MMD Laboratory

Post Covid / Post Vac Syndrome

The role of SARS-CoV-2 Spike Proteins

Prof. Dr. Brigitte König

TABLE OF CONTENTS

The role of SARS-CoV-2 spike proteins in post Covid / post vac syndrome 2
Causes of post covid/post vac syndrome....2
SARS-CoV-2 spike protein (S protein) - host receptor binding 2
SARS-CoV-2 spike protein (S protein) - cell tropism....3
SARS-CoV-2 spike protein (S protein) - Pathogenesis 3
Detection methods around the SARS-CoV-2 spike protein 4
Analysis of persistent SARS-CoV-2 spike proteins....4
Quantitative determination of the SARS-CoV-2 spike protein in plasma/serum 4
Quantitative determination of the SARS-CoV-2 spike protein in exosomes 4
Quantitative determination of the SARS-CoV-2 spike protein in immune cells (PBMC) 5
Analysis of persistent vaccine mRNA 5
Detection of vaccine mRNA in exosomes....5
Detection of vaccine mRNA in immune cells (PBMC)....6
Detection of vaccine mRNA in breast milk 6
Analysis of SARS-CoV-2 persistence....6
Detection of SARS-CoV-2 RNA in serum (highly sensitive) 7
Detection of SARS-CoV-2 RNA in immune cells 7
Detection of SARS-CoV-2 RNA in faeces 7
Detection of SARS-CoV-2 RNA in semen....7
Detection of residual dnA and/or RNA from the vaccines....8
Integration of the vaccine mRNA into the genome 8
Detection of the vaccine mRNA spike sequence in the cell nucleus 9
Detection of the SV-40 enhancer of the SARS-CoV-2 mRNA expression vectors 9
Detection of Pfizer/Moderna expression vectors (plasmids) in intestinal bacteria 9
Selected literature....11/12

THE ROLE OF SARS-COV-2 SPIKE PROTEINS IN POST COVID/POST VAC SYNDROME

CAUSES OF POST COVID/POST VAC SYNDROME

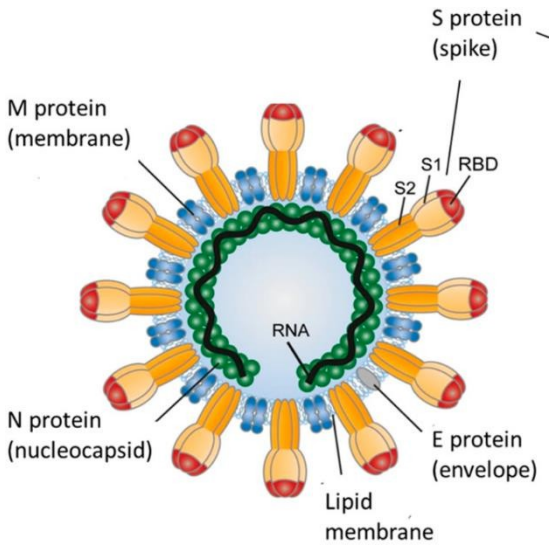
The current hypotheses of the underlying pathophysiology, which very probably often occur in combination and are also mutually dependent, include the following:

- The triggering of impaired immune tolerance and associated autoimmunity after acute viral infection (post-Covid) or through exposure to the vaccine antigen (post-VAC). Microvascular and macrovascular thromboembolic events and unrepaired tissue damage
- a dysbiosis of the intestinal microbiome
- Low levels of stress hormones, smouldering inflammatory reactions, metabolic changes
- Mitochondrial dysfunction
- reactivated viral infections, such as CMV, EBV or other herpes viruses
- persistent SARS-CoV-2 viruses and/or spike proteins (infection/vaccination) in tissues or blood.

THE SPIKE PROTEIN IS A MULTIFUNCTIONAL PROTEIN THAT CONTRIBUTES TO HOST RECEPTOR BINDING, CELL TROPISM AND PATHOGENESIS

SARS-COV-2 SPIKE PROTEIN (S-PROTEIN) - HOST RECEPTOR BINDING

SARS-CoV-2 (coronavirus with severe acute respiratory syndrome, which is responsible for the disease COVID-19) uses the spike proteins of its envelope to infect primarily the cells that are located on the membrane express the enzyme angiotensin converting enzyme 2 (ACE2). The ACE2 (angiotensin converting enzyme) acts as the main receptor.



