SARS-CoV-2 pandemic and vaccine side effects
Part 2: Covid-19 mRNA vaccines and the human molecular biology

A discussion about important molecular biological risk factors with emphasis on the mRNA vaccines used during the Covid-19 pandemic

An initial entry into this blog informs about the essentials of immunology and vaccination*. A basic understanding of immunology helps follow the description of molecular biological risk factors related to vaccines used throughout the Covid-19 pandemic. There are three main types of vaccines against SARS-CoV-2. The conventional method of developing vaccines is to trigger an immune response based on an inactivated virus, as was chosen by Sinopharm. The AstraZeneca vaccine works on a "replication-defective recombinant adenoviral vector," and the Pfizer-BioNTech and Moderna vaccines are mRNA vaccines. An entertaining video clip for recalling the interaction of messenger RNA and DNA can be found on the internet. WHO also provides a video clip explaining how the mRNA vaccines work.

The function of mRNA vaccines

To remember how the mRNA vaccines work, here is a short reminder. The messenger RNA injected in the upper arm stimulates the organism of the vaccinated individual to synthesize the "spike protein," an essential part of the virus. The messenger RNA is "read" within the cell's Ribosome to "produce" the spike protein. The organism of the vaccinated person recognizes, what was synthesized as "foreign", and develops an immune response against the spike protein. The idea is that when the Covid-19 virus attacks, immunity against the spike protein of the virus, is already stimulated and prevents the virus from entering the cells of the vaccinated person.

Reverse transcription and impaired DNA repair

A crucial point is the question, what happens with the "spike protein" synthesized within the vaccinated individual after it creates the immunity against the virus. Another concern involves whether the mRNA injected finds its way into the cell's nucleus, and alters the DNA there, a process called "reverse transcription". Initially, the public was assured that the synthesized "spike protein" eventually would vanish and the DNA within the nucleus won't be altered by the mRNA injected through the vaccine. It turned out that this affirmation might not be entirely accurate. In vitro experiments showed that reverse transcription takes place and interferes with the setting up of the "adaptive" immunity.

The aim of a vaccine should be to create a specific, "adaptive" immunity against an invading germ. The main task to achieve this rests with the B- and T- cells through a rather complicated process described as V(D)J Recombination. It is known from clinical studies that patients exhibit an insufficient adaptive immune system while severely suffering from Covid-19 infection (1, 2). In vitro experiments with a cell line showed that the spike protein was found in the cell nucleus interfering with the V(D)J Recombination process and damaging the DNA repair. DNA repair is a vital mechanism that prevents cancer development, besides many other valuable effects. The authors of the publication concluded that "what had been observed in the cell line might not only

take place in severe Covid-19 infection but also might be an aftereffect of vaccines based on the full-length of the spike protein" (Jiang, H. and Mei, YF: Sars-CoV-2 spike impairs DNA damage repair and inhibits V(D)J recombination in vitro) **. The publication was retracted but still is available through google search.

Another publication implies that the vaccine's mRNA finds its way into the nucleus and is still available. The intention was to find out why PCR tests in patients are still positive long after they overcome the infection. It turned out that in the culture of human cells, reverse-transcribed SARS-CoV-2 RNA could be found integrated into the genome of cells (3). What the native virus could achieve might also be possible for the vaccine mRNA. That could be demonstrated in vitro in a human liver cell line for the BioNTech mRNA vaccine (4).

Whether the result of the two publications is proof for the claim that mRNA vaccines are products of genetic engineering is still debated since the definition of genetic engineering involves the genetic code in the nucleus. The mainstream media rejected that on the ground that the paper about the DNA investigation was technically not sound, and the paper, therefore, was retracted. A scientist close to the pharmaceutical industry objected the second paper, about the liver cell line. The comment to the publisher claimed that in vitro results cannot be extrapolated to what happens in healthy individuals, and the vaccine dose in the experiment was much higher than would have been used in vivo.

