLIVILFIIFLMILFFICCCTGCGSACFSK CHNCCDEYGGHNDVVIKASHDD

Novel **SARS**_S2 MFIFLLFLTSTSGSDDLDRALSGIAAEQDRNTREVFAQVKQMY 32

KTPTLKYFGGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADAG
FMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYT
AALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQN
VLYENQKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNA
QALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITG
RLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRV
DFCGKGYHLMSFPQAAPHGVVFLHVITYVPSQERNFTTAPAIC
HEGKAYFPREGVVFVNGTSWFITQRNFFSPQIITTDNTFVSGN
CDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLG
DISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYI
KWPWYVWLGFIAGLIAIVMVTILLCCMTSCCSCCLKGACSCGS CCKFDEDDSEPVLKGVKLHYT

Novel **MERS**_S2 MIHSVFLMFLLTPTESDCKLPLGQSLCALPDPSTLTTPRSVR 33

SVPGEMRLASIAFNHPIQVDQLNSSYFKLSIPTNFSFGVTQEYI
QTTIQKVTVDCKQYVCNGFQKCEQLLREYGQFCSKINQALH
GANLRQDDSVRNLFASVKSSQSSPIIPGFGGDFNLTLLEPVSIS
TGSRARSARIAEDLLFDKVTIADPGYMQGYDDCMQQGPASAR
DLICAQYVAGYKVLPLMDVNMEAAYTSSLLGSIAGVGWTA
GLSSFAAIPFAQSIFYRLNGVGITQQVLSNQKLIANKFNQAL
GAMQTGFTTTNEAFQKVQDAVNNNAQALSKLASELSNTFG
AISASIGDIIQRLDVLEQDAQIDRLINGRLTTLNAFVAQQLVRS
ESAALSAQLAKDKVNECVKAQSKRSGFCGQGTHIVSFVUNA
PNGLYFMHVGYYPSNHIEVVSAYGLCDAANPTNCIAPVNGY
FIKTNTRIVDEWSYTGSSFYAPEPITSLNTKYVAPQVTYQNI
STNLPPLLGNSTGIDFQDELDEFFKNVSTSIPIFGSLTQINTTL

LDLTYEMLSLQQVVKALNESYIDLKELGNYTYYNKWP Novel **Trimeric**
MFIFLLFLTSTSGSDDLDRALSGIAAEQDRNTREVFAQVKQMY 34 **SARS**_S2

KTPTLKYFGGFNFSQILPDPLKPTKRSFIEDLLFNKVTLADAG
FMKQYGECLGDINARDLICAQKFNGLTVLPPLLTDDMIAAYT
AALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQN
VLYENQKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNA
QALNTLVKQLSSNFGAISSVLNDILSRLDKVEAEVQIDRLITG
RLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRV
DFCGKGYHLMSFPQAAPHGVVFLHVITYVPSQERNFTTAPAIC
HEGKAYFPREGVVFVNGTSWFITQRNFFSPQIITTDNTFVSGN
CDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTSPDVDLG

DISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYI
KWPWYVWLGFIAGLIAIVMTILLCCMTSCCSCLKGACSCGS CCKFDEDDSEPVLKGVKLHYT

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

TABLE-US-00014 TABLE 13 MeV Nucleic Acid Sequences SEQ ID Description Sequence NO:

GC_F_MEASLES_TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT 35 B3.1

CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA Sequence, NT (5'

GAAATATAAGAGCCACCATGGGTCTCAAGGTGAACGTC UTR, ORF, 3'

TCTGCCGTATTCATGGCAGTACTGTAACTCTCCAAACA UTR)

CCCGCCGGTCAAATTCATTGGGGCAATCTCTCTAAGAT Sequence Length:

AGGGGTAGTAGGAATAGGAAGTGCAAGCTACAAAGTT 1864

ATGACTCGTTCCAGCCATCAATCATTAGTCATAAAATT

AATGCCCAATATAACTCTCCTCAATAACTGCACGAGGG

TAGAGATTGCAGAATACAGGAGACTACTAAGAACAGTT

TTGGAACCAATTAGGGATGCACTTAATGCAATGACCCA

GAACATAAGGCCGGTTCAGAGCGTAGCTTCAAGTAGGA

GACACAAGAGATTTGCGGGAGTAGTCCTGGCAGGTGCG

GCCCTAGGTGTTGCCACAGCTGCTCAGATAACAGCCGG

CATTGCACTTCACCGGTCCATGCTGAACTCTCAGGCCAT

CGACAATCTGAGAGCGAGCCTGGAAACTACTAATCAGG

CAATTGAGGCAATCAGACAAGCAGGGCAGGAGATGAT

ATTGGCTGTTCAAGGTGTCCAAGACTACATCAATAATG

AGCTGATACCGTCTATGAACCAGCTATCTTGTGATCTA

ATCGGTCAGAAGCTCGGGCTCAAATTGCTTAGATACTA

TACAGAAATCCTGTCATTATTTGGCCCCAGCCTACGGG

ACCCCATATCTGCGGAGATATCTATCCAGGCTTTGAGTT

ATGCACTTGGAGGAGATATCAATAAGGTGTTAGAAAAG

CTCGGATACAGTGGAGGCGATTTACTAGGCATCTTAGA

GAGCAGAGGAATAAAGGCTCGGATAACTCACGTCGAC

ACAGAGTCTACTTCATAGTCCTCAGTATAGCCTATCCG

ACGCTGTCCGAGATTAAGGGGGTGATTGTCCACCGGCT

AGAGGGGGTCTCGTACAACATAGGCTCTCAAGAGTGGT

ATACCACTGTGCCAAGTATGTTGCAACCCAAGGGTAC

CTTATCTCGAATTTTGATGAGTCATCATGTACTTTTCATG

CCAGAGGGGACTGTGTGCAGCCAAAATGCCTTGTACCC

GATGAGTCTCTGCTCCAAGAATGCCTCCGGGGGTCCA

CCAAGTCTGTGCTCGTACACTCGTATCCGGGTCTTTTG

GGAACCGGTTCAATTTATCACAAGGGAACCTAATAGCC

AATTGTGCATCAATTTCTTTGTAAGTGTTACACAACAGGT

ACGATTATTAATCAAGACCCTGACAAGATCCTAACATA

CATTGCTGCCGATCGCTGCCCGGTAGTCGAGGTGAACG

GCGTGACCATCCAAGTCGGGAGCAGGAGGTATCCAGA

CGCTGTGTACTIONGCACAGAATTGACCTCGGTCCTCCCAT

ATCATTGGAGAGGTTGGACGTAGGGACAAATCTGGGG

AATGCAATTGCCAATTGGAGGATGCCAAGGAATTGTT

GGAATCATCGGACCAGATATTGAGAAGTATGAAAGGTT

TATCGAGCACTAGCATAGTCTACATCCTGATTGCAGTG

TGTCTTGGAGGGTTGATAGGGATCCCCACTTTAATATGT

TGCTGCAGGGGGCGTTGTAACAAAAGGGAGAACAAG

TTGGTATGTCAAGACCAGGCCTAAAGCCTGACCTTACA

GGAACATCAAATCCTATGTAAGATCGCTTTGATGATA

ATAGGCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTT

GGGCCTCCCCCAGCCCCTCCTCCCCTTCCCTGCACCCGT

ACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC GC_F_MEASLES_

ATGGGTCTCAAGGTGAACGTCTCTGCCGTATTCATGGC 36 B3.1

AGTACTGTAACTCTCCAAACACCCGCGGTCAAATTC ORF Sequence, NT

ATTGGGGCAATCTCTCTAAGATAGGGGTAGTAGGAATA
GGAAGTGCAAGCTACAAAGTTATGACTCGTTCCAGCCA
TCAATCATTAGTCATAAAATTAATGCCCAATATAACTCT
CCTCAATAACTGCACGAGGGTAGAGATTGCAGAATACA
GGAGACTACTAAGAACAGTTTTTGGAACCAATTAGGGAT
GCACTTAATGCAATGACCCAGAACATAAGGCCGGTTCA
GAGCGTAGCTTCAAGTAGGAGACACAAGAGATTTGCG
GGAGTAGTCCTGGCAGGTGCGGCCCTAGGTGTTGCCAC
AGCTGCTCAGATAACAGCCGGCATTGCACTTCACCGGT
CCATGCTGAACTCTCAGGCCATCGACAATCTGAGAGCG
AGCCTGGAACTACTAATCAGGCAATTGAGGCAATCAG
ACAAGCAGGGCAGGAGATGATATTGGCTGTTCAGGGTG
TCCAAGACTACATCAATAATGAGCTGATACCGTCTATG
AACCAGCTATCTTGTGATCTAATCGGTCAGAAGCTCGG
GCTCAAATTGCTTAGATACTATACAGAAATCCTGTCATT
ATTTGGCCCCAGCCTACGGGACCCCATATCTGCGGAGA
TATCTATCCAGGCTTTGAGTTATGCACTTGGAGGAGAT
ATCAATAAGGTGTTAGAAAAGCTCGGATACAGTGGAG
GCGATTTACTAGGCATCTTAGAGAGCAGAGGAATAAAG
GCTCGGATAACTCACGTCGACACAGAGTCCTACTTCAT
AGTCCTCAGTATAGCCTATCCGACGCTGTCCGAGATTA
AGGGGGTGATTGTCCACCGGCTAGAGGGGGTCTCGTAC
AACATAGGCTCTCAAGAGTGGTATACCACTGTGCCAA
GTATGTTGCAACCCAAGGGTACCTTATCTCGAATTTTGA
TGAGTCATCATGTACTTTCATGCCAGAGGGGACTGTGT
GCAGCCAAAATGCCTTGTACCCGATGAGTCCTCTGCTC
CAAGAATGCCTCCGGGGGTCCACCAAGTCCTGTGCTCG
TACACTCGTATCCGGGTCTTTTGGGAACCGGTTCAATTT
ATCACAAGGGAACCTAATAGCCAATTGTGCATCAATTC
TTTGTAAAGTGTACACAACAGGTACGATTATTAATCAA
GACCCTGACAAGATCCTAACATACATTGCTGCCGATCG
CTGCCCGGTAGTCGAGGTGAACGGCGTGACCATCCAAG
TCGGGAGCAGGAGGTATCCAGACGCTGTGTACTTGCAC
AGAATTGACCTCGGTCTCCCATATCATTGGAGAGGTT
GGACGTAGGGACAAATCTGGGGAATGCAATTGCCAAA
TTGGAGGATGCCAAGGAATTGTTGGAATCATCGGACCA
GATATTGAGAAGTATGAAAGGTTTATCGAGCACTAGCA
TAGTCTACATCCTGATTGCAGTGTGTCTTGGAGGGTTGA
TAGGGATCCCCACTTTAATATGTTGCTGCAGGGGGCGT
TGTAACAAAAAGGGAGAACAAGTTGGTATGTCAAGAC
CAGGCCTAAAGCCTGACCTTACAGGAACATCAAATCC TATGTAAGATCGCTTTGA
GC_F_MEASLES_G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT 37 B3.1
ATAAGAGCCACCATGGGTCTCAAGGTGAACGTCTCTGC mRNA Sequence
CGTATTCATGGCAGTACTGTTAACTCTCCAAACACCCG (assumes T100
CCGGTCAAATTCATTGGGGCAATCTCTCTAAGATAGGG tail)
GTAGTAGGAATAGGAAGTGCAAGCTACAAAGTTATGA mRNA Sequence
CTCGTTCCAGCCATCAATCATTAGTCATAAAATTAATGC Length: 1925
CCAATATAACTCTCCTCAATAACTGCACGAGGGTAGAG
ATTGCAGAATACAGGAGACTACTAAGAACAGTTTTGGA
ACCAATTAGGGATGCACTTAATGCAATGACCCAGAACA
TAAGGCCGGTTCAGAGCGTAGCTTCAAGTAGGAGACAC
AAGAGATTTGCGGGAGTAGTCCTGGCAGGTGCGGCCCT
AGGTGTTGCCACAGCTGCTCAGATAACAGCCGGCATTG
CACTTCACCGGTCCATGCTGAACTCTCAGGCCATCGAC

AATCTGAGAGCGAGCCTGGAACTACTAATCAGGCAAT
TGAGGCAATCAGACAAGCAGGGCAGGAGATGATATTG
GCTGTTCAAGGTGTCCAAGACTACATCAATAATGAGCT
GATACCGTCTATGAACCAGCTATCTTGTGATCTAATCG
GTCAGAAGCTCGGGCTCAAATTGCTTAGATACTATA
CAAATCCTGTCATTATTTGGCCCCAGCCTACGGGACCC
CATATCTGCGGAGATATCTATCCAGGCTTTGAGTTATGC
ACTTGGAGGAGATATCAATAAGGTGTTAGAAAAGCTCG
GATACAGTGGAGGCGATTTACTAGGCATCTTAGAGAGC
AGAGGAATAAAGGCTCGGATAACTCACGTCGACACAG
AGTCTACTTCATAGTCCTCAGTATAGCCTATCCGACGC
TGTCCGAGATTAAGGGGGTATTGTCCACCGGCTAGAG
GGGGTCTCGTACAACATAGGCTCTCAAGAGTGGTATAC
CACTGTGCCCAAGTATGTTGCAACCCAAGGGTACCTTA
TCTCGAATTTTGATGAGTCATCATGTAATTTTCATGCCAG
AGGGGACTGTGTGCAGCCAAAATGCCTTGTACCCGATG
AGTCTCTGCTCCAAGAATGCCTCCGGGGGTCCACCAA
GTCCTGTGCTCGTACACTCGTATCCGGGTCTTTTGGGAA
CCGGTTCATTTTATCACAAAGGAACCTAATAGCCAATT
GTGCATCAATTCTTTGTAAGTGTTACACAACAGGTACG
ATTATTAATCAAGACCCTGACAAGATCCTAACATACAT
TGCTGCCGATCGCTGCCCGGTAGTCGAGGTGAACGGCG
TGACCATCCAAGTCGGGAGCAGGAGGTATCCAGACGCT
GTGTAATTTGCACAGAATTGACCTCGGTCTCCCATATCA
TTGGAGAGGTTGGACGTAGGGACAAATCTGGGGAATG
CAATTGCCAAATTGGAGGATGCCAAGGAATTGTTGGAA
TCATCGGACCAGATATTGAGAAGTATGAAAGGTTTATC
GAGCACTAGCATAGTCTACATCCTGATTGCAGTGTGTC
TTGGAGGGTTGATAGGGATCCCCACTTTAATATGTTGCT
GCAGGGGGCGTTGTAACAAAAAGGGAGAACAAGTTGG
TATGTCAAGACCAGGCCTAAAGCCTGACCTTACAGGAA
CATCAAAATCCTATGTAAGATCGCTTTGATGATAATAG
GCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTTGGGC
CTCCCCCAGCCCCCTCCTCCCCTTCTGCACCCGTACCC
CCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGCAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAATCTAG GC_F_MEASLES_
TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT 38 D8
CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA Sequence, NT (5'
GAAATATAAGAGCCACCATGGGTCTCAAGGTGAACGTC UTR, ORF, 3'
TCTGTCATATTCATGGCAGTACTGTTAACTCTTCAAACA UTR)
CCCACCGGTCAAATCCATTGGGGCAATCTCTCTAAGAT Sequence Length:
AGGGGTGGTAGGGGTAGGAAGTGCAAGCTACAAAGTT 1864
ATGACTCGTTCAGCCATCAATCATTAGTCATAAAGTT
AATGCCCAATATACTCTCCTCAACAATTGCACGAGGG
TAGGGATTGCAGAATACAGGAGACTACTGAGAACAGTT
CTGGAACCAATTAGAGATGCACTTAATGCAATGACCCA
GAATATAAGACCGTTCAGAGTGTAGCTTCAAGTAGGA
GACACAAGAGATTTGCGGGAGTTGTCTGGCAGGTGCG
GCCCTAGGCGTTGCCACAGCTGCTCAAATAACAGCCG
TATTGCACTTACCAGTCCATGCTGAACTCTCAAGCCAT
CGACAATCTGAGAGCGAGCCTAGAACTACTAATCAGG
CAATTGAGGCAATCAGACAAGCAGGGCAGGAGATGAT

ATTGGCTGTTTCAGGGTGTCCAAGACTACATCAATAATG
AGCTGATACCGTCTATGAATCAACTATCTTGTGATTTAA
TCGGCCAGAAGCTAGGGCTCAAATTGCTCAGATACTAT
ACAGAAATCCTGTCATTATTTGGCCCCAGCTTACGGGA
CCCCATATCTGCGGAGATATCTATCCAGGCTTTGAGCT
ATGCGCTTGGAGGAGATATCAATAAGGTGTTGGAAAAG
CTCGGATACAGTGGAGGTGATCTACTGGGCATCTTAGA
GAGCAGAGGAATAAAGGCCCGGATAACTCACGTGAC
ACAGAGTCCTACTTCATTGTA CT CAGTATAGCCTATCCG
ACGCTATCCGAGATTAAGGGGGTGATTGTCCACCGGCT
AGAGGGGGTCTCGTACAACATAGGCTCTCAAGAGTGGT
ATACCACTGTGCCCAAGTATGTTGCAACCCAAGGGTAC
CTTATCTCGAATTTTGATGAGTCATCATGCACTTTCATG
CCAGAGGGGACTGTGTGCAGCCAGAATGCCTTGTACCC
GATGAGTCCTCTGCTCCAAGAATGCCTCCGGGGGTCCA
CTAAGTCCTGTGCTCGTACACTCGTATCCGGGTCTTTCG
GGAACCGGTTCATTTTATCACAGGGGAACCTAATAGCC
AATTGTGCATCAATCCTTTGCAAGTGTTACACAACAGG
ACAATCATAATCAAGACCCTGACAAGATCCTAACAT
ACATTGCTGCCGATCACTGCCCGGTGGTCGAGGTGAAT
GGCGTGACCATCCAAGTCGGGAGCAGGAGGTATCCGG
ACGCTGTGTA CT TGCACAGGATTGACCTCGGTCTCTCC
ATATCTTTGGAGAGGTTGGACGTAGGGACAAATCTGGG
GAATGCAATTGCTAAGTTGGAGGATGCCAAGGAATTGT
TGGAGTCATCGGACCAGATATTGAGGAGTATGAAAGGT
TTATCGAGCACTAGTATAGTTTACATCCTGATTGCAGTG
TGTCTTGGAGGATTGATAGGGATCCCCGCTTTAATATGT
TGCTGCAGGGGGCGTTGTAACAAGAAGGGAGAACAAG
TTGGTATGTCAAGACCAGGCCTAAAGCCTGATCTTACA
GGAACATCAAATCCTATGTAAGGTC ACTCTGATGATA
ATAGGCTGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTT
GGGCCTCCCCCAGCCCCCTCCTCCCCTTCTGCACCCGT
ACCCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGGC GC_F_MEASLES_
ATGGGTCTCAAGGTGAACGTCTCTGT CATATT CATGGC 39 D8
AGTACTGTAACTCTTCAAACACCCACCGGTCAAATCC ORF Sequence, NT
ATTGGGGCAATCTCTCTAAGATAGGGGTGGTAGGGGTA
GGAAGTGCAAGCTACAAAGTTATGACTCGTTCCAGCCA
TCAATCATTAGTCATAAAGTTAATGCCCAATATAACTCT
CCTCAACAATTGCACGAGGGTAGGGATTGCAGAATACA
GGAGACTACTGAGAACAGTTCTGGAACCAATTAGAGAT
GCACTTAATGCAATGACCCAGAATATAAGACCGGTTC
GAGTGTAGCTTCAAGTAGGAGACACAAGAGATTTGCGG
GAGTTGTCTTGGCAGGTGCGGCCCTAGGCGTTGCCACA
GCTGCTCAAATAACAGCCGGTATTGCACTTCACCAAGTC
CATGCTGAACTCTCAAGCCATCGACAATCTGAGAGCGA
GCCTAGAACTACTAATCAGGCAATTGAGGCAATCAGA
CAAGCAGGGCAGGAGATGATATTGGCTGTT CAGGGTGT
CCAAGACTACATCAATAATGAGCTGATACCGTCTATGA
ATCAACTATCTTGTGATTTAATCGGCCAGAAGCTAGGG
CTCAAATTGCTCAGATACTATA CAGAAATCCTGTCATT
ATTTGGCCCCAGCTTACGGGACCCCATATCTGCGGAGA
TATCTATCCAGGCTTTGAGCTATGCGCTTGGAGGAGAT
ATCAATAAGGTGTTGGAAAAGCTCGGATACAGTGGAG
GTGATCTACTGGGCATCTTAGAGAGCAGAGGAATAAAG

GCCCCGATAACTCACGTGACACAGAGTCCTACTTCAT
TGTAICTAGTATAGCCTATCCGACGCTATCCGAGATTA
AGGGGGTGATTGTCCACCGGCTAGAGGGGGTCTCGTAC
AACATAGGCTCTCAAGAGTGGTATAACCACTGTGCCAA
GTATGTTGCAACCCAAGGGTACCTTATCTCGAATTTTGA
TGAGTCATCATGCACTTTCATGCCAGAGGGGACTGTGT
GCAGCCAGAATGCCTTGTACCCGATGAGTCCTCTGCTC
CAAGAATGCCTCCGGGGGTCCACTAAGTCCTGTGCTCG
TACTCTCGTATCCGGGTCTTTCGGGAACCGGTTCATTTT
ATCACAGGGGAACCTAATAGCCAATTGTGCATCAATCC
TTTGCAAGTGTTACACAACAGGAACAATCATAATCAA
GACCTGACAAGATCCTAACATACATTGCTGCCGATCA
CTGCCCGGTGGTCGAGGTGAATGGCGTGACCATCCAAG
TCGGGAGCAGGAGGTATCCGGACGCTGTGTACTTGCAC
AGGATTGACCTCGGTCTCCCATATCTTTGGAGAGGTT
GGACGTAGGGACAAATCTGGGGAATGCAATTGCTAAGT
TGGAGGATGCCAAGGAATTGTTGGAGTCATCGGACCAG
ATATTGAGGAGTATGAAAGGTTTATCGAGCACTAGTAT
AGTTTACATCCTGATTGCAGTGTGTCTTGGAGGATTGAT
AGGGATCCCCGCTTTAATATGTTGCTGCAGGGGGCGTT
GTAACAAGAAGGGAGAACAAGTTGGTATGTCAAGACC
AGGCCTAAAGCCTGATCTTACAGGAACATCAAATCCT ATGTAAGGTCACTCTGA
GC_F_MEASLES_G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT 40 D8
ATAAGAGCCACCATGGGTCTCAAGGTGAACGTCTCTGT

mRNA Sequence CATATTCATGGCAGTACTGTAACTCTTCAAACACCCAC (assumes T100
CGGTCAAATCCATTGGGGCAATCTCTCTAAGATAGGGG tail)

TGGTAGGGGTAGGAAGTGCAAGCTACAAAGTTATGACT Sequence Length:

CGTTCAGCCATCAATCATTAGTCATAAAGTTAATGCC 1925

CAATATAACTCTCCTCAACAATTGCACGAGGGTAGGGA
TTGCAGAATACAGGAGACTACTGAGAACAGTTCTGGAA
CCAATTAGAGATGCACTTAATGCAATGACCCAGAATAT
AAGACCGGTTCAAGAGTGTAGCTTCAAGTAGGAGACACA
AGAGATTTGCGGGAGTTGTCCTGGCAGGTGCGGCCCTA
GGCGTTGCCACAGCTGCTCAAATAACAGCCGGTATTGC
ACTTACCAGTCCATGCTGAACTCTCAAGCCATCGACA
ATCTGAGAGCGAGCCTAGAACTACTAATCAGGCAATT
GAGGCAATCAGACAAGCAGGGCAGGAGATGATATTGG
CTGTTCAAGGGTGTCCAAGACTACATCAATAATGAGCTG
ATACCGTCTATGAATCAACTATCTTGTGATTTAATCGGC
CAGAAGCTAGGGCTCAAATTGCTCAGATACTATACAGA
AATCCTGTCAATATTTGGCCCCAGCTTACGGGACCCCAT
ATCTGCGGAGATATCTATCCAGGCTTTGAGCTATGCGC
TTGGAGGAGATATCAATAAGGTGTTGGAAAAGCTCGGA
TACAGTGGAGGTGATCTACTGGGCATCTTAGAGAGCAG
AGGAATAAAGGCCCGGATAACTCACGTGACACAGAG
TCCTACTTCATTGTAICTAGTATAGCCTATCCGACGCTA
TCCGAGATTAAGGGGGTGATTGTCCACCGGCTAGAGGG
GGTCTCGTACAACATAGGCTCTCAAGAGTGGTATAACA
CTGTGCCCAAGTATGTTGCAACCCAAGGGTACCTTATC
TCGAATTTGATGAGTCATCATGCACTTTCATGCCAGAG
GGGACTGTGTGCAGCCAGAATGCCTTGTACCCGATGAG
TCCTCTGCTCCAAGAATGCCTCCGGGGGTCCACTAAGT
CCTGTGCTCGTACACTCGTATCCGGGTCTTTCGGGAACC

GGTTCATTTTATCACAGGGGAACCTAATAGCCAATTGT
GCATCAATCCTTTGCAAGTGTTACACAACAGGAACAAT
CATTAATCAAGACCCTGACAAGATCCTAACATACATTG
CTGCCGATCACTGCCCGGTGGTCGAGGTGAATGGCGTG
ACCATCCAAGTCGGGAGCAGGAGGTATCCGGACGCTGT
GTACTTGCACAGGATTGACCTCGGTCTCCCATATCTTT
GGAGAGGTTGGACGTAGGGACAAATCTGGGGAATGCA
ATTGCTAAGTTGGAGGATGCCAAGGAATTGTTGGAGTC
ATCGGACCAGATATTGAGGAGTATGAAAGGTTTATCGA
GCACTAGTATAGTTTACATCCTGATTGCAGTGTGTCTTG
GAGGATTGATAGGGATCCCCGCTTTAATATGTTGCTGC
AGGGGGCGTTGTAACAAGAAGGGAGAACAAGTTGGTA
TGTC AAGACCAGGCCTAAAGCCTGATCTTACAGGAACA
TCAAAATCCTATGTAAGGTCACCTCTGATGATAATAGGC
TGGAGCCTCGGTGGCCAAGCTTCTTGCCCCTTGGGCCTC
CCCCAGCCCCTCCTCCCCTTCTGCACCCGTACCCCCG
TGGTCTTTGAATAAAGTCTGAGTGGGCGGCAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAATCTAG
GC_H_MEASLES_TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT 41 B3
CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA Sequence, NT (5'
GAAATATAAGAGCCACCATGTCAACCGCAACGAGACCG UTR, ORF, 3'
GATAAATGCCTTCTACAAAGATAACCCTTATCCCAAGG UTR)
GAAGTAGGATAGTTATTAACAGAGAACATCTTATGATT Sequence Length:
GACAGACCCTATGTTCTGCTGGCTGTTCTGTTTCGTCATG 2065
TTTCTGAGCTTGATCGGATTGCTGGCAATTGCAGGCATT
AGACTTCATCGGGCAGCCATCTACACCGCGGAGATCCA
TAAAGCCTCAGTACCAATCTGGATGTGACTAACTCCA
TCGAGCATCAGGTCAAGGACGTGCTGACACCACTCTTT
AAAATCATCGGGGATGAAGTGGGCCTGAGAACACCTC
AGAGATTCACTGACCTAGTGAAATTCATCTCGGACAAG
ATTA AATTCCTTAATCCGGATAGGGAGTACGACTTCAG
AGATCTCACTTGGTGCATCAACCCGCCAGAGAGGATCA
AACTAGATTATGATCAATACTGTGCAGATGTGGCTGCT
GAAGAGCTCATGAATGCATTGGTGA ACTCAACTCTACT
GGAGACCAGAACAACCACTCAGTTCCTAGCTGTCTCAA
AGGGAAACTGCTCAGGGCCCACTACAATCAGAGGTCA
ATTCTCAAACATGTCGCTGTCCTTGTGGACTTGTACTT
AGGTTCGAGGTTACAATGTGTCATCTATAGTCACTATGA
CATCCAGGGAAATGTATGGGGGAACCTACCTAGTTGAA
AAGCCTAATCTGAACAGCAAAGGGTCAGAGTTGTCACA
ACTGAGCATGTACCGAGTGTGGTGAAGTAGGTGTGATCA
GAAACCCGGGTTTGGGGGCTCCGGTGTTCATATGACA
AACTATTTGAGCAACCAGTCAGTAATGGTCTCGGCAA
CTGTATGGTGGCTTTGGGGGAGCTCAA ACTCGCAGCCC
TTTGTACGGGGACGATTCTATCATAATCCCTATCAGG
GATCAGGGAAAGGTGTCAGCTTCCAGCTCGTCAAGCTG
GGTGTCTGGAAATCCCCAACCGACATGCAATCCTGGGT
CCCCTTATCAACGGATGATCCAGTGGTAGACAGGCTTT
ACCTCTCATCTCACAGAGGTGTCATCGCTGACAATCAA
GCAAATGGGCTGTCCCGACAACACGAACAGATGACA
AGTTGCGAATGGAGACATGCTTCCAGCAGGCGTGTA
GGTAA AATCCAAGCACTCTGCGAGAATCCCGAGTGGGT
ACCATTGAAGGATAACAGGATTCTTCATACGGGGTCC

TGTCTGTTGATCTGAGTCTGACGGTTGAGCTTAAAATCA
AAATTGCTTCGGGATTTCGGGCCATTGATCACACACGGC
TCAGGGATGGACCTATACAAATCCAACCTGCAACAATGT
GTATTGGCTGACTATTCCGCCAATGAGAAATCTAGCCT
TAGGCGTAATCAACACATTGGAGTGGATAACCGAGATTC
AAGGTTAGTCCCAACCTCTTCACTGTCCCAATTAAGGA
AGCAGGGCAAGACTGCCATGCCCCAACATACCTACCTG
CGGAGGTGGACGGTGATGTCAAACCTCAGTTCCAACCTG
GTGATTCTACCTGGTCAAGATCTCCAATATGTTTTGGCA
ACCTACGATACCTCCAGGGTTGAGCATGCTGTGGTTTA
TTACGTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTA
TCCTTTTAGGTTGCCTATAAAGGGGGTCCCAATCGAAC
TACAAGTGGAATGCTTCACATGGGATCAAAAACCTCTGG
TGCCGTCACCTTCTGTGTGCTTGCGGACTCAGAATCCGGT
GGACTTATCACTCACTCTGGGATGGTGGGCATGGGAGT
CAGCTGCACAGCTACCCGGGAAGATGGAACCAATCGC
AGATAATGATAATAGGCTGGAGCCTCGGTGGCCAAGCT
TCTTGCCCCTTGGGCCTCCCCCAGCCCCCTCCTCCCCTT
CCTGCACCCGTACCCCGTGGTCTTTGAATAAAGTCTG AGTGGGCGGC GC_H_MEASLES_
ATGTCACCGCAACGAGACCGGATAAATGCCTTCTACAA 42 B3
AGATAACCCTTATCCCAAGGGAAGTAGGATAGTTATTA ORF Sequence, NT
ACAGAGAACATCTTATGATTGACAGACCCTATGTTCTG
CTGGCTGTTCTGTTCTGTCATGTTTCTGAGCTTGATCGGA
TTGCTGGCAATTGCAGGCATTAGACTTCATCGGGCAGC
CATCTACACCGCGGAGATCCATAAAAGCCTCAGTACCA
ATCTGGATGTGACTAACTCCATCGAGCATCAGGTCAAG
GACGTGCTGACACCACTCTTAAATCATCGGGGATGA
AGTGGGCCTGAGAACACCTCAGAGATTCAGTACCTAG
TGAAATTCATCTCGGACAAGATTAATTCCTTAATCCG
GATAGGGAGTACGACTTCAGAGATCTCACTTGGTGCAT
CAACCCGCCAGAGAGGATCAAACCTAGATTATGATCAAT
ACTGTGCAGATGTGGCTGCTGAAGAGCTCATGAATGCA
TTGGTGAACCTCAACTCTACTGGAGACCAGAACAACCAC
TCAGTTCCTAGCTGTCTCAAAGGGAAACTGCTCAGGGC
CCACTACAATCAGAGGTCAATTCTCAAACATGTCGCTG
TCCTTGTTGGACTTGTACTTAGGTCGAGGTTACAATGTG
TCATCTATAGTCACTATGACATCCCAGGGAATGTATGG
GGGAACCTACCTAGTTGAAAAGCCTAATCTGAACAGCA
AAGGGTCAGAGTTGTCACAACTGAGCATGTACCGAGTG
TTTGAAGTAGGTGTGATCAGAAACCCGGGTTTGGGGGC
TCCGGTGTTCCATATGACAAACTATTTTGAGCAACCAG
TCAGTAATGGTCTCGGCAACTGTATGGTGGCTTTGGGG
GAGCTCAAACCTCGCAGCCCTTTGTCACGGGGACGATTC
TATCATAATTCCCTATCAGGGATCAGGGAAAGGTGTCA
GCTTCCAGCTCGTCAAGCTGGGTGTCTGGAAATCCCCA
ACCGACATGCAATCCTGGGTCCCCTTATCAACGGATGA
TCCAGTGGTAGACAGGCTTTACCTCTCATCTCACAGAG
GTGTCATCGCTGACAATCAAGCAAAATGGGCTGTCCCG
ACAACACGAACAGATGACAAGTTGCGAATGGAGACAT
GCTTCCAGCAGGCGTGTAAAGGTAAAATCCAAGCACTC
TGCGAGAATCCCGAGTGGGTACCATTGAAGGATAACAG
GATTCCTTCATACGGGGTCCCTGTCTGTTGATCTGAGTCT
GACGGTTGAGCTTAAAATCAAATGCTTCGGGATTCG
GGCCATTGATCACACACGGCTCAGGGATGGACCTATAC

AAATCCAACCTGCAACAATGTGTATTGGCTGACTATTCC
GCCAATGAGAAATCTAGCCTTAGGCGTAATCAACACAT
TGGAGTGGATACCGAGATTCAAGGTTAGTCCCAACCTC
TTCCTGTCCCAATTAAGGAAGCAGGCGAAGACTGCCA
TGCCCCAACATACCTACCTGCGGAGGTGGACGGTGATG
TCAAACCTCAGTTCCAACCTGGTGATTCTACCTGGTCAA
GATCTCCAATATGTTTTGGCAACCTACGATACCTCCAG
GGTTGAGCATGCTGTGGTTTATTACGTTTACAGCCCAA
GCCGCTCATTTTCTTACTTTTATCCTTTTAGGTTGCCTAT
AAAGGGGGTCCCAATCGAACTACAAGTGGAATGCTTCA
CATGGGATCAAAAACCTCTGGTGCCGTCCTTCTGTGTG
CTTGCGGACTCAGAATCCGGTGGACTTATCACTCACTCT
GGGATGGTGGGCATGGGAGTCAGCTGCACAGCTACCCG GGAAGATGGAACCAATCGCAGATAA
GC_H_MEASLES_G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT 43 B3
ATAAGAGCCACCATGTCACCGCAACGAGACCGGATAA mRNA Sequence
ATGCCTTCTACAAAGATAACCCTTATCCCAAGGGAAGT (assumes T100
AGGATAGTTATTAACAGAGAACATCTTATGATTGACAG tail)
ACCCTATGTTCTGCTGGCTGTTCTGTTTCGTCATGTTTCT Sequence Length:
GAGCTTGATCGGATTGCTGGCAATTGCAGGCATTAGAC 2126
TTCATCGGGCAGCCATCTACACCGCGGAGATCCATAAA
AGCCTCAGTACCAATCTGGATGTGACTAACTCCATCGA
GCATCAGGTCAAGGACGTGCTGACACCACTCTTTAAAA
TCATCGGGGATGAAGTGGGCCTGAGAACACCTCAGAG
ATCACTGACCTAGTGAAATTCATCTCGGACAAGATTA
AATTCCTTAATCCGGATAGGGAGTACGACTTCAGAGAT
CTCACTTGGTGCATCAACCCGCCAGAGAGGATCAAACCT
AGATTATGATCAATACTGTGCAGATGTGGCTGCTGAAG
AGCTCATGAATGCATTGGTGAACCTCAACTCTACTGGAG
ACCAGAACAACCACTCAGTTCCTAGCTGTCTCAAAGGG
AAACTGCTCAGGGCCCACTACAATCAGAGGTCAATTCT
CAAACATGTCGCTGTCCTTGTTGGACTTGTACTTAGGTC
GAGGTTACAATGTGTCATCTATAGTCACTATGACATCC
CAGGGAATGTATGGGGGAACCTACCTAGTTGAAAAGCC
TAATCTGAACAGCAAAGGGTTCAGAGTTGTCACAACTGA
GCATGTACCGAGTGTTTGAAGTAGGTGTGATCAGAAAC
CCGGGTTTGGGGGCTCCGGTGTTCATATGACAAACTA
TTTTGAGCAACCAGTCAGTAATGGTCTCGGCAACTGTA
TGGTGGCTTTGGGGGAGCTCAAACCTCGCAGCCCTTGT
CACGGGGACGATTCTATCATAATTCCCTATCAGGGATC
AGGGAAAGGTGTCAGCTTCCAGCTCGTCAAGCTGGGGTG
TCTGGAAATCCCCAACCGACATGCAATCCTGGGTCCCC
TTATCAACGGATGATCCAGTGGTAGACAGGCTTTACCT
CTCATCTCACAGAGGTGTCATCGCTGACAATCAAGCAA
AATGGGCTGTCCCGACAACACGAACAGATGACAAGTTG
CGAATGGAGACATGCTTCCAGCAGGCGTGTAAGGTAA
AATCCAAGCACTCTGCGAGAATCCCGAGTGGGTACCAT
TGAAGGATAACAGGATTCCCTTCATACGGGGTCCCTGTCT
GTTGATCTGAGTCTGACGGTTGAGCTTAAAATCAAAT
TGCTTCGGGATTCGGGCCATTGATCACACACGGCTCAG
GGATGGACCTATACAAATCCAACCTGCAACAATGTGTAT
TGGCTGACTATTCGCCAATGAGAAATCTAGCCTTAGG
CGTAATCAACACATTGGAGTGGATACCGAGATTCAAGG
TTAGTCCCAACCTCTTCACTGTCCCAATTAAGGAAGCA
GGCGAAGACTGCCATGCCCAACATACCTACCTGCGGA

GGTGGACGGTGATGTCAAACCTCAGTTCCAACCTGGTGA
TTCTACCTGGTCAAGATCTCCAATATGTTTTGGCAACCT
ACGATACCTCCAGGGTTGAGCATGCTGTGGTTTATTAC
GTTTACAGCCCAAGCCGCTCATTCTTACTTTTATCCT
TTTAGGTTGCCTATAAAGGGGGTCCCAATCGAACTACA
AGTGAATGCTTCACATGGGATCAAAAACCTCTGGTGCC
GTCACCTTCTGTGTGCTTGCGGACTCAGAATCCGGTGGA
CTTATCACTCACTCTGGGATGGTGGGCATGGGAGTCAG
CTGCACAGCTACCCGGGAAGATGGAACCAATCGCAGAT
AATGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTCTT
GCCCCTTGGGCCTCCCCCAGCCCCTCCTCCCCTTCCTG
CACCCGTACCCCGTGGTCTTTGAATAAAGTCTGAGTG
GGCGGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AA
AAATC TAG GC_H_MEASLES_
TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACT 44 D8
CACTATAGGGAAATAAGAGAGAAAAGAAGAGTAAGAA Sequence, NT (5'
GAAATATAAGAGCCACCATGTCAACCACAACGAGACCG UTR, ORF, 3'
GATAAATGCCTTCTACAAAGACAACCCCATCCTAAGG UTR)
GAAGTAGGATAGTTATTAACAGAGAACATCTTATGATT Sequence Length:
GATAGACCTTATGTTTTGCTGGCTGTTCTATTTCGTCATG 2065
TTTTCTGAGCTTGATCGGGTTGCTAGCCATTGCAGGCATT
AGACTTCATCGGGCAGCCATCTACACCGCAGAGATCCA
TAAAGCCTCAGCACCAATCTGGATGTAACATAACTCAA
TCGAGCATCAGGTTAAGGACGTGCTGACACCACTCTTC
AAGATCATCGGTGATGAAGTGGGCTTGAGGACACCTCA
GAGATCACTGACCTAGTGAAGTTCATCTCTGACAAGA
TTAAATTCCTTAATCCGGACAGGGAATACGACTTCAGA
GATCTCACTTGGTGTATCAACCCGCCAGAGAGAATCAA
ATTGGATTATGATCAATACTGTGCAGATGTGGCTGCTG
AAGAACTCATGAATGCATTGGTGAACATACTACTG
GAGACCAGGGCAACCAATCAGTTCCTAGCTGTCTCAA
GGGAAACTGCTCAGGGCCCACTACAATCAGAGGCCAAT
TCTCAAACATGTCGCTGTCCCTGTTGGACTTGTATTTAA
GTCGAGGTTACAATGTGTCATCTATAGTCACTATGACA
TCCCAGGGAATGTACGGGGGAACCTACCTAGTGGAAAA
GCCTAATCTGAGCAGCAAAGGGTCAGAGTTGTCACAAC
TGAGCATGCACCGAGTGTGTTGAAGTAGGTGTTATCAGA
AATCCGGGTTTGGGGGCTCCGGTATTCCATATGACAAA
CTATCTTGAGCAACCAGTCAGTAATGATTTTCAGCAACT
GCATGGTGGCTTTGGGGGAGCTCAAGTTCGCAGCCCTC
TGTCACAGGGAAGATTCTATCACAATCCCTATCAGGG
ATCAGGGAAGGTGTCAGCTTCCAGCTTGTCAGGCTAG
GTGTCTGGAAATCCCAACCGACATGCAATCCTGGGTC
CCCCTATCAACGGATGATCCAGTGATAGACAGGCTTTA
CCTCTCATCTCACAGAGGCGTTATCGCTGACAATCAAG
CAAAATGGGCTGTCCCGACAACACGGACAGATGACAA
GTTGCGAATGGAGACATGCTTCCAGCAGGCGTGTAAGG
GTAAAATCCAAGCACTTTGCGAGAATCCCGAGTGGACA
CCATTGAAGGATAACAGGATTCCTTCATACGGGGTCTT
GTCTGTTGATCTGAGTCTGACAGTTGAGCTTAAATCA
AAATTGTTTCAGGATTCGGGCCATTGATCACACACGGT

TCAGGGATGGACCTATACAAATCCAACCACAACAATAT

GTATTGGCTGACTATCCCGCCAATGAAGAACCTGGCCT
TAGGTGTAATCAACACATTGGAGTGGATACCGAGATTC
AAGGTTAGTCCCAACCTCTTCACTGTTCCAATTAAGGA
AGCAGGCGAGGACTGCCATGCCCCAACATACCTACCTG
CGGAGGTGGATGGTGTGTCAAACCTCAGTTCCAATCTG
GTGATTCTACCTGGTCAAGATCTCCAATATGTTCTGGCA
ACCTACGATACTTCCAGAGTTGAACATGCTGTAGTTTAT
TACGTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTAT
CCTTTTAGGTTGCCTGTAAGGGGGGTCCCCATTGAATTA
CAAGTGGAAATGCTTCACATGGGACCAAAAACCTCTGGTG
CCGTCACCTTCTGTGTGCTTGCGGACTCAGAATCTGGTGG
ACATATCACTCACTCTGGGATGGTGGGCATGGGAGTCA
GCTGCACAGCCACTCGGGAAGATGGAACCAGCCGCAG
ATAGTGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTC
TTGCCCTTGGGCCTCCCCCAGCCCCTCCTCCCCTTCC
TGCACCCGTACCCCGTGGTCTTTGAATAAAGTCTGAG TGGGCGGC GC_H_MEASLES_
ATGTCACCACAACGAGACCGGATAAATGCCTTCTACAA 45 D8
AGACAACCCCATCCTAAGGGAAGTAGGATAGTTATTA ORF Sequence, NT
ACAGAGAACATCTTATGATTGATAGACCTTATGTTTTGC
TGGCTGTTCTATTCGTCATGTTTCTGAGCTTGATCGGGT
TGCTAGCCATTGCAGGCATTAGACTTCATCGGGCAGCC
ATCTACACCGCAGAGATCCATAAAAGCCTCAGCACCAA
TCTGGATGTAACCTCAATCGAGCATCAGGTTAAGG
ACGTGCTGACACCACTCTTCAAGATCATCGGTGATGAA
GTGGGCTTGAGGACACCTCAGAGATTCAGTACTGACCTAGT
GAAGTTCATCTCTGACAAGATTAATTCCTTAATCCGG
ACAGGGAATACGACTTCAGAGATCTCACTTGGTGTATC
AACCCGCCAGAGAGAATCAAATTGGATTATGATCAATA
CTGTGCAGATGTGGCTGCTGAAGAACTCATGAATGCAT
TGGTGAACCTCAACTCTACTGGAGACCAGGGCAACCAAT
CAGTTCCTAGCTGTCTCAAAGGGAACTGCTCAGGGCC
CACTACAATCAGAGGCCAATTCTCAAACATGTGCTGT
CCCTGTTGGACTTGTATTTAAGTCGAGGTTACAATGTGT
CATCTATAGTCACTATGACATCCCAGGGAATGTACGGG
GGAACCTACCTAGTGGAAAAGCCTAATCTGAGCAGCAA
AGGGTCAGAGTTGTCACAACCTGAGCATGCACCGAGTGT
TTGAAGTAGGTGTTATCAGAAATCCGGGTTTGGGGGCT
CCGGTATTCCATATGACAAACTATCTTGAGCAACCAGT
CAGTAATGATTCAGCAACTGCATGGTGGCTTTGGGGG
AGCTCAAGTTCGCAGCCCTCTGTACAGGGAAGATTCT
ATCACAATTCCTATCAGGGATCAGGGAAAGGTGTCAG
CTTCCAGCTTGTCAGCTAGGTGTCTGGAAATCCCCAA
CCGACATGCAATCCTGGGTCCCCCTATCAACGGATGAT
CCAGTGATAGACAGGCTTTACCTCTCATCTCACAGAGG
CGTTATCGCTGACAATCAAGCAAAATGGGCTGTCCCGA
CAACACGGACAGATGACAAGTTGCGAATGGAGACATG
CTTCCAGCAGGCGTGTAAGGGTAAAATCCAAGCACTTT
GCGAGAATCCCGAGTGGACACCATTGAAGGATAACAG
GATTCCTTCATACGGGGTCTTGTCTGTTGATCTGAGTCT
GACAGTTGAGCTTAAAATCAAATTTGTTTCAGGATTCG
GGCCATTGATCACACACGGTTCAGGGATGGACCTATAC
AAATCCAACCACAACAATATGTATTGGCTGACTATCCC
GCCAATGAAGAACCTGGCCTTAGGTGTAATCAACACAT
TGGAGTGGATAACCGAGATTCAGGTTAGTCCCAACCTC