It appears that SARS-CoV-2 can also utilise other structures on the cell surface as receptors, e.g. integrins. Other entry mechanisms are also conceivable, but these play a subordinate role.

Figure 1: Structure of SARS-CoV-2, an RNA virus encoding a nucleocapsid phosphoprotein (N), a membrane glycoprotein (M), an envelope (E), a spike glycoprotein (S) and a non-structural protein.

SARS-COV-2 SPIKE PROTEIN (S-PROTEIN) - CELL TROPISM

ACE2, the receptor for the SARS-CoV-2 virus, is membrane-bound on the surface of several cell types. ACE2 is found in high concentrations in particular on the mucous membrane of the upper respiratory tract, the gastrointestinal tract, in the ciliated epithelium of the fallopian tubes, in the endothelium, in blood platelets and in soluble form in plasma. The virus can therefore penetrate many organs/tissues and lead to functional disorders.

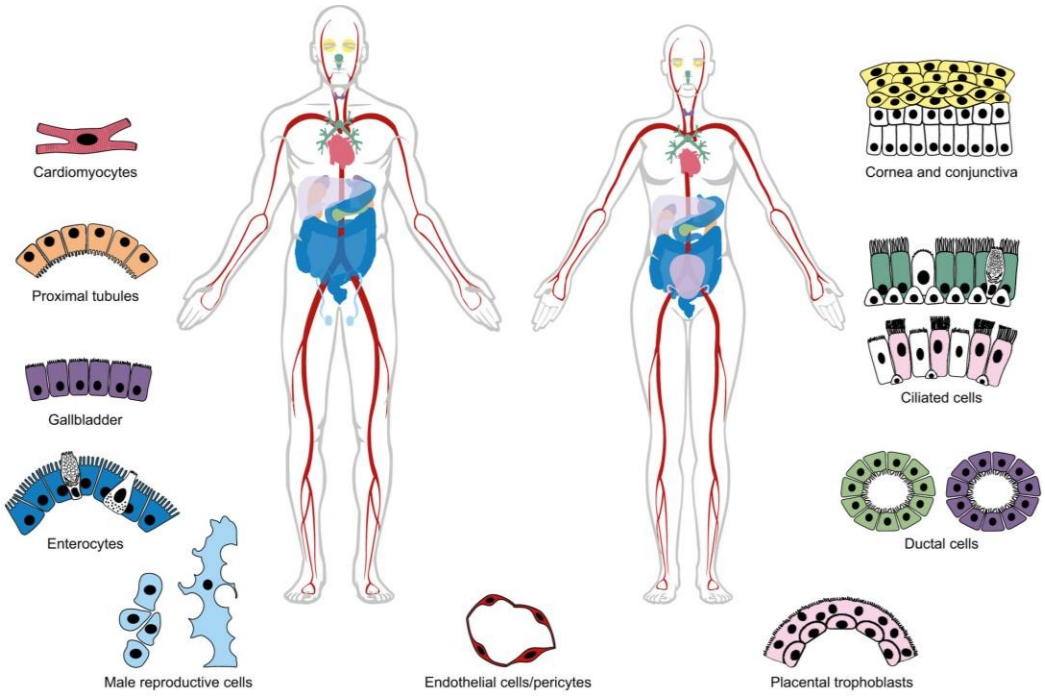


Figure 2: Tissue with high concentrations of ACE2, the receptor for SARS-CoV-2.

SARS-COV-2 SPIKE PROTEIN (S-PROTEIN) - PATHOGENESIS

The SARS-CoV-2 spike protein is not only used by the virus to enter a target cell. The SARS-CoV-2 S protein also exerts direct effects on human cells in the absence of other viral components. Free spike protein also binds to ACE-2, for example, as well as to specific acetylcholine receptors (nicotinic acetylcholine receptors; nAChRcI) and can cause potential toxicological problems.

There is increasing evidence that the SARS-CoV-2 spike protein directly damages mitochondria and/or alters the bioenergetics of mitochondria. These effects have been demonstrated in brain cells, heart muscle cells and muscle cells in particular.

Figure 3: The mitochondrion

DETECTION METHODS FOR THE SARS-COV-2 SPIKE PROTEIN

With a few exceptions (quantitative determination of spike proteins in plasma/serum), the test assays listed below are not suitable for high throughput. In order to achieve a high sensitivity and specificity with an optimum detection limit, the individual test steps are laboratory and personnel intensive. Most of the processing steps cannot be automated. Depending on the test, it can therefore take up to 10 days to provide the results.

