

¹Is mRNA vaccine a vaccine or a gene therapy?

Menahem Brégégère, PhD, Molecular biology & genetics

Irène Fermont, MD, Immuno-hematologist, Pharmacovigilance

Short answer

Vaccination with mRNA has nothing to do with gene therapy. Gene therapy introduces genetic material in order to correct or replace a defective gene, as a treatment of genetic disease or a cancer.

Pfizer-BioNTech mRNA vaccine enables cells to temporarily express the Spike protein at their surface. It does not enter the nucleus. This limited exposure of the antigen is sufficient to trigger the immune response, without interference with cellular gene structure or function.

This vaccine confers immunity by means of a single protein. It does not introduce an infectious agent, even inactivated, into the cells. This new technology therefore has definite advantages in terms of specificity and safety.

To Know more (article)

1/ What is gene therapy?

The purpose of gene therapy in humans is to replace a gene or modify its expression, or to add a new function to the cells, in order to treat a disease in progress.

Gene therapy is defined by the US Food and Drug Administration (FDA) as "***a technique that modifies a person's genes to treat or cure disease***. Gene therapies can work by several mechanisms: - replacing a disease-causing gene with a healthy copy of the gene; -inactivating a disease-causing gene that is not functioning properly; - introducing a new or modified gene into the body to help treat a disease. Gene therapy products are being studied to treat diseases including cancer, genetic diseases, and infectious diseases" ².

2/ What is a messenger RNA?

The genetic information of a cell, which governs its biological functions, is specified by its genomic DNA. To be expressed, this information needs to be translated in the form of proteins, which are the effector molecules of the living cell.

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² US Food & Drug Administration, "What is Gene Therapy".

<https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy#:~:text=Human%20gene%20therapy%20seeks%20to,to%20treat%20or%20cure%20disease.&text=Replacing%20a%20disease%20causing%20gene%20with%20a%20healthy%20copy%20of%20the%20gene>

Rather than using DNA as a template to synthesize proteins, evolution has developed an intermediary molecule, messenger RNA (mRNA), which is a transient RNA copy of the DNA gene, that encodes instructions for protein assembly³[2]

3/ What is this RNA vaccine?

The Pfizer-BioNTech vaccine consists of the mRNA of the SARS-CoV-2, coding for the protein 'Spike' or 'S'; the mRNA is encapsulated in lipid microdroplets. When it enters the cytoplasm, this mRNA is translated into protein S, and the product is expressed at the cell surface. Then the immune system identifies this protein as a foreign antigen, and triggers the immune response. This method allows to reach immunity without introducing an infectious agent, which significantly increases its safety^{4, 5}[3],[4].

4/ Does a RNA vaccine interfere with cell genes?

At no time does mRNA interact with the cell nucleus or DNA. It is rapidly degraded by cellular enzymes without leaving traces. Its only function consists in temporarily enabling the cells to produce and express the S protein. Gene structure and function remains intact in the cells, let alone in their progeny⁶[5].

5/ Is the mRNA vaccine a real vaccine?

Unlike gene therapy, the purpose of RNA vaccine is neither to treat an existing disease, nor to correct a genetic defect, nor to modify cell physiology, but to produce an immunogenic protein and expose it to the immune system, in order to activate an immune response. It is a preventive therapy.

Classically, a vaccine is defined as "a substance containing a virus or a bacteria in a form that is not harmful, given to a person or an animal to prevent them from getting the disease that the virus or bacteria causes" [6]⁷.

With the advent of the new technologies, host cells can be educated to produce the immunogen (antigen) themselves, so that the definition needs to be updated: a vaccine is "a product that stimulates a person's immune system to produce immunity to a specific disease, protecting the person from that disease. Vaccines are usually administered through

³ S. Brenner, F. Jacob et M. Meselson, « An unstable intermediate carrying information from genes to ribosomes for protein synthesis. », Nature, vol. 190, 1961, p. 576-581.

National Human Genome Research Institute, "Messenger RNA".
<https://www.genome.gov/genetics-glossary/messenger-rna> .

⁴ N. Pardi, M. J. Hogan, F.W. Porter, and D. Weissman, "mRNA vaccines – a new era in vaccinology". Nature Reviews Drugs Discovery, vol. 17, 2018, p. 261-279. <https://www.nature.com/articles/nrd.2017.243>

⁵ J. Corum, and C. Zimmer, "How the Pfizer-BioNTech Vaccine Works". New York Times, 2020.
<https://www.nytimes.com/interactive/2020/health/pfizer-biontech-covid-19-vaccine.html> .

⁶ B. Dupuy, "Experts: mRNA vaccine for COVID 19 does not alter RNA". AP News, September 4, 2020.
<https://apnews.com/article/9340521654> .

⁷ Cambridge Dictionary, "Vaccine". <https://dictionary.cambridge.org/fr/dictionnaire/anglais/vaccine> .

needle injections, but can also be administered by mouth or sprayed into the nose"[7] ⁸. mRNA vaccines obviously fit this definition.

6/ Can mRNA sometimes integrate into genomic DNA?

As we have seen, the function of mRNA is to be translated into protein and then degraded. mRNA integration into the genome requires its prior conversion into DNA, an operation carried out by a particular enzyme called reverse transcriptase (RT). Reverse transcriptase is produced by retroviruses, such as HIV (AIDS virus), and enables integration of a RNA viral genome as DNA in infected cells [8]⁹.

But COVID 19 is not a retrovirus, and does not have a reverse transcriptase. A fortiori the mRNA vaccine, which codes only for the S protein, does not either. Hence mRNA reverse transcription can never occur, neither after COVID infection, nor after vaccination.

7/ Conclusion

mRNA vaccines have nothing to do with gene therapy.

Gene therapy introduces genetic material in order to correct or replace a defective gene, as a treatment of a genetic disease or cancer.

Whereas viral mRNA in the vaccine temporarily enables cells to express the spike protein on their surface, without entering the nucleus. This limited exposure is sufficient to trigger the immune response, without interfering with structure or function of the cell genome.

This mRNA vaccine confers immunity by means of a single protein. It does not introduce an infectious agent, even inactivated, into the cells. This method therefore has definite advantages in terms of specificity and safety.

⁸ Centers for Disease Control and Prevention, Definition of terms: "Vaccine".

<https://www.cdc.gov/vaccines/vac-gen/imz-basics.htm> .

⁹ A. Telesnitsky, and S. P. Goff, "Reverse transcriptase and the generation of retroviral DNA". In: Retroviruses. Cold Spring Harbor (NY): Cold Spring Harbor Laboratory Press, 1997.

<https://www.ncbi.nlm.nih.gov/books/NBK19383/>