TTCACTGTTCCAATTAAGGAAGCAGGCGAGGACTGCCA
TGCCCCAACATACCTACCTGCGGAGGTGGATGGTGATG
TCAAACCTCAGTTCCAATCTGGTGATTCTACCTGGTCAAG
ATCTCCAATATGTTCTGGCAACCTACGATACTTCCAGA
GTTGAACATGCTGTAGTTTATTACGTTTACAGCCCAAGC
CGCTCATTCTTACTTTTATCCTTTTAGGTTGCCTGTAA
GGGGGGTCCCCATTGAATTACAAGTGGAATGCTTCACA
TGGGACCAAAAACCTCTGGTGCCGTCACCTTCTGTGTGCTT
GCGGACTCAGAATCTGGTGGACATATCACTCACTCTGG
GATGGTGGGCATGGGAGTCAGCTGCACAGCCACTCGGG AAGATGGAACCAGCCGCAGATAG
GC_H_MEASLES_G*GGGAAATAAGAGAGAAAAGAAGAGTAAGAAGAAAT 46 D8
ATAAGAGCCACCATGTCACCACAACGAGACCGGATAA mRNA Sequence
ATGCCTTCTACAAAGACAACCCCCATCCTAAGGGAAGT (assumes T100
AGGATAGTTATTAACAGAGAACATCTTATGATTGATAG tail)
ACCTTATGTTTTGCTGGCTGTTCTATTCGTCATGTTTCTG Sequence Length:
AGCTTGATCGGGTTGCTAGCCATTGCAGGCATTAGACT 2126
TCATCGGGCAGCCATCTACACCGCAGAGATCCATAAAA
GCCTCAGCACC AATCTGGATGTA ACTA ACTCAATCGAG
CATCAGGTTAAGGACGTGCTGACACCACTCTTCAAGAT
CATCGGTGATGAAGTGGGCTTGAGGACACCTCAGAGAT
TCACTGACCTAGTGAAGTTCATCTCTGACAAGATTA
TTCCTTAATCCGGACAGGGAATACGACTTCAGAGATCT
CACTTGGTGTATCAACCCGCCAGAGAGAATCAAATTGG
ATTATGATCAATACTGTGCAGATGTGGCTGCTGAAGAA
CTCATGAATGCATTGGTGA ACTCAACTCTACTGGAGAC
CAGGGCAACCAATCAGTTCCTAGCTGTCTCAAAGGGAA
ACTGCTCAGGGCCC ACTACAATCAGAGGCCAATTCTCA
AACATGTCGCTGTCCCTGTTGGACTTGTATTTAAGTCGA
GGTTACAATGTGTCATCTATAGTCACTATGACATCCCA
GGGAATGTACGGGGGA ACTTACCTAGTGGAAAAGCCT
AATCTGAGCAGCAAAGGGTCAGAGTTGTCACA ACTGAG
CATGCACCGAGTGT TTTGAAGTAGGTGTTATCAGAAATC
CGGGTTTGGGGGCTCCGGTATTCCATATGACAAACTAT
CTTGAGCAACCAGTCAGTAATGATTCAGCAACTGCAT
GGTGGCTTTGGGGGAGCTCAAGTTCGCAGCCCTCTGTC
ACAGGGAAGATTCTATCACAATTCCTATCAGGGATCA
GGGAAAGGTGTCAGCTTCCAGCTTGTCAAGCTAGGTGT
CTGGAAATCCCCAACCGACATGCAATCCTGGGTCCCC
TATCAACGGATGATCCAGTGATAGACAGGCTTTACCTC
TCATCTCACAGAGGCGTTATCGCTGACAATCAAGCAAA
ATGGGCTGTCCCGACAACACGGACAGATGACAAGTTGC
GAATGGAGACATGCTTCCAGCAGGCGTGTAAGGGTAA
AATCCAAGCACTTTGCGAGAATCCCGAGTGGACACCAT
TGAAGGATAACAGGATTCCCTTCATACGGGGTCTTGTCT
GTTGATCTGAGTCTGACAGTTGAGCTTAAAATCAAAT
TGTTTCAGGATTCGGGCCATTGATCACACACGGTTCAG
GGATGGACCTATACAAATCCAACCACAACAATATGTAT
TGGCTGACTATCCCGCCAATGAAGAACCTGGCCTTAGG
TGTAATCAACACATTGGAGTGGATACCGAGATTCAAGG
TTAGTCCCAACCTCTTCACTGTTCCAATTAAGGAAGCA
GGCGAGGACTGCCATGCCCCAACATACCTACCTGCGGA
GGTGGATGGTGATGTCAA ACTCAGTTCCAATCTGGTGA
TTCTACCTGGTCAAGATCTCCAATATGTTCTGGCAACCT
ACGATACTTCCAGAGTTGAACATGCTGTAGTTTATTAC

GTTTACAGCCCAAGCCGCTCATTTTCTTACTTTTATCCT
TTTAGGTTGCCTGTAAGGGGGTCCCCATTGAATTACA
AGTGAATGCTTCACATGGGACCAAAAACCTCTGGTGCC
GTCACTTCTGTGTGCTTGCGGACTCAGAATCTGGTGGA
CATATCACTCACTCTGGGATGGTGGGCATGGGAGTCAG
CTGCACAGCCACTCGGGAAGATGGAACCAGCCGCAGA
TAGTGATAATAGGCTGGAGCCTCGGTGGCCAAGCTTCT
TGCCCCTTGGGCCTCCCCCAGCCCCTCCTCCCCTTCT
GCACCCGTACCCCGTGGTCTTTGAATAAAGTCTGAGT
GGGCGGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAT CTAG MeV mRNA Sequences
GC_F_MEASLES_UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC 69 B3.1
UCACUUAUAGGGAAUUAAGAGAGAAAAGAAGAGUAAAG Sequence, NT (5'
AAGAAUUAUAGAGCCACCAUGGGUCUCAAGGUGAA UTR, ORF, 3'
CGUCUCUGCCGUUAUCAUGGCAGUACUGUUAACUCUC UTR)
CAAACACCCGCCGGUCAAAUUCAUUGGGGCAAUCUCU Sequence Length:
CUAAGAUAGGGGUAGUAGGAAUAGGAAGUGCAAGCU 1864
ACAAAGUUAUGACUCGUUCCAGCCAUCAUAUAGU
CAUAAAUAUUAUGCCCAAUAUAACUCUCCUCAUAAC
UGCACGAGGGUAGAGAUUGCAGAAUACAGGAGACUA
CUAAGAACAGUUUUGGAACCAAUUAGGGAUGCACUU
AAUGCAAUGACCCAGAACAUAAGGCCGGUUCAGAGCG
UAGCUUCAAGUAGGAGACACAAGAGAUUUGCGGGAG
UAGUCCUGGCAGGUGCGGCCCUAGGUGUUGCCACAGC
UGCUCAGAUAAACAGCCGGCAUUGCACUUCACCGGUCC
AUGCUGAACUCUCAGGCCAUCGACAAUCUGAGAGCGA
GCCUGGAAACUACUAAUCAGGCAAUUGAGGCAAUCAG
ACAAGCAGGGCAGGAGAUGAUUAUUGGCUGUUCAGGG
UGUCCAAGACUACAUCAAUAAUGAGCUGAUACCGUCU
AUGAACCAGCUAUCUUGUGAUCUAAUCGGUCAGAAGC
UCGGGCUCAAAUUGCUUAGAUACUUAACAGAAAUCCU
GUCAUUAUUUGGCCCCAGCCUACGGGACCCCAUAUCU
GCGGAGAUUAUCUUAUCCAGGCUUUGAGUUUAGCACUU
GGAGGAGAUUAUCAAUAAGGUGUUAGAAAAGCUCGGA
UACAGUGGAGGCGAUUUACUAGGCAUCUUAAGAGAGC
AGAGGAAUAAAGGCUCGGAUAAUCACGUCGACACAG
AGUCCUACUUAUAGUCCUCAGUAUAGCCUAUCCGAC
GCUGUCCGAGAUUAAGGGGGUGAUUGUCCACCGGCUA
GAGGGGGUCUCGUACAACAUAAGGCUCUCAAGAGUGG
UAUACCACUGUGCCCAAGUAUGUUGCAACCCAAGGGU
ACCUUAUCUCGAUUUUUGAUGAGUCAUCAUGUACUU
UCAUGCCAGAGGGGACUGUGUGCAGCCAAAUGCCUU
GUACCCGAUGAGUCCUCUGCUCCAAGAAUGCCUCCGG
GGGUCCACCAAGUCCUGUGCUCGUACACUCGUAUCCG
GGUCUUUUGGGAACCGGUUCAUUUUUAUCACAAGGGA
ACCUAAUAGCCAAUUGUGCAUCAAUUCUUUGUAAGU
GUUACACAACAGGUACGAUUAUUAUCAAGACCCUGA
CAAGAUCCUAACAUACAUUGCUGCCGAUCGCUGCCCG
GUAGUCGAGGUGAACGGCGUGACCAUCCAAGUCGGGA
GCAGGAGGUUAUCCAGACGCUGUGUACUUGCACAGAAU
UGACCUCGGUCCUCCCAUAUCAUUGGAGAGGUUGGAC
GUAGGGACAAAUCUGGGGAAUGCAAUUGCCAAAUUG
GAGGAUGCCAAGGAAUUGUUGGAAUCAUCGGACCAG

AUAUUGAGAAGUAUGAAAGGUUUUUCGAGCACUAGC
AUAGUCUACAUCCUGAUUGCAGUGUGUCUUGGAGGG
UUGAUAGGGAUCCCCACUUUAAUAUGUUGCUGCAGG
GGGCGUUGUAACAAAAGGGAGAACAAGUUGGUAUG
UCAAGACCAGGCCUAAAGCCUGACCUACAGGAACAU
CAAAAUCCUAUGUAAGAUCGCUUUGAUGAUAAUAGG
CUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCUUGGGC
CUCCCCCAGCCCCUCCUCCCCUUCUGCACCCGUACC
CCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGGC GC_F_MEASLES_
AUGGGUCUCAAGGUGAACGUCUCUGCCGUAUUCAUGG 70 B3.1
CAGUACUGUUAACUCUCCAAACACCCGCCGGUCAAAU ORF Sequence, NT
UCAUUGGGGCAAUCUCUCUAAGAUAGGGGUAGUAGG
AAUAGGAAGUGCAAGCUACAAAGUUAUGACUCGUUC
CAGCCAUCAAUCAUUAGUCAUAAAUUAUUGCCCAAU
AUAACUCUCCUCAAUAAACUGCACGAGGGUAGAGAUUG
CAGAAUACAGGAGACUACUAAGAACAGUUUUGGAAC
CAAUUAGGGAUGCACUAAUGCAAUGACCCAGAACAU
AAGGCCGGUUCAGAGCGUAGCUUCAAGUAGGAGACAC
AAGAGAUUUGCGGGAGUAGUCCUGGCAGGUGCGGCC
UAGGUGUUGCCACAGCUGCUCAGAUAAACAGCCGGCAU
UGCACUUCACCGGUCCAUGCUGAACUCUCAGGCCAUC
GACAAUCUGAGAGCGAGCCUGGAAACUACUAAUCAGG
CAAUUGAGGCAAUCAGACAAGCAGGGCAGGAGAUGA
UAUUGGCUGUUCAGGGUGUCCAAGACUACAUCAAUA
AUGAGCUGAUACCGUCUAUGAACCAGCUAUCUUGUGA
UCUAAUCGGUCAGAAGCUCGGGCUCAAAUUGCUUAGA
UACUAUACAGAAAUCCUGUCAUUUUUGGCCCCAGCC
UACGGGACCCCAUAUCUGCGGAGAUUCUAUCCAGGC
UUUGAGUUAUGCACUUGGAGGAGAUUCAAUAAAGGU
GUUAGAAAAGCUCGGAUACAGUGGAGGCGAUUUACU
AGGCAUCUUAGAGAGCAGAGGAAUAAAGGCUCGGAU
AACUCACGUCGACACAGAGUCCUACUUCAUAGUCCUC
AGUAUAGCCUAUCCGACGCUGUCCGAGAUUAAGGGGG
UGAUUGUCCACCGGCUAGAGGGGGUCUCGUACAACA
AGGCUCUCAAGAGUGGUUAUACCACUGUGCCCAAGU
GUUGCAACCCAAGGGUACCUUAUCUCGAAUUUUGAUG
AGUCAUCAUGUACUUAUGCCAGAGGGGACUGUGU
GCAGCCAAAUGCCUUGUACCCGAUGAGUCCUCUGCU
CCAAGAAUGCCUCCGGGGGUCCACCAAGUCCUGUGCU
CGUACACUCGUAUCCGGGUCUUUUGGGAACCGGUUCA
UUUUUAUCACAAGGGAACCUAAUAGCCAAUUGUGCAUC
AAUUCUUUGUAAGUGUACACAACAGGUACGAUUUAU
UAAUCAAGACCUGACAAGAUCCUAACAUAUUAUGCU
GCCGAUCGCUGCCCGGUAGUCGAGGUGAACGGCGUGA
CCAUCCAAGUCGGGAGCAGGAGGUAUCCAGACGCUGU
GUACUUGCACAGAAUUGACCUCGGUCCUCCAUAUCA
UUGGAGAGGUUGGACGUAGGGACAAAUCUGGGGAAU
GCAAUUGCCAAAUUGGAGGAUGCCAAGGAAUUGUUG
GAAUCAUCGGACCAGAUUUGAGAAGUAUGAAAGGU
UUUUCGAGCACUAGCAUAGUCUACAUCUUGAUUGCAG
UGUGUCUUGGAGGGUUGAUAGGGAUCCCCACUUAA
UAUGUUGCUGCAGGGGGCGUUGUAACAAAAGGGAG
AACAAGUUGGUUUGUCAAGACCAGGCCUAAAGCCUGA
CCUACAGGAACAUCAAAUCCUAUGUAAGAUCGCUU UGA GC_F_MEASLES_

G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA 71 B3.1
UAUAAGAGCCACCAUGGGUCUCAAGGUGAACGUCUCU mRNA Sequence
GCCGUUAUCAUGGCAGUACUGUUAACUCUCCAAACAC (assumes T100
CCGCCGGUCAAAUUCAUUGGGGCAAUCUCUCUAAGAU tail)
AGGGGUAGUAGGAAUAGGAAGUGCAAGCUACAAAGU mRNA Sequence
UAUGACUCGUUCCAGCCAUCAAUCAUUAGUCAUAAAA Length: 1925
UUAAUGCCCAAUAUAACUCUCCUCAAAUAACUGCACGA
GGGUAGAGAUUGCAGAAUACAGGAGACUACUAAGAA
CAGUUUUGGAACCAAUUAGGGAUGCACUAAUGCAA
UGACCCAGAACAUAAGGCCGGUUCAGAGCGUAGCUUC
AAGUAGGAGACACAAGAGAUUUGCGGGAGUAGUCCU
GGCAGGUGCGGCCCUAGGUGUUGCCACAGCUGCUCAG
AUAACAGCCGGCAUUGCACUUCACCGGUCCAUGCUGA
ACUCUCAGGCCAUCGACAAUCUGAGAGCGAGCCUGGA
AAUCUACUAAUCAGGCAAUUGAGGCAAUCAGACAAGCA
GGGCAGGAGAUGAUUUGGCUGUUCAGGGUGUCCAA
GACUACAUCAAAUAAUGAGCUGAUACCGUCUAUGAACC
AGCUAUCUUGUGAUCUAAUCGGUCAGAAGCUCGGGCU
CAAUUGCUUAGAUACUAUACAGAAAUCCUGUCAU
AUUUGGCCCCAGCCUACGGGACCCCAUAUCUGCGGAG
AUUUCUAUCCAGGCUUUGAGUUAUGCACUUGGAGGA
GAUAUCAAUUAGGUGUUAGAAAAGCUCGGAUACAGU
GGAGGCGAUUUACUAGGCAUCUUAGAGAGCAGAGGA
AUAAAGGCUCGGAUAACUCACGUCGACACAGAGUCCU

ACUUCAUAGUCCUCAGUAUAGCCUAUCCGACGCUGUC
CGAGAUUAAGGGGGUGAUUGUCCACCGGCUAGAGGG
GGUCUCGUACAACAUAAGGCUCUCAAGAGUGGUAUACC
ACUGUGCCCAAGUAUGUUGCAACCCAAGGGUACCUUA
UCUCGAAUUUUGAUGAGUCAUCAUGUACUUUCAUGCC
AGAGGGGACUGUGUGCAGCCAAAUGCCUUGUACCCG
AUGAGUCCUCUGCUCCAAGAAUGCCUCCGGGGGUCCA
CCAAGUCCUGUGCUCGUACACUCGUAUCCGGGUCUUU
UGGGAACCGGUUCAUUUUUUCACAAGGGAACCUAAU
AGCCAAUUGUGCAUCAAUUCUUUGUAAGUGUUACAC
AACAGGUACGAUUAAUUAUCAAGACCCUGACAAGAUC
CUAACAUACAUUGCUGCCGAUCGCUGCCCGGUAGUCG
AGGUGAACGGCGUGACCAUCCAAGUCGGGAGCAGGAG
GUAUCCAGACGCUGUGUACUUGCACAGAAUUGACCUC
GGUCCUCCCAUAUCAUUGGAGAGGUUGGACGUAGGG
ACAAAUCUGGGGAAUGCAAUUGCCAAAUUGGAGGAU
GCCAAGGAAUUGUUGGAAUCAUCGGACCAGAUUUUG
AGAAGUAUGAAAGGUUUUUCGAGCACUAGCAUAGUC
UACAUCCUGAUUGCAGUGUGUCUUGGAGGGUUGAUA
GGGAUCCCCACUUAAUUAUGUUGCUGCAGGGGGCGUU
GUAACAAAAAGGGAGAACAAGUUGGUAUGUCAAGAC
CAGGCCUAAAGCCUGACCUUACAGGAACAUCAAAUC
CUAUGUAAGAU CGCUUUGAUGAUAAUAGGCUGGAGC
CUCGGUGGCCAAGCUUCUUGCCCCUUGGGCCUCCCC
CAGCCCCUCCUCCCCUUCUGCACCCGUACCCCGUGG
UCUUUGAAUAAAGUCUGAGUGGGCGGCAAAAAAAAAA
AAA
AAA AAAAAAAAAAAAAAAAAAAAAAAAAAUCUAG
GC_F_MEASLES_UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC 72 D8

UCACUAUAGGGAAAUAAGAGAGAAAAGAAGAGUAAG Sequence, NT (5'
AAGAAAUAUAAGAGCCACCAUGGGGUCUCAAGGUGAA UTR, ORF, 3'
CGUCUCUGUCAUAUUCAUGGCAGUACUGUUAACUCUU UTR)
CAAACACCCACCGGUCAAUCCAUUGGGGCAAUCUCU Sequence Length:
CUAAGAUAGGGGUGGUAGGGGUAGGAAGUGCAAGCU 1864

ACAAAGUUAUGACUCGUUCCAGCCAUCAAUCAUUAGU
CAUAAAGUUAUGCCCAAUAUAACUCUCCUCAACAAU
UGCACGAGGGUAGGGAUUGCAGAAUACAGGAGACUA
CUGAGAACAGUUCUGGAACCAAUUAGAGAUGCACUU
AAUGCAAUGACCCAGAAUAUAAGACCGGUUCAGAGU
GUAGCUUCAAGUAGGAGACACAAGAGAUUUGCGGGA
GUUGUCCUGGCAGGUGCGGCCCUAGGCGUUGCCACAG
CUGCUCAAAUAACAGCCGGUAUUGCACUUCACCAGUC
CAUGCUGAACUCUCAAGCCAUCGACAAUCUGAGAGCG
AGCCUAGAAACUACUAAUCAGGCAAUUGAGGCAAUCA
GACAAGCAGGGCAGGAGAUGAUUUGGCUGUUCAGG
GUGUCCAAGACUACAUCAAAUAUGAGCUGAUACCGUC
UAUGAAUCAACUAUCUUGUGAUUUAUCGGCCAGAA
GCUAGGGCUCAAAUUGCUCAGAUACUAUACAGAAAUC
CUGUCAUUAUUUGGCCCCAGCUUACGGGACCCCAUAU
CUGC GGAGAU AUCUAUCCAGGCUUUGAGCUAUGCGCU
UGGAGGAGAUUCAUAAGGUGUUGGAAAAGCUCGG
AUACAGUGGAGGUGAUCUACUGGGCAUCUUAGAGAG
CAGAGGAAUAAAGGCCCGGAUAACUCACGUCGACACA
GAGUCCUACUUCAUUGUACUCAGUAUAGCCUAUCCGA
CGCUAUCCGAGAUUAAGGGGGUGAUUGUCCACCGGCU
AGAGGGGGUCUCGUACAACAUAGGCUCUCAAGAGUG
GUAUACCACUGUGCCCAAGUAUGUUGCAACCCAAGGG
UACCUUAUCUCGAAUUUUGAUGAGUCAUCAUGCACUU
UCAUGCCAGAGGGGACUGUGUGCAGCCAGAAUGCCUU
GUACCCGAUGAGUCCUCUGCUCCAAGAAUGCCUCCGG
GGUCCACUAAGUCCUGUGCUCGUACACUCGUAUCCG
GGUCUUUCGGGAACCGGUUCAUUUUAUCACAGGGGA
ACCUAAUAGCCAAUUGUGCAUCAAUCCUUUGCAAGUG
UUACACAACAGGAACAUAUAUAUCAAGACCCUGAC
AGAUAUCCUAACAUAUAUUGCUGCCGAUCACUGCCCGG
UGGUCGAGGUGAAUGGCGUGACCAUCCAAGUCGGGA
GCAGGAGGUAUCCGGACGCUGUGUACUUGCACAGGAU
UGACCUCGGUCCUCCCAUAUCUUUGGAGAGGUUGGAC
GUAGGGACAAAUCUGGGGAAUGCAAUUGCUAAGUUG
GAGGAUGCCAAGGAAUUGUUGGAGUCAUCGGACCAG
AUUUGAGGAGUAUGAAAGGUUUUUCGAGCACUAGU
AUAGUUUACAUCCUGAUUGCAGUGUGUCUUGGAGGA
UUGAUAGGGAUCCCCGCUUUAUAUGUUGCUGCAGG
GGGCGUUGUAACAAGAAGGGAGAACAAGUUGGUAUG
UCAAGACCAGGCCUAAAGCCUGAUCUUACAGGAACAU
CAAAAUCCUAUGUAAGGUCACUCUGAUGAUAAUAGG
CUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCUUGGGC
CUCCCCCAGCCCCUCCUCCCCUCCUGCACCCGUACC
CCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGGC GC_F_MEASLES_
AUGGGUCUCAAGGUGAACGUCUCUGUCAUAUUCAUG 73 D8
GCAGUACUGUUAACUCUUCAAACACCCACCGGUCAA ORF Sequence, NT
UCCAUUGGGGCAAUCUCUCUAAGAUAGGGGUGGUAG
GGGUAGGAAGUGCAAGCUACAAAGUUAUGACUCGUU

CCAGCCAUCAUCAUUAGUCAUAAAGUUAUGCCCAA
UAUAACUCUCCUCAACAAUUGCACGAGGGUAGGGAUU
GCAGAAUACAGGAGACUACUGAGAACAGUUCUGGAA
CCAAUUAGAGAUGCACUUAUGCAAUGACCCAGAAUA
UAAGACCGGUUCAGAGUGUAGCUUCAAGUAGGAGAC
ACAAGAGAUUUGCGGGAGUUGUCCUGGCAGGUGCGG
CCCUAGGCGUUGCCACAGCUGCUCAAUAACAGCCGG
UAUUGCACUUCACCAGUCCAUGCUGAACUCUCAAGCC
AUCGACAAUCUGAGAGCGAGCCUAGAAACUACUAAUC
AGGCAAUUGAGGCAAUCAGACAAGCAGGGCAGGAGA
UGAUAUUGGCUGUUCAGGGUGUCCAAGACUACAUCA
AUAAUGAGCUGAUACCGUCUAUGAAUCAACUAUCUU
GUGAUUUAAUCGGCCAGAAGCUAGGGUCUCAAUUGC
UCAGAUACUAUACAGAAAUCCUGUCAUUUUUGGCC
CAGCUUACGGGACCCCAUAUCUGCGGAGAUUCUAUC
CAGGCUUUGAGCUAUGCGCUUGGAGGAGAUUCAAU
AAGGUGUUGGAAAAGCUCGGAUACAGUGGAGGUGAU
CUACUGGGCAUCUUAGAGAGCAGAGGAAUAAAGGCC
GGAUAACUCACGUCGACACAGAGUCCUACUUCAUUGU
ACUCAGUAUAGCCUAUCCGACGCUAUCGAGAUUAAG
GGGGUGAUUGUCCACCGGCUAGAGGGGGUCUCGUACA
ACAUAGGCUCUCAAGAGUGGUUAUACCACUGUGCCCAA
GUAUGUUGCAACCCAAGGGUACCUUAUCUCGAAUUUU
GAUGAGUCAUCAUGCACUUUCAUGCCAGAGGGGACUG
UGUGCAGCCAGAAUGCCUUGUACCCGAUGAGUCCUCU
GCUCCAAGAAUGCCUCCGGGGGUCACUAAGUCCUGU
GCUCGUACACUCGUAUCCGGGUCUUUCGGGAACCGGU
UCAUUUUUAUCACAGGGGAACCUAAUAGCCAAUUGUGC
AUCAAUCCUUUGCAAGUGUUACACAACAGGAACAAUC
AUUAAUCAAGACCCUGACAAGAUCUUAACAUACAUG
CUGCCGAUCACUGCCCGGUGGUCGAGGUGAAUGGCGU
GACCAUCCAAGUCGGGAGCAGGAGGUAUCCGGACGCU
GUGUACUUGCACAGGAUUGACCUCGGUCCUCCCAUAU
CUUUGGAGAGGUUGGACGUAGGGACAAAUCUGGGGA
AUGCAAUUGCUAAGUUGGAGGAUGCCAAGGAAUUGU
UGGAGUCAUCGGACCAGAUUAUUGAGGAGUAUGAAAG
GUUUUUCGAGCACUAGUAUAGUUUACAUCUGAUUG
CAGUGUGUCUUGGAGGAUUGAUAGGGAUCCCCGCUU
UAAUAUGUUGCUGCAGGGGGCGUUGUAACAAGAAGG
GAGAACAAGUUGGUAUGUCAAGACCAGGCCUAAAGCC
UGAUCUACAGGAACAUCAAAAUCCUAUGUAAGGUC ACUCUGA GC_F_MEASLES_
G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA 74 D8
UAUAAGAGCCACCAUGGGUCUCAAGGUGAACGUCUCU mRNA Sequence
GUCAUAUUCAUGGCAGUACUGUUAACUCUCAAACAC (assumes T100
CCACCGGUCAAUCCAUUGGGGCAAUCUCUCUAAGAU tail)
AGGGGUGGUAGGGGUAGGAAGUGCAAGCUACAAAGU Sequence Length:
UAUGACUCGUUCCAGCCAUCAAUCAUUAGUCAUAAAG 1925
UUAAUGCCCAAUAUAACUCUCCUCAACAAUUGCACGA
GGGUAGGGAUUGCAGAAUACAGGAGACUACUGAGAA
CAGUUCUGGAACCAAUUAGAGAUGCACUUAUUGCAA
UGACCCAGAAUUAAGACCGGUUCAGAGUGUAGCUUC
AAGUAGGAGACACAAGAGAUUUGCGGGAGUUGUCCU
GGCAGGUGCGGCCCUAGGCGUUGCCACAGCUGCUCAA
AUAACAGCCGGUAUUGCACUUCACCAGUCCAUGCUGA

GUGCAGAUGUGGCUGCUGAAGAGCUCAUGAAUGCAU
UGGUGAACUCAACUCUACUGGAGACCAGAACAACCAC
UCAGUUCCUAGCUGUCUCAAGGGAAACUGCUCAGGG
CCCACUACAAUCAGAGGUCAAUUCUCAACAUGUCGC
UGUCCUUGUUGGACUUGUACUUAAGGUCGAGGUACA
AUGUGUCAUCUAUAGUCACUAUGACAUCCCAGGGAAU
GUAUGGGGGAAACCUACCUAGUUGAAAAGCCUAAUCU
GAACAGCAAAGGGUCAGAGUUGUCACAACUGAGCAU
GUACCGAGUGUUUGAAGUAGGUGUGAUCAGAAACCC
GGGUUUGGGGGCUCCCGGUGUCCAUAUGACAAACUA
UUUUGAGCAACCAGUCAGUAAUGGUCUCGGCAACUGU
AUGGUGGCUUUGGGGGAGCUCAAACUCGCAGCCCUU
GUCACGGGGACGAUUCUAUCAUAAUCCCUAUCAGGG
AUCAGGGAAAGGUGUCAGCUUCCAGCUCGUAAGCUG
GGUGUCUGGAAAUCCCCAACCGACAUGCAAUCCUGGG
UCCCCUUAUCAACGGAUGAUCCAGUGGUAGACAGGCCU
UUACCUCUCAUCUCACAGAGGUGUCAUCGCUGACAAU
CAAGCAAAAUGGGCUGUCCCGACAACACGAACAGAUG
ACAAGUUGCGAAUGGAGACAUGCUUCCAGCAGGCGUG
UAAAGGUAAAUAUCCAAGCACUCUGCGAGAAUCCCGAG
UGGGUACCAUUGAAGGAUAACAGGAUUCUUAUAC
GGGUUCCUGUCUGUUGAUCUGAGUCUGACGGUUGAG
CUUAAAUAUAAAUUGCUUCGGGAUUCGGGCCAUUG
AUCACACACGGCUCAGGGAUGGACCUAUACAAAUCCA
ACUGCAACAAUGUGUAUUGGCUGACUAUUCGCCAAU
GAGAAUCUAGCCUUAAGGCGUAAUCAACACAUUGGA
GUGGAUACCGAGAUUCAAGGUUAGUCCAACCUCUUC
ACUGUCCCAAUUAAGGAAGCAGGCGAAGACUGCCAUG
CCCCAACAUACCUACCUUGCGGAGGUGGACGGUGAUGU
CAAACUCAGUCCAACCUGGUGAUUCUACCUGGUCAA
GAUCUCCAUAUUGUUUGGCAACCUACGAUACCUCCA
GGGUUGAGCAUGCUGUGGUUUUAUACGUUUACAGCC
CAAGCCGCUCAUUUUCUUAUUUUAUCCUUUUAGGUU
GCCUAUAAAGGGGGUCCCAAUCGAACUACAAGUGGAA
UGCUUCACAUGGGAUCAAAAACUCUGGUGCCGUCACU
UCUGUGUGCUUGCGGACUCAGAAUCCGGUGGACUUAU
CACUCACUCUGGGAUGGUGGGCAUGGGAGUCAGCUGC
ACAGCUACCCGGGAAGAUGGAACCAAUCGCAGAUAAU
GAUAAUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGC
CCCUUGGGCCUCCCCCAGCCCCUCCUCCCCUUCUGC
ACCCGUACCCCGUGGUCUUUGAAUAAAGUCUGAGUG GCGGC GC_H_MEASLES_
AUGUCACCGCAACGAGACCGGAUAAAUGCCUUCUACA 76 B3
AAGAUAACCCUUAUCCAAGGGAAGUAGGAUAGUUA ORF Sequence, NT
UUAACAGAGAACAUCUUAUGAUUGACAGACCCUAUG
UUCUGCUGGCUGUUCUGUUCGUCAUGUUUCUGAGCUU
GAUCGGAUUGCUGGCAAUUGCAGGCAUUAGACUUCA
UCGGGCAGCCAUCUACACCGCGGAGAUCCAUAAAAGC
CUCAGUACCAAUCUGGAUGUGACUAAUCUCCAUCGAGC
AUCAGGUCAAGGACGUGCUGACACCACUCUUUAAA
CAUCGGGGAUGAAGUGGGCCUGAGAACACCUCAGAGA
UUCACUGACCUAGUGAAAUUCUUCUGGACAAGAUUA

AAUUCUUAUCCGGAUAGGGAGUACGACUUCAGAG
AUCUCACUUGGUGCAUCAACCCGCCAGAGAGGAUCAA

ACUAGAUUAUGAUCAAUACUGUGCAGAUGUGGCUGC
UGAAGAGCUCAUGAAUGCAUUGGUGAACUCAACUCU
ACUGGAGACCAGAACAACCACUCAGUUCCUAGCUGUC
UCAAGGGAAACUGCUCAGGGCCACUACAAUCAGAG
GUCAAUUCUCAACAUGUCGCUGUCCUUGUUGGACUU
GUACUUAGGUCGAGGUUACAAUGUGUCAUCAUAGU
CACUAUGACAUCCCAGGGAAUGUAUGGGGGAACCUAC
CUAGUUGAAAAGCCUAAUCUGAACAGCAAAGGGUCA
GAGUUGUCACAACUGAGCAUGUACCGAGUGUUUGAA
GUAGGUGUGAUCAGAAACCCGGGUUUGGGGGCUCCG
GUGUCCAUAUGACAAACUAUUUUGAGCAACCAGUCA
GUAUUGGUCUCGGCAACUGUAUGGUGGCUUUGGGGG
AGCUCAAACUCGCAGCCCUUUGUCACGGGGACGAUUC
UAUCAUAAUUCCCUAUCAGGGAUACAGGGAAAGGUGU
CAGCUUCCAGCUCGUAAGCUGGGUGUCUGGAAAUCC
CCAACCGACAUGCAAUCCUGGGUCCCCUUAUCAACGG
AUGAUCCAGUGGUAGACAGGCUUUACCUCUCAUCUCA
CAGAGGUGUCAUCGCUGACAAUCAAGCAAAAUGGGCU
GUCCCGACAACACGAACAGAUGACAAGUUGCGAAUGG
AGACAUGCUCUCCAGCAGGCGUGUAAAGGUAAAUAUCA
AGCACUCUGCGAGAAUCCCGAGUGGGUACCAUUGAAG
GAUAACAGGAUUCUUAUACGGGGUCCUGUCUGUUG
AUCUGAGUCUGACGGUUGAGCUUAAAAUCAAAAUUG
CUUCGGGAUUCGGGCCAUUGAUCACACACGGCUCAGG
GAUGGACCUAUACAAAUCCAACUGCAACAAUGUGUAU
UGGCUGACUAUUCGCCAAUGAGAAAUCUAGCCUAG
GCGUAAUCAACACAUUGGAGUGGAUACCGAGAUUCA
AGGUUAGUCCCAACCUCUUCACUGUCCCAAUUAAGGA
AGCAGGCGAAGACUGCCAUGCCCCAACAUACCUACCU
GCGGAGGUGGACGGUGAUGUCAAAACUCAGUCCAACC
UGGUGAUUCUACCUGGUCAGAUCUCCAUAUGUUU
UGGCAACCUACGAUACCUCCAGGGUUGAGCAUGCUGU
GGUUUAUUACGUUUACAGCCAAGCCGCUCAUUUUCU
UACUUUUAUCCUUUUAGGUUGCCUAUAAAGGGGGUC
CAAUUCGAACUACAAGUGGAAUGCUUCACAUGGGAUC
AAAACUCUGGUGCCGUCACUUCUGUGUGCUUGCGGA
CUCAGAAUCCGGUGGACUUUACACUCACUCUGGGAUG
GUGGGCAUGGGAGUCAGCUGCACAGCUACCCGGGAAG AUGGAACCAAUCGCAGAUAA
GC_H_MEASLES_G*GGGAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA 77 B3
UAUAAGAGCCACCAUGUCACCGCAACGAGACCGGAUA mRNA Sequence
AAUGCCUUCUACAAAGAUAAACCUUAUCCCAAGGGAA (assumes T100
GUAGGAUAGUUUAUUAACAGAGACAUCUUAUGAUUG Tail)
ACAGACCCUAUGUUCUGCUGGCUGUUCUGUUCGUCAU Sequence Length:
GUUUCUGAGCUUGAUCGGAUUGCUGGCAAUUGCAGG 2126
CAUUAGACUUCAUCGGGCAGCCAUCUACACCGCGGAG
AUCCAUAAAAGCCUCAGUACCAAUCUGGAUGUGACUA
ACUCCAUCGAGCAUCAGGUCAAGGACGUGCUGACACC
ACUCUUUAAAAUCAUCGGGGAUGAAGUGGGCCUGAG
AACACCUCAGAGAUUCACUGACCUAGUGAAAUUCAUC
UCGGACAAGAUUAAAUCCUUAUCCGGAUAGGGAG
UACGACUUCAGAGAUUCACUUGGUGCAUCAACCCGC
CAGAGAGGAUCAAAACUAGAUUAUGAUCAAUACUGUG
CAGAUUGGCUGCUGAAGAGCUCAUGAAUGCAUUGG
UGAACUCAACUCUACUGGAGACCAGAACAACCACUCA

GUUCCUAGCUGUCUCAAGGGAAACUGCUCAGGGCCC
ACUACAAUCAGAGGUCAAUUCUCAAAACUUGUCGUCUGU
CCUUGUUGGACUUGUACUUAGGUCGAGGUUACAAUG
UGUCAUCUAUAGUCACUAUGACAUCCAGGGAAUGUA
UGGGGGAACCUACCUAGUUGAAAAGCCUAAUCUGAAC
AGCAAAGGGUCAGAGUUGUCACAACUGAGCAUGUACC
GAGUGUUUGAAGUAGGUGUGAUCAGAAACCCGGGUU
UGGGGGCUCCGGUGUCCAUAUGACAAACUAUUUUG
AGCAACCAGUCAGUAAUGGUCUCGGCAACUGUAUGGU
GGCUUUGGGGAGCUCAAACUCGCAGCCCUUUGUCAC
GGGGACGAUUCUAUCAUAAUUCCUAUCAGGGAUACAG
GGAAAGGUGUCAGCUUCCAGCUCGUCAAGCUGGGUGU
CUGGAAAUCCCCAACCGACAUGCAAUCCUGGGUCCCC
UUAUCAACGGAUGAUCCAGUGGUAGACAGGCUUUACC
UCUCAUCUCACAGAGGUGUCAUCGCUGACAAUCAAGC
AAAAUGGGCUGUCCCGACAACACGAACAGAUGACAAG
UUGCGAAUGGAGACAUGCUUCCAGCAGGCGUGUAAA
GGUAAAAUCCAAGCACUCUGCGAGAAUCCCGAGUGGG
UACCAUUGAAGGAUAACAGGAUUCUUAUACGGGG
UCCUGUCUGUUGAUCUGAGUCUGACGGUUGAGCUUA
AAAUCAAAAUUGCUUCGGGAUUCGGGCCAUUGAUCAC
ACACGGCUCAGGGAUGGACCUAUACAAAUCCAACUGC
AACAAUGUGUAUUGGCUGACUAUUCCGCCAAUGAGA
AAUCUAGCCUUAGGCGUAUAACAACAUAUGGAGUGG
AUACCGAGAUUCAAGGUUAGUCCCAACCUCUUCACUG
UCCCAAUUAAGGAAGCAGGCGAAGACUGCCAUGCCCC
AACAUACCUACCUAGCGGAGGUGGACGGUGAUGUCAA
CUCAGUUCCAACCUGGUGAUUCUACCUUGUCAAGAUC
UCCAAUAUGUUUUGGCAACCUACGAUACCUCCAGGGU
UGAGCAUGCUGUGGUUUUAUUACGUUUACAGCCCAAGC
CGCUCAUUUUCUUAUUUUUACCUUUUAGGUUGCCUA
UAAAGGGGGUCCCAAUCGAACUACAAGUGGAAUGCU
UCACAUGGGAUCAAAAACUCUGGUGCCGUCACUUCUG
UGUGCUUGCGGACUCAGAAUCCGGUGGACUUAUCACU
CACUCUGGGAUGGUGGGCAUGGGAGUCAGCUGCACAG
CUACCCGGGAAGAUGGAACCAAUCGCAGAUAAUGAUA
AUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCU
UGGGCCUCCCCCAGCCCCUCCUCCCCUCCUGCACCC
GUACCCCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCG
GCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUCUAG GC_H_MEASLES_
UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGAC 78 D8
UCACUAUAGGGAAUAAGAGAGAAAAGAAGAGUAAG Sequence, NT (5'
AAGAAUAUAAGAGCCACCAUGUCACCACAACGAGAC UTR, ORF, 3'
CGGAUAAAUGCCUUCUACAAAGACAACCCCAUCCUA UTR)
AGGGAAGUAGGAUAGUUUAUUAACAGAGAACAUCUUA Sequence Length:
UGAUUGAUAGACCUUAUGUUUUGCUGGCUGUUCUAU 2065
UCGUCAUGUUUCUGAGCUUGAUCGGGUUGCUAGCCAU
UGCAGGCAUUAGACUUAUCGGGCAGCCAUCUACACC
GCAGAGAUCCAUAAAAGCCUCAGCACCAAUCUGGAUG
UAACUAACUCAUUCGAGCAUCAGGUUAAGGACGUGCU
GACACCACUCUUAAGAUAUCGGUGAUGAAGUGGGC
UUGAGGACACCUCAGAGAUUCACUGACCUAGUGAAGU

UCAUCUCUGACAAGAUUAAAUCCUUAUCCGGACAG
GGAUACGACUUCAGAGAUUCACUUGGUGUAUCAAC
CCGCCAGAGAGAAUCAAAUUGGAUUAUGAUCAAUAC
UGUGCAGAUGUGGCUGCUGAAGAACUCAUGAAUGCA
UUGGUGAACUCAACUCUACUGGAGACCAGGGCAACCA
AUCAGUUCUAGCUGUCUCAAGGGAAACUGCUCAGG
GCCACUACAAUCAGAGGCCAAUUCUCAACAUGUCG
CUGUCCUGUUGGACUUGUAUUUAAGUCGAGGUUAC
AAUGUGUCAUCUAUAGUCACUAUGACAUCCAGGGAA
UGUACGGGGGAACUUAACCUAGUGGAAAAGCCUAAUC
UGAGCAGCAAAGGGUCAGAGUUGUCACAACUGAGCA
UGCACCGAGUGUUUGAAGUAGGGUGUUAUCAGAAAUC
CGGGUUUGGGGGUCUCCGGUAUCCAUAUGACAAACUA
UCUUGAGCAACCAGUCAGUAAUGAUUUCAGCAACUGC
AUGGUGGCUUUGGGGGAGCUCAGUUCGCAGCCCUCU
GUCACAGGGAAGAUUCUAUCACAAUCCCUAUCAGGG
AUCAGGGAAAGGUGUCAGCUUCCAGCUUGUCAAGCUA
GGUGUCUGGAAAUCCCCAACCGACAUGCAAUCCUGGG
UCCCCCUAUCACCGAUGAUCCAGUGAUAGACAGGCU
UUACCUCUCAUCUCACAGAGGCGUUAUCGCUGACAAU
CAAGCAAAAUGGGCUGUCCCGACAACACGGACAGAUG
ACAAGUUGCGAAUGGAGACAUGCUUCCAGCAGGCGUG
UAAGGGUAAAAUCCAAGCACUUUGCGAGAAUCCCGAG
UGGACACCAUUGAAGGAUAACAGGAUCCCUUCAUACG
GGGUCUUGUCUGUUGAUCUGAGUCUGACAGUUGAGC
UUAAAUCAAAAUUGUUUCAGGAUUCGGGCCAUUGA
UCACACACGGUUCAGGGAUGGACCUAUACAAAUCCAA
CCACAACAAUAUGUAUUGGCUGACUAUCCCGCCAAUG
AGAACCUGGCCUUAGGUGUAAUCAACACAUUGGAG
UGGAUACCGAGAUUCAAGGUUAGUCCCAACCUCUUCA
CUGUCCAAUUAAGGAAGCAGGCGAGGACUGCCAUGC
CCACAUAACCUACCUAGGAGGUGGAUGGUGAUGUC
AAACUCAGUCCAAUCUGGUGAUUCUACCUAGGUCUAG
AUCUCCAAUAUGUUCUGGCAACCUACGAUACUUCAG
AGUUGAACAUGCUGUAGUUUAUUACGUUUACAGCCC
AAGCCGCUCAUUUUCUUAUUUAUCCUUUUAGGUUG
CCUGUAAGGGGGGUCCCCAUUGAAUACAAGUGGAA
UGCUCACAUGGGACCAAAAACUCUGGUGCCGUCACU
UCUGUGUGCUUGCGGACUCAGAAUCUGGUGGACAU
UCACUCACUCUGGGAUGGUGGGCAUGGGAGUCAGCUG
CACAGCCACUCGGGAAGAUGGAACCAGCCGCAGAUAG
UGAUAAUAGGCUGGAGCCUCGGUGGCCAAGCUUCUUG
CCCCUUGGGCCUCCCCCAGCCCCUCCUCCCCUCCUG
CACCCGUACCCCGUGGUCUUUGAAUAAAGUCUGAGU GGGCGGC GC_H_MEASLES_
AUGUCACCACAACGAGACCGGAUAAAUGCCUUCUACA 79 D8
AAGACAACCCCAUCCUAAGGGAAGUAGGAUAGUUUAU ORF Sequence, NT
UAACAGAGAACAUCUUAUGAUUGAUAGACCUUAUGU
UUUGCUGGCUGUUCUAUUCGUCAUGUUUCUGAGCUU
GAUCGGGUUGCUAGCCAUUGCAGGCAUUAGACUUCAU
CGGGCAGCCAUCUACCCGCAGAGAUCCAUAAAAGCC
UCAGCACCAUUCUGGAUGUAACUAAUCUAAUCGAGCA
UCAGGUUAAGGACGUGCUGACACCACUCUUCAAGAUC
AUCGGUGAUGAAGUGGGCUUGAGGACACCUCAGAGA
UUCACUGACCUAGUGAAGUUCAUCUCUGACAAGAUUA

AAUUCUUAUCCGGACAGGGAAUACGACUUCAGAGA
UCUCACUUGGUGUAUCAACCCGCCAGAGAGAAUCAA
UUGGAUUAUGAUCAAUACUGUGCAGAUGUGGCUGCU
GAAGAACUCAUGAAUGCAUUGGUGAACUCAACUCUAC
UGGAGACCAGGGCAACCAAUCAGUCCUAGCUGUCUC
AAAGGGAAACUGCUCAGGGCCCACUACAAUCAGAGGC
CAAUUCUCAAAACUUGUCGCUGUCCCUGUUGGACUUGU
AUUUAAGUCGAGGUUACAAUGUGUCAUCUAUAGUCA
CUAUGACAUCCCAGGGAAUGUACGGGGGAACUUACCU
AGUGGAAAAGCCUAAUCUGAGCAGCAAAGGGUCAGA
GUUGUCACAACUGAGCAUGCACCGAGUGUUUGAAGU
AGGUGUUAUCAGAAAUCCGGGUUUGGGGGCUCCGGU
AUUCCAUAUGACAAACUAUCUUGAGCAACCAGUCAGU
AAUGAUUUCAGCAACUGCAUGGUGGCUUUGGGGGAG
CUCAAGUUCGCAGCCCUCUGUCACAGGGAAGAUUCUA
UCACAAUUCCCUAUCAGGGAUCAGGGAAGGUGUCAG
CUUCCAGCUUGUCAAGCUAGGUGUCUGGAAAUCCCCA
ACCGACAUGCAAUCCUGGGUCCCCUAUCAACGGAUG
AUCCAGUGAUAGACAGGCUUUACCUCUCAUCUCACAG
AGGCGUUAUCGCUGACAAUCAAGCAAAAUGGGCUGUC
CCGACAACACGGACAGAUGACAAGUUGCGAAUGGAGA
CAUGCUCUCCAGCAGGCGUGUAAGGGUAAAAUCCAAGC
ACUUUGCGAGAAUCCCGAGUGGACACCAUUGAAGGAU
AACAGGAUUCUUCUAUCGGGGUCUUGUCUGUUGAUC
UGAGUCUGACAGUUGAGCUUAAAAUCAAAAUUGUUU
CAGGAUUCGGGCCAUUGAUACACACGGUUCAGGGAU
GGACCUAUACAAUCCAACCACAACAAUAUGUAUUGG
CUGACUAUCCCGCCAUGAAGAACCUGGCCUUAGGUG
UAAUCAACACAUUGGAGUGGAUACCGAGAUUCAAGG
UUAGUCCCAACCUCUUCACUGUCCAAUUAAGGAAGC
AGGCGAGGACUGCCAUGCCCCAACAUACCUACCUGCG
GAGGUGGAUGGUGAUGUCAAAUCUCAGUCCAAUCUG
GUGAUUCUACCUGGUCAAGAUCCCAAUAUGUUCUGG
CAACCUACGAUACUCCAGAGUUGAACAUUGCUGUAGU
UUUUUACGUUUACAGCCCAAGCCGCUCAUUUUCUUC
UUUUUACCUUUUAGGUUGCCUGUAAGGGGGGUCCCCA
UUGAAUUACAAGUGGAAUGCUUCACAUGGGACCAA
AACUCUGGUGCCGUCACUUCUGUGUCUUGCGGACUC
AGAAUCUGGUGGACAUUACACUCACUCUGGGAUGGU
GGGCAUGGGGAGUCAGCUGCACAGCCACUCGGGAAGAU GGAACCAGCCGCAGAUAG
GC_H_MEASLES_G*GGGAAUAAGAGAGAAAAGAAGAGUAAGAAGAAA 80 D8
UAUAAGAGCCACCAUGUCACCACAACGAGACCGGAUA mRNA Sequence
AAUGCCUUCUACAAAGACAACCCCAUCCUAAGGGAA (assumes T100
GUAGGAUAGUUAUUAACAGAGAACAUCUUAUGAUUG tail)
AUAGACCUUAUGUUUUGCUGGCUGUUCUAUUCGUCA Sequence Length:
UGUUUCUGAGCUUGAUCGGGUUGCUAGCCAUUGCAG 2126
GCAUUAGACUUCUUCGGGCAGCCAUCUACACCCGCAGA
GAUCCAUAAAAGCCUCAGCACCAAUCUGGAUGUAACU
AACUCAUUCGAGCAUCAGGUUAAGGACGUGCUGACAC
CACUCUUCAGAUCUUCGGUGAUGAAGUGGGCUUGA
GGACACCUCAGAGAUUCACUGACCUAGUGAAGUUCAU
CUCUGACAAGAUUAAAUCCUUAUCCGGACAGGGAA
UACGACUUCAGAGAUUCACUUGGUGUAUCAACCCGC
CAGAGAGAAUCAAAUUGGAUUAUGAUCAAUACUGUG