ANALYSIS OF PERSISTENT SARS-COV-2 SPIKE PROTEINS

It is currently not possible to distinguish between the spike proteins of the different SARS-CoV-2 variants and the spike protein after vaccination. We are working hard to differentiate the spike proteins and clearly assign them to the virus variants or the SARS-CoV-2 vaccination.

QUANTITATIVE DETERMINATION OF THE SARS-COV-2 SPIKE PROTEIN IN PLASMA/SERUM

The free SARS-CoV-2 spike protein, which is not bound to antibodies, is detected. Detection is carried out by ELISA. The detection limit is 4.5pg/ml. Each detection of the spike protein must be compared with the symptoms.

- The spike protein is detected by ELISA. The detection limit is 4.5pg/ml serum.

We are unable to detect the spike protein bound to antibodies. We therefore recommend the parallel determination of total anti-SARS-CoV-2 IgG as well as the quantitative determination of the neutralising capacity of IgG antibodies against the original SARS-CoV-2 virus (WUHAN) and the alpha, beta, gamma, delta and omicron variants (our order form VIII; point 1.1).

THE DETECTION OF THE SARS-COV-2 SPIKE PROTEIN IN PLASMA/SERUM IS A CLEAR INDICATION OF PERSISTENT SPIKE PROTEIN.

QUANTITATIVE DETERMINATION OF THE SARS-COV-2 SPIKE PROTEIN IN EXOSOMES

An important communication network between cells consists of extracellular vesicles (EVs) that are constantly released from one cell and later taken up by another cell, which could be located in a distant organ. Small vesicles, called exosomes, can deliver a diverse collection of biologically active molecules, including mRNA, microRNAs (miRNAs), proteins and lipids.

It has been shown that the SARS-CoV-2 proteins, as well as the proteins produced, are packaged in extracellular vesicles (exosomes) after vaccination and distributed to tissues/organs via the bloodstream. In this way, the SARS-CoV-2 spike protein can be transported in exosomes to organs with a higher density of relevant receptors for the spike protein.

- The spike proteins are detected in purified exosomes from approximately 4 ml of serum/plasma.

THE DETECTION OF THE SARS-COV-2 SPIKE PROTEIN IN EXOSOMES IS A CLEAR INDICATION OF A SYSTEMIC EFFECT OF THE SPIKE PROTEIN.

QUANTITATIVE DETERMINATION OF THE SARS-COV-2 SPIKE PROTEIN IN IMMUNE CELLS (PBMC)

Spike proteins are primarily found in tissues/organs that have a high density of ACE-2 as a virus receptor. This means that the spike proteins cannot be detected in serum.

Conventional immunological knowledge teaches us that antigen-presenting cells (especially macrophages) can recognise extracellular potentially pathogenic particles with the help of a number of suitable receptors. "capture". These particles are then broken down by endocytosis or phagocytosis (depending on the particle dimension and the cell type), "processed" into small peptides (approx. 30 amino acids) (i.e. digested) and finally sent for further degradation.

The spike protein present somewhere in the body is therefore taken up by macrophages and can be detected in these, which represent a fraction in the immune cells.

- The spike proteins are detected in purified immune cells (1x10).[6]

THE DETECTION OF THE SARS-COV-2 SPIKE PROTEIN IN IMMUNE CELLS IS A CLEAR INDICATION OF THE PRODUCTION OF THE SPIKE PROTEIN IN THE BODY.

A negative result for the SARS-CoV-2 spike protein does not rule out its presence in the body. If persistent SARS-CoV-2 spike protein is still suspected, the test must be repeated (plasma/serum; exosomes, immune cells).

ANALYSIS OF PERSISTENT VACCINE MRNA

Vaccine mRNA is a possible source of persistent SARS-CoV-2 spike proteins in vaccinated individuals. As the sequence of the vaccine mRNA differs from the sequence of SARS-CoV-2, the vaccine mRNA can be clearly distinguished from the virus RNA.

The detection of vaccine mRNA covers Comirnaty (BioNTech/Pfizer) and Spikevax (Moderna) as well as Vaxzevria (AstraZeneca).

DETECTION OF VACCINE MRNA IN EXOSOMES

Studies have shown that vaccine mRNA can still be detectable in serum 1 month after vaccination. It is unlikely that vaccine mRNA will be detectable in serum for a long time after vaccination.