Risk assessment of the mRNA vaccines and the reaction of the pro-vaccine camp

One controversial issue is the possibility of reverse transcription of the mRNA from the vaccines. Another question is what additional effect the mRNA of the vaccine has once the production of a "foreign" spike protein has been achieved. It is claimed that the mRNA doesn't simply disappear finally but might cause serious side effects (5). A most recent publication of the Journal of "Food and Chemical Toxicology" concluded in the abstract that "a comprehensive risk/benefits assessment of the mRNA vaccines questions them as positive contributors to public health".

The aggressive, hatred response to the publication indicates that an open, unbiased scientific discussion about the pros and cons of the mRNA Covid-19 vaccines are no longer possible. Not the paper's scientific content is discussed, but the credibility and integrity of the authors are questioned. Even false allegations served an Institute for Strategic Dialog to discredit the paper's content claiming it to be a preprint, but that's untrue since it went through the referee process. The fury of the pro-vaccine camp probably is explained in that the manuscript was read about 250.000 times within three weeks on ResearchGate.

The "engineered" spike protein and its side effects

The paper from Seneff et al. (5) could be interpreted as a risk assessment based on the interference of the vaccines with the "molecular biology of the human cells". Possible adverse effects of the mRNA vaccines are explained by relevant findings in immunity, virology, and vaccinology. Over 220 citations allow us to trace back the affirmations and argue against them. Finally, the authors tried to verify the claims about the risk involved in using the mRNA

vaccines with data from the "Food and Drug Administration's Vaccine Adverse Event Reporting System (VAERS)" in the USA.

The vaccine's mRNA is dissimilar from the mRNA of the virus

The mRNA vaccines technique, as a "genetic vaccination tool," are useful for creating immunity against cancer (6), and some rarely occurring metabolic disorders, such as Fabry disease, an inherited condition from the parents interfering with the lipid and fat metabolism, for which a definitive therapy is not available (7). The technique requires that the mRNA be transported into the cell, overcomes the innate immunogenicity, and finally stimulates the required adaptive immunity against the exogenous RNA (8). The various method used to achieve that goal, however, makes the mRNA of the vaccine to be somewhat dissimilar from the exogenous RNA of the virus and might interfere in numerous ways with the cellular homeostasis with the possibility of severe side effects and, unfortunately, also death for very unfortunate recipients of the vaccine. For those with an essential background in molecular biology, microbiology, and medicine, the paper of Seneff et al. (2022) (5) is an interesting and exciting excurse through immunology and associated fields. Yet, all the details cannot be reviewed here. The principal potential harmful effects are mentioned in the headline of the publication. It involves the suppression of the innate immune system and the functions of exosomes, microRNAs, and G-quadruplexes.

Suppression of the innate immunity by mRNA vaccines

A vital component of the innate immunity are cytokines, including the interferons (IFN). There are three types of IFNs, of which type I is of specific interest. Type one is subdivided into IFN-α and IFN-β. There are more than 17 subtypes functioning within the immune system against viral infection, neoplasms, and autoimmune diseases. There is a whole range of IFN regulatory factors (9) out of which the IRF9 is essential for regulating immunity against viruses, genetic alterations, and tumors (10). Once the Covid-19 virus enters the cell facilitated by the spike glycoprotein, the cell starts to produce microRNAs. MicroRNA are recently recognized as important tools for gene regulations. They can travel to any given tissue, for instance, to the microglia of the nervous system. In the case of SARS-CoV-2, the infection suppresses the IRF9, which prompts pro-inflammatory gene expression and activates the human microglia. Microglia are macrophages of the central nervous system. Macrophages are found in almost all human tissue produced by monocytes, which belong to the white blood cells. This chain of events creates neuroinflammation, with explains several neurological symptoms observed in Covid-19 infection (11). What is described here about "inflammation" could happen in almost all tissues of the organism and, unfortunately, is not restricted to the infection. The vaccine spike protein synthesized by the immune system of the vaccinated individual not only has the same effect as the exogenic spike glycoprotein but is designed to be particularly effective. Unfortunately, the effectiveness also means that the vaccine impairs the type I IFN protective roles, such as innate immunity as the first attempt to fight against viruses and bacteria. Still, it also enhances the risk of developing cancer through several complex regulations. The effectiveness of the vaccine's mRNA is achieved, among other tricks, by codon optimization.