CAGAUGUGGCUGCUGAAGAACUCAUGAAUGCAUUGG
UGAACUCAACUCUACUGGAGACCAGGGCAACCAAUCA
GUUCCUAGCUGUCUCAAGGGAAACUGCUCAGGGCCC
ACUACAAUCAGAGGCCAAUUCUCAAAACAUGUCGCUGU
CCCUGUUGGACUUGUAUUUAAGUCGAGGUUACAAUG
UGUCAUCUAUAGUCACUAUGACAUCCCAGGGAAUGUA
CGGGGGAACUUACCUAGUGGAAAAGCCUAAUCUGAGC
AGCAAAGGGUCAGAGUUGUCACAACUGAGCAUGCACC
GAGUGUUUGAAGUAGGUGUUUUCAGAAAUCCGGGUU
UGGGGGCUCCGGUAUUCCAUAUGACAAACUAUCUUGA
GCAACCAGUCAGUAAUGAUUUCAGCAACUGCAUGGGUG
GCUUUGGGGGAGCUCUAGUUCGCAGCCCUCUGUCACA
GGGAAGAUUCUAUCACAAUUCUUAUCAGGGAUUCAGG
GAAAGGUGUCAGCUUCCAGCUUGUCAAGCUAGGUGUC
UGGAAAUCCCCAACCGACAUGCAAUCCUGGGUCCCCC
UAUCAACGGAUGAUCCAGUGAUAGACAGGCCUUUACCU
CUCAUCUCACAGAGGCGUUUUCGCUGACAAUCAAGCA
AAAUGGGCUGUCCCGACAACACGGACAGAUGACAAGU
UGCGAAUGGAGACAUGCUUCCAGCAGGCGUGUAAGG
GUAAAUAUCAAGCACUUUGCGAGAAUCCCGAGUGGAC
ACCAUUGAAGGAUAACAGGAUUCUUAUCACGGGGUC
UUGUCUGUUGAUCUGAGUCUGACAGUUGAGCUUAAA
AUCAAAAUUGUUUCAGGAUUCGGGCCAUUGAUCACAC
ACGGUUCAGGGAUUGGACCUAUACAAAUCCAACCACAA
CAAUAUGUAUUGGCUGACUAUCCCGCCAAUGAAGAAC
CUGGCCUUAGGUGUAAUCAACACAUUGGAGUGGAUA

CCGAGAUUCAAGGUUAGUCCCAACCUCUUCACUGUUC
CAAUUAAGGAAGCAGGCGAGGACUGCCAUGCCCCAAC
AUACCUACCUGCGGAGGUGGAUGGUGAUGUCAAACUC
AGUUCCAAUCUGGUGAUUCUACCUGGUCAAGAUCUCC
AAUAUGUUCUGGCAACCUACGAUACUUCAGAGUUGA
ACAUGCUGUAGUUUAUUACGUUUACAGCCCAAGCCGC
UCAUUUUCUACUUUUUACCUUUUAGGUUGCCUGUA
AGGGGGGUCCCCAUUGAAUACAAGUGGAAUGCUUC
ACAUGGGACCAAAAACUCUGGUGCCGUCACUUCUGUG
UGCUUGCGGACUCAGAAUCUGGUGGACAUUACACUCA
CUCUGGGAUUGGUGGGCAUGGGAGUCAGCUGCACAGCC
ACUCGGGAAGAUGGAACCAGCCGCAGAUAGUGAUAA
UAGGCUGGAGCCUCGGUGGCCAAGCUUCUUGCCCCU
GGGCCUCCCCCAGCCCCUCCUCCCCUCCUGCACCCG
UACCCCGUGGUCUUUGAAUAAAGUCUGAGUGGGCGG
CAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAUCUAG

TABLE-US-00015 TABLE 14 MeV Amino Acid Sequences SEQ ID Description Sequence NO:
GC_F_MEASLES_MGLKVNVS AVFMAVLLTLQTPAGQIHWGNLSKIGVV 47 B3.1
GIGSASYKVMTRSSHQSLVIKLPNITLLNNCTRVEIA ORF Sequence, AA
EYRLLRRTVLEPIRDALNAMTQNI RPVQSVASSRRHK
RFAGVVLAGAALGVATAAQITAGIALHRSMLNSQAID
NLRASLETTNQAIEAIRQAGQEMILAVQGVQDYINNE
LIPSMNQLSCDLIGQKLGLKLLRYYTEILSLFGPSLRDP
ISAEISIQALS YALGGDINKVLEKLGYSGGDLLGILESR

GIKARITHVDTESYFIVLSIAYPTLSEIKGVIVHRLEGVS
YNIGSQEWYTTVPKYVATQGYLISNFDESSCTFMPEG
TVCSQNALYPMSPLLQECLRGSTKSCARTLVSGSFGN
RFILSQGNLIANCASILCKCYTTGTIINQDPDKILTYIAA
DRCPVVEVNGVTIQVGSRRYPDAVYLHRIDLGPPISE
RLDVGTNLGNAIAKLEDAKELLESDQILRSMKGLSST
SIVYILIAVCLGGLIGIPTLICCCRGRCNKKGEQVGMSR PGLKPDLTGTSKSYVRSL*
GC_F_MEASLES_D8 MGLKVNVSVIFMAVLLTLQTPTGQIHWGNLSKIGVVG 48 ORF Sequence, AA
VGSASYKVMTRSSHQSLVIKLMFNITLLNNCTRVGIAE
YRLLRRTVLEPIRDALNAMTQNIRPVQSVASSRRHHR
FAGVVLAGAALGVATAAQITAGIALHQSMNLNSQAIDN
LRASLETTNQAIEAIRQAGQEMILAVQGVQDYINNELI
PSMNQLSCDLIGQKLGKLLRYYTEILSLFGPSLRDPIS
AEISIQALSALGGDINKVLEKLGYSGGDLLGILESRI
KARITHVDTESYFIVLSIAYPTLSEIKGVIVHRLEGVSY
NIGSQEWYTTVPKYVATQGYLISNFDESSCTFMPEGT
VCSQNALYPMSPLLQECLRGSTKSCARTLVSGSFGNR
FILSQGNLIANCASILCKCYTTGTIINQDPDKILTYIAAD
HCPVVEVNGVTIQVGSRRYPDAVYLHRIDLGPPISE
LDVGTNLGNAIAKLEDAKELLESDQILRSMKGLSSTS
IVYILIAVCLGGLIGIPALICCCRGRCNKKGEQVGMSRP GLKPDLTGTSKSYVRSL*
GC_H_MEASLES_B3 MSPQRDRINAFYKDNPHYKGSRIVINREHLMIDRPYVL 49 ORF Sequence, AA
LAVLFVFMFLSLIGLLAIAGIRLHRAAIYTAIEIHKSLSTN
LDVTNSIEHQVKDVLTPLFKIIIGDEVGLRTPQRFTDLV
KFISDKIKFLNPDREYDFRDLTWCINPPERIKLDYDQY
CADVAAEELMNALVNSTLLETTRTTTQFLAVSKGNCS
GPTTIRGQFNSMSLSLLDLYLGRGYNVSSIVTMTSQG
MYGGTYLVEKPNLNSKGESELSQLSMYRVFEVGVIRNP
GLGAPVFHMTNYFEQPVSNGLGNCMVALGELKLAAL
CHGDDSIIPYQGSQKGVSFQLVKLG VVKSPTDMQSW
VPLSTDDPVDRLYLSSHARGVIADNQAQWAVPTTRT
DDKLRMETCFQQACKGKIQALCENPEWVPLKDNRIPS
YGVLSVDLSLTVELKIKIASGFGPLITHGSGMDLYKSN
CNNVYWLTIIPMRNLALGVINTLEWIPRFK VSPNLFTV
PIKEAGEDCHAPTYLPAEVDGDVKLSSNLVILPGQDL
QYVLATYDTSRVEHAVVYVYSPSRFSFYFPFRLPIK
GVPIELQVECFTWDQKLWCRHFCVLADSESGGLITHS GMVGMGVSCATREDGTNR*
GC_H_MEASLES_D8 MSPQRDRINAFYKDNPHPKGSRIVINREHLMIDRPYVL 50 ORF Sequence, AA
LAVLFVFMFLSLIGLLAIAGIRLHRAAIYTAIEIHKSLSTN
LDVTNSIEHQVKDVLTPLFKIIIGDEVGLRTPQRFTDLV
KFISDKIKFLNPDREYDFRDLTWCINPPERIKLDYDQY
CADVAAEELMNALVNSTLLETTRATNQFLAVSKGNCS
GPTTIRGQFNSMSLSLLDLYLSRGYNVSSIVTMTSQGM
YGGTYLVEKPNLSSKGESELSQLSMHRVFEVGVIRNPG
LGAPVFHMTNYLEQPVSNDFSNMVALGELKFAALC
HREDSITIPYQGSQKGVSFQLVKLG VVKSPTDMQSW
VPLSTDDPVIDRLYLSSHARGVIADNQAQWAVPTTRTD
DKLRMETCFQQACKGKIQALCENPEWVPLKDNRIPSY
GVLSVDLSLTVELKIKIVSGFGPLITHGSGMDLYKSNH
NNMYWLTIIPMKNLALGVINTLEWIPRFK VSPNLFTV
PIKEAGEDCHAPTYLPAEVDGDVKLSSNLVILPGQDL
QYVLATYDTSRVEHAVVYVYSPSRFSFYFPFRLPV
RGVPIELQVECFTWDQKLWCRHFCVLADSESGGHITH SGMVGMGVSCATREDGTSRR*

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 fusion 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 Flagellin Nucleic Acid Sequences SEQ ID Name Sequence NO: NT (5'

TCAAGCTTTTGGACCCTCGTACAGAAGCTAATACGACTCACTAT 51 UTR, ORF,

AGGGAATAAGAGAGAAAAGAAGAGTAAGAAGAAATATAAG 3' UTR)

AGCCACCATGGCACAAGTCATTAATACAAACAGCCTGTGCTG
 TTGACCCAGAATAACCTGAACAAATCCCAGTCCGCACTGGGCA
 CTGCTATCGAGCGTTTGTCTTCCGGTCTGCGTATCAACAGCGCG
 AAAGACGATGCGGCAGGACAGGCGATTGCTAACCGTTTTACCG
 CGAACATCAAAGGTCTGACTCAGGCTTCCCGTAACGCTAACGA
 CGGTATCTCCATTGCGCAGACCACTGAAGGCGCGCTGAACGAA
 ATCAACAACAACCTGCAGCGTGTGCGTGAACCTGGCGGTTTCAGT
 CTGCGAATGGTACTAACTCCCAGTCTGACCTCGACTCCATCCAG
 GCTGAAATCACCCAGCGCCTGAACGAAATCGACCGTGTATCCG
 GCCAGACTCAGTTC AACGGCGTGAAAGTCCTGGCGCAGGACAA
 CACCCTGACCATCCAGGTTGGTGCCAACGACGGTGAAACTATC
 GATATTGATTTAAAAGAAATCAGCTCTAAAACACTGGGACTTG

ATAAGCTTAATGTCCAAGATGCCTACACCCCGAAAGAACTGC
TGTAACCGTTGATAAACTACCTATAAAAATGGTACAGATCCT
ATTACAGCCCAGAGCAATACTGATATCCAAACTGCAATTGGCG
GTGGTGCACACGGGGGTTACTGGGGCTGATATCAAATTTAAAGA
TGGTCAATACTATTTAGATGTTAAAGGCGGTGCTTCTGCTGGTG
TTTATAAAGCCACTTATGATGAACTACAAAGAAAGTTAATAT
TGATACGACTGATAAACTCCGTTGGCAACTGCGGAAGCTACA
GCTATTCGGGGAACGGCCACTATAACCCACAACCAAATTGCTG
AAGTAACAAAAGAGGGTGTGATACGACCACAGTTGCGGCTCA
ACTTGCTGCAGCAGGGGTTACTGGCGCCGATAAGGACAATACT
AGCCTTGTAAACTATCGTTTGAGGATAAAAACGGTAAGGTTA
TTGATGGTGGCTATGCAGTGAAAATGGGCGACGATTTCTATGC
CGCTACATATGATGAGAAAACAGGTGCAATTACTGCTAAAACC
ACTACTTATACAGATGGTACTGGCGTTGCTCAAACCTGGAGCTGT
GAAATTTGGTGGCGCAAATGGTAAATCTGAAGTTGTTACTGCT
ACCGATGGTAAGACTTACTTAGCAAGCGACCTTGACAAACATA
ACTTCAGAACAGGCGGTGAGCTTAAAGAGGTTAATACAGATAA
GACTGAAAACCCACTGCAGAAAATTGATGCTGCCTTGGCACAG
GTTGATACACTTCGTTCTGACCTGGGTGCGGTTTCAGAACCGTTT
CAACTCCGCTATACCAACCTGGGCAATACCGTAAATAACCTG
TCTTCTGCCCCTAGCCGTATCGAAGATTCCGACTACGCAACCGA
AGTCTCCAACATGTCTCGCGCGCAGATTCTGCAGCAGGCCGGT
ACCTCCGTTCTGGCGCAGGCGAACCAGGTTCCGCAAAACGTCC
TCTCTTTACTGCGTTGATAATAGGCTGGAGCCTCGGTGGCCATG
CTTCTTGCCCCTTGGGCCTCCCCCAGCCCCTCCTCCCCTTCTG
CACCCGTACCCCGTGGTCTTTGAATAAAGTCTGAGTGGGCGG C ORF
ATGGCACAAGTCATTAATACAAACAGCCTGTCGCTGTTGACCC 52 Sequence,
AGAATAACCTGAACAAATCCCAGTCCGCACTGGGCACTGCTAT NT
CGAGCGTTTGTCTTCCGGTCTGCGTATCAACAGCGCGAAAGAC
GATGCGGCAGGACAGGCGATTGCTAACCGTTTTACCGCGAACA
TCAAAGGTCTGACTCAGGCTTCCCGTAACGCTAACGACGGTAT
CTCCATTGCGCAGACCACTGAAGGCGCGCTGAACGAAATCAAC
AACAACCTGCAGCGTGTGCGTGAACCTGGCGGTTTCAGTCTGCGA
ATGGTACTAACTCCCAGTCTGACCTCGACTCCATCCAGGCTGAA
ATCACCCAGCGCCTGAACGAAATCGACCGTGTATCCGGCCAGA
CTCAGTTCAACGGCGTGAAAGTCTGGCGCAGGACAACACCCT
GACCATCCAGGTTGGTGCCAACGACGGTGAAACTATCGATATT
GATTTAAAAGAAATCAGCTCTAAAACACTGGGACTTGATAAGC
TTAATGTCCAAGATGCCTACACCCCGAAAGAACTGCTGTAAC
CGTTGATAAACTACCTATAAAAATGGTACAGATCCTATTACA
GCCAGAGCAATACTGATATCCAAACTGCAATTGGCGGTGGTG
CAACGGGGGTTACTGGGGCTGATATCAAATTTAAAGATGGTCA
ATACTATTTAGATGTTAAAGGCGGTGCTTCTGCTGGTGTTTATA
AAGCCACTTATGATGAACTACAAAGAAAGTTAATATTGATAC
GACTGATAAACTCCGTTGGCAACTGCGGAAGCTACAGCTATT
CGGGGAACGGCCACTATAACCCACAACCAAATTGCTGAAGTAA
CAAAGAGGGTGTGATACGACCACAGTTGCGGCTCAACTTGC
TGCAGCAGGGGTTACTGGCGCCGATAAGGACAATACTAGCCTT
GTAAAACCTATCGTTTGAGGATAAAAACGGTAAGGTTATTGATG
GTGGCTATGCAGTGAAAATGGGCGACGATTTCTATGCCGCTAC
ATATGATGAGAAAACAGGTGCAATTACTGCTAAAACCACTACT
TATACAGATGGTACTGGCGTTGCTCAAACCTGGAGCTGTGAAAT
TTGGTGGCGCAAATGGTAAATCTGAAGTTGTTACTGCTACCGAT
GGTAAGACTTACTTAGCAAGCGACCTTGACAAACATAACTTCA

GAACAGGCGGTGAGCTTAAAGAGGTTAATACAGATAAGACTG
AAAACCCACTGCAGAAAATTGATGCTGCCTTGGCACAGGTTGA
TACTTTCGTTCTGACCTGGGTGCGGTTTCAGAACCGTTTCAACT
CCGCTATCACCAACCTGGGCAATACCGTAAATAACCTGTCTTCT
GCCCGTAGCCGTATCGAAGATTCCGACTACGCAACCGAAGTCT
CCAACATGTCTCGCGCGCAGATTCTGCAGCAGGCCGGTACCTC
CGTTCTGGCGCAGGCGAACCAGGTTCCGCAAACGTCCTCTCTT TACTGCGT mRNA

G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAAUAUAA 53 Sequence
GAGCCACCAUGGCACAAGUCAUUAUACAAACAGCCUGUCGC (assumes
UGUUGACCCAGAAUAACCUGAACAAAUCCAGUCCGCACUGG T100 tail)

GCACUGCUAUCGAGCGUUUGUCUUCGGGUCUGCGUAUCAACA
GCGCGAAAGACGAUGCGGCAGGACAGGCGAUUGCUAACCGUU
UUACCGCGAACAUCAAGGUCUGACUCAGGCUUCCCGUAACG
CUAACGACGGUAUCUCCAUUGCGCAGACCACUGAAGGCGCGC
UGAACGAAAUCAACAACAACCUGCAGCGUGUGCGUGAACUGG
CGGUUCAGUCUGCGAAUGGUACUAAUCUCCAGUCUGACCUUG
ACUCCAUCCAGGCUGAAAUCACCCAGCGCCUGAACGAAAUCG
ACCGUGUAUCCGGCCAGACUCAGUUAACGGCGUGAAAGUCC
UGGCGCAGGACAACCCUGACCAUCCAGGUUGGUGCCAACG
ACGGUGAAACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUCU
AAAACACUGGGACUUGAUAAGCUUAAUGUCCAAGAUGCCUAC
ACCCCGAAAGAAACUGCUGUAACCGUUGAUAUAAACUACCUAU
AAAAAUGGUACAGAUCUUAUACAGCCCAGAGCAAUACUGAU
AUCCAACUGCAAUUGGCGGUGGUGCAACGGGGGUUACUGG
GGCUGAUUCAAAUUUAAAGAUGGUCAAUACUAAUUAGAUG
UUAAAGGCGGUGCUUCUGCUGGUGUUUAUAAAGCCACUUAU
GAUGAAACUACAAAGAAAGUUAUAUUGAUACGACUGAUAA
AACUCCGUUGGCAACUGCGGAAGCUACAGCUAUUCGGGGAAC
GGCCACUUAACCCACAACCAAUUGCUGAAGUAACAAAAGA
GGGUGUUGAUACGACCACAGUUGCGGCUCAACUUGCUGCAGC
AGGGGUUACUGGCGCCGAUAAGGACAAUACUAGCCUUGUAA
AACUAUCGUUUGAGGAUAAAACGGUAAGGUUAUUGAUGGU
GGCUAUGCAGUGAAAUGGGCGACGAUUUCUUAUGCCGCUACA
UAUGAUGAGAAAACAGGUGCAAUUAUCUGCUAAAACACUAC
UUUAUACAGAUGGUACUGGCGUUGCUCAAACUGGAGCUGUGA
AAUUUGGUGGCGCAAUUGGUAAAUCUGAAGUUGUUAUCUGCU
ACCGAUGGUUAGACUUAUCUAGCAAGCGACCUUGACAAACAU
AACUUCAGAACAGGCGGUGAGCUUAAAGAGGUUAUUAACAGA
UAAGACUGAAAACCCACUGCAGAAAUAUGAUGCUGCCUUGGC
ACAGGUUGAUACACUUCGUUCUGACCUUGGGUGCGGUUCAGAA
CCGUUUCAACUCCGCUAUCACCAACCUGGGCAAUACCGUAAA
UAACCUGUCUUCUGCCCGUAGCCGUUAUCGAAGAUUCCGACUA
CGCAACCGAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGCA
GCAGGCCGGUACCUCGUCUUGGCGCAGGCGAACCCAGGUUCC
GCAAACGUCUCUCUUAUCUGCGUUGAUAAUAGGCUGGAGC
CUCGGUGGCCAUGCUUCUUGCCCCUUGGGCCUCCCCCAGCC
CCUCCUCCCCUUCUGCACCCCGUACCCCGUGGUUCUUUGAAU
AAAGUCUGAGUGGGCGGCAAAAAAAAAAAAAAAAAAAAAAAAAA
AAA
AAAUCUAG

UCAAGCUUUUGGACCCUCGUACAGAAGCUAAUACGACUCACU 81 UTR, ORF,
AUAGGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAAUAUA 3' UTR)
AGAGCCACCAUGGCACAAGUCAUUAUACAAACAGCCUGUCG
CUGUUGACCCAGAAUAACCUGAACAAAUCCAGUCCGCACUG

GGCACUGCUAUCGAGCGUUUGUCUUCCGGUCUGCGUAUCAAC
AGCGCGAAAGACGAUGCGGCAGGACAGGCGAUUUGCUAACCGU
UUUACCGCGAACAUCAAAGGUCUGACUCAGGCUUCCCGUAAC
GCUAACGACGGUAUCUCCAUUGCGCAGACCACUGAAGGCGCG
CUGAACGAAAUCAACAACAACCUGCAGCGUGUGCGUGAACUG
GCGGUUCAGUCUGCGAAUGGUACUAAUCUCCAGUCUGACCUC
GACUCCAUCCAGGCUGAAAUCACCCAGCGCCUGAACGAAAU
GACCGUGUAUCCGGCCAGACUCAGUUCAACGGCGUGAAAGUC
CUGGCGCAGGACAACACCCUGACCAUCCAGGUUGGUGCCAAC
GACGGUGAAACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUC
UAAAACACUGGGACUUGAUAAAGCUAAUGUCCAAGAUGCCU
ACACCCCGAAAGAAACUGCUGUAACCGUUGAUAAAACUACCU
AUAAAAAUGGUACAGAUCUUAUACAGCCCAGAGCAAUACUG
AUAUCCAAACUGCAAUUGGCGGUGGUGCAACGGGGGUUACU
GGGGCUGAUUAUCAAUUUAAAAGAUGGUCAAUACUUAUUAGA
UGUUAAAGGCGGUGCUUCUGCUGGUGUUUAUAAAGCCACUU
AUGAUGAAACUACAAAGAAAGUUAUAUUGAUACGACUGAU
AAAACUCCGUUGGCAACUGCGGAAGCUACAGCUAUUCGGGGA
ACGGCCACUAUAACCCACAACCAAUUGCUGAAGUAACAAA
GAGGGUGUUGAUACGACCACAGUUGCGGCUCAACUUGCUGCA
GCAGGGGUUACUGGCGCCGAUAAGGACAAUACUAGCCUUGUA
AAACUAUCGUUUGAGGAUAAAACGGUAAGGUUAUUGAUGG
UGGCUAUGCAGUGAAAUGGGCGACGAUUUCU AUGCCGCUAC
AUAUGAUGAGAAAACAGGUGCAAUUACUGCUAAAACCACUA
CUUAUACAGAUUGGUACUGGCGUUGCUCAAACUGGAGCUGUG
AAAUUUGGUGGCGCAAUUGGUAAAUCUGAAGUUGUUACUGC
UACCGAUGGUAAAGACUUAUUAGCAAGCGACCUUGACAAACA
UAACUUCAGAACAGGCGGUGAGCUUAAAGAGGUUAAUACAG
AUAAGACUGAAAACCCACUGCAGAAAUAUGAUGCUGCCUUGG
CACAGGUUGAUACACUUCGUUCUGACCUGGGUGCGGUUCAGA
ACCGUUUCAACUCCGCUAUCACCAACCUGGGCAAUACCGUAA
AUAACCUGUCUUCUGCCCUGAGCCGUAUCGAAGAUUCCGACU
ACGCAACCGAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGC
AGCAGGCCGGUACCUCCGUUCUGGCGCAGGCGAACCAGGUUC
CGCAAACGUCCUCUCUUUACUGCGUUGAUAAUAGGCUGGAG
CCUCGGUGGCCAUGCUCUUGCCCCUUGGGCCUCCCCCAGC
CCUCCUCCCCUUCUGCACCCGUACCCCCGUGGUCUUUGAA UAAAGUCUGAGUGGGCGGC ORF
AUGGCACAAGUCAUUAUAACAACAGCCUGUCGUCUGUUGACC 82 Sequence,
CAGAAUAACCUGAACAAAUCCAGUCCGCACUGGGCACUGCU NT
AUCGAGCGUUUGUCUUCGGUCUGCGUAUCAACAGCGCGAAA
GACGAUGCGGCAGGACAGGCGAUUUGCUAACCGUUUACCGCG
AACAUCAAAGGUCUGACUCAGGCUUCCCGUAACGCUAACGAC
GGUAUCUCCAUUGCGCAGACCACUGAAGGCGCGCUGAACGAA
AUCAACAACAACCUGCAGCGUGUGCGUGAACUGGCGGUUCAG
UCUGCGAAUUGGUACUAACUCCAGUCUGACCUCGACUCCAUC
CAGGCUGAAAUCACCCAGCGCCUGAACGAAAUCGACCGUGUA
UCCGGCCAGACUCAGUUAACGGCGUGAAAGUCCUGGCGCAG
GACAACACCCUGACCAUCCAGGUUGGUGCCAACGACGGUGAA
ACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUCUAAAACACU
GGGACUUGAUAAAGCUUAAUGUCCAAGAUGCCUACACCCCGAA
AGAAACUGCUGUAACCGUUGAUAAAACUACCUAUAAAAAUG
GUACAGAUCCUAUUACAGCCCAGAGCAAUACUGAUAUCCAAA
CUGCAAUUGGCGGUGGUGCAACGGGGGUUACUGGGGCUGAU
AUCAAUUUAAAAGAUGGUCAAUACUUAUUAGAUGUUAAAGG

CGGUGCUUCUGCUGGUGUUUAUAAAGCCACUUAUGAUGAAA
CUACAAAGAAAGUUAUUAUUGAUACGACUGAUAAAACUCCG
UUGGCAACUGCGGAAGCUACAGCUAUUCGGGGAACGGCCACU
AUAACCCACAACCAAUUGCUGAAGUAACAAAAGAGGGUGU
UGAUACGACCACAGUUGCGGCUCAACUUGCUGCAGCAGGGGU
UACUGGGCGCCGAUAAGGACAAUACUAGCCUUGUAAAACUAUC
GUUUGAGGAUAAAACGGUAAGGUUAUUGAUGGUGGCUAUG
CAGUGAAA AUGGGCGACGAUUUCUAUGCCGCUACAUAUGAU
GAGAAAACAGGUGCAAUACUGCUAAAACCACUACUUAUACA
GAUGGUACUGGCGUUGCUCAAACUGGAGCUGUGAAAUUUGG
UGGCGCAA AUGGUAAAUCUGAAGUUGUACUGCUACCGAUG
GUAAGACUUACUUAGCAAGCGACCUUGACAAACAUAACUUCA
GAACAGGCGGUGAGCUUAAAGAGGUUAAUACAGAUAAAGACU
GAAAACCCACUGCAGAAAAUUGAUGCUGCCUUGGCACAGGUU
GAUACACUUCGUUCUGACCUGGGUGCGGUUCAGAACCGUUUC
AACUCCGCUAUCACCAACCUGGGCAAUACCGUAAAUAACCG
UCUUCUGCCCGUAGCCGUUUCGAAGAUUCCGACUACGCAACC
GAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGCAGCAGGCC
GGUACCUCG UUCUGGGCGCAGGGCGAACCAGGUUCCGCAAAC GUCCUCUCUUUACUGCGU
mRNA G*GGGAAAUAAGAGAGAAAAGAAGAGUAAGAAGAAAUAUAA 83 Sequence
GAGCCACCAUGGCACAAGUCAUUAUACAACAGCCUGUCGC (assumes
UGUUGACCCAGAAUAACCUGAACAAAUCCAGUCCGCACUGG T100 tail)
GCACUGCUAUCGAGCGUUUGUCUUCGGGUCUGCGUAUCAACA
GCGCGAAAGACGAUGCGGCAGGACAGGGCGAUUGCUAACCGUU
UUACCGCGAACAUCAAAAGGUCUGACUCAGGCUUCCCGUAACG
CUAACGACGGUAUCUCCAUUGCGCAGACCACUGAAGGCGCGC
UGAACGAAAUCAACAACAACCUGCAGCGUGUGCGUGAACUGG
CGGUUCAGUCUGCGAAUGGUACUAACUCCAGUCUGACCUCG
ACUCCAUCCAGGCUGAAAUCACCCAGCGCCUGAACGAAAUCG
ACCGUGUAUCCGGCCAGACUCAGUUCAACGGCGUGAAAGUCC
UGGCGCAGGACAACACCCUGACCAUCCAGGUUGGUGCCAACG
ACGGUGAAACUAUCGAUAUUGAUUUAAAAGAAAUCAGCUCU
AAAACACUGGGACUUGAUAAAGCUUAAUGUCCAAGAUGCCUAC
ACCCCGAAAGAAACUGCUGUAACCGUUGAUAAAACUACCUAU
AAAAUUGGUACAGAUCCUAUUACAGCCCAGAGCAAUACUGAU
AUCCAACUGCAAUUGGCGGUGGUGCAACGGGGGUUACUGG
GGCUGAUAUCAAUUUAAAGAUGGUCAAUACUAAUUAGAUG
UUAAAGGCGGUGCUUCUGCUGGUGUUUAUAAAGCCACUUAU
GAUGAAACUACAAGAAAGUUAUAUUGAUACGACUGAUAA
AACUCCGUUGGCAACUGCGGAAGCUACAGCUAUUCGGGGAAC
GGCCACUAUAACCCACAACCAAUUGCUGAAGUAACAAAAGA
GGGUGUUGAUACGACCACAGUUGCGGCUCAACUUGCUGCAGC
AGGGGUUACUGGCGCCGAUAAGGACAAUACUAGCCUUGUAA
AACUAUCGUUUGAGGAUAAAACGGUAAGGUUAUUGAUGGU
GGCUAUGCAGUGAAA AUGGGCGACGAUUUCUAUGCCGCUACA
UAUGAUGAGAAAACAGGUGCAAUACUGCUAAAACCACUAC
UUAUACAGAUGGUACUGGCGUUGCUCAAACUGGAGCUGUGA
AAUUUGGUGGGCGCAA AUGGUAAAUCUGAAGUUGUACUGCU
ACCGAUGGUAAAGACUUAACUUAAGCAAGCGACCUUGACAAACAU
AACUUCAGAACAGGCGGUGAGCUUAAAGAGGUUAAUACAGA
UAAGACUGAAAACCCACUGCAGAAAAUUGAUGCUGCCUUGGC
ACAGGUUGAUACACUUCGUUCUGACCUGGGUGCGGUUCAGAA
CCGUUUCAACUCCGCUAUCACCAACCUGGGCAAUACCGUAAA
UAACCUGUCUUCUGCCCGUAGCCGUUUCGAAGAUUCCGACUA

CGCAACCGAAGUCUCCAACAUGUCUCGCGCGCAGAUUCUGCA
 GCAGGCCGGUACCUCUCCGUUCUGGCGCAGGCCGAACCAGGUUCC
 GAAAACGUCCUCUCUUACUGCGUUGAUAAUAGGCUGGAGC
 CUCGGUGGCCAUGCUUCUUGCCCCUUGGGCCUCCCCCAGCC

CCUCCUCCCCUUCUGCACCCGUACCCCGUGGUCUUUGAAU
 AAAGUCUGAGUGGGCGGCAAAAAAAAAAAAAAAAAAAAAAA
 AAA
 AAA
 AAAUCUAG

TABLE-US-00018 TABLE 17 Flagellin Amino Acid Sequences SEQ ID Name Sequence NO: ORF
 MAQVINTNSLSLLTQNNLNKSQSALGTAIERLSSGLRINSKDDAA 54 Sequence,

GQAIANRFTANIKGLTQASRNANDGISIAQTTEGALNEINNNLQRV AA
 RELAVQSANGTNSQSDDLDSIQAEITQRLNEIDRVSGQTQFNGVKVL
 AQDNTLTIQVGANDGETIDIDLKEISSKTLGLDKLNVQDAYTPKET
 AVTVDKTTYKNGTDPITAQSNTDIQTAIGGGATGVTGADIKFKDG
 QYYLDVKGASAGVYKATYDETTKKNIDTTDKTPLATAEATAI
 RGTATITHNQIAEVTKEGVDTTTVAQAALAAAGVTGADKDNLSLV
 KLSFEDKNGKVIDGGYAVKMGDDFYAATYDEKTGAITAKTTTYT
 DGTGVAQTGAVKFGGANGKSEVVTATDGKTYLASDLKHNFRF
 GGELKEVNTDKTENPLQKIDAALAQVDTLRSDLGAVQNRFNSAIT
 NLGNTVNNLSSARSRIEDSDYATEVSNMSRAQILQQAGTSVLAQA NQVPQNVLSLLR Flagellin-

MAQVINTNSLSLLTQNNLNKSQSALGTAIERLSSGLRINSKDDAA 55 GS linker-
 GQAIANRFTANIKGLTQASRNANDGISIAQTTEGALNEINNNLQRV circumspor-
 RELAVQSANSTNSQSDDLDSIQAEITQRLNEIDRVSGQTQFNGVKVL ozoite
 AQDNTLTIQVGANDGETIDIDLKQINSQTLGLDTLNVQQKYKVS protein
 TAATVTGYADTTIALDNSTFKASATGLGGTDQKIDGDLKFDDTT (CSP)

KYYAKVTVTGGTGKDGYYEVSVDKTNGEVTLAGGATSPLTGGLP
 ATATEDVKNVQVANADLTEAKAALTAAGVTGTASVVKMSYTDN
 NGKTIDGGLAVKVGDDYYSATQNKDGSISINTTKYTADDGTSKTA
 LNKLGGADGKTEVVSIGGKTYAASKAEGHNFKAQPDLAEEAATT
 TENPLQKIDAALAQVDTLRSDLGAVQNRFNSAITNLGNTVNNLTS
 ARSRIEDSDYATEVSNMSRAQILQQAGTSVLAQANQVPQNVLSLL
 RGGGGSGGGGSMAPDPNANPNANPNANPNANPNANPNANPNANPN
 NPANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPN
 ANPNANPNKNNQGNGQGHNMPNDPNRNVN DENANANN AVKNNN
 NEEPSDKHIEQYLKIKNSISTEWSPCSVTCGNGIQVRIKPGSANKP
 KDEL DYENDIEK KICKMEKCSSVFNVVNS Flagellin-

M MAPDPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPN 56 RPVT
 ANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNANPNKNN linker-
 QGNGQGHNMPNDPNRNVN DENANANN AVKNNN NEEPSDKHIEQ circumspor-
 LKKIKNSISTEWSPCSVTCGNGIQVRIKPGSANKPKDEL DYENDIEK ozoite
 KICKMEKCSSVFNVVNSRPVTMAQVINTNSLSLLTQNNLNKSQSA protein
 LGTAIERLSSGLRINSKDDAAGQAIANRFTANIKGLTQASRNAND (CSP)

GISIAQTTEGALNEINNNLQRVRELAVQSANSTNSQSDDLDSIQAEIT
 QRLNEIDRVSGQTQFNGVKVLAQDNTLTIQVGANDGETIDIDLKQI
 NSQTLGLDTLNVQQKYKVS DTAAATVTGYADTTIALDNSTFKASAT
 GLGGTDQKIDGDLKFDDTTGKYYAKVTVTGGTGKDGYYEVSVD
 KTNGEVTLAGGATSPLTGGLPATATEDVKNVQVANADLTEAKAA
 LTAAGVTGTASVVKMSYTDNNGKTIDGGLAVKVGDDYYSATQ
 KDGSISINTTKYTADDGTSKTALNKLGGADGKTEVVSIGGKTYAA
 SKAEGHNFKAQPDLAEEAATTENPLQKIDAALAQVDTLRSDLG
 AVQNRFN SAITNLGNTVNNLTSARSRIEDSDYATEVSNMSRAQILQ QAGTSVLAQANQVPQNVLSLLR

TABLE-US-00019 TABLE 18 Human Metapneumovirus Mutant Amino Acid Sequences SEQ ID Strain
Sequence NO: HMPV_SC_MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEV
85 DSCAV1_4MMV_DVENLTCSDGPSLIKTELDTKSALRELKTVSADQLAREEQIENPGSGSFVLG
AIALGVAAAAAVTAGVAICKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LAFVRELKDFVSKNLTRALNKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFIL
CGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWY
CQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYP
KVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQ
DADTVTIDNTVYQLSKVEGEQHVIVKGRPVSSSFDPIKFPEDQFNVALDQVFE
NIENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIKKTKKPTG APPELSGVTNNGFIPHN
HMPV_SC_MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEV 86
DSTRIC_4MMV_DVENLTCSDGPSLIKTELDTKSALRELKTVSADQLAREEQIENPGSGSFVLG
AIALGVAAAAAVTAGVAICKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFIL
CGVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWY
CQNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYP
KVSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQ
DADTVTIDNTVYQLSKVEGEQHVIVKGRPVSSSFDPIKFPEDQFNVALDQVFE
NIENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIKKTKKPTG APPELSGVTNNGFIPHN
HMPV_SC_MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEV 87
DM_Krarup_DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG T74LD185P
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFIL
GVYGGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADTVTIDNTVYQLSKVEGEQHVIVKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIKKTKKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEV 88
TM_Krarup_DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG
T74LD185PD454N AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFIL
GVYGGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADTVTIDNTVYQLSKVEGEQHVIVKGRPVSSSFDPIKFPENQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIKKTKKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEV 89
4M_Krarup_DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG
T74LS170LD185P AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFIL
GVYGGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYACLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPCK
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADTVTIDNTVYQLSKVEGEQHVIVKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIKKTKKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEV 90
5M_Krarup_DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG
T74LS170LD185PD454N AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV

LATAVRELKDFVLKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPENQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MS WKVVIIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLPVG 91
DM_Krarup_DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG E51PT74L
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MS WKVVIIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLPVG 92
TM_Krarup_DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG
E51PT74LD454N AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPENQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MS WKVVIIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG 93
StabilizeAlpha DVENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG T74L
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MS WKVVIIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG 94
StabilizeAlpha_DLENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG V55L
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVIIIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MS WKVVIIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG 95
StabilizeAlpha_DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG S170L
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVLKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC

VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVILIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_SC_MS WKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG 96
StabilizeAlpha_DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG T174W
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLWRANKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETR GDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVILIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_SC_4M_MS WKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG 97
Stabilize_DLENLTCSDGPSLIKTELDLLKSALRELKTVSADQLAREEQIENPGSGSFVLG Alpha_
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV V55LT74L5170LT174W
LATAVRELKDFVLKNLWRANKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETR GDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVILIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_MS WKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLPVG 98 ProlineStab_
DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG E51P
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETR GDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVILIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_MS WKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG 99 ProlineStab_
DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG D185P
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIPDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETR GDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVILIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_MS WKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG 100 ProlineStab_
DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG D183P
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCPIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNYA CLLREDQGWYC
QNAGSTVYYPNEKDCETR GDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIIVILIAVLGSSMILVSIFIIIKTKTKPTGA PPELSGVTNNGFIPHN
HMPV_MS WKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRTGWYTNVFTLEVG 101 ProlineStab_

DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG E131P
AIALGVAAAAAVTAGVAIAKTIRLPSEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNACLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIVILIIVLGSSMILVSIFIIIKTKKPTGA PPELSGVTNNGFIPHN
HMPV_ MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG 102 ProlineStab_

DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG D447P
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNACLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFPPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIVILIIVLGSSMILVSIFIIIKTKKPTGA PPELSGVTNNGFIPHN
HMPV_ MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG 103

TrimerRepulsion DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG D454N
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNACLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPENQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIVILIIVLGSSMILVSIFIIIKTKKPTGA PPELSGVTNNGFIPHN
HMPV_ MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG 104

TrimerRepulsion DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG E453N
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQFNRRFLNVVRQFS
DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNACLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPQDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIVILIIVLGSSMILVSIFIIIKTKKPTGA PPELSGVTNNGFIPHN
HMPV_ MSWKVVIIFSLITPQHGLKESYLEESCSTITEGYLSVLRGTWYTNVFTLEVG 105 Stabilize

DVENLTCSDGPSLIKTELDLTKSALRELKTVSADQLAREEQIENPGSGSFVLG AlphaF196W
AIALGVAAAAAVTAGVAIAKTIRLESEVTAINNALKKTNEAVSTLGNGVRV
LATAVRELKDFVSKNLTRAINKNKCDIDDLKMAVSFSQWNRFLNVVRQFS

DNAGITPAISLDLMTDAELARAVPNMPTSAGQIKLMLLENRAMVRRKGFGLI
GVYGSSVIYMVQLPIFGVIDTPCWIVKAAPSCSEKKGNACLLREDQGWYC
QNAGSTVYYPNEKDCETRGDHVFCDTAAGINVAEQSKECNINISTTNYPC
VSTGRHPISMVALSPLGALVACYKGVSCSIGSNRVGIKQLNKGCSYITNQD
ADVTIDNTVYQLSKVEGEQHVIKGRPVSSSFDPIKFPEDQFQVALDQVFENI
ENSQALVDQSNRILSSAEKGTGFIIVILIIVLGSSMILVSIFIIIKTKKPTGA PPELSGVTNNGFIPHN

TABLE-US-00020 TABLE 19 Human Metapneumovirus Mutant Nucleic Acid Sequences SEQ ID Strain
Nucleic Acid Sequence NO: HMPV_SC_ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA
106 DSCAV1_4MMV CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT

CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCTGCAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CTTTGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCCTGAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAGGCTTCGGCATTCTGTGTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTT
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCAACGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAAC HMPV_SC_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 107 DSTRIC_4MMV
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCTGCAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC

GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAGGCTTCGGCATTCTGTGTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATAACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCT
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGCACCAGTGGCATGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC HMPV_SC_DM_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 108 Krarup_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74LD185P
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTGAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA
CCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGCGG
TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA
TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA
GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC
CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC
GGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCAG
CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG
ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG
CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA
CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC
TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC
GTGTTCTGTGATAACCGCCGCTGGAATCAATGTGGCCGAGC
AGAGCAAAGAGTGCAACATCAACATCAGCACCACCAACT
ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT

GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATAACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAAC
HMPV_SC_TM_ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 109 Krarup_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74LD185PD454N
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTACACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTGAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA
CCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGCGG
TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA
TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA
GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC
CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC
GGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCAG
CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG
ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG
CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA
CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC
TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC
GTGTTCTGTGATAACCGCCGTGGAATCAATGTGGCCGAGC
AGAGCAAAGAGTGCAACATCAACATCAGCACCACT
ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATAACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAAC
HMPV_SC_4M_ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 110 Krarup_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74L5170LD185P

CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA
CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCGG
TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA
TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA
GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC
CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC
GGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCAG
CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG
ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG
CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA
CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC
TACCCTAACGAGAAGGACTGCGAGACAAGAGGGCGACCAC
GTGTTCTGTGATAACGCCGCTGGAATCAATGTGGCCGAGC
AGAGCAAAGAGTGCAACATCAACATCAGCACCACT
ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCCAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTGAG
AACATCGAGAATTCACAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_5M_ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 111 Krarup_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74LS170LD185PD454N
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTGA
CCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCGG
TTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGAA

TCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTGA
GCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGGC
CAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGAC
GGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCAG
CGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATCG
ACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTAG
CGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGGA
CCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTAC
TACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCAC
GTGTTCTGTGATAACCGCCGCTGGAATCAATGTGGCCGAGC
AGAGCAAAGAGTGCAACATCAACATCAGCACCACCAACT
ATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATAACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC

TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTTCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_DM_ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 112 Krarup_E51PT74L
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGCCTGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTCTGTGATAACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA

AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTTCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_TM_ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 113 Krarup_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT E51PT74LD454N
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGCCTGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGGCGACCA
CGTGTCTGTGATAACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCAACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGAACCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTTCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_SC_ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 114 StabilizeAlpha_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T74L
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG

AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCCGACCA
CGTGTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGATC
AGCTGAGCAAGGTGGAAGGCCAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAAC
HMPV_SC_ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 115 StabilizeAlpha_
CACCT_CAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT V55L
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACCTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT

GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGGCGAC
CACGTGTTCTGTGATAACGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTT
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAAC HMPV_SC_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 116 StabilizeAlpha_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT S170L
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCAGCATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGGCGAC
CACGTGTTCTGTGATAACGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTT
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG

GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCCAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAAC HMPV_SC_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 117 StabilizeAlpha_
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT T174W
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGTGGCGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGGCGAC
CACGTGTTCTGTGATAACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTT
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCCAACAGCACGTGATC

AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAAC HMPV_SC_4M_
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 118 StabilizeAlpha_

CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT V55LT74L5170LT174W
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACCTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGCTCAAGAGCGCCCTGAGAGA
ACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGAA
CAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGAG
CCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAGC
AGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGCTTAAGAACC
TGTGGCGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTTCTGTGATAACGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCAACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATAACCGTGACCATCGACAACACCGTGATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTCACAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_Proline ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 119 Stab_E51P
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGCCTGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC

GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATAACGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTT
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAAC HMPV_Proline
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 120 Stab_D185P
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCCCTG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTCTGTGATAACGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT

GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATAACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAAC
HMPV_Proline ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 121 Stab_D183P
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTACACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCCCTATCGACG
ACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTCTGTGATAACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCAACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATAACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAAC
HMPV_Proline ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 122 Stab_E131P
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT

CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGCCTAGCGA
AGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACGA
GGCCGTGAGCACACTCGGCAATGGCGTTAGAGTGCTGGCC
ACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAACC
TGACACGGGCCATTAACAAGAACAAGTGCGACATCGACG
ACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGCG
GTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGGA
ATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCTG
AGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCGG
CCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCGA
CGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGCA
GCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGATC
GACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTGTA
GCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGAGG
ACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTGTA
CTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGACCA
CGTGTCTGTGATACCGCCGCTGGAATCAATGTGGCCGAG
CAGAGCAAAGAGTGCAACATCAACATCAGCACCAACCAAC
TATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTCTAT
GGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGTATA
AGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGGGCAT
CATCAAGCAGCTGAACAAGGGCTGCAGCTACATCACCAAC
CAGGACGCCGATACCGTGACCATCGACAACACCGTGTATC
AGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATCAAGG
GCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGTTCCC
TGAGGATCAGTTCCAGGTGGCCCTGGACCAGGTGTTTCGAG
AACATCGAGAATTCACAGGCTCTGGTGGACCAGTCCAACA
GAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGCTTCAT
CATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTCCATG
ATCCTGGTGTCCATCTTCATCATTATCAAGAAGACCAAGA
AGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTGACCAA CAATGGCTTCATCCCTCACAAC
HMPV_Proline ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 123 Stab_D447P
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTGAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG

AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATAACGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG

TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCCCACCTATCAAGT
TCCCTGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAAC HMPV_Tramer
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 124 RepulsionD454N
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTGAGAAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATAACGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC

TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGAACCAGTTCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAAC HMPV_Trimer
ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 125 RepulsionE453N
CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCGACATCGAC
GACCTGAAGATGGCCGTGTCTTTAGCCAGTTCAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATAACCGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTT
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTCAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCGCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAAC HMPV_Stabilize

ATGAGCTGGAAGGTGGTCATCATCTTCAGCCTGCTGATCA 126 AlphaF196W

CACCTCAGCACGGCCTGAAAGAGAGCTACCTGGAAGAGT
CCTGCAGCACCATCACAGAGGGCTACCTGTCTGTGCTGAG
AACCGGCTGGTACACCAACGTGTTCACTGGAAGTGGGC
GACGTCGAGAATCTGACATGCTCTGATGGCCCTAGCCTGA
TCAAGACCGAGCTGGATCTGACCAAGAGCGCCCTGAGAG
AACTCAAGACCGTGTCTGCCGATCAGCTGGCCAGAGAGGA
ACAGATCGAGAATCCTGGCAGCGGCAGCTTTGTGCTGGGA
GCCATTGCTCTTGAGTGGCTGCTGCTGCAGCTGTTACAG
CAGGCGTGGCCATCGCTAAGACCATCAGACTGGAAAGCG
AAGTGACCGCCATCAACAACGCCCTGAAGAAGACAAACG
AGGCCGTCAGCACACTCGGCAATGGCGTTAGAGTGCTGGC
CACAGCCGTGCGCGAGCTGAAGGACTTCGTGTCCAAGAAC
CTGACACGGGCCATTAACAAGAACAAGTGCAGACATCGAC
GACCTGAAGATGGCCGTGTCCTTTAGCCAGTGGAACCGGC
GGTTTCTGAACGTCGTGCGGCAGTTTAGCGACAACGCCGG
AATCACACCAGCCATCAGCCTGGACCTGATGACAGATGCT
GAGCTGGCTAGAGCCGTGCCTAACATGCCTACATCTGCCG
GCCAGATCAAGCTGATGCTCGAGAATAGAGCCATGGTCCG
ACGGAAGGCTTCGGCATTCTGATTGGCGTGTACGGCAGC
AGCGTGATCTATATGGTGCAGCTGCCTATCTTCGGCGTGA
TCGACACACCCTGCTGGATTGTGAAGGCCGCTCCTAGCTG
TAGCGAGAAGAAGGGCAATTACGCCTGCCTGCTGAGAGA
GGACCAAGGCTGGTATTGTCAGAACGCCGGCAGCACCGTG
TACTACCCTAACGAGAAGGACTGCGAGACAAGAGGCGAC
CACGTGTTCTGTGATAACGCCGCTGGAATCAATGTGGCCG
AGCAGAGCAAAGAGTGCAACATCAACATCAGCACCACCA
ACTATCCCTGCAAGGTGTCCACCGGCAGGCACCCTATTTC
TATGGTGGCTCTGTCTCCTCTGGGAGCCCTGGTGGCTTGT
ATAAGGGCGTGTCTGTAGCATCGGCAGCAACAGAGTGG
GCATCATCAAGCAGCTGAACAAGGGCTGCAGCTACATCAC
CAACCAGGACGCCGATACCGTGACCATCGACAACACCGTG
TATCAGCTGAGCAAGGTGGAAGGCGAACAGCACGTGATC
AAGGGCAGACCTGTGTCCAGCAGCTTCGACCCTATCAAGT
TCCCTGAGGATCAGTTCAGGTGGCCCTGGACCAGGTGTT
CGAGAACATCGAGAATTCCCAGGCTCTGGTGGACCAGTCC
AACAGAATCCTGTCTAGCGCCGAGAAGGGAAACACCGGC
TTCATCATCGTGATCATCCTGATCGCCGTGCTGGGCAGCTC
CATGATCCTGGTGTCCATCTTCATCATTATCAAGAAGACC
AAGAAGCCCACCGGCCTCCTCCAGAACTGAGCGGAGTG
ACCAACAATGGCTTCATCCCTCACAAC Human Metapneumovirus mRNA Sequences HMPV_SC_

AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 127 DSCAV1_4MMV

CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUUCUGCAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCUUUGCCGUGCGCGAGCUGAAGGACUUC

GUGUCCAAGAACCUGACACGGGCCCUGAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUACACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GUGUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCU AACGA
GAAGGACUGCGAGACAAGAGGGCACCACGUGUUCUGUG
AUACCGCCGUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAUCAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGGAUCAGUUCAACGUGGCCUUGGACCAGGUGUUCG
AGAACAUCGAGAAUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACA AUGGCUUCAUCCCUCACAAC HMPV_SC_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 128 DSURIC_4MMV
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUUCUGCAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUACACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GUGUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCU AACGA

GAAGGACUGCGAGACAAGAGGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUC AAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGU UCCC
UGAGCACCAGUGGCAUGUGGCCUUGGACCAGGUGUUCGA
GAACAUCGAGAAU UCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUC AUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCUCCAGAACUGAGCGGAGU
GACCAACA AUGGCUUCAUCCUCACAAC HMPV_SC_DM_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 129 Krarup_U74LD185P
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACC GGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUACAGCAGGCGUGGCCAU CGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGC GACAUCCUGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUUCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA

AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUC AAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGU UCCC
UGAGGAUCAGUUCAGGUGGCCUUGGACCAGGUGUUCG

AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCUCCUGGUGUCCAUCUUCUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_UM_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 130 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74LD185PD454N
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCAGAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUUGCUGAGCUGGCUAGAGCCGUGCCUAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAUUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGAACCAGUUCAGGUGGCCUUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_4M_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 131 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74L5170LD185P
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU

GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACA
GUGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAUACACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGCGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGUGGAAUCAUUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGGAUCAGUCCAGGUGGCCUUGGACCAGGUGUUCG
AGAACAUCGAGAAUCCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACA AUGGCUUCAUCCCUCACAAC HMPV_SC_5M_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 132 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74LS170LD185PD454N
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACA
GUGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAUACACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCCUAGAGCCGUGCCUAA

CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGAACCAGUUCAGGUGGCCUUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCACAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCACCGGCGCUCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCUCACAAC HMPV_SC_DM_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 133 Krarup_E51PU74L
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCAGAUUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUUCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC

GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCAGGUGGGCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_UM_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 134 Krarup_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA E51PU74LD454N
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUUGCUGAGCUGGCUAGAGCCGUGCCUAA
AUGCCUACAUCUGCCGGCCAGAUAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGUGGAAUCAUUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACCUAUCUCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGAACCAGUUCAGGUGGGCCUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_

AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 135 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U74L
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCAGAUUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUUGCUGAGCUGGCUAGAGCCGUGCCUAA
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC

AGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAAACGA
GAAGGACUGCGAGACAAGAGGGCACCACGUGUUCUGUG
AUACCGCCGCUUGGAAUCAAUUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCAGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUUCAGGUGGCCCUUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAUAUGGCUUCAUCCCUCACAAC HMPV_SC_

AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 136 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA V55L
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACCUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG

AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUACACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCAGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGGAUCAGUCCAGGUGGCCUUGGACCAGGUGUUCG
AGAAUCAUCGAGAAUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCUGGUGUCCAUCUUAUCAUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACA AUGGCUUCAUCCCUCACAAC HMPV_SC_
AUGAGCUGGAAGGUGGUC AUCAUCUUCAGCCUGCUGAU 137 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA S170L
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUACAGCAGGCGUGGCCAU CGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGCUUAAGAACCUGACACGGGCCAUUAACAAGAACA
GUGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAUACACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG

CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAUAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUCCAGGUGGCCUUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGUCCUCCAGAACUGAGCGGAG
UGACCAACAUAUGGCUUCAUCCCUCACAAC HMPV_SC_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 138 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA U174W
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGUGGCGGGCCAUAACAAGAACA
GUGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAUACACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAUAUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC

UGAGGAUCAGUCCAGGUGGCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUCCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_SC_4M_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 139 SUabilizeAlpha_
CACACCUCAGCACGGCCUGAAAGAGAGAGCUACCUGGAAGA V55LU74L5170LU174W
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACCUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGCUCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGCUUAAGAACCUGUGGGCGGGCCAUAACAAGAACA
GUGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAG
CCAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGGAUCACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGA
GAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGCGCAGCACCCGUGUACUACCCUAAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUUGGAAUCAUUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGGAUCAGUCCAGGUGGCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUCCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_Proline
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 140 SUab_E51P
CACACCUCAGCACGGCCUGAAAGAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGCCUGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG

CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUUCUGAGCUGGCCUAGAGCCGUGCCUAA
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCCGUGUACUACCCUAA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGUGGAAUCAUUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGGAUCAGUCCAGGUGGCCUUGGACCAGGUGUUCG
AGAACAUCGAGAAUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUCUAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_Proline
AUGAGCUGGAAGGUGGUCUAUCAUCUUCAGCCUGCUGAU 141 SUab_D185P
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG

UGCGACAUCCCUGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU

AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCU AACGA
GAAGGACUGCGAGACAAGAGGGCACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGGAUCAGUCCAGGUGGCCUCUGGACCAGGUGUUCG
AGAACAUCGAGAAUCCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCUGGUGUCCAUCUUAUCAUAUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACA AUGGCUUCAUCCCUCACAAC HMPV_Proline
AUGAGCUGGAAGGUGGUAUCAUCUUCAGCCUGCUGAU 142 SUab_D183P
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCU GAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCCCUAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCU AACGA
GAAGGACUGCGAGACAAGAGGGCACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA

AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUCCAGGUGGGCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_Proline
AUGAGCUGGAAGGUGGUAUCAUCUUCAGCCUGCUGAU 143 SUab_E131P
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGCCUAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCAGAUUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUUCGUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCAUUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUUCCC
UGAGGAUCAGUCCAGGUGGGCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGA

CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_Proline
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 144 SUab_D447P
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUUCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUC AAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAAC AAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCAGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCCCACCUAUC AAGUCCC
UGAGGAUCAGUUCAGGUGGCCCUUGGACCAGGUGUUCG
AGAACAUCGAGAAUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUC AUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC HMPV_Urimer
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 145 RepulsionD454N
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA

CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGCUGGA
UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUCAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UGAGAACCAGUUCAGGUGGCCUUGGACCAGGUGUUCGA
GAACAUCGAGAAUUC CAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUCAUCAUUAUCAAGAAGAC
CAAGAAGCCACCGGCGCUCCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCUCACAAC HMPV_Urimer
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 146 RepulsionE453N
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG
AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUUCAACCGGCGGUUUCUGAACGUCGUGCGGCAGUUU
AGCGACAACGCCGGAUUCACACCAGCCAUCAGCCUGGAC
CUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCU AAC
AUGCCUACAUCUGCCGGCCAGAUCAAGCUGAUGCUCGAG
AAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUCU
GAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUGC
AGCUGCCUAUCUUCGGCGUGAUCGACACACCUCUGCUGGA

UUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGGC
AAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG
CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUAAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGUCCC
UCAGGAUCAGUUCAGGUGGCCUUGGACCAGGUGUUCGA
GAACAUCGAGAAUUCACAGGCUCUGGUGGACCAGUCCAA
CAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCUU
CAUCAUCGUGAUAUCCUGAUCGCCGUGCUGGGCAGCUC
CAUGAUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGAC
CAAGAAGCCACCGGCGCUCUCCAGAACUGAGCGGAGU
GACCAACAAUGGCUUCAUCCUCACAAC HMPV_
AUGAGCUGGAAGGUGGUCAUCAUCUUCAGCCUGCUGAU 147 SUabilizeAlpha
CACACCUCAGCACGGCCUGAAAGAGAGCUACCUGGAAGA F196W
GUCCUGCAGCACCAUCACAGAGGGCUACCUGUCUGUGCU
GAGAACCGGCUGGUACACCAACGUGUUCACACUGGAAGU
GGGCGACGUCGAGAAUCUGACAUGCUCUGAUGGCCCUAG
CCUGAUCAAGACCGAGCUGGAUCUGACCAAGAGCGCCCU
GAGAGAACUCAAGACCGUGUCUGCCGAUCAGCUGGCCAG

AGAGGAACAGAUUCGAGAAUCCUGGCAGCGGCAGCUUUG
UGCUGGGAGCCAUUGCUCUUGGAGUGGCUGCUGCUGCA
GCUGUUACAGCAGGCGUGGCCAUUCGCUAAGACCAUCAGA
CUGGAAAGCGAAGUGACCGCCAUCAACAACGCCUUGAAG
AAGACAAACGAGGCCGUCAGCACACUCGGCAAUGGCGUU
AGAGUGCUGGCCACAGCCGUGCGCGAGCUGAAGGACUUC
GUGUCCAAGAACCUGACACGGGCCAUUAACAAGAACAAG
UGCGACAUCGACGACCUGAAGAUGGCCGUGUCCUUUAGC
CAGUGGAACCGGCGGUUCUGAACGUCGUGCGGCAGUU
UAGCGACAACGCCGAAUCACACCAGCCAUCAGCCUGGA
CCUGAUGACAGAUGCUGAGCUGGCUAGAGCCGUGCCUAA
CAUGCCUACAUCUGCCGGCCAGAUAAGCUGAUGCUCGA
GAAUAGAGCCAUGGUCCGACGGAAAGGCUUCGGCAUUC
UGAUUGGCGUGUACGGCAGCAGCGUGAUCUAUAUGGUG
CAGCUGCCUAUCUUCGGCGUGAUCGACACACCCUGCUGG
AUUGUGAAGGCCGCUCCUAGCUGUAGCGAGAAGAAGGG
CAAUUACGCCUGCCUGCUGAGAGAGGACCAAGGCUGGUA
UUGUCAGAACGCCGGCAGCACCGUGUACUACCCUAACGA
GAAGGACUGCGAGACAAGAGGCGACCACGUGUUCUGUG
AUACCGCCGCUGGAAUCA AUGUGGCCGAGCAGAGCAAAG
AGUGCAACAUCAACAUCAGCACCAACUAUCCCUGCA
AGGUGUCCACCGGCAGGCACCCUAUUUCUAUGGUGGCUC
UGUCUCCUCUGGGAGCCCUGGUGGCUUGUUAUAAGGGC
GUGUCCUGUAGCAUCGGCAGCAACAGAGUGGGCAUCAUC
AAGCAGCUGAACAAGGGCUGCAGCUACAUCACCAACCAG
GACGCCGAUACCGUGACCAUCGACAACACCGUGUAUCAG

CUGAGCAAGGUGGAAGGCGAACAGCACGUGAUC AAGGG
CAGACCUGUGUCCAGCAGCUUCGACCCUAUCAAGU UCCC
UGAGGAUCAGUCCAGGUGGCCUGGACCAGGUGUUCG
AGAACAUCGAGAAUUCCCAGGCUCUGGUGGACCAGUCCA
ACAGAAUCCUGUCUAGCGCCGAGAAGGGAAACACCGGCU
UCAUCAUCGUGAUCAUCCUGAUCGCCGUGCUGGGCAGCU
CCAUGAUCCUGGUGUCCAUCUUAUCAUUAUCAAGAAGA
CCAAGAAGCCCACCGGCGCUCCUCCAGAACUGAGCGGAG
UGACCAACAAUGGCUUCAUCCCUCACAAC

EQUIVALENTS

[0846] 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.

[0847] All references, including patent documents, disclosed herein are incorporated by reference in their entirety.

Sequence CWU 1

1

14711620DNA Human metapneumovirus 1atgagctgga agtggtgat tatctcagc ctgctgatta cacctcaaca cggcctgaag
60gagagctacc tggaagagag ctgctccacc atcaccgagg gctacctgag cgtgctgcgg 120accggctggt acaccaactg gttcacctg
gagtgggcg acgtggagaa cctgacctgc 180agcgacggcc ctgacctgat caagaccgag ctggacctga ccaagagcgc tctgagagag
240ctgaagaccg tgtccgccga ccagctggcc agagaggaac agatcgagaa cctcggcgag 300agcagattcg tgctggggcg catcgtctg
ggagtcgccg ctgccgctgc agtgacagct 360ggagtggcca ttgtaagac catcagactg gaaagcgagg tgacagccat caacaatgcc
420ctgaagaaga ccaacgaggc cgtgagcacc ctgggcaatg gagtgagagt gctggccaca 480gccgtgcggg agctgaagga cttcgtgagc
aagaactga ccagagccat caacaagaac 540aagtgcgaca tcatgacct gaagatggcc gtgagcttct cccagttcaa cagacggttc
600ctgaacgtgg tgagacagtt ctccgacaac gctggaatca cacctgccat tagcctggac 660ctgatgaccg acgccgagct ggctagagcc
gtgcccaaca tgcccaccag cgtggccag 720atcaagctga tgetggagaa cagagccatg gtgcggagaa agggcttcgg catcctgatt
780ggggtgatg gaagtcctg gatctacatg gtgcagctgc ccatctcgg cgtgatcgac 840acacctgct ggatcgtgaa ggccgctcct
agctgctccg agaagaaagg aaactatgcc 900tgtctgctga gagaggacca ggctgtgtac tgccagaacg ccggaagcac agtgactat
960ccaacagaga aggactgca gaccagaggc gaccacgtgt tctgcgacac cgtgcggga 1020atcaacgtgg ccgagcagag
caaggagtgc aacatcaaca tcagcacaac caactacccc 1080tgcaagtgta gcaccggacg gcaccccatc agcatggtgg ctctgagccc
tctgggcgct 1140ctggtggcct gctataaggg cgtgtctgt agcatcggca gcaatcgggt gggcatcctc 1200aagcagctga acaagggatg
ctctacatc accaaccagg acgccgacac cgtgaccatc 1260gacaacacc tgtaccagct gagcaaggtg gagggcgagc agcacgtgat
caagggcaga 1320cccgtgagct ccagcttca ccccatcaag tccctgagg accagttcaa cgtggccctg 1380gaccaggtgt ttgagaacat
cgagaacagc cagccctgg tggaccagag caacagaatc 1440ctgtccagcg ctgagaaggg caacaccggc tcatcattg tgatcatt
gatcgcctg 1500ctgggcagct ccatgatcct ggtgagcacc tcatcatta tcaagaagac caagaaacc 1560accggagccc ctctgagct
gagcggcgtg accaacaatg gcttcattcc ccacaactga 162021620DNA Human metapneumovirus 2atgtcttga aagtgatgat
catcatttcg ttactcataa caccaccgca cgggctaaag 60gagagttatt tggaagaatc atgtagtact ataactgagg gatacctcag tgtttaaga
120acagctggt actaatgt ctacacatta gaagttggtg atgtgaaaa tcttcatgt 180actgatggac ctgcttaac caaaacagaa
cttgatctaa caaaaagtc ttaagggaa 240ctcaaaacag tctctgctga tcagtggcg agagaggagc aaattgaaaa tccagacaa
300taagatttg tcttagtgct gatagctctc ggagttgcta cagcagcagc agtcacagca 360ggcattgcaa tagccaaaac cataagctt
gagagtgagg tgaatgcaat taaaggtgct 420ctcaaaacaa ctaatgaagc agtatccaca ttagggaatg gtgtgcgggt cctagccact
480gcagtgagag agctaaaaga atgtgtgagc aaaaactgca ctagtgcaat caacaggaac 540aaatgtgaca ttgctgatct gaagatggct
gtcagcttca gtcaattcaa cagaagattt 600ctaaatggtg tgcggcagtt ttacagacat gcagggataa caccagcaat atcattggac
660ctgatgactg atgctgagtt ggccagagct gtatcataca tgccaacatc tgcagggcag 720ataaaactga tgtggagaa ccgcgcaatg
gtaaggagaa aaggatttgg aatcctgata 780ggggtctacg gaagctctgt gattacatg gttaattgc cgatcttgg tgatcatgat
840acaccttgtt ggatcatcaa ggcagctccc tctgtctcag aaaaaaacgg gaattatgct 900tcctcctaa gagaggatca agggtggtat
tgtaaaaatg caggatctac tgttactac 960ccaatgaaa aagactgca aacaagaggt gatcatgttt tttgtgacac agcagcaggg
1020atcaatgtg ctgagcaatc aagagaatgc aacatcaaca tatctactac caactacca 1080tgcaagtca gcacaggaag acacctata

agcatggtg cactatcacc tctcgggtgct 1140ttgggtgctt gctataaagg ggtaagctgc tcgattggca gcaattgggt tggaaatcacc
1200aaacaattac ccaaaggctg ctacatacata accaaccagg atgcagacac tgtaacaatt 1260gacaataccg tgtatcaact aagcaaagt
gaagggtgaac agcatgtaat aaaagggaga 1320ccagtttcaa gcagtttga tccaatcaag tttcctgagg atcagttcaa tgttgcgctt
1380gatcaagtct tcgaaagcat tgagaacagt caggcactag tggaccagtc aaacaaaatt 1440ctaaacagtg cagaaaaagg aaacactggt
ttcattatcg tagtaatttt ggttgcgtgt 1500cttgggtctaa ccatgatttc agtgagcacc atcatcataa tcaagaaaac aaggaagccc
1560acaggagcacc ctccagagct gaattggtgc accaacggcg gtttcatacc acatagttag 162031620DNAHuman
metapneumovirus 3atgtcttggga aagtgtatg tctcatttcg ttactcataa cacctcagca tggactaaaa 60gaaagtatt tagaagaatc
atgtagtact ataactgaag gatatctcag tgttttaaga 120acagggttgg acaccaatgt cttacatta gaagtgggtg atgttgaaaa tcttacatgt
180actgatggac ctacgttaat caaacagaa cttgacctaa ccaaaagtgc ttaagagaa 240ctcaaacag tttctgctga tcagttagcg
agagaagaac aaattgaaaa tcccagacaa 300tcaaggttgg tctaggtgac aatagctctt ggagttgcca cagcagcagc agtcacagca
360ggcattgcaa tagccaaaac tataaggctt gagagtgaag tgaatgcaat caaaggtgct 420ctcaaaacaa ccaatgagcg agtatcaaca
ctaggaaatg gtagtgcgggt cctagccact 480gcagtaagag agctgaaaga atttggagc aaaaacctga ctagtgcgat caacaagaac
540aagtgtgaca ttgctgattt gaagatggtc gtcagcttca gtcagttcaa cagaagattc 600ctaaatgttg tgcggcagtt ttcagacaat
gcagggataa caccagcaat atcattggac 660ctgatgaatg atgctgagct ggccagagct gtatcataca tgccaacatc tgcaggacag
720ataaaaactaa tgttagagaa cctgcaatg gtagggagaa aaggatttgg aatcttgata 780gggggtctacg gaagctctgt gatttacatg
gtccagctgc cgtctttgg tgcataaat 840acacctgtt ggataatcaa ggcagctccc tcttggcag aaaaagatgg aaattatgct
900tgccctctaa gagaggatca aggttggat tgtaaaaatg caggatccac tgtttactac 960ccaaatgaaa aagactgcca aacaagaggt
gatcatgttt ttttgacac agcagcaggg 1020atcaatgttg ctgagcaatc aagagaatgc aacatcaaca tatctaccac caactacca
1080tgc aaagtc gacaggaag acaccctatc agcatggtg cactatcacc tctcgggtgct 1140ttggtagctt gctacaaagg ggttagctgc
tcgactggca gtaatcaggt tggaaatac 1200aaacaactac ctaaaggctg ctacatacata actaaccagg acgcagacac tgtaacaatt
1260gacaactg tgtatcaact aagcaaagt gaggggtgaac agcatgtaat aaaagggaga 1320ccagtttcaa gcagtttga tccaatcagg
ttcctgagg atcagttcaa tgttgcgctt 1380gatcaagtct tgaagcat tgaaaacagt caagcactag tggaccagtc aaacaaaatt
1440ctgaacagt cagaaaaagg aaacactggt ttcattatg taataatttt gattgctgt 1500cttgggttaa ccatgatttc agtgagcacc
atcatcataa tcaaaaaaac aaggaagccc 1560acaggggac ctccggagct gaattggtt accaacggcg gtttcatacc gcatagttag
162041725DNAHuman respiratory syncytial virus 4atggaggtgc caatcctcaa acaaatgca attaccacaa tcttgcctgc
agtcacactc 60tgttctgctt ccagtcacaaa catcactgaa gaattttatc aatcaacatg cagtgcagtt 120agcaaaggct atcttagtgc tctaagaact
ggttggata ctagtgttat aactatagaa 180ttaagtaata tcaaggaaaa taagtgtat ggaacagatg ctaaggtaaa atgataaaa
240caagaattag ataatataa aatgctgta acagaattgc agttgctcat gcaaagcaca 300ccagcagcca acaatcgagc cagaagagaa
ctaccaaggt ttatgaatta tactctcaat 360aatacaaaa ataccaatg aacattaagc aagaaaagga aaagaagatt tcttggcttt
420ttgttagtg ttgatctgc aatcggcagtt ggcttctgct tatctaaagt cctgcaccta 480gaaggggaag tgaacaaaat caaaagtgt
ctactatcca caaacagggc ttagtcagc 540ttatcaaatg gagttagtt ctaaccagc aaagtgttag acctcaaaaa ctatatagat
600aaacagttgt tacctattgt gaacaagca agctgcagca tatcaaacat tgaactgtg 660atagagtcc acaaaaagaa caacagacta
ctagagatta ccaggaatt tagtgtta 720gcaggtgtaa ctacacctgt aagcattat atgttaacta atagtgaatt attacatta 780atcaatgata
tgcctataac aatgatcag aaaaagttaa tgcacaaca tgttcaata 840gttagacagc aaagttactc tatcatgtcc ataataaagg aggaagtctt
agcatatgta 900gtacaattac cactatagtg tgtaatagat acaccctgtt gaaactgca cacatccct 960ctatgtacaa ccaacacaaa
ggaaggttcc aacatctgt taacaagaac cgacagagga 1020tggtattgtg acaatgcagc atcagtatct ttttccac aagctgaac
atgtaaagt 1080caatgcaatc ggtattttg tgacacaatg aacagtttaa cattaccaag tgaagtaaat 1140ctctgcaaca ttgacatatt
caaccccaaa tatgattgca aaattatgac ttcaaaaaca 1200gatgtaagca gctcgttat cacatctcta ggagccattg tgcctatgta tggcaaaact
1260aaatgtacag catccaataa aatcgtggg atcataaaga catttctaa cgggtgtgat 1320tatgtatcaa ataaggggtt ggatactgtg
tctgtaggta atacattata ttatgtaaat 1380aagcaagaag gcaaaagtct ctatgtaaaa ggtgaaccaa taataattt ctatgacca
1440ttagtgtcc cctctgatga attgatgca tcaatatctc aagtcaatga gaagattaac 1500cagagcctag catttattcg taaatccgat
gaattattac ataagtataa tgcgtgtaaa 1560tccaccacaa atatcatgat aactactata attatagtgta ttatagtaatt attgtatca
1620ttaattgacg ttgactgct cctactatgc aaggccagaa gcacaccagt cacactaagt 1680aaggatcaac tgagtgtgat aaataatatt
gcatttagta actga 17255539PRTHuman 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 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 535539PRTHuman

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 5357539PRTHuman

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 535574PRTHuman 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
9atgccaat t caactgtt aattattaca accatgatca tggcatcaca ctgccaaata 60gacatcaca aactacagca ttaggtgta ttgtcaaca
gtccaaagg gatgaagata 120tcacaaact tcgaaacaag atatctaact ctgagtctca taccaaaaat agaagattct 180aactctgtg
gtgaccaaca gatcaagcaa tacaagagg tattgtagat actgatcatt 240cctttatag atggactaag attacagaag gatgtgatag tgactaatca
agaatccaat 300gaaacactg atcccagaac agaacgattc ttggagggg taattggaac tattgctcta 360ggagtagcaa cctcagcaca
aattacagca gcagttgctc tgggtgaagc caagcaggca 420agatcagaca tgaaaaact caaggaagca atcagggaca caataaagc
agtgcagtca 480gttcagagct ctgtaggaaa ttgatagta gcaattaaat cagccagga ttatgtcaac 540aaagaaatcg tgccatcgt
tgcgagacta ggtgtggaag cagcaggact ctagttagg 600attgcattaa cacagcatta ctagaatta acaaatatat ttggtgataa cataggatcg
660ttacaagaaa aaggaataaa attacaaggt atagcatcat tataccgtac aaatcaca 720gaaatattca caacatcaac agttgacaaa
tatgatatt atgatctatt atttacagaa 780tcaataaagg tgagagttat agatgttgat ttgaatgatt actcaataac cctccaagtc 840agactcctt
tattgaccag actgctgaac actcaaatct acaagtaga ttccatata 900tacaatatcc aaaatagaga atggtatct cctcttccca gccatcat
gacgaaaggg 960gcatttctag gtggagcaga tgtcaagaa tgcataagaag cattcagcag ttatatatgc 1020ccttctgac caggattgt
actaaacct gaaatggaga gctgtctatc aggaaacata 1080tcccaatgct caagaaccac agtcacatca gacatagtc ctaggatgc
attgtcaat 1140ggaggagtg ttgcgaattg tataacaact acatgtacat gcaatggtat cggtaataga 1200atcaaccaac cacctgatca
aggagtcaaa attatacac ataaagaatg taatacaata 1260ggtatcaacg gaatgctatt caacacaaac aaagaaggaa ctcttgcat
ctacacacca 1320gacgacataa cattaacaa ttctgttga cttgatccga ttgacatate aatcgagctc 1380acaaggcca aatcagatct
tgaggatca aaagaatgga taagaaggtc aatcaaaag 1440ctagattcta ttggaagttg gcatcaatct agcactaca tcatagttat ttgataatg
1500atgattatat tgttataat taatataaca ataattacaa ttgcaattaa gtattacaga 1560attcaaaaga gaaatcgagt ggatcaaaat

gataagccgt atgtattaac aaacaag 1617101716DNAHuman parainfluenza virus 3 10atggaatact ggaagcacac
caaccacgga aaggatgctg gtaatgagct ggagacatcc 60acagccactc atggcaacaa gtcaccaac aagataacat atatattgtg
gacgataacc 120ctggtgttat tatcaatagt cttcatcata gtgctaacta attccatcaa aagtgaaaag 180gcccgcgaat cattgtaca
agacataat aatgagttta tggagttac agaaaagatc 240caagtggcat cggataatac taatgatcta atacagtacg gagtgaatac aaggcttct
300acaattcaga gtcattgcca gaattatata ccaatatcat tgacacaaca aatatcggat 360cttaggaaat tcattagtga aattacaatt
agaaatgata atcaagaagt gccaccacaa 420agaataaac atgatgtggg tataaaacct ttaaateccag atgatttctg gagatgcacg
480tctggcttc catctttgat gaaaactcca aaaataagat taatgccggg accaggatta 540ttagctatgc caacgactgt tgatggctgt
gtcagaacce cgtccttagt gataaatgat 600ctgatttatg cttacacctc aatctaatt actcgagggt gccaggatat agggaaatca
660tatcaagat tacagatagg gataataact gtaaactcag acttggacc tgacttaaat 720cctaggatct ctacacctt caacataat
gacaatagaa agtcatgttc tctagcactc 780ctaaatacag atgtatatca actgtgttca accccaaaag ttgatgaaag atcagattat
840gcatcatcag gcatagaaga tattgtactt gatattgtca attatgatgg ctcaatctcg 900acaacaagat ttaagaataa taatataagt tttgatcaac
catatgggc attataccca 960tctgttgac caggatata ctacaaggc aaaataat tctcgggta tggaggtctt 1020gaacatcaa
taaatgagaa tgcaatctc aacacaactg ggtgtcctgg gaaaacacag 1080agagactgta atcaagcacc tcatagtcca tggtttctcag
atagaaggat ggccaactct 1140ataattgttg ttgacaaggg cttgaactca gttccaaaa tgaaggatg gacgatatct 1200atgagacaaa
attactgggg gtcagaagga agattactt tactaggtaa caagatctac 1260atatacacia gatctacaag ttggcacagc aagttaaat
taggaataat tgacattact 1320gactacagt atataaggat aaaatggaca tggcataatg tgctatcaag accaggaaac 1380aatgaatgc
catggggaca tcatgtccg gatggatgta taacgggagt atataccgat 1440gcatatccac tcaatcccac aggaagcatt gtatcatctg
tcatattgga ctacaaaaa 1500tcgagagtca accagtcac aacttactca acagcaaccg aaagggtaaa cgagctggct 1560atccgaaaca
aaactctc agctgggtac acaacaacia gctgcattac aactataac 1620aaagggtatt gtttcatat agtagaataa aatcataaaa
gctaaacac atttcaacc 1680atgttgttca aaacagagat tcaaaaagc tgcagt 1716111716DNAArtificial SequenceSynthetic
Polynucleotide 11atggaatact ggaagcacac caaccacggc aaggacgccc gcaacgagct ggaaccagc 60acagccacac
acggcaacia gctgaccaac aagatcacct acatctgtg gaccatcacc 120ctggtgctgc tgagcatcgt gttcatcacc gtgctgacca
atagatcaa gagcgagaag 180gccagagaga gcctgctgca ggacatcaac aacgagtcca tggagtgac cgagaagatc 240caggtggcca
gcgacaacac caacgactg atccagagcg gcgtgaacac ccggctgctg 300accatccaga gccactgca gaactacacc cccatcagcc
tgaccagca gatcagcagc 360ctgcggaagt tcatcagcga gatcaccacc cggaaacgaca accaggaagt gccccccag 420agaatcacc
acgacgtggg catcaagccc ctgaacccc acgatttctg gcggtgtaca 480agcggcctgc ccagcctgat gaagacccc aagatccggc
tgatgcctgg cctggactg 540ctggccatgc ctaccacagt ggatggctgt gtgcggacc ccagcctcgt gatcaacgat 600ctgatctacg
cctacaccag caacctgat acccggggct gccaggatat cggcaagagc 660taccaggtgc tgcagatcgg catcaccacc gtgaactccg
acctggtgcc cgacctgaac 720cctcggatca gccacacctt caatcaaac gacaacagaa agagctgcag cctggctctg 780ctgaacaccg
acgtgtacca gctgtgcagc accccaagg tggacgagag aagcactac 840gccagcagc gcatcgagga tctgtgctg gacatcgtga
actacgacgg cagcatcagc 900accaccggg tcaagaacia caatcagc ttcgaccagc cctaccccg cctgtacct 960tctgtgggcc
ctggcatcta ctacaagggc aagatcatct tctgggcta cggcggcctg 1020gaacaccca tcaacgagaa cgccatctgc aacaccaccg
gctgcctgg caagaccag 1080agagactgca atcaggccag ccacagcccc tggtcagcg accgcagaat ggtaactct 1140atcatcgtgg
tggacaaggg cctgaacagc gtgcccagc tgaagtgtg gacaatcagc 1200atgcgccaga actactgggg cagcagggc agactctgc
tgctgggaaa caagatctac 1260atctacacc ggccaccag ctggcacagc aaactgcagc tgggaatcat cgacatcacc 1320gactacagc
acatccggat caagtggacc tggcacaac tgctgagcag accggcaac 1380aatgagtgcc cttggggcca cagctgccc gatggatgta
tcaccggcgt gtacaccgac 1440gcctacccc tgaatctac cgctccacc gtgtccagcg tgatctgga cagccagaaa 1500agcagagtga
acccgtgat cacatacagc accgccaccg agagagtga cgaactggcc 1560atcagaacia agacctgag cgccggctac accaccacia
gctgeatc acactacaac 1620aagggtact gttccacat cgtggaatc aaccacaagt cctgaacac cttcagccc 1680atgctgttca
agaccgagat cccaagagc tgctcc 1716121617DNAArtificial SequenceSynthetic Polynucleotide 12atgccatca
gcatctgct gatcatcacc acaatgatca tggccagcca ctgccagatc 60gacatcaca agctgcagca cgtgggcgtg ctctgaaca
gccccaggg catgaagatc 120agccagaact tcgagacag ctacctgatc ctgagctga tccccaat cgaggacagc 180aacagctgcg
gcgaccagca gatcaagcag tacaagcggc tgctggacag actgatcacc 240cccctgtacg accgctgcg gctgcagaaa gacgtgatcg
tgaccaacca gaaagcaac 300gagaacaccg accccggcag cgagagattc ttcggcggcg tgatcggcac aatcgccctg 360ggagtggcca
caagcggcca gattacagcc gctgtggccc tgggtggaag caagcaggcc 420agaagcagca tcgagaagct gaaagaggcc atccgggaca
ccaacaaggc cgtgcagagc 480gtgcagtcca gcgtgggcaa tctgatcgtg gccatcaagt cgtgcagga ctactgtaac 540aaagaaatcg
tgccctctat cgcccggctg ggctgtgaag ctgccgact gcagctgggc 600attgccctga cacagcacta cagcagctg accaacatct
tcggcgaaa catcggcagc 660ctgcaggaag agggcattaa gctgcaggga atcggcagcc tctaccgac caacatcacc 720gagatctca
ccaccagcag cgtggataag tacgacatct acgacctgt gttaccag 780agcatcaaag tgcgctgat cgactggac ctgaacgact
acagcatcacc cctgcaagt 840cggtgcccc tgctgaccag actgctgaac accagatct acaagggtga cagcatctcc 900tacaacatc
agaaccgga gttgtacatc cctctgccc gccacattat gaccaaggcc 960gccttctgg gcggagccga cgtgaaagag tgcacgagg
ccttcagcag ctacatctgc 1020cccagcagc ctggtctctg gctgaaccac gagatggaaa gctgctgag cggcaacatc 1080agccagtgc
ccagaaccac cgtgacctc gatcctgc ccagatacgc ctctgtaat 1140ggcggcgtgg tggccaactg catcaccacc acctgtacct
gcaacggcat cggcaaccg 1200atcaaccagc ctcccgatca gggcgtgaag attatcacc acaagagt taacaccatc 1260ggcatcaacg

gcatgctgtt caataccaac aaagaggcca ccttgccctt ctacaccccc 1320gacgatatca cctgaacaa ctccgtgget ctggaccca
tcgacatctc catcgagctg 1380aacaaggcca agagcgacct ggaagagtcc aaagagtgga tccggcggag caaccagaag
1440ctggacteta tccgcagctg gcaccagagc agcaccacca tcatcgtgat cctgattatg 1500atgattatcc tgttcatcat caacattacc
atcatcacta tcgccattaa gtactaccgg 1560atccagaaac ggaaccgggt ggaccagaat gacaagcctt 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 15204062DNAMiddle East respiratory syndrome coronavirus
20atgatacact cagtggttct actgatgttc ttgtaaacac ctacagaaag ttacgttgat 60gtagggccag attctgttaa gtctgcttg attgaggtg
atatacaaca gacctcttt 120gataaaactt ggcctaggcc aattgatgt tctaaggctg acggtattat atacctcaa 180ggccgtacat
attctaacat aactatact tacaagtc ttttcccta tcaggagac 240catgggtgata tgatgttta ctctgcagga catgctacag gcacaactcc
acaaaagtg 300ttgtagccta actattctca ggacgtcaaa cagtttgccta atgggttctg cgtccgtata 360ggagcagctg ccaattccac
tggcactgtt attattagcc catctaccag cgctactata 420cgaaaaattt acctgcttt tatgctgggt tcttcagttg gtaattctc agatggtaaa
480atgggcccgt tctcaatca tactctagtt ctttggccc atggatgtgg cactttact 540agagctttt attgtattct agagcctcgc tctggaate
attgtcctgc tggcaattcc 600tatacttct ttgccacta tcactctct gcaacagatt gttctgatgg caattacaat 660cgtaatgcca gtctgaactc
tttaaggag tatttaatt tacgtaactg cacctttatg 720tacactata acattaccga agatgagatt tttagatggg ttggcattac acaactgct
780caaggtgttc acctctctc atctcggtat gttgattgt acggcggcaa tatgtttcaa 840tttggccact tgctgttta tgatactatt aagtattat
ctatcattcc tcacagtatt 900cgttctatcc aaagtatag aaaagcttgg gctgcctct acgtatataa actcaaccg 960ttaacttcc tgttgatt
ttctgttgat ggttatatac gcagagctat agactgtgg 1020tttaagtatt tgcacaact ccaactgctca tatgaatct tcgatgttga atctggagt
1080tattcagttt cgtcttctga agcaaacct tctggctcag ttgtggaaca ggctgaaggt 1140gttgaatgtg attttcacc tctctgtct
ggcacacctc ctcaggttta taattcaag 1200cgtttgttt ttaccaattg caattataat ctaccacaaat tgcttctact ttttctgtg 1260aatgatttta
ctttagtca aatatctcca gcagcaattg ctgcaactg ttattctca 1320ctgatttgg attattttc ataccactt agtatgaaat ccgatctcag
tgtagttct 1380gctgggtcaa tatccagtt taattataaa cagtccttt ctaatccac atgtttgatc 1440ttagcgactg ttctcataa ccttactact
attactaagc ctcttaagta cagctatatt 1500aacaagtgtc ctctctctt ttctgatgat cgtactgaag tacctcagtt agtgaacct
1560aatcaact caccctgtgt atccattgtc ccatccactg tgtgggaaga cggatgatt 1620tataggaaac aactatctcc acttgaaggt
ggtggctggc ttgtgctag tggctcaact 1680gttgcctga ctgagcaatt acagatgggc tttgtatta cagttcaata tggtagacag
1740accaatagtg tttgccccaa gttgaattt gtaatgaca caaaaattgc ctctcaatta 1800ggcaattgct tggaaatct cctctatggt
gtttcgggccc gttgtgttt tcagaattgc 1860acagctgtag gtgtcagca gcagccttt gttatgatg cgtaccagaa tttagttggc
1920tattattctg atgatggcaa ctactactgt ctgctgctt gtgttagtgt tctgtttct 1980gtcatctatg ataaagaaac taaaaccac
gctactctat ttgtagtgt tgcagtga 2040cacattct ctaccatgtc tcaatactcc cgtctacgc gatcaatgt taaacggcga
2100gattctacat atggccccct tcagacacct gttggtgtg tctaggact tgtaattcc 2160ctttgttcg tagaggactg caagttgct
ctcggtaac ctctctgctc tctctgac 2220acacctaga ctctcacacc tcgactgtg cgtctgtgc cagtgaaat gcgctggca
2280ccattgctt ttaactatcc cattcaggt gatcaacta atagtagtta tttaatta 2340agtataccca ctaattttc ctttgggtg actcaggagt
acattcagac aaccattcag 2400aaagttactg ttgattgta acagtactt tgcaatggt tcagaagtg tgagcaatta 2460ctgcgcgag
atggccagtt ttgtccaaa ataaaccagg ctctccatgg tgccaattt 2520cgccaggatg attctgtacg taattgttt gcgagcgtga aaagctctca
atcctctct 2580atcataccag gtttggagg tgactttaa ttgacactc tagaacctgt ttctatatct 2640actggcagtc gtagtgcag
tagtctatt gaggatttgc tatttgaca agtcaacta 2700gctgatctg gttatatgca aggttacgat gattgtatgc agcaaggtcc agcatcagct
2760cgtgatctta ttgtgctca atagtggct gttataaag tattactcc tttatggat 2820gttaatatgg aagccgctg tacttcatct
ttgctggca gcatagcagg ttgtgctgg 2880actgctggct taccctctt tctgctatt ccattgcac agagtatyt ttataggta
2940aacggtgtg gcattactca acagttctt tcagagaacc aaaagcttat tgccaataag 3000tttaatcagg ctctgggagc tatgcaaca
ggcttcaact caactaatga agcttttgg 3060aaggttcagg atgctgtgaa caaatgca caggctctat ccaattagc tagcagacta
3120tcaataact ttgtgctat ttccgctct attggagaca tcatacaacg tctgtatgt 3180ctcgaacagg acgccccaaat agacagact
attaatggcc gttgacaac actaatgtct 3240tttggctc acgactgtg tcttccgaa tcagctgctc ttccgctca attggctaaa
3300gataaagtca atgagtgtg caaggcaaa tcaagcgtt ctggatttg cgtcaagcc 3360acacatatag tctctttg ttgaaatgcc
cctaatggcc ttactttat geatgttgg 3420tattacccta gcaaccat tgaggtgtt tctgcttatg gctttgca tgcagctaac
3480cctactaatt gtagacccc ttgtaattgc tacttatta aaactaataa cactaggatt 3540gttgatgagt ggtcatatac tggctcctc
ttctatgac ctgagccat cactctctt 3600aataactaagt atgtgcacc acagtgaca taccaaaaca ttctactaa cctcctct
3660cctctctcgc gcaattccac cgggattgac ttcaagatg agttggatga gttttcaaa 3720aatgttagca ccagtatacc taatttgg
tcttaaacac agattaatac tacattact 3780gatcttacct acgagatgtt gctcttcaa caagttgta aagcccttaa tgagtctac
3840atagacctta aagagcttg caattact tattacaaca aatggcctg gtacattgg 3900cttggttca ttgctgggct ttgtcctta
gctctatgct tcttctcat actgtctgc 3960actggtgtg gcacaaactg tatgggaaaa ctaagtgt atcgtgtg tgatagatac
4020gaggaatac acctcagcc gcataaggt catgttcaat aa 4062214062DNAArtificial SequenceSynthetic
Polynucleotide 21atgatacact cagtggttct actgatgttc ttgtaaacac ctacagaaag ttacgttgat 60gtagggccag attctgttaa

gtctgctgt atgaggtg atatacaaca gactttctt 120gataaaactt ggcctagcc aattgatgt tctaaggctg acggtattat atacctca
180ggccgtacat atttaacat aactatcact tatcaagtc ttttcccta tcagggagac 240catggtgata tgatgttta ctctgcagga
catgctacag gcacaactcc acaaaagtg 300ttttagta actatttca ggacgtcaaa cagtttgta atgggttgt cgtccgata
360ggagcagctg ccaattccac tggcactgt attattagcc catctaccag cgctactata 420cgaaaaattt acctgcttt tatgtcgggt
tcttcagtgt gtaatttctc agatggtaaa 480atgggcccgt tctcaatca tactctagt ctttggccc atggatgtgg cactttactt 540agagctttt
attgtattct ggagcctcgc tctggaaate attgtctgc tggcaatcc 600tatacttct ttgccactta tcacactcct gcaacagatt gttctgatgg
caattacaat 660cgtaatgcca gctgaactc tttaaggag tatttaatt tacgtaactg cacctttatg 720tacacttata acattaccga agatgagatt
ttagagtgtt ttggcattac acaaactgct 780caaggtgttc acctctctc atctcggtat gttgattgt acggcggcaa tatgttcaa 840tttgccacct
tgctgttta tgatactatt aagtattatt ctatcattcc tcacagtatt 900cgttctatcc aaagtgatag aaaagctgg gctgctctc acgtataaa
acttcaaccg 960ttaactttcc tgttgattt ttctgtgat gttatatac gcagagctat agactgtgtt 1020ttaatgatt tgcacaact cactgctca
tatgaatcct tcgatgtga atctggagtt 1080tattcagttt cgtcttctga agcaaaacct tctggctcag ttgtggaaca ggctgaaggt
1140gttgaatgt attttccac tctctgtct ggcacacctc ctcaagttta taattcaag 1200cgtttgtttt ttaccaattg caattataat ctaccaat
tgcttact ttttctgtg 1260aatgatttta ctgtagta aatatccca gcagcaattg ctgcaactg ttattctca 1320ctgattttgg attactttc
ataccactt agtatgaaat ccgatctcag tgttagttct 1380gctgttccaa tatccagtt taattataaa cagctctttt ctaatccac atgtttgatt
1440ttagcagctg ttctcataa cttactact attactaagc ctcttaagta cagctatatt 1500aacaagtct cctgctctct ttctgatgat
cgtactgaag tacctcagtt agtgaacgct 1560aatcaactact cacctgtgt atccattgtc ccatccactg tgtggaaga cgggtgatt
1620tataggaac aactatctcc acttgaaggt ggtggctggc ttgttctag tggctcaact 1680gttgccatga ctgagcaatt acagatgggc
tttgattta cagtcaata tggtagacac 1740accaatagtg tttgcccac gcttgaatt gctaatagaca caaaaattgc ctctcaatta
1800ggcaattgct tggaaatct cctctatggt gtttcgggccc gttgtttt tcagaattgc 1860acagctgtag gtttcgaca gcagcgttt
gtttatgat cgtaccagaa tttagttggc 1920tattattctg atgatggcaa ctactactgt ttgcgtgctt gtttagtgt tctgtttct 1980gtcatctatg
ataaagaac taaaaccac gctactctat ttgtagtgt tgcagtgtga 2040cacatttct ctaccatgtc tcaatactcc cgttctacgc gatcaatgt
taaaggcga 2100gattctacat atggccccct tcagacacct gttggttgc tcttaggact ttttaattcc 2160tcttgttgc tagaggactg
caagttgctt cttgtcaat ctctctgtgc tcttctgac 2220acacctagta ctctcaacc tcgactgtg cctctgttc caggtgaaat gcgcttggca
2280tccattgctt ttaactatcc tattcaggtt gatcaactta atagtagtta ttttaatta 2340agtatacca ctaattttc ctttgggtg actcaggagt
acattcagac aaccattcag 2400aaagttactg ttgattgaa acagtactgt tgcaatggtt tcagaagtg tgagcaatta 2460ctgcgcgagt
atggccagtt ttgtccaaa ataaaccagg ctctccatgg tgcaattta 2520cgccaggatg attctgtacg taattgttt gcgagcgtga aaagctctca
atcatctct 2580atcataccag gttttggagg tgactttaa ttgacacttc tggaaactgt ttctatatct 2640actggcagtc gtagtgcacg
tagtctatt gaggattgc tatttgaca agtcaactata 2700gctgatctg gttatagca aggttacgat gattgatgc agcaaggtcc agcatcagct
2760cgtgatctta tttgtctca atagtggct gttacaag tattacctcc tttatggat 2820gttaatatgg aagccgcgta tacttcatct
ttgcttggca gcatagcagg ttttggctgg 2880actgctgctg tatectctt tctgctatt ccatttgcac agagtatctt ttataggta
2940aacggtgtg gcattactca acaggttctt tcagagaacc aaaagcttat tgcaataag 3000ttaatcagg ctctgggagc tatgcaaaa
ggcttacta caactaatga agctttcag 3060aaggttcagg atgctgtgaa caacaatgca caggctctat ccaattagc tagcgagcta
3120tctaactt ttgtgctat ttccgctct attggagaca tcatacaac tcttgatgtt 3180ctcgaacagg acgcccacat agacagactt
attaatggcc gtttgacaac actaaatgt 3240tttgttgcac agcagctgt tcttccgaa tcagctgctc ttccgctca attggctaaa
3300gataaagta atgagtgtg caaggcaaa tccaagcgtt ctgattttg cggtaaggc 3360acacatatag tctcctttg tgtaaatgc
cctaagcc tttactcat gcatgttgg 3420tattacccta gcaaccacat tgagttggt tctgcttatg gctttgca tgcagctaac
3480cctactaatt gtagagccc ttttaagtc tactttata aaactaata cactaggatt 3540gttgatgagt ggcatatac tggctcctc
ttctatgca ctgagccat tacctcctt 3600aataactaag atgttgcac acaggtgaca taccaaaaca ttctactaa cctccctct
3660cctctctcgc gcaattccac cgggattgac ttcaagatg agttggatga gttttcaaa 3720aatgtagca ccagtatacc taatttgg
tcctaacac agattaatac tacattactc 3780gatcttacct acgagatgtt gctcttcaa caagtgta aagccctaa tgactctac
3840atagacctta aagagcttgg caattact tattacaaca aatggcctg gtacattgg 3900cttggttca ttgctgggct tttgcctta
gctctatgct tcttctcat actgtctgc 3960actggttgc gcacaaactg tatgggaaaa ctttaagtga atcgttgtg tgatagatac
4020gaggaatag acctcagacc gcataaggtt catgttact aa 4062221845DNAArtificial SequenceSynthetic
Polynucleotide 22atgatccact cgtgttct cctcatgtc ctgtgacc cactgagc agactgcaag 60ctcccgtgg gacagctct
gtgtgcctg cctgacactc ctgactct gacccacgc 120tccgtcgggt cggctcctgg cgaatgcgg ctggcctca tgccttcaa
tcaccaate 180caagtgatc agctgaatag ctctatttc aagcttcca tccccagaa ctctcgttc 240ggggtcacc aggagtacat
ccagaccaca atcagaagg tcaccgtcga ttgcaagca 300tacgtgtgca acggcttca gaagtgcgag cagctgctga gagaatcgg
gcagtttgc 360agcaagatca accagcctc gcatggagct aacttgcgc aggacactc cgtgcgcaac 420ctcttgcct ctgtgaagtc
atcccagtc tccccatca tcccgggatt cggaggggac 480ttcaactga cctctctgga gccctgtctg atcagaccg gtagcagatc
ggcgcgctca 540gccattgaag atcttctgt cgacaaggtc accatcgcgc atcccgggca catgcaggga 600tacgacgact gtagcagca
gggaccagcc tccgcgaggg acctcatctg cgcgcaatac 660gtggccgggt acaagtgtc gctcctctg atggatgta acatggagcc
cgttatact 720ctgctcctgc tggctctat cgcggcctg ggttgaccg ccggctctc ctcttccc 780gtatccct ttgcacaatc
cattttctac cggctcaac gcgtgggcat tactcaaaa 840gtcctgtcgg agaaccagaa gttgatgca acaagttca atcagccct
gggggcatg 900cagactgat tctactagc taacgaagc ttccagaag tccaggacgc tgtgaacaac 960aacgcccagg cgtctcaaaa