However, exosomes, i.e. extracellular vesicles, are used to transport mRNA, including the vaccine mRNA. Exosomes can take up their cargo anywhere in the body and also distribute it.

- The mRNA is quantitatively detected in purified exosomes from approximately 4 ml of serum/plasma using RT-PCR

THE DETECTION OF VACCINE MRNA IN EXOSOME UNCELLS IS A CLEAR INDICATION OF THE PERSISTENCE OF VACCINE MRNA.

DETECTION OF VACCINE MRNA IN IMMUNE CELLS (PBMC)

Viral RNA is recognised as foreign by human cells and thus triggers defence reactions that impair its translation into proteins and at the same time control its degradation. The SARS-CoV-2 spike glycoprotein mRNA was "humanised" in order to stabilise the mRNA and thus improve its translation. Thus, a guanine-methylated cap, 3'- and 5'-untranslated regions (UTRs) copied from those of human proteins, and finally a long poly(A) tail were added. Replacement of uridines with pseudouridines or (even better) with methylpseudouridine prevents recognition as foreign mRNA by the Toll-Like Receptors (TLR) and subsequent activation of IFN type I.

It is not known whether the vaccine mRNA can persist in immune cells, e.g. in long-lived memory cells. It is also not yet known whether macrophages reabsorb the vaccine mRNA located in exosomes.

- The mRNA is quantitatively detected in purified immune cells ($1x10^6$) using RT-PCR.

THE DETECTION OF VACCINE MRNA IN IMMUNE CELLS IS A CLEAR INDICATION OF THE PERSISTENCE OF VACCINE MRNA.

DETECTION OF VACCINE MRNA IN BREAST MILK

Several studies have shown that the mRNA of the Pfizer/Moderna COVID-19 vaccine is present in the expressed breast milk (EBM) of breastfeeding women.

To detect the mRNA, the entire breast milk and an enriched exosome fraction of the breast milk (approx. 3 ml) are analysed.

- The mRNA is quantitatively detected in unfractionated breast milk (1ml) as well as in purified exosomes from approximately 4ml of breast milk using RT-PCR.

the detection of maternal milk mRNA is not evidence of the formation of spike proteins and is not indicative of possible cumulative vaccine mRNA expression following frequent breastfeeding in infants.

ANALYSIS OF A SARS-COV-2 PERSISTENCE

A comprehensive meta-analysis by Cevik et al. indicates that viral shedding (as detected by PCR) can persist over longer periods of time with broad sampling. The maximum duration of viral RNA excretion was 83 days in the upper respiratory tract, 59 days in the lower respiratory tract, 126 days in stool samples and 60 days in serum samples. However, small amounts of material were used for the analyses (serum, stool).

An important question regarding the persistence of post Covid / post vac symptoms remains:

- **Do the symptoms correlate with a possible persistence of the virus in different compartments?**

DETECTION OF SARS-COV-2 RNA IN SERUM (HIGHLY SENSITIVE)

The detection of RNA in the blood during the acute phase of COVID-19 correlated with the risk of PASC in various studies, although RNA is generally barely detectable in these patients after several months (Su et al., 2022).

- All viruses present in approximately 4 ml of serum/plasma are concentrated by means of ultracentrifugation. They are then analysed for SARS-CoV-2 RNA using quantitative RT-PCR.

DETECTION OF SARS-COV-2 RNA IN IMMUNE CELLS

Viral RNA is recognised as foreign by human cells, triggering defence reactions that impair its translation into proteins and at the same time control its degradation. It is not known whether the SARS-CoV-2 virus can persist in immune cells, e.g. in long-lived memory cells. It is also not yet known whether macrophages reabsorb the virus that is located somewhere in the body.

- The SARS-CoV-2-specific mRNA is quantitatively detected in purified immune cells ($1x10^6$) using RT-PCR. We use three different segments of SARS-CoV-2 mRNA, coding for the receptor binding site of the SARS-CoV-2 spike protein (RBD), the spike protein outside RBD (S), and the envelope protein (E).

