Letter to Editor

Will the mRNA Vaccines Interfere with One's DNA?

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Abstract:

As the number of COVID-19 cases continues to rise with over 65 million recorded cases and more than 1.5 million mortalities as of early December, the race against time to find a vaccine intensifies. In recent years, there has been growing interest in mRNA-based technology for the development of prophylactic vaccines against infectious diseases and even for cancers and allergies. The prospects for mRNA vaccines are very promising because of their high potency, capacity for rapid development and potential for low-cost manufacture and safe administration. However, until now, no vaccines using this technology have made it this far in clinical trials thus there have been concerns on the therapeutic and possible adverse effects and claims especially on social media that the vaccines will alter the DNA. This article discusses the unique attributes of mRNA vaccines and current challenges and expectations within the context of the COVID-19 pandemic.

Keywords: COVID-19; pandemic; vaccine; mRNA; DNA

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The Pfizer-BioNTech and Moderna COVID-19 vaccines are mRNA (messenger RNA) vaccines that rely upon the mRNA to induce an immune response and produce protective antibodies. During the process of transcription, RNA polymerase makes a copy of a gene from its DNA to mRNA as signaled by the cell. The mRNA sequences in the cell is a direct copy of the DNA sequences in our genes[1,2].

The mRNA strand exits the nucleus and enters the cytoplasm (with a carrier lipid nanoparticle). The mRNA which carries the genetic message then attaches to the ribosomes, where translation occurs, which codes for amino acids to make proteins[1].

The vaccine mRNA instructs the ribosomes to create the S-proteins. These are spikes on the coronavirus which acts as the antigen. These antigens will leave the cell and triggers the body's immune system to produce neutralizing antibodies [3].

The antigens (S-protein) produced by the mRNA are biologically inert. They will induce an immune response, but they will not cause any other biological effect, they are harmless. Thus, DNA makes RNA makes protein. Once the mRNA has created a protein, it is then broken down into individual nucleotides to be reused by the cell.

The mRNA only reads the DNA information and carries it to the ribosomes which produce the S-protein antigen. As mRNA, it does not need to persist any longer after the protein has been made. RNA is an inherently unstable molecule and is rapidly degraded[4].

The instability of RNA is why public health experts have been concerned about the logistics of distribution of RNA vaccines. The Pfizer-BioNTech vaccines must be stored at the arctic temperature of –70 °C [5]. The Moderna vaccine remains stable in a standard –20 °C freezer for up to six months, under refrigeration (2–8 °C) for up to 30 days and at room temperature for up to 12 hours [6].

Our DNA lies in the nucleus of the cell surrounded by a double-membrane. It allows the mRNA to leave the nucleus, but blocks them from entering it. So the vaccine mRNA cannot enter the nucleus until it is broken down into smaller single nucleotides which are harmless. Even if it could get into the nucleus, the DNA has protective mechanisms to deal with it.

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Hence, the vaccine mRNA cannot interact with our DNA[3].

If anything, the use of mRNA is safer than whole virus or DNA delivery because the mRNA is not infectious and cannot be integrated into the host genome [3,4]. DNA vaccines need to reach the nucleus to be decoded, while mRNA is processed directly in the cytoplasm.

We are only 9 months into the vaccine trails and therefore do not have long-term safety data. The mRNA vaccines can cause short-lived side-effects, including pain at the injection site, fever, muscle aches and pains, headache and fatigue [5]. In the short term, there are no safety signals.

With the approval for the use of the Pfizer-BioNTech vaccine in the UK and pending Emergency Use Authorization (EUA) in the US, will enable post-marketing surveillance and pharmacovigilance to evaluate the effectiveness of the vaccine in real world experience and the lookout for rare and major adverse effects following immunizations (AEFI)[7].

There is the small possibility that the S-protein could induce some immune cross-reactivity that leads to an auto-immune disorder but there are no red flags thus far [8]. Similarly, we also do not have any long-term data on the effectiveness of the vaccine. Does the immune response wanes over time? What is the duration of protection, a few months or a few years? Efficacy results reported for each vaccine were based on similar analyses — the number of participants who developed symptoms of COVID-19 and then had laboratory confirmations of infection, either one week after receiving the second of two vaccine doses spaced three weeks apart, in the case of the Pfizer-BioNTech trial, or two weeks after a two-shot, 28-day regimen with the Moderna vaccine. The Pfizer-BioNTech study of more than 43,000 volunteers confirmed 170 cases of COVID-19 cases, with 162 of those occurring among people given placebo shots resulting in vaccine efficacy of 95% [5]. The Moderna-NIH study registered 196 COVID-19 cases, 185 of which arose in the placebo group, yielding a point estimate vaccine efficacy of 94% [9]. The phase 3 trials were designed primarily to consider symptomatic disease. We still do not know whether the vaccines will prevent the transmission of the virus or simply keep people from becoming as sick upon infection.

We are hopeful that the vaccines will have some effect on transmission. If particles breathed out by asymptomatic or pre-symptomatic cases during talking and breathing transmits the coronavirus, then a vaccine that reduces symptoms would also reduce that. Or the vaccine by reducing a person's viral loads in the upper airway also cuts the amount they can transmit. Better still like the conjugated vaccines (pneumococcal and meningococcal), by conferring mucosal immunity, sterilizes the upper airway and prevents its emission into the air space and reducing spread of the coronavirus.

Thus far only the researchers at Oxford, using the viral vector Astra Zeneca vaccines have hinted that testing showed the vaccinated group in the UK had fewer asymptomatic infections, which means they'd be less likely to unwittingly spread the disease themselves.

Conflicts of Interest: Nil

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