gctggcctcc gaactcagca acaccttcgg agccatcagc 1020gcatcgatcg gtgacataat tcagcggctg gacgtgctgg agcaggacgc
ccagatcgac 1080cgccctcatca acggacggct gaccaccttg aatgccttcg tggcacaaca gctggtcg 1140agcgaatcag cggcacttcc
cgcccaactc gccaaaggaca aagtcaacga atcgctgaag 1200gcccagtcga agaggtccgg tttctgcggt caaggaacce atattgtgct
cttcgctgctg 1260aacgcgcca acggtctgta ctttatgcac gtcggctact acccgagca tcatatcgaa 1320gtggtgctcg cctacggcct
gtgcgatgcc gtaaccca ctaactgtat tgcctctgtg 1380aacggatatt ttattaagac caacaacacc cgcattgtgg acgaatggc
atacaccgg 1440ctgctcttct acgcgcccga gccatcact tactgaaca ccaatacgt ggctccgca 1500gtgacctacc agaactctc
cacaatttg cgcgcggcgc tgctcggaaa cagcaccgga 1560attgatttcc aagatgaact ggacgaatc tcaagaacg tgtccactc
cattccaac 1620ttcgggaagcc tgacacagat caacaccacc ctctcgacc tgacctaga gatgctgagc 1680cttcaacaag tggtaagcc
cctgaacgag agctacatcg acctgaagga gctgggcaac 1740tatacctact acaacaagt gcccggacaag attgaggaga ttctgtcga
aatctaccac 1800attgaaaacg agatcgccag aatcaagaag ctatcgcg aagcc 1845234071DNAArtificial
SequenceSynthetic Polynucleotide 23atggaaaccc ctgcccagct gctgttctg ctgctgctgt ggctgcctga taccaccggc
60agctatgtgg acgtgggccc cgatagcgtg aagtcgcct gctcgaagt ggacatccag 120cagaccttt tcgacaagac ctggcccaga
cccacgacg tgccaagc cgacggcacc 180atctatccac aaggccggac ctacagcaac ataccatta cctaccaggc cctgttcca
240atcaagggc accacggcga tatgtactg tactctgccc gccacgccac cggcaccaca 300ccccagaaac

tgctctggc caactacagc caggacgtga agcagttgc caacggctc 360gtcgtgcccga ttggcggcgc tgccaatagc accggcacg
tgatcatcag cccagcacc 420agcggcca tccggaagat ctaccccgc tcatgctgg gcagctcctg gggcaattc 480agcgcggca
agatggggcgt gttctcaac cacacctg tgctgctgc cgatggctg 540ggcacactgc tgagagcct ctactgcatc ctggaacca
gaagcggca ccaactgcct 600gcccgaata gctacaccag ctccgccc taccacacac cgcaccgca ttgctccgac 660ggcaactaca
accggaacgc cagcctgaac agcttcaag agtacttca cctgcggaac 720tgacacttca tctacaccta caatatcacc gaggacgaga
tctggaatg gttcggcacc 780accagaccg cccagggcgt gcaactgtc agcagcagat acgtggacct gtagggcggc 840aacatgtcc
agtttccac cctgcccgtg tacgaccca tcaagtacta cagcatcacc 900ccccacagca tccggtccat ccagagcgc agaaaagct
ggggcgcct ctacgtgac 960aagctgcagc cctgacctt cctgctggac ttacgctgg acggctacat cagacgggc 1020atcactgctg
gcttcaacga cctgagccag ctgactgct cctacgagag ctccgactg 1080gaaagcggcg tctacagcgt gtccagctt caggccaagc
ctagcggcag cgtggtggaa 1140caggtgagg gctggaatg cgactcagc cctctgctga gggcaccac tcccaggtg 1200tacaactca
agcggctggt gttaccaac tgcaattaca acctgacaa gctgctgagc 1260ctgttctccg tgaacgactt cacctgtagc cagatcagcc
ctgcccctat tcccagcaac 1320tgctacagca gctgatcct ggactactt agtaccccc tgagcatgaa gtccgatctg 1380agcgtgctc
cgcgggacc catcagccag tcaactaca agcagagctt cagcaacct 1440acctgctga ttctggccc cgtgcccac aatctgacca
ccatcaccaa gccctgaag 1500tacagctaca tcaacaagt cagcagactg ctgtccgagc accggaccga agtccccag 1560ctcgtgaagc
ccaaccagta cagcccctgc gttccatcg tcccagcag cgtgtgggag 1620gacggcgact actacagaaa gcagctgagc ccctggaag
gcccgggatg gctggtggct 1680tctggaagca cagtggccat gaccgagcag ctgcagatgg gcttggcat caccgtgag 1740tacggcaccg
acaccaacag cgtgtgccc aagctggaat tcccgaatga caccaagatc 1800gccagccagc tgggaaactg cgtggaatac tccctgtatg
gctgtccgg accgggctg 1860ttccagaatt gcacagcag gggagtgccg cagcagagat tctgtacga tccctaccag 1920aacctgctg
gtactacag cgacgacggc aattactact gctgcccggc ctgtgtgctc 1980gtgcccgtg cctgtatc cagaaaagag acaagacc
acgccacact gttcggctc 2040gtggcctg agcacatcag ctccacctg agccagtact cccgctccac cgggtccatg 2100ctgaagcgg
gagatagc ctacggccc ctgcagacac ctgtgggatg tgtgctggc 2160ctcgtgaaca gctccctgt tgtggaagat tgcaagctg
cctgggcca gagcctgtg 2220gccctgccc ataccctag caccctgacc cctagaagcg tgcctctgt gcccggcga 2280atcgggctg
ctctatcgc ctcaatcac ccatcagc tggaccagct gaactcagc 2340acttcaagc tgagatccc cacaactt agctcggcg
tgaccagga gtacatccag 2400accacaatcc agaaagtgc cgtggactgc aagcagtagc tgtgcaacgg ctctcagaag 2460tgcaacagc
tgctgcgca gtacggccag ttctgagca agatcaacca gccctgcac 2520ggcgccaacc tgagacagga tgacagcgtg cggaacctg
tgccagcgt gaaaagcagc 2580cagtcagcc ccatcctcc tggctcggc ggcacttca acctgacct gctggaacct 2640gttccatca
gcaccggctc cagaagcgc agatccgcca tggaggacct gctgtcagc 2700aaagtgaaca ttgcccagcc cggctacatg cagggtacg
acgattgcat gcagcaggc 2760ccagccagc caggggatct gatctgtgccc cagtatgtgg cggctaca ggtgctgccc 2820cccctgatg
acgtgaacat ggaagcggc tacacctca gctgctggg ctctattgct 2880ggcgtgggat ggacagccgg cctgtctagc ttgcccga
tcccttgc cagagcacc 2940ttctaccggc tgaacggcgt gggcatcaca caacaggtg tgagcgagaa ccagaagctg 3000atcgccaaca
agttaacca ggcactggc gccatgcaga cggcttcc caccaccaac 3060gagccttca gaaagtgca ggacgcccgtg acaacaacg
cccagctct gagcaagctg 3120gectccgagc tgagcaatac ctccgccc atcagcgcct ccatcggcga catcatccag 3180cggctggagc
tgctggaaca ggacggccag atcagccggc tgatcaacgg cagactgacc 3240acctgaacg cctctgtggc acagcagctc gtgcggagc
aatctccc cctgtctgct 3300cagctggcca aggacaaagt gaacagctg gtgaagggc agtccaagc gagcggctt 3360gtggccag
gcaccacat cgtgtctt gctgtgaatg cccccacgg cctgtactt 3420atgcactggt gctattacc cagcaaccac atcaggtgg
tgtccgcta tggcctgtg 3480gacggcga atctacca ctgtatccc cccgtgaac gctacttcat caagaccaac 3540aacaccggga
tctggagca gtgtctac acaggcagca gcttctagc ccccagccc 3600atcacctccc tgaacacca atactggcc cccaagtga
cataccagaa catctcacc 3660aacctgccc ctccactgt gggaaattcc accggcatg acttccagga cgagctggac 3720gagttctca
agaacgtgt cactccat cccaacttgc gcagcctgac ccagataac 3780accactctg tggacctgac ctacagatg ctgctcctg

aacaggtcgt gaaagccctg 3840aacgagagct acatcgacct gaaagagctg gggaactaca cctactacaa caagtggcct 3900tggtacatt
ggctgggctt tatcgccggc ctgggtggccc tggccctgtg cgtgttcttc 3960atcctgtgct gcaccggctg cggcaccaat tgcattgggca
agctgaaatg caaccgggtgc 4020tgcgacagat acgaggaata cgacctggaa cctcaciaag tgcattgtgca c 4071241353PRTMiddle
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 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 615271353PRTMiddle 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 1350281353PRTMiddle 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 1350291255PRTHuman 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 60aagaagagt aagaagaaat ataagagcca ccatgggtct
caaggtgaac gtctctgccg 120tattcatggc agtactgtta actctcaaaa caccgcggc tcaattcat tggggcaatc 180tctctaagat
aggggtagta ggaataggaa gtgcaagcta caaagtattg actcgttcca 240gccatcaatc attagtcata aaattaatgc ccaatataac tctctcaat
aactgcacga 300gggtagagat tgcagaatac aggagactac taagaacagt tttggaacca attaggggatg 360cacttaatgc aatgaccag
aacataaggc cggttcagag cgtagcttca agtaggagac 420acaagagatt tgcggggagta gtctggcag gtgcggcct aggtgttgc
acagctgtc 480agataacagc cggcattgca ctaccgggt ccatgctgaa ctctcaggcc atcgacaatc 540tgagagcgag cctggaaact
actaatcagg caattgaggc aatcagacaa gcagggcagg 600agatgatatt ggctgttcag ggtgtccaag actacatcaa taatgagctg
ataccgtcta 660tgaaccagct atcttctgat ctaatcggtc agaagctcgg gctcaattg ctagatact 720atacagaaat cctgtcatta
tttgcccca gctacggga cccatattc gggagatat 780ctaccaggc tttgagttat gcactggag gagatatcaa taagtgta
gaaaagctc 840gatacagtg aggcgattta ctaggcatc tagagagcag aggaataaag gctcggataa 900ctcagctga cacagagtc
tactcatag tctcagat agcctatcc acgtgtccg 960agattaagg ggtgattgc caccgctag aggggtctc gtacaacata
ggctctcaag 1020agtgttatac cactgtccc aagtattg caaccaagg gtacctatc tgaatttg 1080atgagtcac atgtacttc
atgccagagg ggactgtg cagccaaaat gcttctacc 1140cgtagctc tctgtccaa gaatgcctcc ggggtccac caagctctg
gtctgtacac 1200cgtatccg gtcttttggg aaccggttca tttatcaca agggaacctata atagccaatt 1260gtgcatcaat tctttgtaag
tgttacaaa caggtacgat tattaatcaa gacctgaca 1320agatcctaac atacattgct gccgatcgt gcccgtagt cgaggtgaac
ggcgtgacca 1380tccaagtcgg gagcaggagg tatccagacg ctgtgtactt gcacagaatt gacctcggc 1440ctccatatac attggagagg
ttggacgtag ggacaaatc ggggaatgca attgccaat 1500tggaggatgc caaggaattg ttggaatcat cggaccagat attgagaagt
atgaaaggt 1560tatcgagcac tagcatagtc tacatctga ttgcagtgt tcttggaggg ttgataggga 1620ccccacttt aatatgttc
tgcagggggc gttgtaacaa aaaggagaa caagtggta 1680gtcaagacc aggctaaag cctgacctta caggaacatc aaaatcctat
gtaagatgc 1740ttgatgata ataggctgga gctcgggtgg ccaagcttct tccccctgg gctcccc 1800agccctct cccctctg
caccgtacc cccgtgtct ttgaataaag tctgagtg 1860cggc 1864361653DNAArtificial SequenceSynthetic
Polynucleotide 36atgggtctca aggtgaacgt ctctgccgta tcatggcag tactgttaac tctccaaaca 60cccgcggc aaattcattg
gggcaatctc tctaagatag ggttagtagg aataggaagt 120gcaagctaca aagtatgac tcttccagc catcaatcat tagtcataaa attaatgcc
180aatataact tctcaataa ctgcacgagg gtagagattg cagaatacag gagactacta 240agaacagttt tgaaccaat tagggatgca
cttaatgcaa tgaccagaa cataagggc 300gttcagagcg tagcttcaag taggagacac aagagattg cgggagtagt cctggcaggt
360gccccttag gtgttccac agctgtcag ataacagccg gcattgcaat taccggctc 420atgctgaact ctaggccat cgacaatctg
agagcgagcc tggaaactac taatcaggca 480attgaggcaa tcagacaagc agggcaggag atgatattgg ctgttcaggg tgccaagac
540tatcatcaata atgagctgat accgtctatg aaccagctat ctgtgatct aatcggtcag 600aagctcgggc tcaattgct tagatactat
acagaaatc tgtcattat tggccccagc 660ctacgggacc ccatatctgc ggagatatct atccaggctt tgagttatgc acttggagga
720gatataata aggtgttaga aaagctcggga tacagtggag gcgatttact aggcattta 780gagagcagag gaataaaggc tggataact
cacgtcaca cacagtctca ctcatagtc 840ctcagtatag cctatccgac gctgtccgag attaggggg tgattgtcca cggctagag
900ggggtctct acaataggt ctctcaagag tggatataca ctgtgcccga gtatgttga 960accaagggt acctatctc gaattttgat
gagtcacat gtacttcat gccagagggg 1020actgtgtgca gcaaaatgc ctgtaccg atgagctctc tctccaaga atgctcgg
1080gggtccaca agtctgtgc tctacactc gtatccgggt ttttgggaa ccggttatt 1140ttatcacaag ggaacctaat agccaattg
gcatcaatc tttgtaagt ttacacaaca 1200ggtacgatta ttaatacaaga cctgacaag atcctaacat acattgctgc ctagctctg
1260ccgtagtgc aggtgaacgg cgtgaccatc caagtcggga gcaggagta tccagacgt 1320gtgtacttgc acagaattga cctcggctct
cccatatcat tggagaggtt ggacgtaggg 1380acaatctgg ggaatgcaat tgccaaattg gaggatgcca aggaattgtt ggaatcag
1440gaccagat tgagaagtat gaaaggtta tgcagcacta gcatagtcta cactctgatt 1500gcagtgtgct ttggagggtt gatagggat
cccacttaa tatgttctg cagggggcgt 1560gtaacaaaa agggagaaca agttggtatg tcaagaccag gcctaaagcc tgacctaca
1620ggaacatcaa aatcctatg aagatcgtt tga 1653371925DNAArtificial SequenceSynthetic Polynucleotide
37ggggaataa gagagaaaag aagagtaaga agaaataa gagccaccat ggtctcaag 60gtgaacgtct ctgccgtatt catggcagta
ctgttaactc tccaaacacc cggcgtcaa 120attcattgg gcaatctct taagatagg gtagtaggaa taggaagtgc aagctacaaa
180gttatgact gtccagcca tcaatcatta gtataaaat taatgcccata taactctc 240ctcaataact gcacgagggt agagattgca
gaatacagga gactactaag aacagtttg 300gaaccaatta gggatgcaat taatgcaatg accagaaca taaggccgt tgcagagcga
360gttcaagta ggagacaaa gagatttgc ggagtagtc tggcaggtgc ggcctaggt 420gttgcacag ctgctcagat aacagccggc
attgacttc accggtccat gctgaactct 480caggccatc acaatctgag agcgagcctg gaaactacta atcaggcaat tgaggcaatc

540agacaagcag ggcaggagat gatattggct gttcagggtg tccaagacta catcaataat 600gagctgatac cgtctatgaa ccagctatct
tgtgatctaa tcggtcagaa gctcgggctc 660aaattgctta gatactatac agaaactctg tcattatttg gccccagcct acgggacccc
720atatctcggg agatatctat ccaggctttg agttatgcac ttggaggaga tatcaataag 780gtgttagaaa agctcggata cagtggaggc
gatttactag gcactttaga gacagagga 840ataaaggctc ggataactca cgtcgacaca gactcctact tcatagtctc cagtatagcc
900tatccgacgc tgtccgagat taaggggggtg attgtccacc ggctagaggg ggtctctac 960aacataggct ctcaagagtg gtataccat
gtgcccaagt atgttgaac ccaagggtac 1020cttatctcga attttgatga gtcacatgt actttcatgc cagaggggac tgtgtgcagc
1080caaatgcct tgtaccgat gactcctctg ctccaagaat gcctccgggg gtcaccaag 1140tctctgtctc gtacactcgt atccgggtct
tttgggaacc ggttcatttt atcacaaggg 1200aacctaag ccaattgtgc atcaattctt tgaagtgtt acacaacagg tacgattatt
1260aatcaagacc ctgacaagat ctaacatac attgtgcgc atcgtgccc ggtagtcgag 1320gtgaacggcg tgaccatcca agtcgggagc
aggaggtatc cagacgctgt gtacttgcac 1380agaattgacc tcggtcctcc catatcattg gagaggttg acgtagggac aaatctgggg
1440aatgcaattg ccaattgga ggatgccaa gaattgttg aatcatcgga ccagatattg 1500agaagtatga aaggtttatc gagcactagc
atagtctaca tctgattgc agtgtgtctt 1560ggagggttga tagggatccc cactttaata tgttctgca gggggcgttg taacaaaaag
1620ggagaacaag ttggtatgc aagaccaggc ctaaagctg acctacagg aacatcaaaa 1680tctatgtaa gatcgtttg atgataatg
gctggagcct cgggtgcca gcttcttgc 1740ccttgggct cccccagcc cctctcccc tctctgacc cgtaccccc tggtctttga
1800ataaagtctg agtgggaggc aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa 1860aaaaaaaa aaaaaaaaa
aaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa 1920tctag 1925381864DNAArtificial SequenceSynthetic
Polynucleotide 38tcaagcttt ggaccctct acagaagctc atacgactca ctataggga ataagagaga 60aaagaagagt aagaagaat
ataagagcca ccatgggtct caaggtgaac gtctctgca 120tattcatggc agtactgtta actctcaaa caccaccgg tcaatccat tggggcaat
180tctctaatag aggggtgta gggtaggaa gtgcaagctc caaagtatg actcgtcca 240gccatcaatc attagtata aagttatgc
ccaatatac tctctcaac aattgcacga 300gggtaggat tgcagaatac aggagactac tgagaacagt tctggaacca attagagatg
360cacttaatgc aatgaccag aatataagac cgggtcagag ttagcttca agtaggagac 420acaagagatt tgcgggagtt gtctggcag
gtcgggacct aggcgttgc acagtgtctc 480aaataacagc cgttattgca ctaccagct ccatgctgaa ctctcaagcc atcgacaatc
540tgagagcag ctagaaact actaatcagg caattgaggc aatcagacaa gcagggcagg 600agatgatatt ggctgttcag ggtgtccaag
actacatcaa taatgagctg ataccgtctc 660tgaatcaact atcttctgat ttaatcgcc agaagctagg gctcaattg ctgagatac
720atacagaaat cctgtcatta tttggccca gcttaccgga ccccatatct gggagatata 780ctatccaggc ttgagctat gcgcttggag
gagatatcaa taaggtgtg gaaaagctc 840gatacagtg aggtgatctc ctgggcatct tagagagcag aggaataaag gcccggataa
900ctcactcga cacagagctc tactcattg tactcagat agcctatccg acgctatccg 960agattaaggg ggtgattgtc caccggctag
agggggtctc gtacaacata ggctctcaag 1020agtgtatc cactgtccc aagtattg caaccaagg gtacctatc tgaatttg
1080atgagctac atgcacttc atccagagg ggactgtgtg cagccagaat gcttctacc 1140cgtagagctc tctgtccaa gaatcctcc
gggggtccc taagtctgt gctctgacac 1200ctgtatccg gcttctggg aaccggttca tttatcaca gggaacctc atagccaatt
1260gtgcatcaat ccttctcaag tttacaca cagaacaat cattaatcaa gacctgaca 1320agatcctaac atacattgct gccatcact
gcccgtggt cgaggtgaat ggcgtgacca 1380tccaagctcg gacagaggg tatccggagc ctgtgtactt gcacaggatt gacctggctc
1440ctccatatac tttggagagg ttggacgtg ggacaaatct ggggaatgca attgctaagt 1500tgaggatgc caaggaattg ttgagctat
cggaccagat attgaggagt atgaaaggtt 1560tatcgagcac tagtatagtt tacatcctga ttgagctgtg tcttggagga ttgatagga
1620ccccgctt aatatgttc tgcagggggc gttgtaacaa gaaggagaa caagttgta 1680tgaagacc aggcctaaag cctgatctc
caggaacatc aaaatcctat gtaaggtcac 1740tctgatgata ataggctgga gcctcggtg ccaagcttct tccccctg gcctcccc
1800agccccct cccctctc caccgtacc cccgtgtct tgaataaag tctgagttg 1860cgcc 1864391653DNAArtificial
SequenceSynthetic Polynucleotide 39atgggtctca aggtgaactc ctctgcata tcatggcag tactgttaac tctcaaca
60cccaccgctc aaatccattg gggcaatctc tctaatagag gggtgttagg ggtaggaagt 120gcaagctaca aagttatgac tcttccagc
catcaatcat tagcataaa gtaatgccc 180aatataactc tctcaacaa ttgcagagg gtagggattg cagaatacag gagactactg
240agaacagttc tgaaccaat tagagatgca cttaatgca tgaccagaa tataagaccg 300gttcagagt tagcttcaag taggagacac
aagagattg cgggagttg cctggcaggt 360gcggccctag gcgttgcac agctgctca ataacagccg gtattgact taccagctc
420atgctgaact ctcaagccat cgacaactc agagcagcc tagaaactac taatcagca 480attgaggca tcagacaagc agggcaggag
atgatattg ctgttcagg tgccaagac 540tatatcaata atgagctgat accgtctatg aatcaactat ctgtgattt aatcggccag
600aagctaggc tcaattgct cagatactat acagaatcc tgcattatt tggccccagc 660ttacgggacc ccatatctc ggagatatt
atccaggctt tgagctatgc gcttggagga 720gatataca atggttggaa aaagctcggaa tacagtggag gtgatctact gggcatctta
780gagagcagag gaataaaggc ccgataact cacgtcgaca cagagctca ctctattgta 840ctcagtatag cctatccgac gctatccgag
attaagggg tgattgcca ccggctagag 900ggggtctctg acaacatagg ctctcaagag tggatacca ctgtgcccc gtagttgca
960accaaggg acctatctc gaatttgat gactcatc gacttcat gccagagggg 1020actgtgtgca gccagaatgc ctgtaccg
atgagctctc tctccaaga atgcctcgg 1080gggtccacta agctctgtc tctacactc gtatccgggt ctctgggaa ccggttcat
1140ttatcacagg ggaacctaat agccaattg gcatcaatcc tttgcaagt ttacacaaca 1200ggaacaatca ttaatcaaga cctgacaag
atcctaact acattgtgc ctagactgc 1260ccggtgctc aggtgaatgg cgtgaccatc caagtcggga gcaggaggtc tccggacgt
1320gtgacttgc acaggattga cctcgctct cccatattt ttgagaggtt ggactaggg 1380acaaatctg ggaatgcaat tgctaagttg
gaggtgcca aggaattgtt ggagctatc 1440gaccagatata ttaggagat gaaaggttta tcagcacta gtatgttta catcctgatt

1500gcagtgtgct ttggaggatt gatagggatc cccgctttaa tatgttgctg cagggggcgt 1560tgaacaaga agggagaaca agttggtatg
tcaagaccag gcctaaagcc tgatcttaca 1620ggaacatcaa aatcctatgt aaggctactc tga 1653401925DNAArtificial
SequenceSynthetic Polynucleotide 40ggggaaataa gagagaaaag aagagtaaga agaataataa gagccaccat gggctc
60gtgaacgtct ctgtcatatt catggcagta ctgttaactc ttcaaacacc caccggctcaa 120atccattggg gcaatctctc taagatagg
gtggtagggg taggaagtgc aagctacaaa 180gttatgactc gttccagcca tcaatcatta gtcataaagt taatgcccata tataactctc
240ctcaacaatt gcacgagggt agggattgca gaatacagga gactactgag aacagttctg 300gaaccaatta gagatgactc taatgcaatg
accagaata taagaccggt tcagagtgtg 360gcttcaagta ggagacacaa gagatttgcg ggagttgtcc tggcaggtgc ggccttaggc
420gttgccacag ctgctcaaat aacagccggt attgcactc accagtccat gctgaactct 480caagccatcg acaatctgag agcgagccta
gaaactacta atcaggcaat tgaggcaatc 540agacaagcag ggcaggagat gatattggct gttcaggggtg tccaagacta catcaataat
600gagctgatac cgtctatgaa tcaatctct tgtgatttaa tggccagaa gctagggctc 660aaattgctca gatactatac agaaatctg
tcattattg gccccagctt acgggacccc 720atattctgagg agatatctat ccaggctttg agctatgcgc ttggaggaga tatcaataag
780gtgttgaaa agctcggata cagtggaggt gatctactgg gcatcttaga gagcagagga 840ataaaggccc ggataactca cgtcgacaca
gagctctact tcattgtact cagtatagcc 900tatccgacgc tatccgagat taaggggggtg attgtccacc ggctagaggg ggtctcgtac
960aacataggct ctcaagagtg gtataccact gtgcccaggt atgttgcaac ccaagggtac 1020cttatctega attttgatga gtcacatgc
acttctatgc cagagggggac tgtgtgcagc 1080cagaatgcct tgtaccgat gagtctctg ctccaagaat gcctccgggg gtcactaag
1140tctctgtctc gtactcgt atccgggtct tccgggaacc ggttcattt atcacagggg 1200aacctaag ccaattgtc atcaatcct
tgcaagtgt acacaacagg acaatcatt 1260aatcaagacc ctgacaagat ctaacatac attgctgcc atactgcc ggtggtcgag
1320gtgaatggcg tgaccatcca agtcgggagc agggaggtatc cggacgctgt gtaactgcaac 1380aggattgacc tggctctc catatctttg
gagaggttg acgtagggac aatctgggg 1440aatgcaattg ctaagtgtga ggatgccaag gaattgttg agtcatcgga ccagatattg
1500aggagatga aagtttact gagcactagt atagttaca tctgattgc agtgtgtctt 1560ggaggattga taggatccc cgccttaata
tgttctgca gggggcgttg taacaagaag 1620ggagaacaag ttggtatgc aagaccagc ctaaagcctg atcttacagg aacatcaaaa
1680tctatgtaa ggtcactctg atgataatag gctggagcct cgggtggccaa gcttcttgc 1740cctgggct cccccagcc cctctcccc
ttctgcacc cgtaccccc tggtcttga 1800ataaagtctg agtggggcggc aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa
1860aaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa 1920tctag 1925412065DNAArtificial
SequenceSynthetic Polynucleotide 41tcaagcttt ggaccctct acagaagta atacgactca ctataggga atagagaga
60aaagaagagt aagaagaat ataagagcca ccatgtcacc gcaacgagac cggataaatg 120cctctacaa agataacct tatccaagg
gaagtaggt agttattaac agagaacatc 180ttatgattga cagaccctat gtctctgctg ctgttctgt ctgactgtt ctgagcttga 240tcggattgct
ggcaattgca ggcattagac tcatcgggc agccatctac accgcggaga 300tcataaaag cctcagtacc aatctggatg tgactaactc
catcgagcat caggtcaagg 360acgtctgac accactctt aaaatcatc gggatgaagt gggcctgaga acactcaga 420gattcactga
cctagtgaaa tcatctcgg acaagattaa atctctaat ccggatagg 480agtacgactc cagagatctc acttgggtgca tcaaccgcc
agagaggatc aaactagatt 540atgatcaata ctgtgcagat gtggctgctg aagagctcat gaatgcattg gtgaactcaa 600ctctactgga
gaccagaaca accactcagt tctagctgt ctcaaagga aactgtcag 660ggcccactac aatcagaggt caattctca acatgtcgt
gtcctgttg gactgtact 720tagtgcagg ttacaatgt tcatctatag tcaactatgac atcccaggga atgtatgggg 780gaacctact
agttgaaaag ctaactctga acagcaaagg gtcagagttg tcaactga 840gcatgtaccg agtgtttgaa gtaggtgtga tcgaaaccc
gggtttgggg gctccggtgt 900tccatagc aaactttt gagcaaccag tcagtaatgg tctcggaac tgatgttg 960cttggggga
gtcaaacctc gcagccctt gtcaggggga cgttctatc ataattcct 1020atcagggatc agggaaagt gtcagctcc agctcgtcaa
gtcgggtgct tggaaatccc 1080caaccgacat gcaatctg gtcctctat caacggatga tccagtggta gacaggttt 1140acctctcatc
tcacagaggt gtcacgctg acaatcaagc aaaatgggt gtcggacaa 1200cacgaacaga tgacaagttg cgaatggaga catgctcca
gcaggcgtgt aaagtaaaa 1260tccaagcact ctgcgagaat cccgagtggg taccattgaa ggataacagg attcctcat 1320acggggtcct
gtctgtgat ctgagtctga cgttgagct taaaatcaaa atgctcgg 1380gattcgggcc atgtacaca cacggctcag ggtggacct
atacaaatcc aactgcaaca 1440atgtgtattg gctgactatt ccgcaatga gaaactagc cttagcgta atcaacacat 1500tgagtggtg
accgagatc aaggttagtc ccaactctt cactgtcca ataaaggaag 1560cagcgaaga ctgcatgcc ccaacatacc tacctcggga
ggtggacggt gatgcaaac 1620tcagttcaa cctggtgatt ctacctgctc aagatctcca atattttt gcaacctacg 1680atacctccag
ggtgagcat gctgtggtt attacgtta cagcccaagc cgtcattt 1740cttacttta tcttttagg ttgcataaa aggggtccc aatgaacta
caagtggaat 1800gcttcatg ggtcaaaaa ctctgtgccc gtcactctg tgtctgctg gactcagaat 1860ccggtggact tactctac
tctgggatg tggcatggg agtcagctgc acagctacc 1920gggaagatg aaccaatgc agataatg aataggctg agctcgtg
gccaagctc 1980ttgcccctg ggcctcccc cagccctcc tccctctc gaccctac cccctggtc 2040ttgaataaa gctgagtg
gcggc 2065421854DNAArtificial SequenceSynthetic Polynucleotide 42atgtcaccgc aacgagaccg gataatgcc
ttctacaaag ataacctta tccaagga 60agtaggatg ttattaacag agaactctt atgattgaca gacctatgt tctgctgct 120gttctgtc
tcatgttct gagctgac ggattgctg caattgcagg cattagactt 180catcgggcag ccatctacac cgggagatc cataaaagcc
tcagtacaa tctggatgtg 240actaactcca tcgagatca ggtcaaggac gtgctgacac cactcttaa aatcatcggg 300gatgaagtg
gctgagaac acctcagaga tcaactgacc tagtgaatt catctcggac 360aagattaat tcttaatcc gtagaggag tacgactca
gagatctac ttggtgcatc 420aacccggcag agaggatcaa actagattat gatcaact gtcagatgt ggtgctgaa 480gagctcatg
atgcattggt gaactcaact ctactggaga ccagaacaac cactcagttc 540ctagctgtct caaagggaa ctgctcaggg cccactacaa

tcagaggta atttcaaac 600atgtcgtgt ccttgttga ctgtacta ggtcagggtt acaatgttc atctatagtc 660actatgacat
cccagggat gtaggggga acctacatg ttgaaaagcc taatctgaac 720agcaaagggt cagagttgtc acaactgagc atgtaccag
tgtttgaagt aggtgtgatc 780agaaccggt gtttgggggc tccggtgtc catatgaaa actatttga gcaaccagtc 840agtaagtgt
tcggcaactg tatggtgctt ttgggggagc tcaaactgc agcccttgt 900cacggggagc attctatcat aattccctat cagggatcag
ggaaaggtgt cagctccag 960ctcgtcaagc tgggtgtctg gaaatccca accgacatgc aatctgggt cccctatca 1020acggatgatc
cagtggtaga caggctttac ctctcatctc acagaggtgt catcgtgac 1080aatcaagcaa aatgggctgt cccgacaaca cgaacagatg
acaagttcgc aatggagaca 1140tgctccagc aggcgtgtaa aggtaaaat caagcactct gcgagaatcc cgagtgggta 1200ccattgaagg
ataacaggat tcttcatac ggggtcctgt ctgtgatct gagtctgacg 1260gttgagctta aatcaaaaat tgcttcggga ttcgggcat tgatcacaca
cggtcaggg 1320atggacctat acaaatcaa ctgcaacaat gtgtattggc tgactatcc gccatgaga 1380aatctagct

taggegtat caacacattg gagtgatc cgagattcaa ggtagtccc 1440aacctctca ctgtcccaat taaggaagca ggcaagact
gccatcccc aacataccta 1500cctgcggagg tggacggtga tgcaaacct agttccaacc tggtagttct acctggtcaa 1560gatctccaat
atgttttggc aacctagat acctcagggt ttgagcatgc tgtggttat 1620tacgtttaca gcccaagcgc ctattttct tacttttate ctttaggtt
gcctataaag 1680ggggtcccaa tgaactaca agtggatgc ttacatggg atcaaaaact ctggtgccgt 1740cattctgtg tgcttgcgga
ctcagaatcc ggtggacta tcaactcctc tgggatggtg 1800ggcatgggag tcagctgcac agctaccgg gaagatggaa ccaatcgcag ataa
1854432126DNAArtificial SequenceSynthetic Polynucleotide 43ggggaaataa gagagaaaag aagagtaaga agaaataa
gagccacat gtcaccgaa 60cgagaccgga taaatgctt ctacaagat aacccttacc ccaagggaag taggatagtt 120attaacagag
aacatctat gattgacaga cctatgtc tgctggctgt tctgtctc 180atgttttga gcttgatcgg attgctggca attgcaggca ttagactca
tcgggcagcc 240atctacaccg cggagatcca taaaagcctc agtaccatc tggatgtgac taactcctc 300gagcatcagg tcaaggacgt
gctgacacca ctcttaaaa tcatcgggga tgaagtgggc 360ctgagaacac ctacagatg cactgaccta gtgaaattca tctcggaca
gattaaattc 420cttaatccg ataggagta cacttcaga gatctcact ggtgatcaa cccgccagag 480aggatcaaac tagattatga
tcaactgtg gcagatgtg ctgctgaaga gctcatgaat 540gcattggtga actcaactct actggagacc agaacaacca ctcagttct agctgtctca
600aagggaaact gctcaggccc cactacaatc agaggtcaat tctcaaatc gtcgtgtcc 660ttgtggact tgtagtagg tcgaggttac
aatgtgcat ctatagtcac tatgacatcc 720cagggaatgt atgggggaaac ctacctagtt gaaaagccta atctgaacag caaagggtca
780gagttgtcac aactgagcat gtaccgagtg ttgaagtag gtgtgatcag aaaccgggt 840ttgggggctc cgggttcca tatgacaac
tattttgagc aaccagtcag taatgtctc 900ggcaactgta tgggtgctt gggggagctc aaactcgcag cctttgtca cggggacgat
960ctatcataa tccctatca gggatcagg aaaggtgca gcttccagct cgtcaagctg 1020ggtgtctgga aatcccaac cgacatgcaa
tctgggtcc cttatcaac ggatgatcca 1080gtgtagaca ggctttacct ctatctcac agaggtgca tcgtgaca tcaagcaaaa
1140tgggtgtcc cgacaacag aacagatgac aagtgcgaa tggagacatg ctccagcag 1200gctgtaaaag gtaaatcca agcactcgc
gagaatccc agtgggtacc attgaaggat 1260aacaggatc ctctacagc ggtcctgtct gttgatcga gctgacggt tgagcttaaa
1320atcaaaattg ctccgggatt cgggccattg atcacacag gtcagggat ggacctatc 1380aaatccaact gcaacaatgt gtattggtg
actattccgc caatgagaaa tctagccta 1440ggcgtaatca acacattgga tggataccg agattcaagg ttatcccaa cctcttact
1500gtcccaatta aggaagcagg cgaagactgc catgccccaa catacctacc tgcggaggtg 1560gacggtgatg tcaactcag ttcaacctg
gtgattctac ctggtcaaga tctcaaat 1620gttttgcaa cctacgatac ctccagggtt gagcatgctg tggttatta cgtttacagc
1680ccaagcctc cattttcta cttttatct tttaggttgc ctataaagg ggtcccaatc 1740gaactacaag tggatgctt cacatgggat
caaaaactct ggtgctgca ctctgtgtg 1800cttgcggact cagaatccg tggacttacc actcactctg gtaggtggg catgggagtc
1860agctgcag ctaccggga agatggaacc aatgcagat aatgataa ggctggagcc 1920tcggtggcca agcttctgc ccttgggccc
tccccccagc cctctctc ctctctgc 1980ccgtacccc gtggtctttg aataaagtct gagtgggagg caaaaaaaaa aaaaaaaaaa
2040aaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa 2100aaaaaaaa aaaaaaaaa atctag
2126442065DNAArtificial SequenceSynthetic Polynucleotide 44tcaagcttt ggacctcgt acagaagcta atagactca
ctataggga ataaagaga 60aaagaagat aagaagaaat ataaagacca ccatgtcacc acaacgagac cggataaatg 120ccttctaca
agacaacccc catcctaagg gaagtaggat agttattaac agagaacatc 180ttatgattga tagacctat gttttgctgg ctgtctatt ctgcatggtt
ctgagctga 240tcgggttct agccattgca ggcattagac ttatcgggc agcatctac accgagaga 300tccataaaag ctcagcacc
aatctggatg taactaact aatcgagcat caggttaag 360actgctgac accactctc aagatcatg gtgatgaagt gggcttgagg
acacctcaga 420gattcactga ctagtgaag ttatctctg acaagattaa attcttaat cggacagggt 480aatacactc cagagatctc
acttgggtga tcaacccgc agagagaatc aaattgatt 540atgatcaata ctgtcagat gtggtgctg aagaactcat gaatcattg gtgaactcaa
600ctctactgga gaccaggga accaatcagt tctagctgt ctcaaggga aactgctcag 660ggccactac aatcagaggc caattctca
acatgtcgt gtcctgttg gactgtatt 720taagtcagg ttacaatgtg tcatctatag tcaatgac atcccaggga atgtacgggg
780gaacttacct agtggaaaag ctaactctga gcagcaaagg gtcagagttg tcaactga 840gcatgcaccg agtgtttgaa ttaggtgta
tcagaaatcc gggtttggg gctccggtat 900tccatgatg aaactatct gagcaaccag tcagtaatga tttagcaac tgcatggtg
960ctttgggga gctcaagttc gcagcctct gtcacaggga agattctatc acaattcct 1020atcagggatc agggaaagt gtcagcttc
agcttgcga gctaggtgct tggaaatccc 1080caaccgacat gcaatctgg gtcctctat caacggatga tccagtata gacaggctt
1140acctctatc tcacagagc gttatcctg acaatcaagc aaaaagggt gtcggaca 1200cacggacaga tgacaagttg cgaatggaga
catgctcca gcaggctgt aagggtaaa 1260tcaagcact ttgcgagaat cccgagtgga caccattgaa ggataacagg attcttcat

1320acggggtctt gtctgtgat ctgagtctga cagttgagct taaatcaaa attgttcag 1380gattcgggcc attgatcaca cacggttcag
ggatggacct atacaaatcc aaccacaaca 1440atatgtattg gctgactatc ccgccaatga agaacctggc cttaggtgta atcaacacat
1500tgagtgat accgagattc aaggttagtc ccaacctctt cactgttcca attaaggaag 1560caggcgagga ctgcatgcc ccaacatacc
tacctgcgga ggtggatggt gatgcaaac 1620tcagtccaa tctggtgatt ctacctggtc aagatctcca atatgtctg gcaacctag
1680atactccag agttgaacat gctgtagttt attacgttta cagcccaagc cgtcatttt 1740cttacttta tcttttagg ttgctgtaa
gggggggtccc cattgaatta caagtggaat 1800gcttcatg ggaccaaaaa ctctggtgcc gtcactctg tgtgctgcg gactcagaat
1860ctggtggaca tactactcac tctgggatgg tgggcatggg agtcagctgc acagccactc 1920gggaagatgg aaccagccgc agatagtgat
aataggctgg agcctcgggtg gccaagcttc 1980ttgccccctg ggctcccc cagccccctc tccccctct gcacctgac cccctggctc
2040tttgaataaa gtctgagtgg gcggc 2065451854DNAArtificial SequenceSynthetic Polynucleotide 45atgtcaccac
aacgagaccg gataaatgcc ttctacaaag acaaccccc tctaaggga 60agtaggatag ttattaacag agaacatctt atgattgata gacctatgt
tttctggct 120gttctattcg tcatgtttct gagcttgatc ggggtgctag ccattgcagg cattagactt 180catcgggcag ccatctacac
cgcagagatc cataaaagcc tcagaccaa tctggatgta 240actaactcaa tcgagcatca ggtaaggac gtgctgacac cactctcaa
gatcatcgg 300gatgaagtgg gcttggagac acctcagaga tctactgacc tagtgaagtt catctctgac 360aagattaaat tcttaatcc
ggacaggga tacgacttca gagatctcac ttggtgtatc 420aacccgccag agagaatcaa attggattat gatcaatact gtgcagatgt
ggctgctgaa 480gaactcatga atgcattggt gaactcaact ctactggaga ccagggcaac caatcagttc 540ctagctgtct caaagggaaa
ctgctcaggg cccactaaa tcagaggcca attctcaaac 600atgtcgtgt cctgttggga ctgtattta agtcgaggtt acaatgtgc atctatagtc
660actatgacat cccagggaat gtacggggga acttacctag tggaaaagcc taatctgac 720agcaaagggt cagagttgc acaactgagc
atgcaccgag tgtttgaagt aggtgtatc 780agaaatccgg gttgggggc tccggtatc catatgacaa actatcttga gcaaccagtc
840agtaatgatt tcagcaactg catggtggct ttgggggagc tcaagttcgc agccctctgt 900cacagggaag attctatcac aatccctat
cagggatcag ggaaaggtgt cagctccag 960ctgtcaagc tagtgtctg gaaatcccc accgacatgc aatcctgggt cccctatca
1020acggatgac cagtgataga caggctttac ctctcatc acagaggcgt tctcgtgac 1080aatcaagcaa aatgggctgt cccgacaaca
cggacagatg acaagtgcg aatggagaca 1140tgcctcagc agcgtgtaa gggtaaaatc caagcattt gcgagaatcc cgagtggaca
1200ccattgaagg ataacaggat tcttcatac ggggtcttct ctgttgatct gactctgaca 1260gttgagctta aatcaaaaat tgttcagga
ttcgggcat tgatcacaca cggctcaggg 1320atggacctat acaaatcaa ccacaacaat atgtattggc tgactatccc gccaatgaag
1380aacctggcct taggtgtaat caacacattg gactggatc cgagattcaa ggtagtccc 1440aacctcttca ctgtccaat taaggaagca
ggcaggact gccatcccc aacataccta 1500cctgcggagg tggatggtga tctcaaac acgtccaatc tgggtattct acctggtaaa
1560gatctcaat atgttctg gc aacctacgat actccagag tgaacatgc ttagttat 1620tacgtttaca gccaagecg ctctttct
tactttatc ctttaggtt gctgtaaag 1680gggggtcccc tgaattaca agtggatgc ttcacatggg accaaaaact ctggtgcctg
1740cactctgtg tcttgcgga ctcagaatct ggtggacata tctactc tgggatggtg 1800ggcatgggag tcagctgac agccactcg
gaagtggaa ccagccgcag atag 1854462126DNAArtificial SequenceSynthetic Polynucleotide 46ggggaaataa
gagagaaaag aagagtaaga agaaataa gagccaccat gtcaccaca 60cgagaccgga taaatgcct ctacaagac aacccccatc
ctaagggaag taggatagtt 120attaacagag aacatctt atgtgataga cctatgtt tctggtctgt tctattcgtc 180atgttctga gcttgatcgg
gttctagcc attgcagga ttagacttca tgggcagcc 240atctacaccg cagagatcca taaaagcctc agcacaatc tggatgtaac
taactcaatc 300gagcatcagg ttaaggactg gctgacacca ctctcaaga tcatcgtgga tgaagtgggc 360ttgaggacac ctcagagatt
cactgaccta gtgaagtca tctctgacaa gattaaatc 420cttaatccgg acagggaata cgacttcaga gatctcactt ggtgtatcaa cccgccagag
480agaatcaaat tggattatga tcaactgtg gcagatggtg ctgctgaaga actcatgaa 540gcattggtga actcaactct actggagacc
agggcaaca atcagttct agctgtctca 600aagggaact gctcagggcc cactacaatc agaggcaat tctcaaatc gctgctgccc
660ctgttgact tgtatttaag tcgaggttac aatgtgcat ctatagtcac tatgacatcc 720cagggaatgt acgggggaac ttacctagtg
gaaaagccta atctgagcag caaagggtca 780gagttgac aactgagcat gcaccagtg tttgaagtag gtgtatcag aatccgggt
840ttgggggctc cgtattcca tatgacaaac tatctgagc aaccagtcag taatgattc 900agcaactgca tgggtgctt gggggagctc
aagttgcag cctctgtca cagggaagat 960tctacaaa tccctatca gggatcagg aaaggtgca gcttccagct tctcaagta
1020ggtgtctgga aatccccaac cgacatgca tctggtgcc cctatcaac ggatgatcca 1080gtgatagaca gctttacct ctcatctac
agaggcgtta tctctgacaa tcaagcaaaa 1140tgggctgtcc cgacaacacg gacagatgac aagttgcgaa tggagacatg ctccagcag
1200gctgtgaagg gtaaatcca agcacttgc gagaatccc agtgagacc attgaaggat 1260aacaggattc ctctacagg gctctgtct
gttgatctga gctgacagt tgacttaaa 1320atcaaaattg ttcaggatt cgggccattg atcacacag gtcagggat ggacctatac
1380aaatcaacc acaacaat atgttggctg actatccgc caatgaagaa cctggcctta 1440ggtgtaatca acacattgga gtggataccg
agattcaagg ttagtccaa cctcttact 1500gttcaata aggaagcagg cgaggactgc catgccccaa catacctacc tgcggaggtg
1560gatggtgatg tcaactcag ttcaatctg gtgattctac ctggtcaaga tctcaatat 1620gttctggcaa cctacgatac ttccagatt
gaacatctg tagttatta cgtttacagc 1680ccaagccgt catttctta cttttact tttaggtg ctgtaagggg ggtccccatt
1740gaattacaag tggatgctt cacatgggac caaaaactct ggtgccgta ctctgtgtg 1800cttgcggact cagaatctgg tggacatc
actcactctg ggatggtgg catgggagtc 1860agctgcacag cactcggga agatggaacc agccgcagat agtgataata ggctggagcc
1920tcggtggcca agcttctgc ccttgggcc tccccagc cctctccc ctctctgac 1980ccgtacccc gtggtctttg aataaagtct
gagtgggcgg caaaaaaaaa aaaaaaaaaa 2040aaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa
2100aaaaaaaa 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 Ser