THE DETECTION OF SARS-COV-2 MRNA IN IMMUNE CELLS IS A CLEAR INDICATION OF THE PERSISTENCE OF THE VIRUS

DETECTION OF SARS-COV-2 RNA IN STOOL

One of the largest autopsy series of patients with COVID-19 to date showed clear evidence of infection of the small intestine by SARS-CoV-2. Thus, SARS-CoV-2 is capable of infecting the gastrointestinal tract. This postulated gastrointestinal tract tropism of SARS-CoV-2 corresponds to the fact that other betacoronaviruses that infect mammals can cause gastrointestinal diseases.

Previous studies indicate that the intestines of people with POST COVID are a virus reservoir.

- The total RNA is isolated from an aliquot of a stool sample and analysed for the presence of SARS-CoV-2 RNA.

DETECTION OF SARS-COV-2 RNA IN SEMEN

The testis is one of the tissues with a high density of angiotensin-converting enzyme-2 (ACE-2), the binding sites for SARS CoV-2. Autopsy reports have shown viral invasion of the testis. Whether the male reproductive organ is a site of viral persistence has not been clarified. Equally unclear is the possible effect of viral persistence on sperm quality.

- All viruses contained in approximately 4 ml of semen are concentrated by means of ultracentrifugation. They are then analysed for SARS-CoV-2 RNA using quantitative RT-PCR.

A negative result for SARS-COV-2 PERSISTENCE (RNA DETECTION) DOES NOT EXCLUDE ITS PRESENCE IN THE BODY.

A POSITIVE RESULT FOR SARS-COV-2 PERSISTENCE (RNA DETECTION) IS NOT EVIDENCE OF INFECTIOUS VIRUS AND/OR SPIKE PROTEIN PRODUCTION.

DETECTION OF RESIDUAL DNA AND/OR RNA FROM THE VACCINES

Vaccine-specific analyses can be used to analyse various body fluids (e.g. blood, saliva, semen), immune cells (especially monocytes/macrophages) and tissue for vaccine residues. The vaccine residues can be either mRNA or DNA based.

We offer a test that includes 4 target sequences: 1) the vaccination spike (Pfizer, Moderna, Janssen), 2) the "Ori" sequence of the transcription plasmid (VaxOri), which was used for vaccine production; 3) the SV40 enhancer sequence of the transcription plasmid used for vaccine production;
4) a control sequence (RNAaseP). This is a test in which the SV40 enhancer offers the highest sensitivity. The SV40 enhancer is only present on the transcription plasmid in the Pfizer vaccine, so an SV40 target failure with spike-positive qPCR would indicate a Moderna vaccination and not a Pfizer vaccination. The RNaseP assay confirms that you have properly isolated DNA and/or RNA from the tissue. The VaxOri is included in both Moderna and Pfizer, but not in Janssen.

A logic matrix for deducing which vaccine is in the sample material is shown in the table below. This becomes more complicated when vaccines are mixed in the same patient, but presumably the last vaccine administered will dominate the signal.

TARGET SEQUENCE	RESULT	VACCINE
SPIKE VAX	Positive	Pfizer
SPIKE ORI	Positive	Pfizer
SPIKE SV40	Positive	Pfizer
RNASEP	positive	Control ok
SPIKE VAX	Positive	Moderna
SPIKE ORI	Positive	Moderna
SPIKE SV40	Negative	Moderna
RNASEP	positive	Control ok
SPIKE VAX	Positive	Janssen
SPIKE ORI	Negative	Janssen
SPIKE SV40	Negative	Janssen
RNASEP	positive	Control ok

INTEGRATION OF THE VACCINE MRNA INTO THE GENOME

Does part of the RNA in an mRNA vaccination also pass into the DNA - i.e. does it become incorporated into our cells? Many people are concerned about this question. The central question of the possible integration of the vaccine mRNA into our human genome is all the more topical as plasmid DNA has been detected in some vaccine batches.
Although it can be assumed that plasmid DNA is degraded in our cells (in the cytosol), transport into the cell nucleus cannot be ruled out. The plasmid DNA in the Pfizer vaccine contains the "SV40 enhancer", which enables transport into the cell nucleus (nuclear localisation signal (NLS)).

DETECTION OF THE VACCINE MRNA SPIKE SEQUENCE IN THE CELL NUCLEUS

We therefore offer the detection of DNA with the inoculation mRNA spike sequence in the cell nucleus.

- The cell nucleus is first isolated from immune cells or other cell types (e.g. oral mucosa cells, sperm cells). The total DNA is isolated from the cell nuclei. This is checked for the presence of the spike sequence of the vaccine (Pfizer, Moderna, Janssen).