Codon optimization and effectiveness of mRNA vaccines

Among the features of the secondary structure of the mRNAs of the vaccines is a high guanine-cytosine content amounting to 53% in Pfizer's BNT162b2 and 61% in Moderna mRNA -1273, while the native mRNA from the virus accounts for 36%. The high GC content can result in Guanine quadruplex (G-quadruplex), a process called codon optimization used in biotechnology therapeutics. The technique improves the quantity of polypeptide and proteins with potentially unfavorable results, particularly for mRNA vaccines (12) and, among other effects, is related to neurological diseases (13).

In this context, particular attention was given recently to the human prion protein (PrP) (14). The protein on the cell surface has several physiological functions within the nervous and immune systems. The gene of the prion protein has multiple G4-forming sequences. A hypothesis linked G-quadruplex formation to the rare event of "misfolding" PrP into PrPsc, which is discussed as one factor related to Alzheimer's disease (15). Misfolding might happen when the prion binds to its mRNA. Also, the spike glycoprotein of the virus has "prion-like characteristics" (16), as well as the spike protein of the vaccines.

Recently, Spongiform Encephalitis (Creutzfeldt-Jakob Disease) cases were reported after vaccination from Turkey (17). The pharmaceutical sector quickly rejected reports about the mad cow disease following vaccination as fake news. While writing this manuscript, additional reports about several cases in various countries appeared again in the international press (The Epoch Times, 5th June 2022).

The role of exosomes in mRNA vaccine side effects

Codon optimization is not the only "smart" technique to enhance the vaccine's effectiveness. These techniques let the vaccine produce spike glycoprotein up to 60 days after vaccination. The long-lasting production of spike glycoprotein was detected after investigating lymphoid tissue where the mRNA was found in the "germinal centers" (18). The lymphoid tissue and the neurological system mentioned here as examples are not the only possible predilection for the side effects of the mRNA vaccines. Many other systems of the organism can be involved. As mentioned above, the glycoprotein spike-initiated production of microRNAs traveling quickly utilizing exosomes to almost any given organism's location.

In health and disease, cells release extracellular vesicles, which assure normal physiological function but are also related to abnormalities. There are two kinds of vesicles, ectosomes, and exosomes. The vesicles can contain various "constitutions" of a cell, such as DNA, RNA, lipids, and other metabolites (19). Exosomes are involved in "cellular communication" and are therefore related to a broad spectrum of the function of the organisms. In the context of mRNA vaccines, this mirrors the immune response to the viral infection and even aggravates the pathogenicity of the mRNA vaccines. With the exosomes, through the bloodstream, the vaccine-initiated spike glycoproteins travel, as mentioned above, to other locations, causing inflammation with the subsequent reaction of the given organic system with system-specific symptoms. The symptoms are diagnosed as myocarditis, myocardial infarction, thromboembolism, autoimmune diseases, and neurological diseases. Since the Immune system, as mentioned above, might be

impaired, so is the repair mechanism for DNA. The result also might be side effects in the long run, such as developing cancer and blood diseases in the future.

Fortunately, our immune system is good enough to fight back even against the "smartest" vaccine development program. The spike glycoprotein can also be attacked, and fragments are taken away from t-killer cells within and outside of the cell. Finally, the risk of experiencing an adverse effect after vaccination by no means necessitates that those vaccinated will be affected. Up to now, millions and millions of people have been vaccinated without suffering from severe side effects. Still, those unfortunate individuals suffering from a severe disease, being disabled for the rest of their lives, or even dying must be a severe concern to all health authorities.