Arg Arg 610 615511729DNAArtificial SequenceSynthetic Polynucleotide 51tcaagctttt ggaccctcgt acagaagcta atacgactca ctataggga ataagagaga 60aaagaagagt aagaagaaat ataagagcca ccatggcaca agtcattaat acaaacgcc 120tgcgctgtt gaccagaat aacctgaaca aatcccagtc cgcactgggc actgctatcg 180agcgtttgct tccggtctg cgtatcaaca gcgcgaaaga cgatgcggca ggacaggcga 240ttgctaaccg tttaccgcg aacatcaaag gtctgactca ggcttccgt aacgctaacc 300acggtatctc cattgcgcag accactgaag gcgcgctgaa cgaaatcaac aacaactgc 360agcgtgtgcg tgaactggcg gttcagtctg cgaatgtac taactcccag tctgacctg 420actccatcca ggctgaaatc acccagcgcc tgaacgaaat cgaccgtgta tccggccaga 480ctcagttcaa cgcgctgaaa gtctggcgc aggacaacac cctgacctc caggttggtg 540ccaacgacgg tgaactatc gatattgatt taaaagaaat cagctctaaa acactgggac 600ttgataagct taatgtccaa gatgcctaca ccccgaaaga aactgctgta accgttgata 660aaactaccta taaaatggt acagatccta ttacagcca gagcaatact gatatccaaa 720ctgcaattgg cgggtggtgca acggggggtta ctggggctga tatcaaat tt aaagatggtc 780aatactatt agatgtaaa ggcggtgctt ctgctggtgt ttataaagcc acctatgatg 840aaactacaaa gaaagttaat attgatacga ctgataaac tccgttgga actgcggaag 900ctacagctat tccggggaacg gccactataa cccacaacca aattgctgaa gtaacaaaag 960agggtgttga tacgaccaca gttgcggctc aacttctgc agcaggggtt actggcgccg 1020ataaggacia tactagcctt gtaaaactat cgtttgagga taaaacggg aaggttattg 1080atggtggcta tgcagtgaaa atggcgagc atttctatgc cgtacatat gatgagaaaa 1140caggtgcaat tactgctaaa accactactt atacagatgg tactggcgtt gctcaaactg 1200gagctgtgaa atttggtggc gcaaatgta aatctgaagt tgttactgct accgatgta 1260agacttactt agcaagcgac cttgacaac ataacttcag aacaggcggg gagcttaaag 1320aggtaatac agataagact gaaaaccac tgcagaaaat tgatgctgcc ttggcacagg 1380ttgataact tcttctgac ctgggtgcgg ttcagaaccg ttcaactcc gctatcacca 1440acctgggcaa taccgtaaat aactgtctt ctgcccgtag cgtatcgaa gattccgact 1500acgcaaccga agtctccaac atgtctcgcg cgcagattct gcagcaggcc ggtacctccg 1560ttctggcgca ggcaaccag gttccgcaaa acgtctctc ttactgctg tgataatagg 1620ctggagcctc ggtggccatg cttctggcc cttgggcctc ccccagccc ctctcccct 1680tctcgaccc gtaccccct ggtctttgaa taaagtctga gtggcgccg

1729521518DNAArtificial SequenceSynthetic Polynucleotide 52atggcacaag tcattaatac aaacagcctg tcgctgttga cccagaataa cctgaacaaa 60tcccagtcg cactgggcac tgctatcgag cgtttgtctt ccggtctgcg tataacagc 120gcgaaagac atgcggcagg acaggcgatt gtaaccggt ttaccgcgaa catcaaagg 180ctgactcagg ctcccgtaa cgtaacgac ggtatctcca ttgcgcagac cactgaaggc 240gcgctgaacg aatcaacaa caacctgcag cgtgtgcgtg aactggcggg ttagtctgcg 300aatggtacta actcccagtc tgacctgac tccatccagg ctgaaatcac ccagcgcctg 360aacgaaatcg accgtgtatc cggccagact cagttaacg gcgtgaaagt cctggcgag 420gacaacacc tgaccatcca ggttggtgcc aacgacggg aactatcga tattgattta 480aaagaaatca gctctaaaac actgggactt gataagctta atgtccaaga tgcctacacc 540ccgaaagaaa ctgctgtaac cgttgataaa actacctata aaaatggtac agatcctatt 600acagcccaga gcaatactga tatccaaact gcaattggcg gtggtgcaac ggggggttact 660ggggctgata tcaaatltaa agatggtcaa tactatttag atgttaaagg cgggtcttct 720gctggtgttt ataaagccac ttatgatgaa actacaaaga aagttaat tgatcagact 780gataaaactc cgttggaac tgcggaagct acagctattc ggggaacggc cactataacc 840cacaacaaa ttgctgaagt aacaaaagag ggtgttgata cgaccacagt tgcggctcaa 900cttctgagcag caggggttac tggcgccgat aaggacaata ctagccttgt aaaactatcg 960tttgaggata aaaacggtaa ggttattgat ggtggctatg cagtgaaat gggcgacgat 1020ttctatgccg ctacatatga tgagaaaaca ggtgcaatta ctgctaaaac cactacttat 1080acagatggtta ctggcgttgc tcaaactgga gctgtgaaat ttggtggcgc aaatggtaaa 1140tctgaagttg ttactgctac cgatggtgaa acttacttag caagcgacct tgacaaacat 1200aacttcagaa caggcgggtg gcttaaagag gtaatacag ataagactga aaaccactg 1260cagaaaattg atgctgcctt ggcacaggtt gatacactc gttctgacct ggggtcggtt 1320cagaaccgtt tcaactccgc taccaccaac ctgggcaata ccgtaataa cctgtcttct 1380gcccgtagcc gtatcgaaga ttccgactac geaacggaag tctccaacat gtctcgcg 1440cagattctgc agcaggccgg tactcctgt ctggcgagc gaaaccaggt tccgcaaac 1500gtctctctt tactgctg 1518531790RNAArtificial SequenceSynthetic Polynucleotide 53ggggaaauaa

gagagaaaag aagaguaaga agaaauuaa gagccaccau ggcacaaguc 60auuaauaaca acagccuguc gcuguugacc cagaauaacc ugaacaaauc ccaguccgca 120cugggcacug cuaucgagcg uuugucuucc ggucugcgu ucaacagcgc gaaagacgau 180gcggcaggac aggcgauugc uaaccguuuu accgcgaaca ucaaaggucu gacucaggcu 240ucccguaacg cuaacgacgg uaucuccauu gcgcagacca cugaaggcgc gcugaacgaa 300aucaacaaca accugcagcg ugugcgugaa cuggcgguuu agucugcga ugguaauaac 360uccagucug accucgacuc cauccaggcu gaaauaccc agcgcugaa cgaaaucgac 420cguguaucg gccagacua guucaacggc gugaagucc uggcgagga caacaccug 480accauccagg uuggugccaa cgacggugaa acuaucgaa uugauuuuaa agaaaucagc 540ucuaaaacac ugggacuuga uaagcuuaa guccaagaug ccuacacccc gaaagaaacu 600gcuguaaccg uugauaaaac uaccuuaaaa auugguacag auccuauuac agcccagagc 660aaauacugaa uccaacugc aauggcggu ggugcaacgg ggguuacug ggucugauuac 720aaauuuuaag auggucaaua cuuuuagau guuaaaggcg gugcuucugc ugguguuuuau 780aaagccacu augaugaaac uacaaagaaa guuaauuug auacgacuga uaaaacuccg 840uuggcaacug cgaagcuac agcuauucgg ggaacggcca cuuaaccca caacaaaau 900gcugaaguu caaaagaggg uguugauacg accacaguug cggcucaacu ugcugcagca 960gggguuuacug gcgccgaa ggacaauacu agccuuguaa aacuaucguu ugagguaaaa 1020aacgguaagg uuauugaugg uggcuagca gugaauuug gcgacgaaau cuaugccgu 1080acauaugaug agaaaacagg ugcauuuacu gcuaaaacca cuacuuauc agaugguacu 1140ggcguugcuc aaacuggagc ugugaaauuu gguggcgcaa augguaaauc ugaaguuguu 1200acugcuaccg augguaaagc uuacuuaagca agcgaccuug acaaacuaa cuucagaaca 1260ggcggugagc uuaaagaggu uauuacagau aagacugaaa

accacugca gaaaauugau 1320gcugccuugg cacagguuga uacacuucgu ucugaccugg gugcgguuca gaaccguuuc
1380aacuccgca uaccaaccu gggcauacc guaaauaacc ugucuucgc ccguagccgu 1440aucgaagauu ccgacuacgc
aaccgaaguc uccaacaugu cucgcgcga gauucugcag 1500caggccggua ccuccguucu ggcgaggcg aaccagguuc
cgaaaacgu ccucuuuuu 1560cugcguugau aauaggcugg agccucggug gccaugcuuc uugcccuug ggccucucc
1620cagccucc ucccuuccu gcaccguac ccccgugguc uuugaauaaa gucugagugg 1680gcggcaaaaa aaaaaaaaa
aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa 1740aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaucug
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 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 690571620RNAHuman

metapneumovirus 57augagcugga aggguggau uaucuucagc cugcugauua caccucaaca cgcccugaag 60gagagcuacc
uggaagagag cugcuccacc aucaccgagg gcuaccugag cgugcugcgg 120accggcuggu acaccaacgu guaccaccug
gaggugggcg acguggagaa ccugaccugc 180agcgacggcc cuagccugau caagaccgag cuggaccuga ccaagagcgc
ucugagagag 240cugaagaccg uguccgccga ccagcuggcc agagaggaac agaucgagaa ccucggcag 300agcagauucg
ugcuggggcg caucgcucug ggagucgccc cugccgcugc agugacagcu 360ggaguggcca uugcuaagac caucagacug
gaaagcgagg ugacagccau caacaugcc 420cugaagaaga ccaacgaggg cgugagcacc cugggcaaug gagugagagu
gcuggccaca 480gccgugcggg agcugaagga cuucgugagc aagaaccuga ccagagccau caacaagaac 540aagugcgaca
ucgaugaccu gaagauggcc gugagcuucu ccaguucaa cagacgguuc 600cugaacuggg ugagacaguu cuccgacaac
gcuggaauca caccugccau uagccuggac 660cugaugaccg acgcccagcu ggcuagagcc gugcccaaca ugcccaccag
cgcuggccag 720aucaagcuga ugcuggagaa cagagccaug gugcggagaa agggcuucgg cauccugauu 780gggguguaug
gaagcuccgu gaucucaug gugcagcugc ccaucuucgg cgugaucgac 840acaccucgcu ggaucgugaa ggccgcuccu
agcugcuccg agaagaaagg aaacuaugcc 900ugucugcuga gagaggacca gggcugguac ugccagaacg ccggaagcac

aguguacuau 960cccaacgaga aggacugcga gaccagaggc gaccacgugu ucugcgacac cgcugccgga 1020aucaacugg
ccgagcagag caaggagugc aacaucaca ucagcacaac caacuacccc 1080ugcaagguga gcaccggacg gcacccauc
agcauggugg cucugagccc ucugggcgcu 1140cugguggccu gcuauaaggg cguguccugu agcaucggca gcaaucgggu
gggcaucauc 1200aagcagcuga acaagggaug cuccuacauc accaaccagg acgccgacac cgugaccauc 1260gacaacaccg
uguaccagcu gagcaaggug gagggcgagc agcacgugau caagggcaga 1320cccugagcu ccagcuucga cccaucag
uuccugagg accaguuaa cguggccug 1380gaccaggugu uugagaacau cgagaacagc caggcccugg uggaccagag
caacagauc 1440cuguccagcg cugagaaggg caacaccggc uucaucauug ugaucuuu gaucgccgug 1500cugggcagcu
ccaugauccu ggugagcauc uucaucauu ucaagaagac caagaaacc 1560accggagccc cuccugagcu gagcggcgug
accaacaug gcuucauucc ccacaacuga 1620581620RNAHuman metapneumovirus 58augucuugga aagugaugau
caucauuucg uuacucaua caccacagca cgggcuaaag 60gagaguuaau uggaagauc auguaguacu auaacugagg
gauaccucag uguuuuaaga 120acaggcuggu acacuaaugu cuucacauua gaaguuggug auguugaaaa ucuuacaugu
180acugauggac cuagcuuaa caaacagaa cuugaucuaa caaaaagugc uuuaagggaa 240cucaaacag ucucugcuga
ucaguuggcg agagaggagc aaauugaaaa uccagacaa 300ucaaguuug ucuuaggugc gauagcucuc ggaguugcua
cagcagcagc agucacagca 360ggcauugcaa uagccaaaac cauaaggcuu gagagugagg ugaauugcau uaaaggugcu
420cucaaaaaa cuaaugaagc aguauccaca uuagggaaug gugugcgggu ccuagccacu 480gcagugagag agcuaaaaga
auuugugagc aaaaaccuga cuagugcau caacaggaac 540aaaugugaca uugcugaucu gaagauggcu gucagcuca
gucauuuca cagaagauuu 600cuuauguug ugcggcaguu uucagacaau gcagggaaua caccagcau aucauuggac
660cugaugacug augcugaguu ggccagagcu guaucuaca ugccaacauc ugcagggcag 720auaaaaacuga uguuggagaa
ccgcgcaaug guaaggagaa aaggauuugg aauccugaua 780ggggucucag gaagcucugu gauuuacaug guucauuugc
cgauuuuug ugucuaugau 840acaccuuguu ggaucauca ggcagucucc ucuugcucag aaaaaacgg gaauuaugcu
900ugccuccuaa gagaggauca agggugguau uguaaaaug caggaucuac uguuuacuac 960ccaaaugaaa aagacugcga
aacaagaggu gaucauguuu uuugugacac agcagcaggg 1020aucaauguug cugagcauc aagagaugc aacaucaca
uauacuac caacuacca 1080ugcaaaugca gcacaggaag acaccuaua agcaugguug cacuauacc ucucggugcu
1140uugguggcuu gcuauaaagg gguaagcugc ucgauuggca gcaauugggu uggaaucauc 1200aaacaauac ccaaaggcug
cucauacua accaaccagg augcagacac uuaacaauu 1260gacaauaccg uguaucaacu aagcaaguu gaaggugaac
agcauguaau aaaagggaga 1320ccaguuaa gcaguuuuga uccaaucaag uuccugagg aucaguuaa uguugcguu
1380gaucaagucu ucgaaagcau ugagaacagu caggcacuag uggaccaguc aaacaaaau 1440cuuaacagug cagaaaaagg
aaacacuggu uucauuuacg uaguauuuu gguugcuguu 1500cuuggucuaa ccaugauuuc agugagcauc aucaucaua
ucaagaaaac aaggaagccc 1560acaggagc cuccagagcu gaugguguc accaacggcg guuacauacc acauaguug
1620591620RNAHuman metapneumovirus 59augucuugga aagugaugau uucauuucg uuacucaua caccucagca
uggacuuaa 60gaaaguuaau uagaagauc auguaguacu auaacugaag gauaucucag uguuuuaaga 120acagguuggu
acaccaaugu cuuuacauua gaaguuggug auguugaaaa ucuuacaugu 180acugauggac cuagcuuaa caaacagaa
cuugaccuaa caaaagugc uuuaagagaa 240cucaaacag uuucugcuga ucaguugcg agagaagaac aaauugaaaa
uccagacaa 300ucaagguuug uccuaggugc aauagcucu ggaguugcca cagcagcagc agucacagca 360ggcauugcaa
uagccaaaac uuaaggcuu gagagugaag ugaauugcau caaaggugcu 420cucaaaaaca ccaaugaggc aguaucaca
cuaggaaug gagugcgggu ccuagccacu 480gcaguaagag agcugaaaga auuugugagc aaaaaccuga cuagugcgu
caacaagaac 540aagugugaca uugcugauuu gaagauggcu gucagcuca gucaguua cagaagauuc 600cuuauguug
ugcggcaguu uucagacaau gcagggaaua caccagcau aucauuggac 660cugaugaug augcugagcu ggccagagcu
guaucuaca ugccaacauc ugcaggacag 720auaaaacuaa uguuagagaa ccgugcaaug gugaggagaa aaggauuugg
aaucuugaua 780ggggucucag gaagcucugu gauuuacaug guccagcugc cgauuuuug ugucuaaa 840acaccuuguu
ggauaauc ggcagucucc ucuuguucag aaaaagauug aaauuaugcu 900ugccuccuaa gagaggauca agggugguau
uguaaaaaug caggauccac uguuuacuac 960ccaaaugaaa aagacugcga aacaagaggu gaucauguuu uuugugacac
agcagcaggg 1020aucaauguug cugagcauc aagagaugc aacaucaca uaucuaccac caacuacca 1080ugcaaaugca
gcacaggaag acaccuauc agcaugguug cacuauacc ucucggugcu 1140uugguagcuu gcuacaaagg gguuagcugc
ucgacuggca guaaucaggu uggaauaau 1200aaacauc cuuaaggcug cucauacua acuaaccagg acgagacac
uguaacaau 1260gacaacacug uguaucaacu aagcaaguu gagggugaac agcauguaau aaaagggaga 1320ccaguuaa
gcaguuuuga uccaucag uuccugagg aucaguuaa uguugcguu 1380gaucaagucu uugaaagcau ugaaaacagu
caagcacuag uggaccaguc aaacaaaau 1440cugaacagug cagaaaaagg aaacacuggu uucauuuug uauuuuuu
gauugcuguu 1500cuuggguuaa ccaugauuuc agugagcauc aucaucaua ucaaaaaac aaggaagccc 1560acaggggac
cuccggagcu

gaugguguu accaacggcg guuacauacc gcuauguuag 1620601725RNAHuman respiratory syncytial virus
60auggaguugc cauccuca acaaaugca auuaccaca uccuugcugc agucacacuc 60uguuuugcuu ccagucuaaa
caucacugaa gaauuuuac aaucaacug cagugcaguu 120agcaaggcu auuuagugc ucaagaacu gguuguaa

aucaagcauc ucauagucca ugguuuucag auagaaggau ggucacuc 1140auaauguug uigacaaggg cuugaacuca
guuccaaaau ugaagguaug gacgauaucu 1200augagacaaa auuacugggg gucagaagga agauuacuuc uacuagguaa
caagaucuac 1260auauacacaa gaucuacaag uuggcacagc aaguuaaa uaggaauuu uacauuacu 1320gacuacagug
auauaaggau aaauggaca uggcauaug ugcuaucaag accagaaa 1380aaugauguc cauggggaca ucauguccg
gauggaugua uaacgggagu auauaccgau 1440gcuauccac ucauuccac aggaagcauu guaucaucug ucauauugga
cucacaaaa 1500ucgagaguca acccagucuu aacuuaucac acagcaaccg aaaggguaaa cgagcuggcu 1560auccgaaaca
aaacacucuc agcuggguac acaacaacaa gcugcauuac acacuuaac 1620aaaggguuuu guuuucauuu aguagaaaua
aucauuaaa gcuuaaac acuucaacc 1680auguuguuca aaacagagau ucaaaaaagc ugcagu 1716631716RNAArtificial
SequenceSynthetic Polynucleotide 63auggaauacu ggaagcacac caaccagcg aaggacgccc gcaacgagcu gaaaccagc
60acagccacac acggcaacaa gcugaccaac aagaucacu acauccugug gaccaucacc 120cuggugcugc ugagcaucgu
guucauacug gugcugacca auagcauca gagegagaag 180gccagagaga gccugcugca ggacaucac aacgaguca
uggaagugac cgagaagauc 240cagguggcca gcgacaacac caacgaccug auccagagcg gcgugaacac ccggcugcug
300accuaccaga gccacgugca gaacuacac ccaucagcc ugaccagca gaucagcgac 360cugcggaagu ucaucagcga
gaucaccauc cggaacgaca accaggaagu gccccccag 420agaauacacc acgacguggg caucaagccc cugaacccc acgaaucug
gcgguguaca 480agcggcugc ccagccugau gaagacccc aagaucggc ugaugccugg ccuggacug 540cuggccaugc
cuaccacagu ggauggcugu gucgggacc ccagccucgu gaucaacgau 600cugaucucac ccuacaccag caaccugac
accggggcu gccaggauu cggcaagagc 660uaccaggugc ugcagauccg caucaacc gugaacucc accuggugc
cgaccugaac 720ccucggauca gccacacuu caacaucac gacaacagaa agagcugcag ccuggcucug 780cugaacaccg
acguguacca gcugugcagc accccaagg uggacgagag aagcgacuac 840gccagcagcg gcaucgagga uaucgugcug
gacucguga acucagcagc cagcaucagc 900accaccggg ucaagaacaa caaucagc uucgaccagc ccuacggc ccuguaccu
960ucugugggccc cuggcaucua cuacaaggc aagaucacu uccugggcu cggcggccug 1020gaacaccca ucaacgagaa
cgcaucugc aacaccaccg gcugcccug caagaccag 1080agagacugca aucaggccag ccacagccc ugguucagcg
accgagaau gguaacuc 1140aucaucgugg uggacaaggg ccugaacagc gugccaagc ugaagugug gacaucagc
1200augcggcaga acucagggg cagcagggc agacuucugc ugcugggaaa caagaucuac 1260aucuacacc gguccaccag
cuggcacagc aaucugcagc ugggaucuu cgacaucacc 1320gacuacagcg acauccggau caaguggacc uggcacaacg
ugcugagcag acccggaac 1380aaugagugcc cuuggggcca cagcugcccc gauggaugua ucaccggcu guaccagc
1440gccuacccc ugaauccuac cggcucauc guguccagcg ugaucugga cagccagaaa 1500agcagaguga acccgugau
cacaucagc accgccagc agagagugaa cgaucggc 1560aucagaaca agaccugag cgccggcuac accaccacaa
gcugcaucac acacuacaac 1620aaggguacu gcuuccacuu cguggaauc aaccacaagu ccugaacac cuaccagccc
1680augcuguuca agaccagau cccaagagc ugcucc 1716641617RNAArtificial SequenceSynthetic Polynucleotide
64augcccauca gcauccugcu gaucaucacc acaugauca uggccagcca cugccagau 60gacaucacca agcugcagca
cgugggugcug cucgugaaca gcccaggc caugaagau 120agccagaacu ucgagacagc cuaccugau cugagccuga
ucccaagau cgaggacagc 180aacagcugc gcgaccagca gaucaagcag ucaagcggc ugcuggacag acugaucauc
240cccugucagc acggccugc gcugcagaaa gacgugaucg ugaccaacca ggaaagcaac 300gagaacaccg accccggac
cgagagauuc uucggcggc ugaucggc acucgcccug 360ggaguggcca caagcgecca gauuacagcc gcuguggccc
ugguggaagc caagcggc 420agaagcagc ucgagaagcu gaaagaggc auccgggaca ccaacaaggc gcugcagagc
480gucgagucca gcgugggcaa ucugaucug gccaucaagu ccgucagga cuacgugaac 540aaagaaucg ugcccucuu
cgccggcug ggcugugaag cugccggacu gcagcuggc 600auugcccuga cacagcacua cagcagcug accaacauc
ucggcgaca caucggcagc 660cugcagaaa agggcauuu gcugcaggga aucgccagc uguaccgac caaucacc
720gagauuuca ccaccagc cguggauaag uacgacauc acgaccugcu guaccagc 780agcaucaag ugcgugau
cgacuggac cugaacgac acagcaucac ccugcaagug 840cggcugccc ugcugaccag acugcugaac acccagau
acaaggugga cagcaucucc 900uacaacucc agaaccgca gugguacac ccucgccc gccacuuu gaccaagggc
960gccuuucug gcggagccga cgugaaagag ugcucagc ccuucagc cuacaucugc 1020cccagcagc cuggcuucgu
gcugaaccac gagauggaaa gcugccugag cggcaacac 1080agccagugcc ccagaaccac gcugaccucc gacucgugc
ccagauacg cuucgugaau 1140ggcggcug uggccaacug caucaccacc accuguccu gcaacggc cggcaaccg
1200aucaaccagc cuccgauca gggcgugaag auuacacc acaagagug uaacaccauc 1260ggcaucaacg gcaucuguu
cauacacac aaagaggga cccuggccu cuacacccc 1320gacgauuca ccugaacaa cuccguggcu cuggaccca
ucgacaucac caucagcug 1380aacaaggcca agagcaccu ggaagagucc aaagagugga uccggcggag caaccagaag
1440cuggacucua ucggcagcug gcaccagagc agcaccacca uaucugau ccugauuau 1500augauuaucc uguucauc
caacuacac ucaucacua ucgcauuu guacuaccg 1560auccagaaac ggaaccggg ggaccagaau gacaagccc
acugcugac aacaag 1617654062RNAMiddle East respiratory syndrome coronavirus 65augauacacu caguguuuu
acugauguu uuguuaacac cuacagaaag uuacguugau 60guaggggcag auuciguuuu gucugcuugu auugagguu
auauacaaca gaccuuuuu 120gaaaaacu ggccuaggcc auuugauguu ucaagcug acgguuuu auaccuca
180ggccguacu auucuaacu acauacacu uaucaaggc uuuuuccua ucaggagac 240cauggugaua ugauguuuu

agaugguaaa 480augggccgcu ucuucaauca uacucuaguu cuuuugcccg auggaugugg cacuuuacuu 540agagcuuuuu
auuguauucu ggagccucgc ucuggaaauc auuguccgc ugccaauucc 600uauacuucu uugccacuua ucacacuccu
gcaacagauu guucugaugg cauuuacaa 660cguaaugcca gucugaacuc uuuuaaggag uauuuuauuu uacguaacug
caccuuuauug 720uacacuuaa acuuuaccga agaugagauu uuagaguggu uuggcauuac acaacugcu 780caagguguuc
accucuucuc aucucggauu guugauuuigu acggcgcaa uauguucaa 840uuugccaccu ugccuguuuu ugauacuauu
aaguauuuuu cuaucauucc ucacagauu 900cguucuaucc aaagugauag aaaagcuugg gcugccuucu acguauuaa
acuuaaccg 960uuacuucc uguuggauuu uucuguugau gguuauauac gcagagcuau agacuguggu 1020uuuaugauu
ugucacaacu ccacugcuca uaugaauccu ucgauguuga aucuggaguu 1080uauucaguuu cgucuucga agcaaacu
ucuggcucag uuguggaaca ggcugaaggu 1140guugaaugug auuuuucc ucucugucu ggacaccuc cucagguua
uaauuacaag 1200cguuugguuu uuaccaauug cauuuauau cuuaccuuu ugcuuucacu uuuuucugug 1260aaugauuuu
cuuguaguca auuacucca gcagcaauug cuagcaacug uuauucuuca 1320cugauuuugg auuacuuuuc auaccacu
aguauaaaau ccgacucag uguuaguucu 1380gcugguccaa uauccaguu uauuuuauaaa caguccuuuu cuauccac
auguuugauu 1440uuagcgacug uuccucauaa ccuuacuacu auuacuaagc cucuuuagaa cagcuauuu 1500aacaugucu
cucgucuucu uucugaugau cguacugaag uaccucaguu agugaacgcu 1560aucauuacu caccugugu auccauugc
ccaaccacug ugugggaaga cggugauuu 1620uauaggaac aacuaucucc acuugaaggu gguggcuggc uuguugcuag
uggcucaacu 1680guugccauga cugagcauu acagaugggc uuugguauua cagucaaua ugguacagac 1740accauagug
uuugcccaa gcuuuaguuu gcuaaugaca caaaaauugc cucucauuu 1800ggcaauugcg uggaauuuu ccucuauggu
guuucgggccc gugguguuuu ucagaauugc 1860acagcuguag guuucgaca gcagcguuu guuuuugaug cguaccagaa
uuuaguuggc 1920uauuuuucug augauggcaa cuacuacugu uugcgugcuu guuuuagugu uccuguuuu 1980gucaucuaug
auaaagaaac uaaaaccac gcuaucuaau uugguagugu ugcaugugaa 2040cacuuuucu cuaccauguc ucauacucc
cguucucgcu gaucaaugcu uaaacggcga 2100gauucuaau auggccccu ucagacaccu guugguugug uccuaggacu

uguuauucc 2160ucuuguucg uagaggacug caaguugccu cuuggucaau cucucuguc ucuuccugac 2220acaccuagua
cucucacacc ucgagugug cgcucuguuc caggugaaa ggcuuuggca 2280uccauugcuu uuaucucc uauucaggu
gaucaacuua auaguaguu uuuuuuuuu 2340aguauacca cuuuuuuuu cuuuggugug acucaggagu acuuacagac
aaccuucag 2400aauguuacug uugauugua acaguacuu ugcauuguu uccagaagug ugagcauuu 2460cugcgagug
auggccaguu uuguuccaa auaaaccagg cucuccaug ugccauuuu 2520cgccaggaug auucuguacg uauuuuuuu
gagcagcuga aaagcucua aucaucucc 2580aucauaccag guuuuggagg ugacuuuuu uugacacuuc uggaaccugu
uucuaauacu 2640acuggcaguc guagucagc uagugcuuu gaggaauugc uuuuugaca agucacuua 2700gcugaucug
guuuuagca agguuacgau gauugcagc agcaagucc agcaucagcu 2760cgugaucuu uuugucua auauguggcu
gguuacaaag uuuuaccucc ucuuuggau 2820guuuuuuugg aagccgcuu uacuucacu uugcuuggca gcuaucagc
uguuggcugg 2880acugcuggcu uauccuccu ugcugcuuu ccuuugcag agaguauuu uuauagguu 2940aacgguguug
gcuuuacua acagguucu ucagagaacc aaaagcuuu ugccaauuag 3000uuuuuacagc cucugggagc uaugcaaca
ggcuucacua caacuauuga agcuuuucag 3060aagguucagg aucugugaa caacaugca caggcucuau ccauuuagc
uagcgagcu 3120ucuuuuuuu uuggugcuu uuccgcccuc auuggagaca ucauacaacg ucuuuguuu 3180cucgaacagg
acgcccuuu agacagacu auuuuuggc guuugaca acuuuuuugcu 3240uuuuugcag agcagcuuu ucguuccgaa
ucagcugcuc uuuccgcu auuggcuuu 3300gaaauuagcu augagugugu caaggcaca uccaagcguu cugguuuuu
cggucaagc 3360acacuuuag ugucuuuuu uguuuuugc ccuuuugc uuuuacuuu gcauuuuggu 3420uuuuuuccu
gcaaccacu ugagguuuu ucugcuuuu gucuuugcga ugcagcuuu 3480ccuacuuuu guuuuagccc uguuuuugc
uacuuuuuu aaacuauua cacuagguu 3540guuugagug ggucauuuac uggcucguc uucuaugcag cugagccau
uaccucccu 3600aaucuuuag auuuugcag acaggugaca uaccuuuua uuucuuuua ccuccuccu 3660ccucucug
gcauuuccac cggguuugc uuccaagug aguuugauu guuuuuuua 3720aauguuagca ccaguuuacc uuuuuuuggu
uccuuuac aguuuuuac uacuuuac 3780gaucuuuac acgaguuuu gucuuuuua cauuuuuuu aagccuuuu
ugaguuuu 3840auagacuuu aagagcuugg cauuuuuacu uuuuuuua aauggccgug guacuuuug 3900cuugguuu
uugcugggcu uguugccuuu gcucuaugc ucuuuuuac acugucguc 3960acugguugug gcacuuuugc uauuuuuuu
uuuuuuuu auuuuuuu 4020gaggaauagc accucgagc gcauuuugcu cauuuuuu aa
4062671845RNAArtificial SequenceSynthetic Polynucleotide 67augauccu cgguuuuccu ccuauuuu
cuguuacc ccacugagc agacugcaag 60cucccgcugg gacaguccu gugugcug ccugacacuc cuagcacuc gacccacg
120uccgugcggc cggugccugg cgaaugcgg cuggccucca ucgcuuuua ucaccauac 180caaguggauc agcuuauag
cucguuuu aagcugucca ucccacgaa cuucucguu 240gggucacc aggaguacu ccagaccaca auuagaag
ucaccgucga uugcaagca 300uacugugca acggcuucca gaugucgag cagcugcuga gagaauacgg gcuuuuugc
360agcaagaua accagcgcg gcaugagcu aacuugcgc aggacgac ucugcgcaac 420cucuuuugcu cugugaugc
auccagucc ucccacua ucccgggguu cggaggggac 480uucaaccuga ccuccugga gcccugucg aucagaccg
guagcaguc ggcgcgcu 540gcauuuag auuuucguu cgacaaguc accaucgccc auccgggcuu caugcagga

600uacgacgacu guaugcagca gggaccagcc uccgcgaggg accucaucug cgcgcaauac 660guggccgggu acaaagugcu
gccuccucug auggauguga acauggagc cgcuuuauacu 720ucguccugc ucggcucuauc cgcggcgug ggguggaccg
ccggccuguc cuccuucgce 780gcuaucccu uugcacaauc cauuuucuauc cggcucaacg gcgugggcau uacuacaaca
840guccugucgg agaaccagaa guugaucgca aacaaguca aucaggccu gggggccaug 900cagacuggau ucacuacgac
uaacgaagc uuccagaagg uccaggacgc ugugaacaac 960aacgcccagg cgcucucaaa gcuggccucc gaacucagca
acaccuucgg agccaucagc 1020gcaucgaucg gugacauau ucagcggcug gacgugcugg agcaggacgc ccagaucgac
1080cgccucauca acggacggcu gaccaccuug aaugccuucg uggcacaaca gcugguccgg 1140agcgaucag cggcacuuc
cgccaacuc gccaaggaca aagucaacga augcgugaag 1200gcccagucca agagguccgg uuucugcggu caaggaacc
auauuguguc cuucgucgug 1260aacgcgcca acggucugua cuuuaugcac gucggcuacu acccgagca ucauucgaa
1320gugguguccg ccuacggccu gugcgaugcc gcuacccca cuaacuguaug ugcuccugug 1380aacggauauu uuauuaagac
caacaacacc cgcauugugg acgaauuguc auacaccggu 1440ucguccuuc acgcgcccg gccaucacu ucacugaaca
ccaaauacgu ggcuccgca 1500gugaccuacc agaacaucuc caccauuug ccgccgcgc ugcucggaaa cagcaccgga
1560auugauuucc aagaugaacu ggacgaauuc uucaagaacg uguccacuuc cauuccaac 1620uucggaagcc ugacacagau
caacaccacc cuucugcacc ugaccuacga gaugcugagc 1680cuucaacaag uggucaagcc ccugaacgag agcuacaucg
accugaagga gcugggcaac 1740uauaccuacu acaacaagug gccggacaag auugaggaga uucugucgaa aaucuaacc
1800auugaaaacg agaucgccag aaucagaag cuuauccggc aagcc 1845684071RNAArtificial SequenceSynthetic
Polynucleotide 68auggaaacc cugcccagcu gcuguuccug cugcucugu ggcugccuga uaccaccggc 60agcauugugg
acgugggccc cgauagcgug aaguccgcu guaucgaagu ggacaucag 120cagaccuuu ucgacaagac cuggcccaga
ccaucgacg uguccaagcc gcacggcauc 180aucuauccac aaggccggac cuacagcaac aucaccuuu ccuaccaggc ccuguucca
240uaucaaggcg accacggcga uauguacgug uacucugccg gccacgccac cggcaccaca 300cccagaaac uguucguggc
caacuacagc caggacguga agcaguucgc caacggcuuc 360gucgucgga uggcgccgc ugccaauagc accggcacag
ugaucaucag cccagcacc 420agcggacca uccggaagau cuaccgcc uucaugcugg gcagcuccu gggcauuuc
480agcgcaggca agaugggccg guucuucaac cacaccugg ugcugcugcc cgauggcugu 540ggcacacugc ugagaccu
cuacugcauc cuggaacca gaagcggca ccacugccu 600gccggcaua gcuacaccag cuucgccacc uaccacacac ccgccaccga
uugcuccgac 660ggcaacuaca accggaagc cagccugaac agcucaag aguaucuaa ccugcggaac 720ugcaccuua
uguacaccua cauauacc gagcagaga uccuggaug guucggcauc 780accagaccg cccagggcgu gcaccuguuc
agcagcagau acguggaccu guacggcgcc 840aacauguucc aguuugccac ccugcccug uacgacacca ucaaguacia
cagcauac 900cccacagca uccgguccau ccagagcagc agaaaagccu gggccgcuu cuacguguac 960aagcugcagc
cccugaccu ccugcuggac uucagcugg acggcuacu cagacggcc 1020aucgacugcg gcuucaacga ccugagccag
cugcagcug cuuacgagag cuucgacgug 1080gaaagcggcg uguacagcgu guccagcuuc gaggccaagc cuagcggcag
cgugguggaa 1140caggcugagg gcguggaau gcacuucagc ccucugcuga gccggacccc ucccaggug 1200uacaacuua
agcggcuggu guuaccaac ugcauuuaca accugacca gcugcugagc 1260cuguuuccg ugaacgacu caccuguagc
cagauagcc cugccgcau ugccagcaac 1320ugcuacagca gccugaucg ggacuacuuc agcuacccc ugagcaugaa
guccgaucug 1380agcuguccu ccggcgacc caucagccag uucaacuaca agcagagcuu cagcaaccu 1440accugccuga
uucuggccac cgugcccac aaucugacca ccauaccaa gcccugaag 1500uacagcuaca ucaacaagug cagcagacug
cuguccgac accggaccga agugcccag 1560cucgugaacg ccaaccagua cagcccugc guguccauc ugcccagc
cgugugggag 1620gacggcgacu acuacagaaa gcagcugagc cccuggaag gcggcggaug gcugguggcu 1680ucuggaagca
caguggccau gaccgagcag cugcagaugg gcuuuggcau caccgugcag 1740uacggcacc acaccaacag cgugugcccc
aagcuggaau ucgcaauaga cacaagauc 1800gccagccagc ugggaaacug gcuggaauac uccuguaug gcguguccg
acggggcgug 1860uuccagaauu gcacagcagu gggagucgg cagcagagau ucguguacga ugccuaccag 1920aaccucgugg
gcuacuacag gcagcagcc aaauacuacu gccugccggc cugugugucc 1980gugcccugug ccugaucua cgacaagag
acaagacc acgccacacu guucggcucc 2040guggccugcg agcaucag cuccaccaug agccaguacu cccguccac
ccguccaug 2100cugaagcga gagauagc cuacggcccc cugcagacac cugugggaug ugugcugggc 2160cucgugaaca
gcuccuguu uguggaagau ugcaagcugc cccugggcca gagccugugu 2220gccugccag auaccuag caccugacc
ccuagaagc ugcgucugu gccggcgaa 2280augcggcugg ccuacuucgc cuucauac ccauccagc uggaccagcu
gaacuccagc 2340uacuuaagc ugagcaucc cacaacuuc agcuucggcg ugaccagga guacuaccag 2400accacauc
agaaagugac cguggacugc aagcaguac ugugcaacgg cuuucagaag 2460ugcgaacagc ugcugcgca guacggccag
uucugcagca agauacca ggcccugc 2520ggcgccaacc ugagacagga ugacagcgug cggaaccugu ucgcccagcu
gaaaagcagc 2580caguccagcc ccauauccc uggcuucggc ggcacuuua accugaccu gcuggaaccu 2640guguccauca
gcaccggcuc cagaagcgc agauccgca ucgaggaccu gcuguucgac 2700aaagugacca ugcggacc cggcuacau
cagggcuac agauugcau gcagcagggc 2760ccagccagc ccagggauc gaucugugcc caguauggg ccggcuaca
ggugcugccc 2820cccugaugc agugaacau ggaagccgc uaccucca gccugcuggc cucuauugcu 2880ggcguggg
ggacagccg ccugucugc uuugccgca uccuuucgc ccagagcauc 2940uucuaaccgc ugaacggcgu gggcaucaca
caacaggugc ugagcgagaa ccagaagcug 3000aucgccaaca aguuuaacca ggcacuggc gccaugcaga ccggcuucac

caccaccaac 3060gaggccuica gaaaggugca ggacgccgug aacaacaacg cccaggcucu gagcaagcug 3120gccuccgagc
ugagcaauac cuucggcgcc aucagcgcuu ccaucggcga caucauccag 3180cggcuggacg ugcuggaaca ggacgccag
aucgaccgge ugaucacagg cagacugacc 3240accugaacg ccuucguggc acagcagcuc gucgggagcg aaucugccgc
ucugucugcu 3300cagcuggcca aggacaaagu gaacgagucg gugaaggccc aguccaagcg gacgggcuuu 3360uguggccagg
gcaccacau cguguccuuc gucgugaug ccccaacgg ccuguacuuu 3420augcagugg gcuaauacc cagcaaccac
aucgaggugg uguccgccua ugccugugc 3480gacgccgcca auccuacaa cuguaucgc cccgugaacg gcuaucuuau
caagaccaac 3540aacaccggga ucguggacga gugguccuac acaggcagca gcuuuacgc ccccagccc 3600aucaccucc
ugaacacaa auacguggcc cccaaguga cauaccagaa cauccacc 3660aaccugccc cuccacugcu gggaaaucc
accggcaucg acuuccagga cgagcuggac 3720gaguucuuca agaacguguc caccuccauc ccaacuucg gcagccugac
ccagaucac 3780accacucgc uggaccugac cuacgagaug cuguccucg aacaggucgu gaaagcccug 3840aacgagagcu
acaucgaccu gaaagagcug gggaacuaca ccuacuaca caaguggccu 3900ugguacuuu ggcugggcuu uaucgccggc
cugguggccc ugccucugug cguguucuu 3960aaccugugcu gcaccggcug cggcaccuu ugcaugggca agcugaaug
caaccggugc 4020ugcgacagau acgaggaaua cgaccuggaa ccucacaaug ugcaugugca c 4071691864RNAArtificial
SequenceSynthetic Polynucleotide 69ucaagcuuuu ggaccucgu acagaagcua auacgacua cuauaggga auaagagaga
60aaagaagagu aagaagaaau auaagagcca ccaugggucu caaggugaac gucucugccg 120uaucuauggc aguacuguuu
acucuccaaa caccgcccgg ucaaaucuu ugcccgauc 180ucucuaagau agggguagua ggaauaggaa gugcaagcua
caaaguuuug acucguuca 240gccaucau auuagucua aaauuaugc ccauuuaac ucuccucaa aaucgcagc
300ggguagagau ugcagaauac aggagacuac uaagaacagu uuuggaacca auuagggaug 360cacuuauugc aaugaccag
aacauaaggc cgguucagag cguagcuuca aguaggagac 420acaagagau ugcgggagua guccuggcag gucggcccu
aggguuugc acagcugcuc 480agauaacagc cggcauugca cuucaccggu ccaugcugaa cucucaggcc aucgacauc
540ugagagcag ccuggaaacu acuaucagg caauagaggc aaucagaca gcagggcagg 600agaugauuu ggcuguucag
gguguccaag acuaucuaa uauagagcug auaccgucua 660ugaaccagcu aucuugugau cuauccgguc agaagcugc
gcuaaaauug cuuagauacu 720auacagaaau ccugucuuu uuugcccga gccuacggga ccccauucg gcggagauu
780cuauccaggc uuugauuuu gcacuuggag gagauucaa uaagguguua gaaaagcug 840gauacagugg agcgauuuu
cuaggcauc uagagagcag aggaauaaug gcucggauaa 900cucacgucga cacagagucc uacuucuaug uccucaguu
agccuauccg acgcuguccg 960agauuaagg ggugauugc caccggcuag agggggucuc guacaacuaa ggcucuaag
1020agugguauac cacugugccc aaguauug caaccaagg guaccuuac ucgaauuuug 1080augagucac auguacuuuc
augccagagg ggacugugug cagccaaaau gccuuguacc 1140cgaugagucc ucuguccaa gaaugccucc ggggguccac
caaguccugu gcucguacac 1200ucguauccgg gucuuuugg aaccgguuca uuuuacaca agggaaccua auagccauu
1260gugcaucau ucuuuguaag uguuacaca cagguacgau uauuaucua gaccucgaca 1320agaucuaac auacauugc
gccgaucgcu gccggguagu cgaggugaac ggcgugacca 1380uccaagucgg gagcaggagg uauccagacg cuguguacu
gcacagaau gaccucgguc 1440cucccauau auuggagagg uuggacguag ggacaaucg ggggaugca auugccaa
1500uggaggauug caaggaauug uuggaaucau cggaccagau auugagaagu augaaagguu 1560uauagcagc uagcauagc
uacauccuga uugcagugug ucuuggaggg uugauaggga 1620ucccacuau auaugugc ugcagggggc guuguacaa
aaaggagaa caaguuggua 1680ugucaagacc aggccuaag ccugaccuu caggaacac aaaaucuuu guagaucgc
1740uuugaugau auaggcugga gccucggugg ccaagcuuc ugcuccuug gccuccccc 1800agcccuccu cccuuccg
caccguacc cccguggucu uugaauaaug ucugaguggg 1860cggc 1864701653RNAArtificial SequenceSynthetic
Polynucleotide 70augggucuca aggugaacg cucugccgua ucauggcag uacuguaac ucuccaaca 60cccggcggc
aaucuuuug gggcaucuc ucuaagauag gguuagugg auaaggaagu 120gcaagcuaa aaguuaugc ucguaccagc
caucaucau uagucuaaaa auuaugccc 180aauaaacuc uccucauaa cugcagagg guagagauug cagaauacag
gagacuaca 240agaacaguuu uggaaccau uagggaugca cuuaugca ugaccagaa cauaaggccg 300guucagagc
uagcuucaag uaggagac aagagauuug cgggaguagu ccuggcaggu 360gcggccuag guguugccac agcugcucag
auaacagccg gcauugcuc ucaccguc 420augcugaacu cucaggccau cgacaucug agagcagcc uggaacuac
uaucaggca 480auuaggcua ucagacaagc agggcaggag augauuugg cuguucaggg uguccaagc 540uacaucaua
augagcugau accgucuaug aaccgcuau cuugugauc auucggucag 600aagcucgggc ucauuuugc uagauacuau
acagaauc ugucuuuuu ugccccagc 660cuacgggacc ccuauucg gcgagauacu auccaggcu uaguuuugc
acuuggagga 720gauucauaa agguuuuaga aaagcucgga uacaguggag gcgauuuacu aggcacuua 780gagagcagag
gaauaaaggc ucggauaacu cagcugaca cagagucca cuucaugc 840cucaguauag ccuauccgac gcuguccgag
auuaaggggg ugauugucca cggcuagag 900ggggucucg acaacuagc cucucaagag ugguauacca cuguccca
guauuugca 960accuagggu accuuuucg gaauuuugau gagucauca guacuucua gccagagggg 1020acugugugca
gcaaaugc cuuugaccg augaguccc ugcuccaaga augccuccg 1080ggguccacca aguccugc ucguacacuc
guauccgggu cuuugggaa cggguucau 1140uuuacaa ggaaccuaa agccauuug gcaucauuc uuuguaug
uuacaca 1200gguacgaa uuaucuaa ccugacaag auccuacau acuuugcgc gcaucguc 1260ccgguagucg
aggugaacgg cgugaccauc caagcggga gcaggaggua uccagacgu 1320guguacuugc acagaauga ccucggucu

cccuaucou uggagagguu ggacguaggg 1380acaaucugg ggaaucaau ugccaaauug gaggaugcca aggaauuguu
ggaaucaucg 1440gaccagauau ugagaauau gaaagguuuu ucgagcacua gcuaugucua cauccugauu 1500gcaguguguc
uuggaggguu gauagggauc cccacuuuaa uauguugcug cagggggcg 1560uguaacaaaa agggagaaca aguugguau
ucaagaccag gccuaagcc ugaccuuaca 1620ggaacauca aaucuauug aagaucguu uga 1653711925RNAArtificial
SequenceSynthetic Polynucleotide 71ggggaaaua gagagaaaag aagauaaga agaaauuaa gagccaccau gggucuaag
60gugaacgucu cugccguuuu cauggcagua cuguuaacuc uccaaacacc cgccgguca 120auucauuggg gcaaucucuc
uaagauaggg guaguaggaa uaggaagugc aagcuacaaa 180guuauagacuc guuccagcca ucaucauuu gucauuuuu
uaaugccca uuaaacucuc 240cucauuacu gcacgagggg agagauugca gaauacagga gacuacuaag aacaguuuu
300gaaccauuu gggaugcacu uauugcaaug accagaaca uaaggccgg ucagagcgua 360gcuucaagua ggagacaca
gagauuugcg ggaguagucc uggcaggugc ggccuaggu 420guugccacag cugcucagau aacagccggc auugcacuuc
accgguccau gcugaacuc 480caggccaucg acaucugag agcgagccug gaaacuacua aucaggcaau ugaggcauc
540agacaagcag ggcaggagau gauauuggcu guucagggug uccaagacua caucauuuu 600gagcugauac gcucuaugaa
ccagcuauc uugaucuaa ucggucagaa gcucggguc 660aaauugcuu gauacuauac agaaucug ucauuuuu
gccccagccu acgggacccc 720auaucugcgg agauaucuau ccaggcuuug aguuaugcac uuggaggaga uaucauuag
780guguuagaaa agcucggaua caguggaggc gauuuacuag gcauuuaga gagcagagga 840auaaaggcuc ggauaacua
cgucgacaca gaguccuacu ucauaguccu caguauagcc 900uauccgacgc uguccagau uaagggggug auuguccac
ggcuagaggg ggucucguac 960aacauaggcu cucaagagug guauaccacu gugcccaagu auguugcaac ccaagggua
1020cuuauucgca auuuugauga gucaucaug acuuucaugc cagaggggac ugugugcagc 1080caaaugccu uguaccgga
gaguccucug cuccaagaau gccucegggg guccaccaag 1140uccugucuc guacacucgu auccgggucu uuugggaacc
ggucuuuuu aucacaaggg 1200aacuuauag ccaauuguc aucauuuuu uuaaguguu acacaacagg uacgaauuu
1260aaucaagacc cugacaagau ccuaacauac auugcugccg aucgucgccc gguagucgag 1320gugaacggcg ugaccauca
agucgggagc aggagguauc cagacgcugu guacuugcac 1380agaauugacc ucgguccuc caucauuug gagagguug
acgaggggac aaucugggg 1440aaucauuug ccauuugga ggaugccaag gaauguugg aaucaucgga ccagauuu
1500agaauaaga aagguuuuac gagcucuagc auagucuaa uccugauugc agugugucuu 1560ggaggguuu uagggaucc
cucuuaaua uguugcugca gggggcgug uacaaaaag 1620ggagaacaag uugguuguc aagaccaggc cuaaagccug
accuuacagg aacaucaaaa 1680uccuauuaa gaucgcuuug augauuuag gcuggagccu cgguggccaa gcuucugcc
1740ccuugggcu cccccagcc ccuccccc uuccugcacc cguaccccg ugucuuuga 1800auaaagucug aguggggcgc
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa
aaaaaaaaa 1920ucuag 1925721864RNAArtificial SequenceSynthetic Polynucleotide 72ucaagcuuu ggaccucgu
acagaagcu auacgacu cuauaggga auuagagaga 60aaagaagagu aagaagaa auuagagcca caugggucu caagguaac
gucucugua 120uauucauggc aguacuuu acuuuacaa caccaccgg ucauuuccu uggggcauc 180ucucuaagau
aggggugua gggguaggaa gugcaagcu caaauuuug acucguuca 240gccaucauc auuagucua aaguuaugc
ccaauuaac ucuccuac auuugcag 300ggguaggau ugcagaauac aggagacuac ugagaacagu ucuggaaca
auuagagau 360cacuuauugc auuagaccag auuuaagac cguuucagag uguagcuca agugagagc 420acaagagau
ugcgggaguu guccuggcag gugcggccu aggcguugcc acagcugcuc 480aaauaacagc cguuauugc cuuaccagu
ccaugcugaa cucuaagcc aucgacauc 540ugagagcgag ccuagaacu acuaucagc cauuagaggc auacagaca
gcaggcgag 600agaugauuu ggcuguucag gguguccaag acuaucuaa uauugcug auaccgucua 660ugaaucauc
auuugugau uuaucggc agaagcuagg gcuaauuug cucagauac 720auacagaaau ccugucuuu uuuggccca
gcuuacggga cccauaucu gcggagauu 780cuauccaggc uuugagcuu gcgcuuggag gagaucau uaggguguug
gaaaagcucg 840gauacagugg agguagucua cugggcauc uagagagcag aggaauaaag gcccggaua 900cucacgucg
cacagagucc uacuucuuug uacucaguau agccuuccg acgcuuccg 960agauuaagg gguuuguc caccggcug
agggggucuc guacaacua ggcucuaag 1020agugguauac cacugugccc aaguauuug caaccaagg guaccuuac
ucgaauuuug 1080augagucuc augcacuuc augccagagg ggacugugug cagccagaau gccuugucc 1140cgaugagucc
ucugcuccaa gaaugccuc ggggguccac uaguccugc gcucguacac 1200ucguauccgg gcuuucggg aaccgguca
uuuuacaca ggggaaccua auagccaau 1260gugcauau

ccuuugcaag uguuacaca caggaaca auuauca gaccucgaca 1320agaucuaac aucauugc gccgaucacu
gcccgguggu cgagguaau ggcgugacca 1380uccaagucgg gagcaggagg uauccggagc cuguguacu gcacaggau
gaccucgguc 1440cuccauauc uuuggagagg uggacguag ggacaauc ggggaugca auugcuuagu 1500uggaggau
caaggauug uggagucuu cggaccagau auuagggagu augaaaggu 1560uauagcagc uaguauagu ucauccuga
uugcaguguc ucuuggagga uugauaggga 1620ucggcgcuu auuauugc ugcagggggc guuuaaca gaaggagaa
caaguuggua 1680ugucaagacc aggcuaaag ccuagucua caggaacuc aaauccuau gaaaggucac 1740ucugaugua
auaggcugga gccucggug ccaagcuuc ugccccuug gccuccccc 1800agccccu cccuuccg caccguacc
cccgggucu ugaauaaag ucugagugg 1860cgcc 1864731653RNAArtificial SequenceSynthetic Polynucleotide