THE DETECTION OF THE VACCINE-MRNA SPIKE SEQUENCE IN THE CELL NUCLEUS DNA IS EVIDENCE THAT THE VACCINE HAS CROSSED THE NUCLEAR BOUNDARY. THE DETECTION OF DNA WITH THE VACCINE-MRNA SPIKE SEQUENCE IS NOT EVIDENCE FOR THE INTEGRATION OF THE VACCINE-MRNA INTO THE HUMAN GENOME AND IS NOT EVIDENCE FOR CONTINUOUS PRODUCTION OF THE SPIKE PROTEIN.

DETECTION OF THE SV-40 ENHANCER OF THE SARS-COV-2 MRNA EXPANSION VECTORS

We offer the detection of the SV40 enhancer sequence of the Pfizer vaccine in the cell nucleus.

- The cell nucleus is first isolated from immune cells or other cell types (e.g. oral mucosa cells). The total DNA is isolated from the cell nuclei. This is checked for the presence of the SV40 enhancer sequence.

THE DETECTION OF THE SV40-ENHACER SEQUENCE IS NOT EVIDENCE OF INCORPORATION INTO THE HUMAN GENOME. THE DETECTION OF THE SV40-ENHACER SEQUENCE OF THE PFIZER VACCINE (COMIRNATY) IN THE CELL NUCLEUS IS, HOWEVER, EVIDENCE FOR THE PERSISTENCE OF THE VACCINE IN THE HUMAN BODY AND ESPECIALLY IN THE CELL NUCLEUS.

DETECTION OF THE EXPRESSION VECTORS (PLASMIDS) OF PFIZER/MODERNA IN INTESTINAL BACTERIA

Although it can be assumed that contaminating plasmid DNA in the mRNA vaccines (Pfizer, Moderna) is degraded in the human body, transport into our intestines cannot be completely ruled out until evidence to the contrary is provided. Whether the plasmid DNA can then be absorbed into our intestinal bacteria, in particular *Escherichia coli* bacteria, remains to be verified.

We therefore offer the detection of expression vectors (Pfizer, Moderna) in intestinal bacteria.

- Aliquots of a faecal sample are incubated aerobically/anaerobically using the antibiotics kanamycin and neomycin. Plasmids are then isolated from the cultured bacteria. These are checked by PCR for the presence of the expression vectors (plasmids) of the mRNA vaccines (Pfizer, Moderna) (Spike, Vector, SV40).

THE DETECTION OF EXPRESSION VECTORS IS NOT PROOF OF THE CONTINUOUS FORMATION OF SARS-COV-2 SPIKE PROTEINS. HOWEVER, THE DETECTION OF THE SV40 ENHACER SEQUENCE OF THE PFIZER VACCINE (COMIRNATY) IS A PROOF OF THE PERSISTENCE OF THE VACCINE IN THE HUMAN BODY.

SELECTED LITERATURE

Trougakos IP, Terpos E, Alexopoulos H, Politou M, Paraskevis D, Scorilas A, Kastritis E, Andreakos E, Dimopoulos MA. Adverse effects of COVID-19 mRNA vaccines: the spike hypothesis. Trends Mol Med. 2022 Jul;28(7):542-554. doi: 10.1016/j.molmed.2022.04.007. Epub 2022 Apr 21. PMID: 35537987; PMCID: PMC9021367.

Cosentino M, Marino F. Understanding the Pharmacology of COVID-19 mRNA Vaccines: Playing Dice with the Spike? Int J Mol Sci. 2022 Sep 17;23(18):10881. doi: 10.3390/ijms231810881. PMID: 36142792; PMCID: PMC9502275.

Seneff S, Nigh G, Kyriakopoulos AM, McCullough PA. Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs. Food Chem Toxicol. 2022 Jun;164:113008. doi: 10.1016/j.fct.2022.113008. Epub 2022 Apr 15. PMID: 35436552; PMCID: PMC9012513.

Bansal S, Perincheri S, Fleming T, Poulson C, Tiffany B, Bremner RM, Mohanakumar T. Cutting Edge: Circulating Exosomes with COVID Spike Protein Are Induced by BNT162b2 (Pfizer-BioNTech) Vaccination prior to Development of Antibodies: A Novel Mechanism for Immune Activation by mRNA Vaccines. J Immunol. 2021 Nov 15;207(10):2405-2410. doi: 10.4049/jimmunol.2100637. Epub 2021 Oct 15. PMID: 34654691.