Why risks were not detected during the trials– the example of the Ventavia Research Group

However, one would expect that these complex risks to our "molecular biology" would have appeared more obviously during the trial phases. Quite a few papers were published, and some were even discussed in this blog at the beginning of the pandemic, warning to go ahead in haste. All this was ignored, and even the trial phases seem not to be executed as required, judging by the following example (20):

Problems became known during the trial phase III of the Pfizer trials because of a "whistleblower". External research organizations help pharmaceutical companies in phase III trials. For the mRNA product of Pfizer, this was the "Ventavia Research Group". Testing involved 44.000 participants from 153 sides around the world. A regional research director observed mistakes in data collection, in that information were obtained from "unblinded" patients, not well-trained vaccinators, and inadequate follow-up of side effects. Those being vaccinated were not monitored adequately. Research protocols were not followed as agreed upon. Vaccines were not stored keeping the correct temperature. The label of laboratory specimens was not correct. The research director informed her superiors several times without a reaction from their side. Finally, she contacted the US Food and Drug Administration (FDA) and immediately was thrown out by Ventavia. The FDA thanked her for the information but didn't follow up on the issue.

Is there an attempt not to let us know much about vaccinations' side effects?

In the meantime, there is a long list of serious diseases which were not detected during the trial phases. A comprehensive list is difficult to come by since the WHO database does not easily allow data to be compiled as being claimed by media outside the mainstream, such as scienceFiles.org***. Recently it was reported that the database VAERS, mentioned above, altered its data set by taking out several records. Common side effects, such as fever, headache, pain at the injection site, etc., are supposed to be tolerated. Diseases formerly by no means well known, such as Guillain-Barré syndrome, are now almost even known by the public. Myocarditis or Pericarditis is not that seldomly observed in middle-aged males, being public figures as sportsmen. Reports about the side effects of the vaccines for children are entirely missing, and the public is encouraged to vaccinate students and schoolchildren, toddlers, and even babies. The risk of vaccination for pregnant women and the pregnancy outcome remains to be laid open to the public. Children and pregnant women most likely are prone to serious side effects of the

mRNA vaccines, too, given what is known by now about the impact of the vaccines on the complex human biology and the immune system.

Outlook

It was mentioned in a previous entry to this blog that .."What can be done with the omics technology and machinery on hand to design a new vaccine is fascinating". The technique has already proved its value for animal curative medicine and disease prevention. History has shown that any advancement in technology cannot be stopped from being applied. However, before the Covid-19 pandemic, the mRNA technique was used cautiously. Still, it was pushed to the forefront now to fight against the virus, neglecting warning voices even from formerly highly respected experts. At the end of the year 2021 (2564), it became evident that vaccination didn't prevent the infection, nor prevented vaccinated individuals from transmitting the virus to others, and it also might not help to soften the impact of the infection for those suffering from the SARS-CoV-2 disease (21, 22).

Historians might find a reason in the future why a relatively harmless virus caused a standstill in the world at the beginning of the third decennia of the twenty-first century. Finally, it should be concluded whether lockdowns and vaccinations saved human lives from falling victim to the virus or whether more lives were lost because of unsuitable counteractions. However, governments and health authorities, especially in Southeast Asia and Africa, drawn into the calamity, shouldn't be blamed and made responsible for any wrongdoings. The WHO, the pharmaceutical industry, and those in the related field of science being investigators or administrators paved the way for what might be judged later as meaningful management of an emergency or a misguided hazardous experiment. The Thai government tried its best to cushion the damaging aftereffects of the pandemic. The health sector on all levels efficiently cared for the diseased, counteracted the spread of the disease, and efficiently vaccinated the population demanding the treatment.

* Unfortunately, there is a mistake in the conclusion of the "Introduction into Immunology". The forefathers of modern vaccination are Jenner and Pasteur. The Humboldt brothers had their merits for science in the 19th century but had nothing to do with immunology and vaccination.

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***Accessible through Telegram

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Frank P. Schelp is responsible for the content of the manuscript, and points of view expressed might not reflect the stance and policy of the Faculty of Public Health, Khon Kaen University, Thailand

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