73augggucuca aggugaacgu cucugucaua uucauggcag uaciguuaac ucuucaaa 60cccaccgguc aaauccauug
gggcaaucuc ucuagauag gggugguagg gguaggaagu 120gcaagcuaca aaguuaugac ucguuccagc caucauau
uagucuaaaa guuaaugccc 180aaauaaacuc uccucaaaa uugcagagg guagggauug cagaauacag gagacuacug
240agaacaguuc uggaaccau uagagaugca cuuaugcaa ugaccagaa uuaagaccg 300guucagagug uagcuucaag
uaggagacac aagagauug cgggaguugu ccuggcaggu 360gcgcccuag gcguugccac agcugcuaa auaacagccg
guauugcacu ucaccagucc 420augcugaacu cucaagccau cgacaucug agagcgagcc uagaauacac uauacaggca
480auugaggcaa ucagacaagc agggcaggag augauauugg cuguucaggg uguccaagac 540uacaucaaua augagcugau
accgucuaug aaucacuau cuugugauuu aaucggccag 600aagcuagggc ucaauugcu cagauacuau acagaauc
ugucuuuuu uggccccagc 660uuacgggacc ccauucugc ggagauacu auccaggcuu ugagcuugc gcuuggagga
720gauaucaua agguuugga aaagcucgga uacaguggag gugauacu gggcaucuua 780gagagcagag gaauaaaggc
ccggauacu cagcugaca cagagucca cucauugua 840cucaguauag ccuauccgac gcuauccgag auuaaggggg
ugauugucca ccggcuagag 900ggggucucgu acaacuagg cucucaagag ugguaacca cugugccca gaauguugca
960accaagggu accuauucg gaauuuugau gagucauau gcacuuuau gccagagggg 1020acugugugca gccagaugc
cuuguaccg augaguccuc ugcuccaaga augccuccg 1080ggguccaia aguccuguc ucguacacuc guauccgggu
cuucgggaa ccgguucau 1140uuauacaggg ggaaccuau agccaauugu gcauaucc uuugcaagug uuacaca
1200ggaacaaua uuaaucaaga ccugacaag auccuauacu acuuucugc gcaucacugc 1260ccggugugc agguaaug
cgugaccau caagucggga gcaggagga uccggagcu 1320guguacuugc acaggaua ccucgguccu ccauauuu
uggagagguu ggacguagg 1380acaaucugg ggaugcau ugcuaaguug gaggaugcca aggaauuguu ggagucagc
1440gaccagauu uagggaguu gaaagguua ucgagcua guauaguua cauccugau 1500gcagugugc uggaggau
gaauggguc cccguuuua uaguugcug cagggggcgu 1560uguaacaaga agggagaaca aguugguug ucaagaccg
gccaaagcc ugaucuaa 1620ggaacaaua aaucuaugu aagucacuc uga 1653741925RNAArtificial
SequenceSynthetic Polynucleotide 74ggggaaaua gagagaaaag aagauaaga agaaauuaa gagccacau gggucuaag
60gugaacguc cugucuaau cauggcagua cuguuaacuc uucaaacacc caccgguca 120auccauuggg gcaucucuc
uaagauagg gugguagggg uaggaaguc aagcuacaa 180guuaugacuc guuccagca ucauauua gucauaaagu
uaugccca uuaacucuc 240cucaacaau gcacgagggg agggauugca gaauacagga gacuacug aacaguucg
300gaaccaaua gagaugcacu uauugcaug accagaaua uaagaccggu ucagagugua 360gcuucaagua ggagacaca
gagauuugc ggaguugucc ugccagugc ggccuaggc 420guugccacag cugcucaau aacagccggu auugcacuuc
accagucca gcuagauc 480caagcaucg acaucugag agcgagcua gaaacuaua aucaggcau ugaggcauc
540agacaagcag ggcaggagau gauauuggc guucagggug uccaagacua cauaauaau 600gagcugauac gcuuaugaa
ucaacuau ucugauuuua ucggccagaa gcuagggc 660aaauugcuca gauacuauac agaaucug ucauuuuug
gccccagcu acgggacccc 720auaucugcgg agauacuau ccaggcuuug agcuugcgc uggaggaga uaucauaag
780guguuggaaa agcucggaua caguggaggu gacuacugg gcaucuaa gagcagagga 840auaaaggccc ggauaacua
cgucgacaca gaguccuacu ucauugacu caguauagcc 900uauccgagc uauccgagau uaaggggug auugccacc
ggcuagagg ggucugua 960aacauaggc cucaagagug guauaccacu gugcccaagu auguugcaac ccaagggua
1020cuuauucg auuuuga gucaucug acuuuacug cagaggggac ugugcagc 1080cagaugccu uguaccgag
gaguccuc cucaagaau gccuccgggg guccauaag 1140uccugucg guacacucg auccggguc uucgggaacc
gguucauuu aucacagggg 1200aacuaauag ccauuguc aucauucuu ugcaaguguu acacaacagg acauauuu
1260aaucagacc cugacaagau ccauacuau auugcugcc aucacugccc gguggucgag 1320gugaauggcg ugaccauca
agucgggagc agggaua cggagcug guacuugc 1380aggauugacc ucgguccuc cauauuuug gagagguugg
acguagggac aaucugggg 1440aaugcauuug cuuaguuuga ggaugccaag gaauuuugg agucacgga ccagauuuug
1500aggagaua agguuuuau gagcuaugu auaguuaa uccagauugc agugugucuu 1560ggaggauuga uagggauc
cgcuuuuaa uguugcugca gggggcguug uacaagaag 1620ggagaacaag ugguaugc aagaccagc cuaaagccg
aucuuacag acauacaaa 1680uccuaugua ggucacucug augauauag gcuggagccu cgguggcca gcuucugcc
1740ccuugggcu cccccagc ccuccccc uuccugcacc cguaccccg uggucuuuga 1800auaaaguc aguggggcgg
aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1860aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa
aaaaaaaaa 1920ucuag 1925752065RNAArtificial SequenceSynthetic Polynucleotide 75ucaagcuuuu ggaccucg
acagaagcu auacgacu cuauaggga auagagaga 60aaagaagagu aagaagaa auagagcca caugucacc gcaacgagac
cggauaaaug 120ccuucuaa agauaacuu uauccaaagg gaaguaggau aguuuuuac agagaacuc 180uuauugaua
cagaccuau guucugcug cuguucuguu cguauguuu cugagcuuga 240ucggauugc ggcauuugc ggcauuagac
uauucggc agccaucac acccgggaga 300uccauaaaag ccucaguacc auucggagug uacuauac caucgagcau
caggucaagg 360acugcugac accacuuuu auaucucg gggaugaagu gggccugaga acaccuaga 420gauucacuga
ccuagugaaa uauucucgg acaaguuua auuccuuuu ccggauggg 480aguacgacu cagagauc acuuugugca
ucaaccgcc agagaggau aaacuaguu 540augaucaua cugugcagau guggcugcug aagagcua gaugcaug
gugaacua 600cucuacug gaccagaac accacucagu ucuagcugu cuaaaggga acucgucag 660ggcccacuac

aaucagaggu caauucuaa acaugucgcu guccuuguug gacuuguacu 720uaggucgagg uuacaauug ucaucuauag
ucacuaugac aucccagga auguauuggg 780gaaccuaccu aguugaaaag ccuaaucuga acagcaaagg gucagaguug
ucacaacuga 840gcauguaccg aguguuugaa guagguguga ucagaaaccc ggguuugggg gcuccggugu 900uccauaugac
aaacuauuuu gagcaaccag ucaguaaugg ucucggcaac uguauuggug 960cuuuggggga gcuaaacuc gcagccuuu
gucacgggga cgaucuauc auuuuuuccu 1020aucagggauc agggaaaggu gucagcuucc agcucguca gcuggguguc
uggaaaucc 1080caaccgacau gcauuccgg gucccuuau caacggaua uccaguggua gacaggcuu 1140accucuauc
ucacagaggu gucaucgcu acaaucaagc aaaugggcu gucccgaca 1200cacgaacaga ugacaaguug cgauggaga
caugcuucca gcaggcgugu aaagguaaaa 1260uccaagcacu cugcgagaau cccgaguggg uaccuugaa ggauaacagg
auuccuuc 1320acgggguccu gucuguugau cugagucuga cggugagcu uaaaaucaa auugcuuccg 1380gauucgggccc
auugaucaca cacggcucag ggauggaccu aucaaauc aacugcaaca 1440auguguauug gcugacuauu ccgccauga
gaaucuaage cuuaggcgua aucaacacau 1500uggaguggau accgagauuc aagguuaguc ccaaccucu cacugucca
auuaaggag 1560caggcgaga cugcaugcc ccaacauacc uaccucgga gguggacggu gauguaaac 1620ucaguucca
ccuggugauu cuaccugguc aagauucca auauuuuug gcaaccuacg 1680auaccuccag gguugagcau gcugugguu
uuacguua cagccaagc gcucuuuuu 1740cuuacuuuu uccuuuagg uugcuuuuu aggggguccc aaucgaacua
caaguggau 1800gcuucacau ggaucaaaaa cucuggguc gucacuucug ugucucugc gacucagaau 1860ccgguggacu
uacacucac ucugggaggg ugggcauggg agucagcuc acagcuacc 1920gggaagagg aaccaaucgc agauaugau
auuaggcugg agccucggug gccaagcuuc 1980uugcccuug ggccucccc cagccucc ucccuuccu gaccguc
cccgguguc 2040uuugaauaa gucugagugg gggc 2065761854RNAArtificial SequenceSynthetic Polynucleotide
76augucaccgc aacgagaccg gauaaugcc ucucaaaag auaacuuu uccaaggga 60aguaggauag uuauaacag
agaacauuu augauugaca gaccuauug ucugcuggcu 120guucuguucg ucauguuuc gagcuugauc ggauugcugg
cauugcagg cauugacu 180caucgggag ccaucacac cgcggagau cauaaaagcc ucaguacca ucuggaugug
240acuaacuca ucgagcau ggucaaggac gucugacac cacuuuuu aucaucggg 300gaugaaggg gccugagaac
accucagaga uucacugacc uagugaaau caucucggc 360aaguuuuu uccuuuucc ggauagggag uacgacuuca
gagauccac uuggugcau 420aacccgag agaggauca acuauguuu gaucauacu gucgagauu ggcugcuga
480gagcuauga augcauuggu gaacuaacu cuacuggaga ccagaaca cacucaguuc 540cuagcuguc caaagggaa
cugcucaggg ccacuaaca ucagagguca auucuaaac 600augucgcu ccuuguugga cuuguacuua ggucgaggu
acauguguc aucauaguc 660acuauagcau cccagggaau gaauggggga accuaccuag uugaaaagcc uauucgaa
720agcaagggu cagauuguc acaucgagc auguaccgag uguuugaagu agguugauc 780agaaaccgg guuuggggg
uccgguguuc cauugaca acuauuuuga gcaaccaguc 840agaaugguc ucggcaacug uauugggcu uugggggagc
ucaaacucgc agccuuuug 900cacggggagc auucuauc auuuccuau cagggaucag gaaaggugu cagcuuccag
960cucgucaage ugguugucg gaaucucca accgacugc auuccugggu cccuuuauca 1020acggaugau caguggua
caggcuuuac cucuacuc acagaggugu caucgucag 1080aucaagca auugggcu cccgacaaca cgaacagau
acaaguugc auaggagaca 1140ugcuuccagc aggcgugua agguuuuau caacacauug gaguggauac cgagauca
1200ccauugaagg auaacaggau uccuucuauc ggggucug cuuguaucu gagucgagc 1260guugagcu uaucaaaa
ugcuuccggg uucgggccau ugaucacaca cggcucaggg 1320auggacuu acaauccaa cugcaacau guguauuggc
ugacuauucc gcaaugaga 1380aaucuaugcc uaggcguaa caacacauug gaguggauac cgagauca gguuagucc
1440aacucua cuucuccau uaaggaagca ggcaagacu gcaugccc acauaccua 1500ccucggagg ugacgguga
uguaaacuc aguuccaacc ugguuauu accugguca 1560gucuccau auguuuugc aaccuacg accuccaggg
uugagcugc ugguuuuau 1620uacguuua gccaagcc cuuuuuu ucuuuuau cuuuuagggu gcuuuuag
1680gggucucca ucgaucua aguggaagc uucacauagg aucaaaaacu cuggugccg 1740cacuucugug ucuugcgg
cucagaaucc gguggacu uacucacuc uggauggg 1800ggcaugggag ucagcucac agcuaccgg gaagaggaa
ccaucgag auua 1854772126RNAArtificial SequenceSynthetic Polynucleotide 77gggaaaua gagagaaag
aagauaaga agaaauuaa gageccau gucaccgca 60cgagaccgga uaaugccu cuacaagau aaccuuuau ccaagggaag
uaggauuu 120auaacagag acaucuuu gauugacaga ccuauguuc ucugcugcu ucuguucg 180auguuucga
gcuugaucgg auugcuggca auugcaggca uuagacuua ucgggagcc 240aucuacaccg cggagauca uaaaagcc
aguaccauc uggaugagc uauuccau 300gagcaucagg ucaaggagc gcugacaca cuuuuuuu ucaucgggga
ugaaguggg 360cugagaacac cucagauu cacugacua gugaauua ucucgaca gauuuuuu 420cuuauuccg
auagggaga gcacuucaga gacucacu ggugcaua cccgagag 480aggaucaaac uaguuuuga ucauacug
gcagauuggc cugcugaaga gcuaugau 540gcauugguga acuaacuc acuggagacc agaacaaca cucaguucc
agcugucua 600aagggaacu gcucagggcc cacuaaac agagguaau ucuaaacau gucgucucc 660uuguuggacu
uguacuugg ucgagguuac auugucua cuuagucac uaugaucc 720cagggaau augggggaac cuaccuagu
gaaaagccu aucuaacag caaaggguca 780gaguuguc aacugagcau guaccgagug uuugaagu gagugauc
aaaccggg 840uuggggguc cgguguuca uauuugagc aaccaguc uauugguc 900ggcaacug
ugggcuuu gggggagc aacucgag cccuuugca cgggagcau 960ucuaucuaa uccuuauc ggaucagg

aaagguguca gcuuccagcu cgucaagcug 1020ggugucugga auccccaac cgacaugcaa uccugggucc ccuuaucaac
ggauuca 1080gugguagaca ggcuuuaccu cucaucac agagguguca ucgcugacaa ucaagcaaaa 1140ugggcugucc
cgacaacacg aacagaugac aaguugcgaa uggagacug cuuccagcag 1200gcguguaaag guaaaauca agcacucugc
gagaaucccg aguggguacc auugaaggau 1260aacaggauuc cuucaucgg gguccugucu guugaucuga gucugacggu
ugagcuuaaa 1320aucaaaaauug cuucgggguu cgggccauug aucacacacg gcucagggau ggaccuauac 1380aaauccaacu
gcaacaauug guauuggcug acuaucggc caugagaaa ucuagccua 1440ggcguaauca acacauugga guggauaccg
agauucaagg uuaguccaa ccucuucacu 1500gucceaaaua aggaagcagg cgaagacugc caugcccaa cauaccuacc
ugcggaggug 1560gacggugaug ucaaacucag uccaaccug gugauucac cuggucaaga ucuccaaau 1620guuuuggcaa
ccuacgauac cuccaggguu gagcaugcug ugguuuaua cguuacagc 1680ccaagccgcu cauuuucua cuuuuauccu
uuuagguugc cuuaaaagg ggucceaac 1740gaacuacaag uggaugcuu cacauggggu caaaaacucu ggugccguca
cuucugugug 1800cuugcggacu cagaucggg uggacuuauc acucacucug ggauugguggg caugggaguc 1860agcugcacag
cuaccggga agauugaacc auucgcagau augauaaua ggcuggagcc 1920ucgguggcca agcuucugc ccuugggcc
ucccccagc ccuccucc cuuccugcag 1980ccguacccc guggucuuug auaaaagucu gaguggcgg caaaaaaaaa
aaaaaaaaa 2040aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 2100aaaaaaaaa
aaaaaaaaa aucuag 2126782065RNAArtificial SequenceSynthetic Polynucleotide 78ucaagcuuuu ggaccucgu
acagaagcua auacgacuca cuauaggga auaagagaga 60aaagaagagu aagaagaaau auaagagcca ccaugucacc acaacgagac
cggauaaaug 120ccuucuaaca agacaacccc cauccaaagg gaaguaggau aguuuuuac agagaacuc 180uuuagauuga
uagaccuuau guuuugcugg cuguucuuu cgucauguuu cugagcuuga 240ucggguugcu agccauugca ggcuuagac
uucucgggc agccauucac accgcagaga 300uccauaaaag ccucagcacc auucuggaug uacuaacuc auucgagcau
cagguuaagg 360acgucgucac accacucuc aagaucucg gugaugaagu gggcuugagg acaccucaga 420gauucacuga
ccuagugaag uucacucug acaaguuua auuccuuau cggacaggg 480auucgacuu cagagaucuc acuuuggguga
ucaacccgc agagagauc aaauuggau 540augaucaua cugugcagau guggcugcug aagaacuc auugcaug
gugaacuaa 600cucucugga gaccagggca accaaucagu uccuagcugu cucaaaggga aacugcucag 660ggcccacuc
auucagaggc caauucuaa acaugucgcu gucccuug gacuuguuu 720uaagucgagg uuacaugug ucaucuaug
ucacuaugac auccaggga auguacgggg 780gaacuaccu aguggaaaag ccuaucuga gcagcaagg gucagaguug
ucacaacuga 840gcaugcaccg aguuuugaa guaggguua ucagaauc ggguuugggg gcuccguu 900uccauaugac
aaucuaucuu gagcaaccag ucaguauga uuucagcaac ugcauggug 960cuuuggggga gcuaaguuc gcagccucu
gucacaggga agauucuauc acauuuccu 1020aucagggauc agggaaaggu gucagcuucc agcuuguaa gcuagguguc
uggaaaucc 1080caaccgacau gcauuccg gucccccua caacggaua uccagugua gacaggcuu 1140accucucac
ucacagaggc guuucguc acaucaagc aaauugggu guccgaca 1200cacggacaga ugacaaguug cgauggaga
cugcuuca gcaggcgugu aaggguuaaa 1260uccaagcacu uugcgagaau cccagugga caccuuga ggauaacagg
auuccuuc 1320acggggucuu gucuguugau cugagucuga caguugagcu uaaaucua auuguucag 1380gauucgggc
auugaucaca caggguucag ggauggacu auacaaucc aaccacaaca 1440auauguuug gcugacuuc ccgcauga
agaaccggc cuuagguga aucaacacu 1500uggaguggau accgagauuc aagguuagc ccaaccucu cacuguuca
auuaaggag 1560caggcgagga cugcaugcc ccaacauacc uaccugcgga gguggauggu gauguaaac 1620ucaguucca
ucuggugau cuaccugguc aagauuca auauuguc gcaaccuac 1680auacuuccag aguugaacu gcuguuguu
auuacguua cagccaagc gcucuuuu 1740cuuacuuuu uccuuuagg uugccuguaa gggggguc cauugaaua
caugggaa 1800gcuucacug ggacaaaaa cucuggugc gucacuucug ugugcuugc gacucagaau 1860cugguggaca
uucacucac ucuggaugg ugggcauggg agucagcugc acagccac 1920gggaagaug aaccagccgc agauagugau
auuaggcugg agccugug gccaagcuu 1980uugcccuug ggcuccccc cagccucc ucccuuccu gcaccguac
ccccgugguc 2040uuugaauaa gucugagugg gcggc 2065791854RNAArtificial SequenceSynthetic Polynucleotide
79augucaccac aacgagacc gauaaaugc uucuaaaag aacccccca uccuaaggga 60aguaggauag uuuuuacag
agaacucuu augauugau gaccuuauug uuugcuggcu 120guucuaucg ucauguuuc gagcuugauc gguugcuag
ccauugcagg cauuagacu 180aucgggcag caucucac cgcagagau cauaaaagcc ucagacca ucuggaugua
240acuacuaa ucgagcauca gguaaggac gucugacac cacucuaa gaucaucggu 300gaugaagugg gcuaggagc
accucagaga uucacugacc uagugaagu caucucugac 360aagauuaau uccuaaucc ggacaggga uacgacuca
gagaucac uugguuauc 420aaccgccag agagaauca auuggauuu gaucauacu gucagaugu ggcugcugaa
480gaucuauga augcauuggu gaucuaacu cuucggaga ccaggcaac caucaguuc 540cuagcugucu caagggaaa
cugcucagg cccacuaca ucagaggcca auucuaaac 600augucgugu ccuugugga cuuguuuua agucgaggu
acauguguc aucauaguc 660acuauagacu cccagggaau guacggggga acuuaccuag ugaaaagcc uaucugagc
720agcaagggu cagaguugc aacugagc augcaccgag uguuugaagu agguuuuac 780agaaucgg guuuggggg
uccguuuu cauagaca acuaucuga gcaaccagc 840aguaugau ucagcaacug caugguggcu uggggggagc
ucaaguucg agccucugu 900cacagggaag auucuauc auuuccuau cagggaucag ggaagggu cagcuuccg
960cuuguaagc uaggugucg gaaucacca accgacugc auccugggu ccccuauca 1020acggaugauc cagugauaga

caggcuuuac cucucaucuc acagaggcgu uaucgcugac 1080aaucaagcaa aaugggcugu cccgacaaca cggacagaug
acaaguugcg aauggagaca 1140ugcuuccagc aggcguguaa ggguaaaauc caagcacuuu gcgagaaucc cgaguggaca
1200ccauugaagg auaacaggau uccuucuauc ggggucuugu ciguugaucu gagucugaca 1260guugagcuua aaaucaaaa
uguuucagga uucgggccau ugaucacaca cgguucaggg 1320auggaccuau acaaaucac ccacaacaau auguauuggc
ugacuauccc gccaaugaag 1380aacccggccu uagguguaau caacacauug gaguggauac cgagauuca gguuagucc
1440aacccuua ciguuccau uaaggaagca ggcgaggacu gccaugcccc acauaccua 1500ccugcggagg uggaugguga
uguaaacuc aguuccaauc ugguuauuc accuggucaa 1560gaucuccau auguucuggc aaccuacgau acuccagag
uugaacugc uguaguuuu 1620uacguuuaca gcccaagccg cucuuuuu uacuuuuu cuuuuagguu gccuguaagg
1680gggguccca ugaauuaca aguggaagc uucacaggg accaaaaacu cuggugccgu 1740cacuucugug ugcuuugcga
cucagaauuc gguggacaua ucacucacuc uggauggug 1800ggcaugggag ucagcugcac agccacucgg gaagauggaa
ccagcccgag auag 1854802126RNAArtificial SequenceSynthetic Polynucleotide 80ggggaaaua gagagaaa
aagauaaga agaaaua gagccacau gucaccaca 60cgagaccgga uaaugccu cuacaagac aaccucca cuagggag
uaggauugu 120auaacagag acaucuuu gauugauaga ccuuuuuu ugcuggcugu ucuuucugc 180auguuucga

gcuuugcgg guugcuagcc auugcaggca uuagacuua ucgggcagcc 240aucuacaccg cagagaucua uaaaagccu
agcaccuuc uggauguaac uacucauac 300gagcaucagg uuaaggacgu gcugacaca cucuuaaga ucaucgguga
ugaagugggc 360uugaggacac cucagaguu cacugaccua gugaaguua ucucugaca gauuuuuu 420cuuuuuccg
acagggaaua cgacuucaga gaucucacu gguguaucac cccgccagag 480agaaucauu uggaauuga ucauucug
gcagauuggcugcugaaga acuaugaau 540gcauugguga acuaacuc acuggagacc agggcaacca aucaguucc
agcugucua 600aagggaacu gcucagggcc cacuacauc agaggccau ucuaacau gucgucucc 660cuguuggacu
uguuuuuu ucgagguuac auugucacu cuauaguc uagacauc 720cagggaugu acgggggaac uuaccuagug
gaaaagccua aucugagcag caaaggguca 780gaguuguc aacugagcau gcaccgagug uuugaagu guguuucag
aaaucgggu 840uuggggguc cgguuuuca uaugacaac uauucugc aaccaguc uaauguuu 900agcaucgca
uggugccuuu gggggagcuc aaguucgag ccucugua cagggaagau 960ucuaucaca uuccuua gggauccgg
aaaggguca gcuuccagc ugucaagca 1020ggugucugga auucccaac cgacugca uccuggucc ccuaucaac
ggauuca 1080gugauagca gcuuuuacu cuacucac agaggcguu ucgugaca ucaagcaaaa 1140ugggcugucc
cgacaacac gacagaugac aaguugcga uggaagcau cuuccagc 1200gcguguaagg guaaaauca agcacuucg
gagaauccg aguggacac auugaagga 1260aacaggau cuucauacgg ggucuguc guugaucga gucugacag
ugagcuuaa 1320aucauuuug uuucagga cgggccauug aucacacg guucagggau ggaccuauac 1380aaaucaacc
acaacaauu guauuggc acuaucggc caaugaaga ccuggccua 1440gguguauc acacauugga guggauaccg
aguuucaagg uuaguccaa ccuucacu 1500guuccaaua aggaagcagg cgaggacugc caugcccau cauccuacc
ugcggaggug 1560gauggugaug ucaaacucag uuccaauuc gugaucuc cuggucaaga uccaauu 1620guucggca
ccuacgau uuccagaguu gaacugcug uaguuuuuu cguuacagc 1680ccaagccg cuuuuuuu cuuuuuccu
uuuagguugc cuguaagggg gucccauu 1740gaauucaag uggaugcu cacauuggc caaaacuc ggugccgca
cuucugug 1800cuugcggacu cagaucugg uggaucac acucacuc ggauugggg caugggaguc 1860agcugcacag
ccacugggga agauagacc agcccgag aguguaaua ggcuggagcc 1920ucggggcca agcuucugc ccuugggccc
ucccccagc ccuccucc cuuccgac 1980ccguacccc guggucuuu auuaaguc gaguggcgg caaaaaaaaa
aaaaaaaa 2040aaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa 2100aaaaaaaa
aaaaaaaa auuag 2126811729RNAArtificial SequenceSynthetic Polynucleotide 81ucaagcuuu ggaccucg
acagaagcua auacgacua cuauaggga auagagaga 60aaagaagagu aagaagaa auagagcca cauggcaca agucuuuu
acaacagcc 120ugcugucuu gaccagaau aaccugaaca auccaguc gcacugggc acugcuucg 180agcuuugc
uuccggucg cuuaucaac gcgcgaaaga cgauccggca ggacagcgca 240uugcuaccg uuuuaccg acaucaag
gucugacua gcuuccgcu aacgcuacg 300acgguauc cuuugcag accacugaag gcgcgugaa cgaaucac
aacaccugc 360agcugugcg ugaacuggc guucaguc cgaugguac uacuccag ucugaccug 420acuucca
ggcugaauc acccagcgc ugaacgaa cgaccgug uccggccaga 480cucaguuca cggcgugaa guccggcgc
aggacaacac ccugacca cagguuggug 540ccaacgagc ugaacuauc gauuuguu uaaaagaa cagcuaaaa
acacugggac 600uugauaagcu uauugucca gaugccuaca cccgaaaga aacugcugua accguugua 660aaacuucca
uuuuuuggu acagaucua uuacagccc gagcauacu gauuccaa 720cugcauuugg cgguggugca acggggguu
cuggggcuga uaucauuuu aaagauggc 780aaucuuuu agauuuuu ggcggugcu cugcuggugu uuuuuagcc
acuuaugaug 840aaucuaaaa gaaaguuuu auugauacga cuguuuuu uccguuggc acugcggag 900cuacagcuu
ucggggaac gccacuuaa ccacaacca auugcugaa guacaaaag 960aggguuuu uacgaccaca guugcggcuc
aacuugcugc agcagggguu acuggcggc 1020auaaggaca ucuagccu guaaaacu cguuugagga uaaaacggu
aagguuuu 1080auggggcua ugcagugaa augggcgagc auucuaugc gcuaucuu gauagaaaa 1140caggugcau
uacugcuua accacuacu auacagaug uacugcguu gcuaacug 1200gagcugugaa auuuggguc gcaauugga

aaucugaagu uguuacugcu accgauggua 1260agacuuacu agcaagcgac cuugacaaac auaacuucag aacaggcggg
gagcuuaaag 1320agguuaauac agauaagacu gaaaaccac ugcagaaaau ugaugcugcc uggcagagg 1380uugauacac
ucguucugac cugggugcgg uucagaaccg uuucaacucc gcuauacca 1440accugggcaa uaccguaaa aaccugucuu
cugcccguag ccguaucgaa gauuccgacu 1500acgcaaccga agucuccaac augucugcg cgagauucu gcagcaggcc
gguaaccug 1560uucuggcgca ggcgaaccag guuccgaaa aguccucuc uuucugcgu ugauauuagg 1620cuggagccuc
gguggccaug cuucugccc cuugggccc ccccagccc cuccucccu 1680uccugcacc guacccccgu ggucuuugaa
uaaagucuga gugggccc 1729821518RNAArtificial SequenceSynthetic Polynucleotide 82auggcacaag
ucauuauac aacagccug ugcuguuga cccagaaua ccugaacaaa 60uccagucc cacugggcac ugcuaucgag cguuugucuu
ccggucugcg uaucaacagc 120gcgaaagacg augcggcagg acaggcgauu gcuaccguu uuaccgcaa caucaaggu
180cugacucagg cucccguaa cgcuaacgac gguaucucca ugcgcagac cacugaaggc 240gcgcugaacg aaaucaaca
caaccugcag cgugugcgug aacuggcggg ucagucugcg 300aaugguacua acuccaguc ugaccucgac uccaucagg
cugaaucac ccagcggcug 360aacgaaucg accguguauc cggccagacu caguucaacg gcgugaaagu ccuggcgcag
420gacaacccc ugaccauca gguuggugcc aacgacggug aaucuaucga uauugauuuu 480aaagaaa gcucaaaa
acugggacuu gauaagcuu auguccaaga ugccuacacc 540ccgaaagaaa cugcuguaac cguugauaaa acuaccuua
aaaugguac agauccuau 600acagcccaga gcauacuga uauccaaacu gcauuggcg guggugcaac ggggguuacu
660ggggcugau ucauuuuu agauggucaa uacuauuag auguuuagg cggugcuuu 720gcugguguuu auaagccac
uuauaugaa acuacaaaga aaguauauu ugauacgacu 780gauaaaacuc cguuggcaac ugcggaagcu acagcuauuc
ggggaacggc cacuaaacc 840cacaacaaa ugcugaagu acaaaagag gguguugaua cgaccacagu ugcggcuca
900cuugcugcag caggguuac uggcgccgau aaggacaaua cuagccuugu aaaacuucg 960uuugaggaua aaaacggua
gguuauugau gguggcuau cagugaaaau gggcgacgau 1020uucuaugccg cuacauaga ugagaaaaca ggugcauuu
cugcaaaac cacuacuau 1080acagauggua cuggcguugc ucaacugga gcugugaaau ugguggcgc aaugguua
1140ucugaaguug uuacugcuac cgaugguaag acuuacuug caagcgaccu ugacaaacu 1200aacuucagaa caggcgguga
gcuuaaagag guuaauacag auaagacuga aaaccacug 1260cagaaaauug augcugccuu ggcacagguu gauacacuuc
guucugaccu gggugcgguu 1320cagaaccguu ucaacuccg uauaccaac cugggcaaua ccguaaaaua ccugucuuu
1380gccguagcc guaucgaaga uuccgacuac gcaaccgaag ucuccaacu gucucgcg 1440cagauucgc agcaggccg
uaccuccguu cuggcgcagg cgaaccaggu uccgaaaac 1500guccucucu uacugcgu 1518831790RNAArtificial
SequenceSynthetic Polynucleotide 83ggggaaaua gagagaaaag aagauaaga agaaauuaa gagccacau ggcacaagc
60auuaauaca acagccugc gcuguugacc cagaauaacc ugaacaauc ccaguccgca 120cugggcacug cuaucgagc
uuugucucc ggucugcgu ucaacagcgc gaaagacgau 180gcggcaggac aggcgauugc uaaccguuuu accggaaca
ucaagguu gacucaggcu 240uccguaacg cuaacgacgg uaucuauu gcgcagacca cugaaggcgc gcugaacgaa
300aucaacaaca accugcagc ugugcgugaa cuggcgguuc agucugcga ugguaucuaac 360uccagucug accucgac
cauccaggu gaaucacc agcggcugaa cgaaucgac 420cguguaucg gccagacu guucaacggc gugaaagucc
uggcgcagga caaccucc 480accuaccag uggugccaa cgacggugaa acuaucgaa uugauuuua agaaucagc
540ucuaaaacac ugggacuuga uaagcuuau guccaagaug ccuacacc gaaagaaacu 600gcuguaaccg uugauaaa
uaccuauaaa auugguacag auccuauuac agcccagagc 660aaucugua uccaacucg aauggcggg ggugcaaccg
ggguuacug ggcugauau 720aaauuuuau auggucaua cuuuuugau guuaaaggc gugcuucgc ugguguuuu
780aaagccacu augaugaac ucaaaagaa guuaauuug auacgacuga uaaaucucc 840uuggcaacug cggaagcuac
agcuauucg ggaacggcca cuuaaccca caacaaaau 900gcugaagua caaaagagg uguugauacg accacaguug
cggcuacu ugcugcagca 960gggguuacug gcgccgaua ggacaauacu agccuugua aacuucguu ugaggauaaa
1020aacgguaagg uuauaugg uggcuauca gugaaaugg gcgacgauu cuaugccgc 1080acauaugau agaaacagg
ugcauuacu gcuaaaaca cuacuauac agaugguacu 1140ggcguugc aaucuggagc ugugaaauu gguggcga
augguaaauc ugaaguugu 1200acugcuacc augguagac uuacuugca agcagcuug acaacaua cuucagaaca
1260ggcggugagc uuaaagaggu uauacagau aagacugaaa acccagcga gaaauugau 1320gcugccuugg cacagguu
uacacuucg ucugaccug gugcggua gaaccguu 1380aacuccgcu uaccaaccu gggcauacc guaaaauacc
ugucucugc ccgagccgu 1440aucgaaguu ccgacuacg aaccgaagc uccaacagu cucgcgcga gauucgag
1500caggccggu cuuccguu ggcgcaggc aaccagguuc cgcaaacg cuucuuuu 1560cugcguugau auagcug
agccugcgg gccaugcu uggcccuug ggccuccc 1620cagcccucc ucccuuccu gacccguac cccguggc
uuugaauaa gucugagug 1680gcggcaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa
1740aaaaaaaa aaaaaaaaa aaaaaaaaa aaaaaaaaa aaaaucua 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 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 catctcagc ctgctgatca
cacctcagca cggcctgaaa 60gagagctacc tggagagtc ctgcagcacc atcacagagg gctacctgtc tgtctgaga 120accgctggt
acaccaactg gttcacactg gaagtgggag acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga
ccaagagegc cctgagagaa 240ctcaagaccg tctctgccga tcagctggcc agagaggaac agatcgagaa tctggcagc 300ggcagctttg
tgctgggagc cattgctctt ggagtggctg ctgctgcagc ttttacagca 360ggcgtggcca tctgcaagac catcagactg gaaagcgaag
tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctggcaatg gcgttagagt gctggccttt 480gccgtgagcg
agctgaagga ctctgttcc aagaacctga cacgggccct gaacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtcctta
gccagttcaa ccggcgggtt 600ctgaactgc tggcgcagtt tagcgacaac gccggaatca caccagcat cagcctggac 660ctgatgacag
atgctgagct ggctagagcc gtgctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga
aagcttcgg cattctgtgt 780ggcgtgtacg gcagcagcgt gatctatg gtgcagctgc ctatctcgg cgtgatgac 840acacctgct
ggattgtgaa ggccctcct agctgtagcg agaagaagg caattacgcc 900tgctctgta gagaggacca aggtggtat tgcagaacg
ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagagc gaccactgt tctgtgatac cgccgtgga 1020atcaatgtgg
ccgagcagag caagagtgc aacatcaaca tcgaccac caactatcc 1080tgaaggtgt ccaccggcag gcacctatt tctatggtg
ctctgtctcc tctgggagcc 1140ctggtgctt gtataaggc cgtgtctgt agcatggca gcaacagagt gggcatc 1200aagcagctga
acaaggctg cagctacat accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgatcagct gagcaaggtg gaaggcgaac
agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca cctatcaag ttcctgagg atcagttcaa cgtggccctg 1380gaccaggtg
tcgagaacat cgagaattcc caggtctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc tcatcatc
tgatcatcct gatgcctg 1500ctgggcagct ccatgatcct ggtgtccatc tcatcatta tcaagaagac caagaagccc 1560accggcctc
ctccagaact gagcggagtg accaacaatg gcttcatc tcacaac 16171071617DNAArtificial SequenceSynthetic

Polynucleotide 107atgagctgga agtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc
ctgcagcacc atcacagagg gctacctgct tgtgctgaga 120accggctggt acaccaactg gttcacactg gaagtgggcg acgtcgagaa
tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga
tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagcttg tctgaggagc cattgctctt ggagtggctg ctgctgcagc
tgttacagca 360ggcgtggcca tctgcaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc
cgtcagcaca ctcggaatg gcgtagagt gctggccaca 480gccgtgctgc agctgaagga ctctgtctcc aagaacctga cacgggccat
taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttaa cggcggttt 600ctgaacgtcg tgcggcagtt
tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc
tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggctcgg cattctgatt 780ggcgtgtacg gcagcagctg
gatctatatg gtgcagctgc ctatctcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctcct agctgtagcg agaagaagg
caattacgcc 900tgctgctga gagaggacca aggtggtat tgcagaacg cggcagcac cgtgtactac 960cctaacgaga aggactgcga
gacaagaggc gaccacgtgt tctgtgatac cgccgtgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac
caactatccc 1080tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataagg
cgtgtctgt agcatcgga gcaacagagt gggcatcacc 1200aagcagctga acaagggtg cagctacatc accaaccagg acgccgatac
cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttca
ccctatcaag ttcctgagc accagtggca tgtggcctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc
caacagaatc 1440ctgtctagcg ccgagaaggg aacaccggc tcatcatcg tgatcatct gatgcctg 1500ctgggcagct ccatgatcct
ggtgtccatc tcatcatta tcaagaagac caagaagccc 1560accggcgtc ctccagaact gageggagt accaacaatg gcttcatccc
tcacaac 16171081617DNAArtificial SequenceSynthetic Polynucleotide 108atgagctgga agtggtcat catcttcagc
ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgct tgtgctgaga
120accggctggt acaccaactg gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag
ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc
300ggcagcttg tctgaggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgtaagac catcagactg
gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggaatg gcgtagagt gctggccaca
480gccgtgctgc agctgaagga ctctgtctcc aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcctgacct gaagatggcc
gtgtccttta gccagttaa cggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac
660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg
gtccgacgga aaggctcgg cattctgatt 780ggcgtgtacg gcagcagctg gatctatatg gtgcagctgc ctatctcgg cgtgatcgac
840acacctgct ggattgtgaa ggccgctcct agctgtagcg agaagaagg caattacgcc 900tgctgctga gagaggacca aggtggtat
tgcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgtgga
1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcacctatt
tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataagg cgtgtctgt agcatcgga gcaacagagt gggcatcacc
1200aagcagctga acaagggtg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg
gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttca ccctatcaag ttcctgagg atcagttcca ggtggcctg
1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aacaccggc
tcatcatcg tgatcatct gatgcctg 1500ctgggcagct ccatgatcct ggtgtccatc tcatcatta tcaagaagac caagaagccc
1560accggcgtc ctccagaact gageggagt accaacaatg gcttcatccc tcacaac 16171091617DNAArtificial
SequenceSynthetic Polynucleotide 109atgagctgga agtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa
60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgct tgtgctgaga 120accggctggt acaccaactg gttcacactg
gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa
240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagcttg tctgaggagc cattgctctt
ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgtaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc
420ctgaagaaga caaacgaggc cgtcagcaca ctcggaatg gcgtagagt gctggccaca 480gccgtgctgc agctgaagga ctctgtctcc
aagaacctga cacgggccat taacaagaac 540aagtgcgaca tcctgacct gaagatggcc gtgtccttta gccagttaa cggcggttt
600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc
gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggctcgg cattctgatt
780ggcgtgtacg gcagcagctg gatctatatg gtgcagctgc ctatctcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctcct
agctgtagcg agaagaagg caattacgcc 900tgctgctga gagaggacca aggtggtat tgcagaacg ccggcagcac cgtgtactac
960cctaacgaga aggactgcga gacaagaggc gaccacgtgt tctgtgatac cgccgtgga 1020atcaatgtgg ccgagcagag caaagagtgc
aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc
1140ctggtggctt gttataagg cgtgtctgt agcatcgga gcaacagagt gggcatcacc 1200aagcagctga acaagggtg cagctacatc
accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga
1320cctgtgtcca gcagcttca ccctatcaag ttcctgaga accagtcca ggtggcctg 1380gaccaggtgt tcgagaacat cgagaattcc
caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aacaccggc tcatcatcg tgatcatct gatgcctg

1500ctgggcagct ccatgatcct ggtgtccatc tcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg
accaacaatg gtttcatccc tcacaac 16171101617DNAArtificial SequenceSynthetic Polynucleotide 110atgagctgga
aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg
gctacctgct tgtgctgaga 120accggctggt acaccaactg gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc
ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac
agatcgagaa tcttggcagc 300ggcagctttg tctggggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca
tcgctaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctgggcaatg
gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgctt aagaacctga cacgggcat taacaagaac 540aagtgcgaca
tcctgacct gaagatggcc gtgtccttta gccagtcaa cggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca
caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga
tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc
ctatcttcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgctgctga
gagaggacca aggtggtat tctcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgca gacaagagge gaccacgtgt
tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt
ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcgga
gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc
1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttca cctatcaag
ttcctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc
1440ctgtctagcg ccgagaaggg aacaccggc tcatcatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc
tcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagtg accaacaatg gtttcatccc tcacaac
16171111617DNAArtificial SequenceSynthetic Polynucleotide 111atgagctgga aggtggtcat catcttcagc ctgctgatca
cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgct tgtgctgaga 120accggctggt
acaccaactg gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc
tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagctttg
tctggggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag
tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctgggcaatg gcgttagagt gctggccaca 480gccgtgcgcg
agctgaagga cttcgtgctt aagaacctga cacgggcat taacaagaac 540aagtgcgaca tcctgacct gaagatggcc gtgtccttta
gccagtcaa cggcggttt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag
atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga
aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acacctgct
ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgctgctga gagaggacca aggtggtat tctcagaacg
ccggcagcac cgtgtactac 960cctaacgaga aggactgca gacaagagge gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg
ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcacctatt tctatggtgg
ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcgga gcaacagagt gggcatcacc 1200aagcagctga
acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac
agcacgtgat caagggcaga 1320cctgtgtcca gcagcttca cctatcaag ttcctgaga accagttcca ggtggccctg 1380gaccaggtgt
tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aacaccggc tcatcatcg
tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc tcatcatta tcaagaagac caagaagccc 1560accggcgctc
ctccagaact gagcggagtg accaacaatg gtttcatccc tcacaac 16171121617DNAArtificial SequenceSynthetic
Polynucleotide 112atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc
ctgcagcacc atcacagagg gctacctgct tgtgctgaga 120accggctggt acaccaactg gttcacactg cctgtgggcg acgtcgagaa
tctgacatgc 180tctgatggcc ctagcctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga
tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagctttg tctggggagc cattgctctt ggagtggctg ctgctgcagc
tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc
cgtcagcaca ctgggcaatg gcgttagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgctc aagaacctga cacgggcat
taacaagaac 540aagtgcgaca tcagcacct gaagatggcc gtgtccttta gccagtcaa cggcggttt 600ctgaacgtcg tgcggcagtt
tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc
tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt
gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg
caattacgcc 900tgctgctga gagaggacca aggtggtat tctcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgca
gacaagagge gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac
caactatccc 1080tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg
cgtgtcctgt agcatcgga gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac
cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttca

ccctatcaag ttcctgagg atcagttcca ggtggcctg 1380gaccaggtg tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcacatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcacatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gageggagtg accaacaatg gttcatccc tcacaac 16171131617DNAArtificial SequenceSynthetic Polynucleotide 113atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tgaagagtc ctgcagcacc atcacagagg gctacctgic tgtgctgaga 120accggctggt acaccaactg gttcacactg cctgtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc ttttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctgggcaatg gcgtagagt gctggccaca 480gccgtgacgc agctgaagga ctctgtctcc aagaacctga cacgggcat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gttctctta gccagttaa ccggcggtt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctct agctgtagcg agaagaaggg caattacgcc 900tgctctgta gagaggacca aggtggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagagc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtctgt agcatcggca gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tttatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca ccctatcaag ttcctgaga accagtcca ggtggcctg 1380gaccaggtg tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcacatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcacatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gageggagtg accaacaatg gttcatccc tcacaac