Zoe Swank and others, Persistent Circulating Severe Acute Respiratory Syndrome Coronavirus 2 Spike Is Associated With Post-acute Coronavirus Disease 2019 Sequelae, CLINICAL INFECTIOUS DISEASES, Volume 76, Issue 3, 1 February 2023, Pages e487-e490, https://doi.org/10.1093/cid/ciac722

Pesce E, Manfrini N, Cordiglieri C, Santi S, Bandera A, Gobbini A, Gruarin P, Favalli A, Bombaci M, Cuomo A, Collino F, Cricrì G, Ungaro R, Lombardi A, Mangioni D, Muscatello A, Aliberti S, Blasi F, Gori A, Abrignani S, De Francesco R, Biffo S and Grifantini R (2022) Exosomes Recovered From the Plasma of COVID-19 Patients Expose SARS-CoV-2 Spike-Derived Fragments and Contribute to the Adaptive Immune Response. Front. Immunol. 12:785941. doi: 10.3389/fimmu.2021.785941

Clough E, Inigo J, Chandra D, Chaves L, Reynolds JL, Aalinkeel R, Schwartz SA, Khmaladze A, Mahajan SD. Mitochondrial Dynamics in SARS-COV2 Spike Protein Treated Human Microglia: Implications for Neuro-COVID. J Neuroimmune Pharmacol. 2021 Dec;16(4):770-784. doi: 10.1007/s11481-021-10015-6. Epub 2021 Oct 2. Erratum in: J Neuroimmune Pharmacol. 2021 Dec 11;: PMID: 34599743; PMCID: PMC8487226.

Kim ES, Jeon MT, Kim KS, Lee S, Kim S, Kim DG. Spike Proteins of SARS-CoV-2 Induce Pathological Changes in Molecular Delivery and Metabolic Function in the Brain Endothelial Cells. Viruses. 2021 Oct 8;13(10):2021. doi: 10.3390/v13102021. PMID: 34696455; PMCID: PMC8538996.

Huynh TV, Rethi L, Lee TW, Higa S, Kao YH, Chen YJ. Spike Protein Impairs Mitochondrial Function in Human Cardiomyocytes: Mechanisms Underlying Cardiac Injury in COVID-19. Cells. 2023 Mar 11;12(6):877. doi: 10.3390/cells12060877. PMID: 36980218; PMCID: PMC10046940.

Cevik M, Kuppalli K, Kindrachuk J, Peiris M. Virology, transmission, and pathogenesis of SARS-CoV-2 BMJ 2020; 371 :m3862 doi:10.1136/bmj.m3862

Cevik M, Tate M, Lloyd O, et al. SARS-CoV-2, SARS-CoV-1 and MERS-CoV viral load dynamics, duration of viral shedding and infectiousness: a living systematic review and meta-analysis. Lancet Microbe2020; (forthcoming) doi:10.1016/S2666-5247(20)30172-5.Google Scholar

Dean DA, Dean BS, Muller S, Smith LC. Sequence requirements for plasmid nuclear import. Exp Cell Res. 1999 Dec 15;253(2):713-22. doi: 10.1006/excr.1999.4716. PMID: 10585295; PMCID: PMC4152905.

Brogna C, Brogna B, Bisaccia DR, Lauritano F, Marino G, Montano L, Cristoni S, Prisco M, Piscopo M. Could SARS-CoV-2 Have Bacteriophage Behaviour or Induce the Activity of Other Bacteriophages? Vaccines (Basel). 2022 Apr 29;10(5):708. doi: 10.3390/vaccines10050708. PMID: 35632464; PMCID: PMC9143435.

Brogna C, Brogna B, Bisaccia DR, Lauritano F, Marino G, Montano L, Cristoni S, Prisco M, Piscopo M. Could SARS-CoV-2 Have Bacteriophage Behaviour or Induce the Activity of Other Bacteriophages? Vaccines (Basel). 2022 Apr 29;10(5):708. doi: 10.3390/vaccines10050708. PMID: 35632464; PMCID: PMC9143435.

Prasad TK, Rao NM. The role of plasmid constructs containing the SV40 DNA nuclear-targeting sequence in cationic lipid-mediated DNA delivery. Cell Mol Biol Lett. 2005;10(2):203-15. PMID: 16010286.