16171141617DNAArtificial SequenceSynthetic Polynucleotide 114atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tgaagagtc ctgcagcacc atcacagagg gctacctgic tgtgctgaga 120accggctggt acaccaactg gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc ttttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctgggcaatg gcgtagagt gctggccaca 480gccgtgacgc agctgaagga ctctgtctcc aagaacctga cacgggcat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gttctctta gccagttaa ccggcggtt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctct agctgtagcg agaagaaggg caattacgcc 900tgctctgta gagaggacca aggtggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagagc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcacctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtctgt agcatcggca gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tttatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca ccctatcaag ttcctgagg atcagttcca ggtggcctg 1380gaccaggtg tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcacatcg tgatcatcct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcacatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gageggagtg accaacaatg gttcatccc tcacaac 16171151617DNAArtificial SequenceSynthetic Polynucleotide 115atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tgaagagtc ctgcagcacc atcacagagg gctacctgic tgtgctgaga 120accggctggt acaccaactg gttcacactg gaagtgggcg acctcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagctttg tgctgggagc cattgctctt ggagtggctg ctgctgcagc ttttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctgggcaatg gcgtagagt gctggccaca 480gccgtgacgc agctgaagga ctctgtctcc aagaacctga cacgggcat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gttctctta gccagttaa ccggcggtt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatcttcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctct agctgtagcg agaagaaggg caattacgcc 900tgctctgta gagaggacca aggtggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagagc gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc

caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg
cgtgtcctgt agcatcggca gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac
cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca
cctatcaag ttcctgagg atcagtcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc
caacagaate 1440ctgtctagcg ccgagaaggg aaacaccggc tcatcatcg tgatcatcct gatgcctgtg 1500ctgggcagct ccatgatcct
ggtgtccatc tcatcatta tcaagaagac caagaagccc 1560accggcgtc ctcagaact gageggagt accaacaatg gcttcatccc
tcacaac 16171161617DNAArtificial SequenceSynthetic Polynucleotide 116atgagctgga agtggtcat catcttcagc
ctgtgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgct tgtgtgaga
120accggctggt acaccaactg gttcacactg gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag
ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc
300ggcagctttg tctggggagc cattgtcttt ggagtggctg ctgtctcagc ttttacagca 360ggcgtggcca tcgctaagac catcagactg
gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggaatg gcgtagagt gctggccaca
480gccgtgctg agctgaagga cttctgtctt aagaacctg cacgggcat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc
gtgtcttta gccagttcaa ccggcggtt 600ctgaacgtc tgcggcagtt tagcgacaac gccggaatca caccagccat cagctggac
660ctgatgacag atgtgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga tctcgagaa tagagccatg
gtccgacgga aaggctcgg cattctgatt 780ggcgtgtacg gcagcagct gatctatatg gtgcagctgc ctatctcgg cgtgatcagc
840acacctgct ggatttgaa ggccgctct agctgtagcg agaagaagg caattacgcc 900tgctgtgta gagaggacca aggtggtat
tgtcagaac ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagagg gaccagctgt tctgtgatac ccgctgtgga
1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt
tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcacc
1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg
gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca cctatcaag ttcctgagg atcagtcca ggtggccctg
1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaate 1440ctgtctagcg ccgagaaggg aaacaccggc
tcatcatcg tgatcatcct gatgcctgtg 1500ctgggcagct ccatgatcct ggtgtccatc tcatcatta tcaagaagac caagaagccc
1560accggcgtc ctcagaact gageggagt accaacaatg gcttcatccc tcacaac 16171171617DNAArtificial
SequenceSynthetic Polynucleotide 117atgagctgga agtggtcat catcttcagc ctgtgatca cacctcagca cggcctgaaa
60gagagctacc tggaagagtc ctgcagcacc atcacagagg gctacctgct tgtgtgaga 120accggctggt acaccaactg gttcacactg
gaagtgggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa
240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagctttg tctggggagc cattgtcttt
ggagtggctg ctgtctcagc ttttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc
420ctgaagaaga caaacgaggc cgtcagcaca ctcggaatg gcgtagagt gctggccaca 480gccgtgctg agctgaagga cttctgtctc
aagaacctg ggccggccat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtcttta gccagttcaa ccggcggtt
600ctgaacgtc tgcggcagtt tagcgacaac gccggaatca caccagccat cagctggac 660ctgatgacag atgtgagct ggctagagcc
gtgcctaaca tgctacatc tgccggccag 720atcaagctga tctcgagaa tagagccatg gtccgacgga aaggctcgg cattctgatt
780ggcgtgtacg gcagcagct gatctatatg gtgcagctgc ctatctcgg cgtgatcagc 840acacctgct ggatttgaa ggccgctct
agctgtagcg agaagaagg caattacgcc 900tgctgtgta gagaggacca aggtggtat tgtcagaac ccggcagcac cgtgtactac
960cctaacgaga aggactgcga gacaagagg gaccagctgt tctgtgatac ccgctgtgga 1020atcaatgtgg ccgagcagag caaagagtgc
aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc
1140ctggtggctt gttataaggg cgtgtcctgt agcatcggca gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc
accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga
1320cctgtgtcca gcagcttcca cctatcaag ttcctgagg atcagtcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc
caggctctgg tggaccagtc caacagaate 1440ctgtctagcg ccgagaaggg aaacaccggc tcatcatcg tgatcatcct gatgcctgtg
1500ctgggcagct ccatgatcct ggtgtccatc tcatcatta tcaagaagac caagaagccc 1560accggcgtc ctcagaact gageggagt
accaacaatg gcttcatccc tcacaac 16171181617DNAArtificial SequenceSynthetic Polynucleotide 118atgagctgga
agtggtcat catcttcagc ctgtgatca cacctcagca cggcctgaaa 60gagagctacc tggaagagtc ctgcagcacc atcacagagg
gctacctgct tgtgtgaga 120accggctggt acaccaactg gttcacactg gaagtgggcg acctcgagaa tctgacatgc 180tctgatggcc
ctgacctgat caagaccgag ctggatctgc tcaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac
agatcgagaa tcttggcagc 300ggcagctttg tctggggagc cattgtcttt ggagtggctg ctgtctcagc ttttacagca 360ggcgtggcca
tcgctaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcggaatg
gcgtagagt gctggccaca 480gccgtgctg agctgaagga cttctgtctt aagaacctg ggccggccat taacaagaac 540aagtgcgaca
tcgacgacct gaagatggcc gtgtcttta gccagttcaa ccggcggtt 600ctgaacgtc tgcggcagtt tagcgacaac gccggaatca
caccagccat cagctggac 660ctgatgacag atgtgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga
tctcgagaa tagagccatg gtccgacgga aaggctcgg cattctgatt 780ggcgtgtacg gcagcagct gatctatatg gtgcagctgc
ctatctcgg cgtgatcagc 840acacctgct ggatttgaa ggccgctct agctgtagcg agaagaagg caattacgcc 900tgctgtgta

gagaggacca aggctggtat tgcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgca gacaagagge gaccacgtg
tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtg
ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcgga
gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc
1260gacaacaccg tgcatacagc gagcaaggtg gaaggcgaac agcagctgat caagggcaga 1320cctgtgtcca gcagcttcca ccctatcaag
ttcctgagg atcagttcca ggtggccctg 1380gaccaggtg tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc
1440ctgtctagcg ccgagaaggg aacaccggc tcatcatcg tgatcatcct gatcgccctg 1500ctgggcagct ccatgatcct ggtgtccatc
tcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagt accaacaatg gttcatccc tcacaac
16171191617DNAArtificial SequenceSynthetic Polynucleotide 119atgagctgga aggtggtcat catcttcagc ctgctgatca
cacctcagca cggcctgaaa 60gagagctacc tggagagtc ctgcagcacc atcacagagg gctacctgctc tgtgtgaga 120accggctggt
acaccaactg gttcactg cctgtggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga
ccaagagcgc cctgagagaa 240ctcaagaccg tctctgccga tcagctggcc agagaggaac agatcgagaa tctggcagc 300ggcagcttg
tctgggagc cattgctctt ggagtggctg ctgctgcagc tttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag
tgaccgcat caacaacgcc 420ctgaagaaga caaacgagc cgtaagcaca ctggcaatg gcgttagagt gctggccaca 480gccgtgcg
agctgaagga ctctgtctc aagaacctga cacgggcat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gttcctta
gccagttaa ccggcggtt 600ctgaacgtc tggcgagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag
atgctgagct ggctagagcc gtgctaaca tgctacatc tggcgccag 720atcaagctga tctcgagaa tagagccatg gtccgacgga
aaggctcgg cattctgatt 780ggcgtgtac gcagcagcgt gatctatg tgcagctgc ctatctcgg cgtgatcagc 840acaccctgct
ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgctgctga gagaggacca aggctggtat tgcagaacg
ccggcagcac cgtgtactac 960cctaacgaga aggactgca gacaagagge gaccacgtg tctgtgatac cgccgctgga 1020atcaatgtgg
ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtg ccaccggcag gcaccctatt tctatggtgg
ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg cgtgtcctgt agcatcgga gcaacagagt gggcatcacc 1200aagcagctga
acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgcatacagc gagcaaggtg gaaggcgaac
agcagctgat caagggcaga 1320cctgtgtcca gcagcttcca ccctatcaag ttcctgagg atcagttcca ggtggccctg 1380gaccaggtg
tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aacaccggc tcatcatcg
tgatcatcct gatcgccctg 1500ctgggcagct ccatgatcct ggtgtccatc tcatcatta tcaagaagac caagaagccc 1560accggcgctc
ctccagaact gagcggagt accaacaatg gttcatccc tcacaac 16171201617DNAArtificial SequenceSynthetic
Polynucleotide 120atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggagagtc
ctgcagcacc atcacagagg gctacctgctc tgtgtgaga 120accggctggt acaccaactg gttcactg gaagtggcg acgtcgagaa
tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tctctgccga
tcagctggcc agagaggaac agatcgagaa tctggcagc 300ggcagcttg tctgggagc cattgctctt ggagtggctg ctgctgcagc
tgttacagca 360ggcgtggcca tcgctaagac catcagactg gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgagc
cgtcagcaca ctggcaatg gcgttagagt gctggccaca 480gccgtgcg agctgaagga ctctgtctc aagaacctga cacgggcat
taacaagaac 540aagtgcgaca tctctgacct gaagatggcc gttcctta gccagttaa ccggcggtt 600ctgaacgtc tggcgagtt
tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgctaaca tgctacatc
tggcgccag 720atcaagctga tctcgagaa tagagccatg gtccgacgga aaggctcgg cattctgatt 780ggcgtgtac gcagcagcgt
gatctatg tgcagctgc ctatctcgg cgtgatcagc 840acaccctgct ggattgtgaa ggccgctcct agctgtagc agaagaaggg
caattacgcc 900tgctgctga gagaggacca aggctggtat tgcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgca
gacaagagge gaccacgtg tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac
caactatccc 1080tgcaaggtg ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggctt gttataaggg
cgtgtcctgt agcatcgga gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac
cgtgaccatc 1260gacaacaccg tgcatacagc gagcaaggtg gaaggcgaac agcagctgat caagggcaga 1320cctgtgtcca gcagcttcca
ccctatcaag ttcctgagg atcagttcca ggtggccctg 1380gaccaggtg tcgagaacat cgagaattcc caggctctgg tggaccagtc
caacagaatc 1440ctgtctagcg ccgagaaggg aacaccggc tcatcatcg tgatcatcct gatcgccctg 1500ctgggcagct ccatgatcct
ggtgtccatc tcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gagcggagt accaacaatg gttcatccc
tcacaac 16171211617DNAArtificial SequenceSynthetic Polynucleotide 121atgagctgga aggtggtcat catcttcagc
ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggagagtc ctgcagcacc atcacagagg gctacctgctc tgtgtgaga
120accggctggt acaccaactg gttcactg gaagtggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag
ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tctctgccga tcagctggcc agagaggaac agatcgagaa tctggcagc
300ggcagcttg tctgggagc cattgctctt ggagtggctg ctgctgcagc tttacagca 360ggcgtggcca tcgctaagac catcagactg
gaaagcgaag tgaccgcat caacaacgcc 420ctgaagaaga caaacgagc cgtaagcaca ctggcaatg gcgttagagt gctggccaca
480gccgtgcg agctgaagga ctctgtctc aagaacctga cacgggcat taacaagaac 540aagtgccta tcgacgacct gaagatggcc
gtgtcctta gccagttaa ccggcggtt 600ctgaacgtc tggcgagtt tagcgacaac gccggaatca caccagccat cagcctggac
660ctgatgacag atgctgagct ggctagagcc gtgctaaca tgctacatc tggcgccag 720atcaagctga tctcgagaa tagagccatg

gtccgacgga aaggctcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatctcgg cgtgatcgac
840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg caattacgcc 900tgcttctga gagaggacca aggctggtat
tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga gacaagaggg gaccacgtgt tctgtgatac cgccgctgga
1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt
tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggtt gttataaggg cgtgtcctgt agcatcgga gcaacagagt gggcatcacc
1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg
gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca ccctatcaag ttcctgagg atcagttcca ggtggccctg
1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc
ttcatcctg tgatcctct gatcgccgtg 1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc
1560accggcgctc ctccagaact gageggagtg accaacaatg gtttcatccc tcacaac 16171221617DNAArtificial
SequenceSynthetic Polynucleotide 122atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa
60gagagctacc tggagagtc ctgcagcacc atcacagagg gctacctgtc tgtgtgaga 120accggctggt acaccaactg gttcacactg
gaagtgggag acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa
240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagctttg tcttgggagc cattgctctt
ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgtaagac catcagactg cctagcgaag tgaccgcat caacaagcc
420ctgaagaaga caaacgagc cgtcagcaca ctggcaatg gcgtagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc
aagaacctga cacgggcat taacaagaac 540aagtgcgaca tcagcaccat gaagatggcc gtgtcctta gccagttcaa ccggcggttt
600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc
gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgetcgagaa tagagccatg gtccgacgga aaggctcgg cattctgatt
780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatctcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct
agctgtagcg agaagaaggg caattacgcc 900tgcttctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac
960cctaacgaga aggactgcga gacaagaggg gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc
aacatcaaca tcagcaccac caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc
1140ctggtggtt gttataaggg cgtgtcctgt agcatcgga gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc
accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga
1320cctgtgtcca gcagcttcca ccctatcaag ttcctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc
caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcctg tgatcctct gatcgccgtg
1500ctgggcagct ccatgatcct ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc

ctccagaact gageggagtg accaacaatg gtttcatccc tcacaac 16171231617DNAArtificial SequenceSynthetic
Polynucleotide 123atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggagagtc
ctgcagcacc atcacagagg gctacctgtc tgtgtgaga 120accggctggt acaccaactg gttcacactg gaagtgggag acgtcgagaa
tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga
tcagctggcc agagaggaac agatcgagaa tcttggcagc 300ggcagctttg tcttgggagc cattgctctt ggagtggctg ctgctgcagc
tgttacagca 360ggcgtggcca tcgtaagac catcagactg gaaagcgaag tgaccgcat caacaagcc 420ctgaagaaga caaacgagc
cgtcagcaca ctggcaatg gcgtagagt gctggccaca 480gccgtgcgcg agctgaagga cttcgtgtcc aagaacctga cacgggcat
taacaagaac 540aagtgcgaca tcagcaccat gaagatggcc gtgtcctta gccagttcaa ccggcggttt 600ctgaacgtcg tgcggcagtt
tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc
tgccggccag 720atcaagctga tgetcgagaa tagagccatg gtccgacgga aaggctcgg cattctgatt 780ggcgtgtacg gcagcagcgt
gatctatatg gtgcagctgc ctatctcgg cgtgatcgac 840acaccctgct ggattgtgaa ggccgctcct agctgtagcg agaagaaggg
caattacgcc 900tgcttctga gagaggacca aggctggtat tgtcagaacg ccggcagcac cgtgtactac 960cctaacgaga aggactgcga
gacaagaggg gaccacgtgt tctgtgatac cgccgctgga 1020atcaatgtgg ccgagcagag caaagagtgc aacatcaaca tcagcaccac
caactatccc 1080tgcaaggtgt ccaccggcag gcaccctatt tctatggtgg ctctgtctcc tctgggagcc 1140ctggtggtt gttataaggg
cgtgtcctgt agcatcgga gcaacagagt gggcatcacc 1200aagcagctga acaagggctg cagctacatc accaaccagg acgccgatac
cgtgaccatc 1260gacaacaccg tgtatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca
ccctatcaag ttcctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc
caacagaatc 1440ctgtctagcg ccgagaaggg aaacaccggc ttcatcctg tgatcctct gatcgccgtg 1500ctgggcagct ccatgatcct
ggtgtccatc ttcatcatta tcaagaagac caagaagccc 1560accggcgctc ctccagaact gageggagtg accaacaatg gtttcatccc
tcacaac 16171241617DNAArtificial SequenceSynthetic Polynucleotide 124atgagctgga aggtggtcat catcttcagc
ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggagagtc ctgcagcacc atcacagagg gctacctgtc tgtgtgaga
120accggctggt acaccaactg gttcacactg gaagtgggag acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag
ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tgtctgccga tcagctggcc agagaggaac agatcgagaa tcttggcagc
300ggcagctttg tcttgggagc cattgctctt ggagtggctg ctgctgcagc tgttacagca 360ggcgtggcca tcgtaagac catcagactg
gaaagcgaag tgaccgcat caacaagcc 420ctgaagaaga caaacgagc cgtcagcaca ctggcaatg gcgtagagt gctggccaca

480gccgtgctgag agctgaagga ctctgtgtcc aagaacctga cacgggcat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc
gtgtccttta gccagttcaa ccggcggtt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac
660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg
gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatctcgg cgtgatcgac
840acacctgct ggattgtgaa ggccgctct agctgtagcg agaagaagg caattacgcc 900tgctgtgta gagaggacca aggtggtat
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 gggcatcacc
1200aagcagctga acaagggtg cagctacatc accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tttatcagct gagcaaggtg
gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca cctatcaag ttcctcagg accagttcca ggtggccctg
1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aacaccggc
ttcatcctg tgatcctct gatcgcctg 1500ctgggcagct ccatgatcct ggtgtccatc ttatcatta tcaagaagac caagaagccc
1560accggcgtc ctccagaact gacggagtg accaacaatg gttcatccc tcacaac 16171251617DNAArtificial
SequenceSynthetic Polynucleotide 125atgagctgga aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa
60gagagctacc tggagagtc ctgcagcacc atcacagagg gctacctgtc tgtgtgaga 120accggctggt acaccaactg gttcacactg
gaagtggcg acgtcgagaa tctgacatgc 180tctgatggcc ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa
240ctcaagaccg tctctgccga tcagctggcc agagaggaac agatcgagaa tctggcagc 300ggcagctttg tctgggagc cattgctctt
ggagtggctg ctgctgcagc tttacagca 360ggcgtggcca tcgtaagac catcagactg gaaagcgaag tgaccgccat caacaagcc
420ctgaagaaga caaacgaggc cgtcagcaca ctcgcaatg gcttagagt gctggccaca 480gccgtgctg agctgaagga ctctgtgtcc
aagaacctga cacgggcat taacaagaac 540aagtgcgaca tcgacgacct gaagatggcc gtgtccttta gccagttcaa ccggcggtt
600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc
gtgcctaaca tgctacatc tgccggccag 720atcaagctga tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt
780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc ctatctcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctct
agctgtagcg agaagaagg caattacgcc 900tgctgtgta gagaggacca aggtggtat 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 gggcatcacc 1200aagcagctga acaagggtg cagctacatc
accaaccagg acgccgatac cgtgaccatc 1260gacaacaccg tttatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga
1320cctgtgtcca gcagcttcca cctatcaag ttcctcagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc
caggctctgg tggaccagtc caacagaatc 1440ctgtctagcg ccgagaaggg aacaccggc ttcatcctg tgatcctct gatcgcctg
1500ctgggcagct ccatgatcct ggtgtccatc ttatcatta tcaagaagac caagaagccc 1560accggcgtc ctccagaact gacggagtg
accaacaatg gttcatccc tcacaac 16171261617DNAArtificial SequenceSynthetic Polynucleotide 126atgagctgga
aggtggtcat catcttcagc ctgctgatca cacctcagca cggcctgaaa 60gagagctacc tggagagtc ctgcagcacc atcacagagg
gctacctgtc tgtgtgaga 120accggctggt acaccaactg gttcacactg gaagtggcg acgtcgagaa tctgacatgc 180tctgatggcc
ctgacctgat caagaccgag ctggatctga ccaagagcgc cctgagagaa 240ctcaagaccg tctctgccga tcagctggcc agagaggaac
agatcgagaa tctggcagc 300ggcagctttg tctgggagc cattgctctt ggagtggctg ctgctgcagc tttacagca 360ggcgtggcca
tcgtaagac catcagactg gaaagcgaag tgaccgccat caacaagcc 420ctgaagaaga caaacgaggc cgtcagcaca ctcgcaatg
gcttagagt gctggccaca 480gccgtgctg agctgaagga ctctgtgtcc aagaacctga cacgggcat taacaagaac 540aagtgcgaca
tcgacgacct gaagatggcc gtgtccttta gccagttgaa ccggcggtt 600ctgaacgtcg tgcggcagtt tagcgacaac gccggaatca
caccagccat cagcctggac 660ctgatgacag atgctgagct ggctagagcc gtgcctaaca tgctacatc tgccggccag 720atcaagctga
tgctcgagaa tagagccatg gtccgacgga aaggcttcgg cattctgatt 780ggcgtgtacg gcagcagcgt gatctatatg gtgcagctgc
ctatctcgg cgtgatcgac 840acacctgct ggattgtgaa ggccgctct agctgtagcg agaagaagg caattacgcc 900tgctgtgta
gagaggacca aggtggtat 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 gggcatcacc 1200aagcagctga acaagggtg cagctacatc accaaccagg acgccgatac cgtgaccatc
1260gacaacaccg tttatcagct gagcaaggtg gaaggcgaac agcacgtgat caagggcaga 1320cctgtgtcca gcagcttcca cctatcaag
ttcctgagg atcagttcca ggtggccctg 1380gaccaggtgt tcgagaacat cgagaattcc caggctctgg tggaccagtc caacagaatc
1440ctgtctagcg ccgagaaggg aacaccggc ttcatcctg tgatcctct gatcgcctg 1500ctgggcagct ccatgatcct ggtgtccatc
ttatcatta tcaagaagac caagaagccc 1560accggcgtc ctccagaact gacggagtg accaacaatg gttcatccc tcacaac
16171271617RNAArtificial SequenceSynthetic Polynucleotide 127augagcugga agguggucau caucuacg
cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg guaccuguc ugucugaga
120accggcuggu acaccaacgu guacacacug gaagugggag acgucgagaa ucugacaugc 180ucugaugcc 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
cacgggccu gaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucac cggcgguuu
600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu
ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga
aaggcuucgg cauucugugu 780ggcguguacg gcagcagcgu gaucauauug gucgagcugc cuauucgg cgugaucgac
840acaccugcu ggauugugaa ggccgucuccu agcuguagcg agaagaaggc cauuuacgcc 900ugccugcuga gagaggacca
aggcugguau ugucagaac cggcgagcag cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu
ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuauccc
1080ugcaaggugu ccaccggcag gcaccuauu ucuauuggg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggc
cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaaggcgug cagcuacauc accaaccagg
acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga
1320ccugugucca gcagcuucga ccuaucaag uuccugagc aucaguucac cguggccug 1380gaccaggugu ucgagaacau
cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaaggc aaacaccggc ucaucaucg
ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc ucaucauuu ucaagaagac caagaagccc
1560accggcgcuc caccagauc gagcggagug accaacaug gcuuauccc ucacaac 16171281617RNAArtificial
SequenceSynthetic Polynucleotide 128augagcugga aggugguau caucuucagc cugcugauca caccucagca cgccugaaa
60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu
guucacacug gaagugggagc agcugcagaa ucugacauc 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 uacaagaac
540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguucac cggcgguuu 600cugaacgucg ugcggcaguu
uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca
ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugugu
780ggcguguacg gcagcagcgu gaucauauug gucgagcugc cuauucgg cgugaucgac 840acaccugcu ggauugugaa
ggccgucuccu agcuguagcg agaagaaggc cauuuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaac
cggcgagcag cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgucgga
1020aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag
gcaccuauu ucuauuggg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggc cguguccugu agcaucggca
gcaacagagu gggcaucauc 1200aagcagcuga acaaggcgug cagcuacauc accaaccagg acgccgauac cgugaccauc
1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga
ccuaucaag uuccugagc accaguggca ugugcccg 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg
uggaccaguc caacagauc 1440cugucuagcg ccgagaaggc aaacaccggc ucaucaucg ugaucauccu gaucgccgug
1500cugggcagcu ccaugauccu gguguccauc ucaucauuu ucaagaagac caagaagccc 1560accggcgcuc caccagauc
gagcggagug accaacaug gcuuauccc ucacaac 16171291617RNAArtificial SequenceSynthetic Polynucleotide
129augagcugga aggugguau caucuucagc cugcugauca caccucagca cgccugaaa 60gagagcuacc uggaagaguc
cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggagc
agcugcagaa ucugacauc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa
240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc
cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcaagac caucagacug gaaagcgaag
ugaccgccau caacaacgcc 420cugaagaaga caaacgaggc cgucagcaca cucggcaaug gcguuagagu gcuggccaca
480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uacaagaac 540aagugcgaca uccugaccu
gaagauggcc guguccuuua gccaguucac cggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca
caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag
720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucuguu 780ggcguguacg gcagcagcgu
gaucauauug gucgagcugc cuauucgg cgugaucgac 840acaccugcu ggauugugaa ggccgucuccu agcuguagcg
agaagaaggc cauuuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaac cggcgagcag cguguacuac
960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag
caaagagugc aacaucaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauuggg
cucugucucc ucugggagcc 1140cugguggcuu guuauaaggc cguguccugu agcaucggca gcaacagagu gggcaucauc
1200aagcagcuga acaaggcgug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu

gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga ccuaaucaag uucccugagg
aucaguucca gguggccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaau
1440cugucuagcg cggagaaggg aacaccggc uucaucaucg ugaucuccu gaucgccgug 1500cugggcagcu ccaugauccu
gguguccauc uucaucaua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaug
gcucaucc ucacaac 1617131617RNAArtificial SequenceSynthetic Polynucleotide 130augagcugga
agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg
gcuaccuguc ugucugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc
180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga
ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucu ggaguggcug
cugcugcagc uguuacagca 360ggcguggcca ucgcuagac caucagacug gaaagcgaag ugaccgccau caacaacgcc
420cugaagaaga caaacgagc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga
cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca uccugaccu gaagauggcc guguccuuua
gccaguucac cggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac
660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcugagaa
uagagccaug guccgacgga aagguucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuaauug gucgagcugc
cuauucgg cgugaucgac 840acaccugcu ggauugugaa ggccguccu agcuguagcg agaagaaggc cauuacgcc
900ugccugcuga gagaggacca aggcugguau ugucagaacg cggcagcagc cguguacuac 960ccuaacgaga aggacugcga
gacaagaggc gaccacgugu ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagaguc aacaucaca
ucagaccac caacuucc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg cucugucucc ucugggagcc
1140cugguggcuu guuaaaggc cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaaggcug
cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac
agcagcugau caagggcaga 1320ccugugucca gcagcuucga ccuaaucaag uucccugaga accaguucca gguggccug
1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagaau 1440cugucuagcg cggagaaggg
aacaccggc uucaucaucg ugaucuccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucaua
ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaug gcucaucc ucacaac
1617131617RNAArtificial SequenceSynthetic Polynucleotide 131augagcugga agguggucau caucuucagc
cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugucugaga
120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau
caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac
agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca
360ggcguggcca ucgcuagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgagc
cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugcuu aagaaccuga
cacgggccau uaacaagaac 540aagugcgaca uccugaccu gaagauggcc guguccuuua gccaguucac cggcgguuu
600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu
ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcugagaa uagagccaug guccgacgga
aagguucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuaauug gucgagcugc cuauucgg cgugaucgac
840acaccugcu ggauugugaa ggccguccu agcuguagcg agaagaaggc cauuacgcc 900ugccugcuga gagaggacca
aggcugguau ugucagaacg cggcagcagc cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu
ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagaguc aacaucaca ucagaccac caacuucc
1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuaaaggc
cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaaggcug cagcuacauc accaaccagg
acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcagcugau caagggcaga
1320ccugugucca gcagcuucga ccuaaucaag uucccugagg aucaguucca gguggccug 1380gaccaggugu ucgagaacau
cgagaauucc caggcucugg uggaccaguc caacagaau 1440cugucuagcg cggagaaggg aacaccggc uucaucaucg
ugaucuccu gaucgccgug 1500cugggcagcu

ccaugauccu gguguccauc uucaucaua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug
accaacaug gcucaucc ucacaac 16171321617RNAArtificial SequenceSynthetic Polynucleotide 132augagcugga
agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg
gcuaccuguc ugucugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg acgucgagaa ucugacaugc
180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga
ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucu ggaguggcug
cugcugcagc uguuacagca 360ggcguggcca ucgcuagac caucagacug gaaagcgaag ugaccgccau caacaacgcc
420cugaagaaga caaacgagc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga

cuucgugcuu aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucccugaccu gaagauggcc guguccuuua
gccaguuca cccggcgguu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac
660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa
uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gucgagcugc
cuauucgg cgugaucgac 840acaccugcu ggauugugaa ggccgucucc agcuguagcg agaagaagg cauuacgcc
900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga
gacaagaggc gaccacgugu ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagagugc aacaucaca
ucagcaccac caacuaucc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg cucugucucc ucugggagcc
1140cugguggcuu guuauaagg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug
cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac
agcacgugau caagggcaga 1320ccugugucca gcagcuucga ccuaucaag ucccugaga accaguucca gguggccug
1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaagg
aaacaccggc uucaucaucg ugaucuccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucaua
ucaagaagac caagaagcc 1560accggcgcuc caccagaacu gageggagug accaacaug gcuuaucc ucacaac
16171331617RNAArtificial SequenceSynthetic Polynucleotide 133augagcugga aggugguau caucuucagc
cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga
120accggcuggu acaccaacgu guucacacug ccuguggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau
caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac
agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca
360ggcguggcca ucgcuagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgagc
cgucagcaca cucggcaug gcguuagagu gcuggccaca 480gccgucgagc agcugaagga cuucgugucc aagaaccuga
cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguuca cccggcgguu
600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu
ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga
aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gucgagcugc cuauucgg cgugaucgac
840acaccugcu ggauugugaa ggccgucucc agcuguagcg agaagaagg cauuacgcc 900ugccugcuga gagaggacca
aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu
ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuaucc
1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaagg
cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg
acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga
1320ccugugucca gcagcuucga ccuaucaag ucccugagg aucaguucca gguggccug 1380gaccaggugu ucgagaacau
cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaagg aaacaccggc uucaucaucg
ugaucuccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucaua ucaagaagac caagaagcc
1560accggcgcuc caccagaacu gageggagug accaacaug gcuuaucc ucacaac 16171341617RNAArtificial
SequenceSynthetic Polynucleotide 134augagcugga aggugguau caucuucagc cugcugauca caccucagca cggccugaaa
60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu
guucacacug ccuguggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc
ucaagagcgc ccugagagaa 240cucaagaccg ugucugccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc
300ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuagac
caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgagc cgucagcaca cucggcaug
gcguuagagu gcuggccaca 480gccgucgagc agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac
540aagugcgaca ucgacgaccu gaagauggcc guguccuuua gccaguuca cccggcgguu 600cugaacgucg ugcggcaguu
uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca
ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu
780ggcguguacg gcagcagcgu gaucuauaug gucgagcugc cuauucgg cgugaucgac 840acaccugcu ggauugugaa
ggccgucucc agcuguagcg agaagaagg cauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg
ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgucgga
1020aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuaucc 1080ugcaaggugu ccaccggcag
gcaccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaagg cguguccugu agcaucggca
gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc
1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga
ccuaucaag ucccugaga accaguucca gguggccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg
uggaccaguc caacagauc 1440cugucuagcg ccgagaagg aaacaccggc uucaucaucg ugaucuccu gaucgccgug

1500cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaug gcuucaucc ucacaac 16171351617RNAArtificial SequenceSynthetic Polynucleotide 135augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaaguggggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucugc ucaagagcgc ccugagagaa 240cucaagaccg ugucugcccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcuggggagc 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 gccaguuaa cggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucauaug gugcagcugc cuaucuucgg cgugaucgac 840acaccugcu ggauugugaa ggccgucucu agcuguagcg agaagaaggg cauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagucg aacaucaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauuggug cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcagcugau caagggcaga 1320ccugugucca gcagcuucga ccuaucaag uucccugagg aucaguucca gguggccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaaggg aacaccggc uucaucaucg ugaucuccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaug gcuucaucc ucacaac 16171361617RNAArtificial SequenceSynthetic Polynucleotide 136augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaaguggggcg accucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugcccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcuggggagc 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 gccaguuaa cggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucauaug gugcagcugc cuaucuucgg cgugaucgac 840acaccugcu ggauugugaa ggccgucucu agcuguagcg agaagaaggg cauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagucg aacaucaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauuggug cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcagcugau caagggcaga 1320ccugugucca gcagcuucga ccuaucaag uucccugagg aucaguucca gguggccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaaggg aacaccggc uucaucaucg ugaucuccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaug gcuucaucc ucacaac 16171371617RNAArtificial SequenceSynthetic Polynucleotide 137augagcugga agguggucau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaaguggggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugcccga agaucgagaa uccuggcagc 300ggcagcuuug ugcuggggagc 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 gccaguuaa cggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucauaug gugcagcugc cuaucuucgg cgugaucgac

840acaccugcu ggauugugaa ggccgucuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca
aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu
ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc
1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg
cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg
acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga
1320ccugugucca gcagcuucga ccuaucaag uuccugagg aucaguucca gguggccug 1380gaccaggugu ucgagaacau
cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg
ugaucauccu gaucgccgug 1500cugggcagcu ccaugaucuu gguguccauc uucaucauu ucaagaagac caagaagccc
1560accggcgcuc caccagaacu gagcggagug accaacaug gcuucaucc ucacaac 16171381617RNAArtificial
SequenceSynthetic Polynucleotide 138augagcugga agguggucau caucuucagc cugcugauca caccucagca cgccugaaa
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 360ggcugggcca ucgcuagac
caucagacug gaaagcgaag ugaccgccau caacaagcc 420cugaagaaga caaacgagcg cgucagcaca cucggcaaug
gcguuagagu gcuggccaca 480gccgucgcg agcugaagga cuucgucuu aagaaccugu ggccggccau uaacaagaac
540aagugcgaca ucgacgaccu gaagauggcc guguccuuu gccaguucac ccggcgguuu 600cugaacgucg ugcggcaguu
uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca
ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu
780ggcguguacg gcagcagcgu gaucuaauug gugcagcugc cuaucuucgg cgugaucgac 840acaccugcu ggauugugaa
ggccgucuccu agcuguagcg agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg
ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgucgga
1020aucaaugugg ccgagcagag caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag
gcaccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca
gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc
1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga
ccuaucaag uuccugagg aucaguucca gguggccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg
uggaccaguc caacagauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug
1500cugggcagcu ccaugaucuu gguguccauc uucaucauu ucaagaagac caagaagccc 1560accggcgcuc caccagaacu
gagcggagug accaacaug gcuucaucc ucacaac 16171391617RNAArtificial SequenceSynthetic Polynucleotide
139augagcugga agguggucau caucuucagc cugcugauca caccucagca cgccugaaa 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 360ggcgugggcca ucgcuagac caucagacug gaaagcgaag
ugaccgccau caacaagcc 420cugaagaaga caaacgagcg cgucagcaca cucggcaaug gcguuagagu gcuggccaca
480gccgucgcg agcugaagga cuucgucuu aagaaccugu ggccggccau uaacaagaac 540aagugcgaca ucgacgaccu
gaagauggcc guguccuuu gccaguucac ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca
caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag
720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu
gaucuaauug gugcagcugc cuaucuucgg cgugaucgac 840acaccugcu ggauugugaa ggccgucuccu agcuguagcg
agaagaaggg caauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac
960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag
caaagagugc aacaucaaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg
cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc
1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu
gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga ccuaucaag uuccugagg
aucaguucca gguggccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagauc
1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug 1500cugggcagcu ccaugaucuu
gguguccauc uucaucauu ucaagaagac caagaagccc 1560accggcgcuc caccagaacu gagcggagug accaacaug
gcuucaucc ucacaac 16171401617RNAArtificial SequenceSynthetic Polynucleotide 140augagcugga
agguggucau caucuucagc cugcugauca caccucagca cgccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg
gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug ccugugggcg acgucgagaa ucugacaugc

180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugcccga
ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug
cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc
420cugaagaaga caaacgagc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga
cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuua
gccaguucuaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac
660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa
uagagccaug guccgacgga aagguucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc
cuauucgg cgugaucgac 840acaccugcu ggauugugaa ggccgucuccu agcuguagcg agaagaaggc cauuacgcc
900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga
gacaagaggc gaccacgugu ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagagugc aacaucaca
ucagcaccac caacuaucc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg cucugucucc ucugggagcc
1140cugguggcuu guuauaaggc cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaaggcguc
cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac
agcacgugau caagggcaga 1320ccugugucca gcagcuucga ccuaucaag uuccugagg aucaguucca gguggccug
1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg

ccgagaaggc aaacaccggc uucaucaucg ugaucuccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc
uucaucauu ucaagaagac caagaagccc 1560accggcguc succagaacu gagcggagug accaacaug gcuuauccc ucacaac
16171411617RNAArtificial SequenceSynthetic Polynucleotide 141augagcugga aggugguau caucuucagc
cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga
120accggcuggu acaccaacgu guacacacug gaagugggagc acgucgagaa ucugacaugc 180ucugauggcc cuagccugau
caagaccgag cuggaucuga ccaagagcgc ccugagagaa 240cucaagaccg ugucugcccga ucagcuggcc agagaggaac
agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca
360ggcguggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgagc
cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga
cacgggccau uaacaagaac 540aagugcgaca uccugaccu gaagauggcc guguccuuua gccaguucuaa ccggcgguuu
600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu
ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga
aagguucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuauucgg cgugaucgac
840acaccugcu ggauugugaa ggccgucuccu agcuguagcg agaagaaggc cauuacgcc 900ugccugcuga gagaggacca
aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu
ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuaucc
1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggc
cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaaggcguc cagcuacauc accaaccagg
acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga
1320ccugugucca gcagcuucga ccuaucaag uuccugagg aucaguucca gguggccug 1380gaccaggugu ucgagaacau
cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaaggc aaacaccggc uucaucaucg
ugaucuccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc
1560accggcguc succagaacu gagcggagug accaacaug gcuuauccc ucacaac 16171421617RNAArtificial
SequenceSynthetic Polynucleotide 142augagcugga aggugguau caucuucagc cugcugauca caccucagca cggccugaaa
60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu
guacacacug gaagugggagc acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga
ccaagagcgc ccugagagaa 240cucaagaccg ugucugcccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc
300ggcagcuuug ugcugggagc cauugcucuu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuaagac
caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgagc cgucagcaca cucggcaaug
gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac
540aagugcccua ucgacgaccu gaagauggcc guguccuuua gccaguucuaa ccggcgguuu 600cugaacgucg ugcggcaguu
uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca
ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aagguucgg cauucugauu
780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc cuauucgg cgugaucgac 840acaccugcu ggauugugaa
ggccgucuccu agcuguagcg agaagaaggc cauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg
ccggcagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgucgga
1020aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuaucc 1080ugcaaggugu ccaccggcag

gcaccuauu ucuauggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca
gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc
1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga
ccuaucaag uuccugagg aucaguucca gguggccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg
uggaccaguc caacagauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucuccu gaucgccug
1500cugggcagcu ccaugauccu gguguccauc uucaucaua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu
gagcggagug accaacaug gcuucaucc 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
cauugcucu ggaguggcug cugcugcagc uguuacagca 360ggcugggcca ucgcuaagac caucagacug ccuagcgaag
ugaccgccau caacaacgcc 420cugaagaaga caaacgagc cgucagcaca cucggcaaug gcguuagagu gcuggccaca
480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu
gaagauggcc guguccuuu gccaguuaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca
caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag
720aucaagcuga ugcucgagaa uagagccaug guccgacgga aagguucgg cauucugauu 780ggcguguacg gcagcagcgu
gaucuauaug gugcagcugc cuauucgg cgugaucgac 840acaccugcu ggauugugaa ggccguccu agcuguagcg
agaagaaggg cauuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac
960ccuacgaga aggacugcga gacaagaggc gaccagugu ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag
caaagaguc aacaucaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg
cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc
1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu
gagcaaggug gaaggcgaac agcacgugau caagggcaga 1320ccugugucca gcagcuucga ccuaucaag uuccugagg
aucaguucca gguggccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagauc
1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucuccu gaucgccug 1500cugggcagcu ccaugauccu
gguguccauc uucaucaua ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaug
gcuucaucc 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 cauugcucu ggaguggcug
cugcugcagc uguuacagca 360ggcugggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc
420cugaagaaga caaacgagc cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga
cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ucgacgaccu gaagauggcc guguccuuu
gccaguuaa ccggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac
660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa
uagagccaug guccgacgga aagguucgg cauucugauu 780ggcguguacg gcagcagcgu gaucuauaug gugcagcugc
cuauucgg cgugaucgac 840acaccugcu ggauugugaa ggccguccu agcuguagcg agaagaaggg cauuacgcc
900ugccugcuga gagaggacca aggcugguau ugucagaacg ccggcagcac cguguacuac 960ccuacgaga aggacugcga
gacaagaggc gaccagugu ucugugauac cgccgucgga 1020aucaaugugg ccgagcagag caaagaguc aacaucaca
ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauggugg cucugucucc ucugggagcc
1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug
cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac
agcacgugau caagggcaga 1320ccugugucca gcagcuucc accuaucaag uuccugagg aucaguucca gguggccug
1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaaggg
aaacaccggc uucaucaucg ugaucuccu gaucgccug 1500cugggcagcu ccaugauccu gguguccauc uucaucaua
ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaug gcuucaucc 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 cauugcucu ggaguggcug cugcugcagc uguuacagca
360ggcugggcca ucgcuaagac caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgagc

cgucagcaca cucggcaaug gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga
cacgggccau uaacaagaac 540aagugcgaca ugcagcaccu gaagauggcc guguccuuua gccaguuaa cggcgguuu
600cugaacgucg ugcggcaguu uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu
ggcuagagcc gugccuaaca ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga
aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu gaucauauug gucgagcugc cuaucuucgg cgugaucgac
840acaccugcu ggauugugaa ggccgcuccu agcuguagcg agaagaaggg cauuuacgcc 900ugccugcuga gagaggacca
aggcugguau ugucagaacg cggcgagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu
ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuauccc
1080ugcaaggugu ccaccggcag gcaccuauu ucuauuggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg
cguguccugu agcaucggca gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg
acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacugau caagggcaga
1320ccugugucca gcagcuucga ccuaucaag uucccugaga accaguucca gguggcccug 1380gaccaggugu ucgagaacau
cgagaauucc caggcucugg uggaccaguc caacagauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg
ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc
1560accggcgcuc cuccagaacu gageggagug accaacaug gcuucaucc ucacaac 16171461617RNAArtificial
SequenceSynthetic Polynucleotide 146augagcugga aggugguau caucuucagc cugcugauca caccucagca cggccugaaa
60gagagcuacc uggaagaguc cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu
guucacacug gaagugggcg acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga
ccaagagcgc ccugagagaa 240cucaagaccg ugucugcccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc
300ggcagcuuug ugcugggagc cauugcucu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuagac
caucagacug gaaagcgaag ugaccgccau caacaacgcc 420cugaagaaga caaacgagc gcucagcaca cucggcaaug
gcguuagagu gcuggccaca 480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac
540aagugcgaca ugcagcaccu gaagauggcc guguccuuua gccaguuaa cggcgguuu 600cugaacgucg ugcggcaguu
uagcgacaac gccggaauca caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca
ugccuacauc ugccggccag 720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu
780ggcguguacg gcagcagcgu gaucauauug gucgagcugc cuaucuucgg cgugaucgac 840acaccugcu ggauugugaa
ggccgcuccu agcuguagcg agaagaaggg cauuuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg
cggcgagcac cguguacuac 960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga
1020aucaaugugg ccgagcagag caaagagugc aacaucaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag
gcaccuauu ucuauuggugg cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca
gcaacagagu gggcaucauc 1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc
1260gacaacaccg uguaucagcu gagcaaggug gaaggcgaac agcacugau caagggcaga 1320ccugugucca gcagcuucga
ccuaucaag uucccucagg aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg
uggaccaguc caacagauc 1440cugucuagcg ccgagaaggg aaacaccggc uucaucaucg ugaucauccu gaucgccgug
1500cugggcagcu ccaugauccu gguguccauc uucaucauu ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu
gagcggagug accaacaug gcuucaucc ucacaac 16171471617RNAArtificial SequenceSynthetic Polynucleotide
147augagcugga aggugguau caucuucagc cugcugauca caccucagca cggccugaaa 60gagagcuacc uggaagaguc
cugcagcacc aucacagagg gcuaccuguc ugugcugaga 120accggcuggu acaccaacgu guucacacug gaagugggcg
acgucgagaa ucugacaugc 180ucugauggcc cuagccugau caagaccgag cuggaucuga ccaagagcgc ccugagagaa
240cucaagaccg ugucugcccga ucagcuggcc agagaggaac agaucgagaa uccuggcagc 300ggcagcuuug ugcugggagc
cauugcucu ggaguggcug cugcugcagc uguuacagca 360ggcguggcca ucgcuagac caucagacug gaaagcgaag
ugaccgccau caacaacgcc 420cugaagaaga caaacgagc gcucagcaca cucggcaaug gcguuagagu gcuggccaca
480gccgugcgcg agcugaagga cuucgugucc aagaaccuga cacgggccau uaacaagaac 540aagugcgaca ugcagcaccu
gaagauggcc guguccuuua gccaguggaa cggcgguuu 600cugaacgucg ugcggcaguu uagcgacaac gccggaauca
caccagccau cagccuggac 660cugaugacag augcugagcu ggcuagagcc gugccuaaca ugccuacauc ugccggccag
720aucaagcuga ugcucgagaa uagagccaug guccgacgga aaggcuucgg cauucugauu 780ggcguguacg gcagcagcgu
gaucauauug gucgagcugc cuaucuucgg cgugaucgac 840acaccugcu ggauugugaa ggccgcuccu agcuguagcg
agaagaaggg cauuuacgcc 900ugccugcuga gagaggacca aggcugguau ugucagaacg cggcgagcac cguguacuac
960ccuaacgaga aggacugcga gacaagaggc gaccacgugu ucugugauac cgccgcugga 1020aucaaugugg ccgagcagag
caaagagugc aacaucaca ucagcaccac caacuauccc 1080ugcaaggugu ccaccggcag gcaccuauu ucuauuggugg
cucugucucc ucugggagcc 1140cugguggcuu guuauaaggg cguguccugu agcaucggca gcaacagagu gggcaucauc
1200aagcagcuga acaagggcug cagcuacauc accaaccagg acgccgauac cgugaccauc 1260gacaacaccg uguaucagcu
gagcaaggug gaaggcgaac agcacugau caagggcaga 1320ccugugucca gcagcuucga ccuaucaag uucccugagg
aucaguucca gguggcccug 1380gaccaggugu ucgagaacau cgagaauucc caggcucugg uggaccaguc caacagauc

1440cugucuagcg ccgagaaggg aacaccggc uucaucaugc ugaucauccu gaucgccgug 1500cugggcagcu ccaugauccu
gguguccauc uucaucauu ucaagaagac caagaagccc 1560accggcgcuc cuccagaacu gagcggagug accaacaug
gcuucaucce ucacaac 1617

* * * * *

[Images](#)

[Add to Shopping Cart](#)

[View Shopping Cart](#)

[Hit List](#)

[Prev](#)

[Next](#)

[Top](#)

[Help](#)

[Home](#)

[Boolean](#)

[Manual](#)

[Number](#)

[PTDLs](#)