

Pfizer and Moderna mRNA Vaccines Attack Bone Marrow Stem Cells and Drastically Alter Gene Expression

Researchers are also using LNPs/mRNA for gene editing. Three studies reviewed.

By [Dr. William Makis](#)

Theme: [Science and Medicine](#)

Global Research, September 11, 2023

[COVID Intel](#) 9 September 2023

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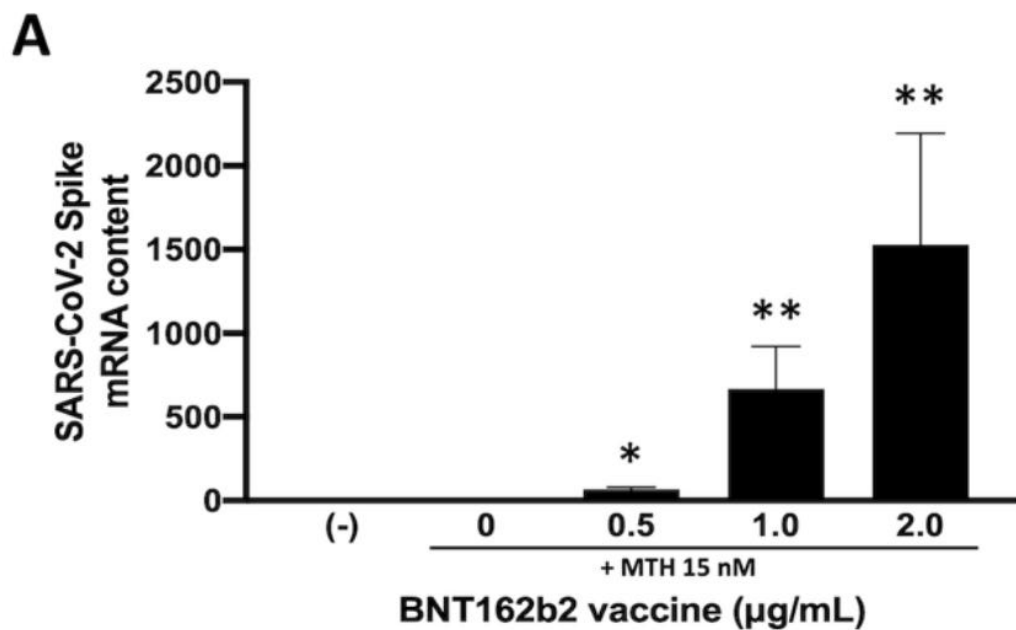
I review three recent papers:

- [Sep. 7, 2023 - Zurlo et al](#) - The anti-SARS-CoV-2 BNT162b2 vaccine suppresses mithramycin-induced erythroid differentiation and expression of embryo-fetal globin genes in human erythroleukemia K562 cells
- [Jul. 27, 2023 - Breda et al](#) - In vivo hematopoietic stem cell modification by mRNA delivery
- [Jan. 22, 2023 - Puccetti et al](#) - Biodrug Delivery Systems: Do mRNA Lipid Nanoparticles Come of Age?

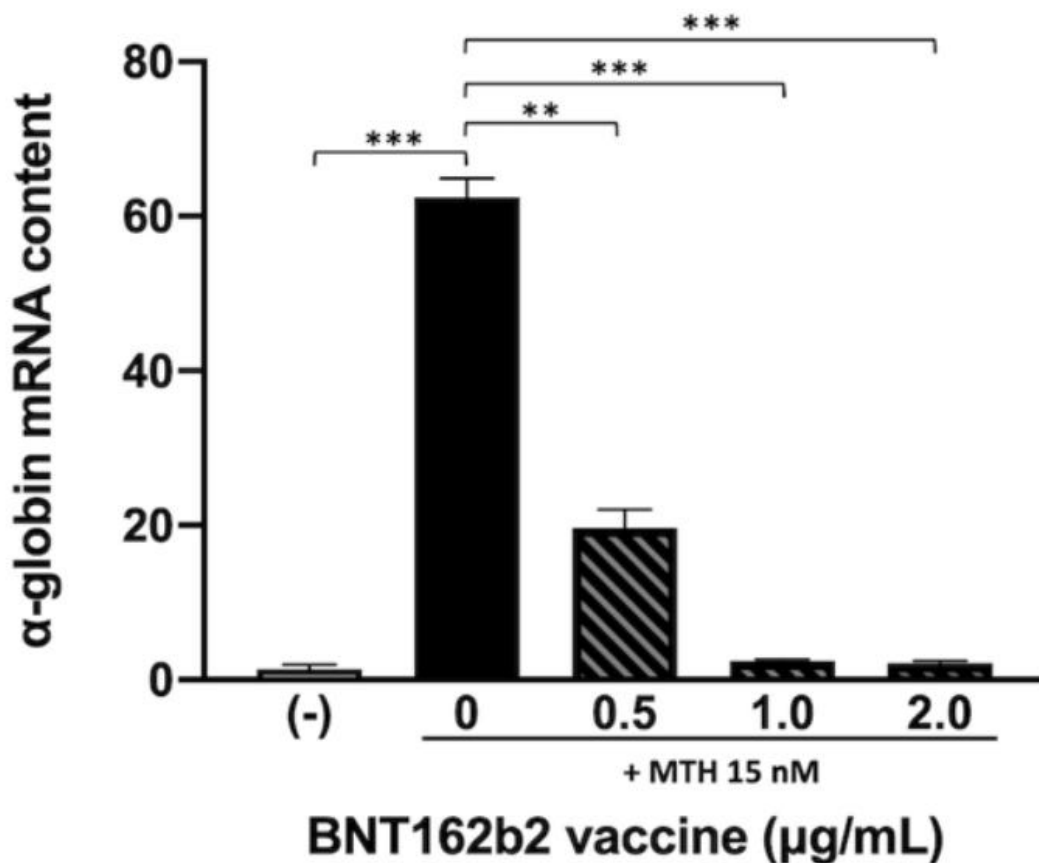
[Sep. 7, 2023 - Zurlo et al](#) - The anti-SARS-CoV-2 BNT162b2 vaccine suppresses mithramycin-induced erythroid differentiation and expression of embryo-fetal globin genes in human erythroleukemia K562 cells

- Italian researchers treated K562 stem cells with increasing concentrations of Pfizer COVID-19 mRNA vaccine
- What are K562 stem cells? - K-562 are lymphoblast cells isolated from the bone marrow of a 53-year-old chronic myelogenous leukemia patient. The K-562 cell line is widely used in immune system disorder and immunology research.
- What are lymphoblast cells? Immature white blood cells that develop into healthy immune cells called lymphocytes. In leukemia, lymphoblasts don't mature, instead they multiply rapidly in bone marrow and interfere with all blood cell production.
- researchers were able to inhibit the growth of stem cells as Pfizer dose increased

- Spike protein levels also increased with higher Pfizer mRNA doses
- Spike protein increased expression of pro-inflammatory genes through up-regulation of NF- κ B
- Spike protein drastically decreased expression of several globin genes
- Spike protein suppressed erythroid differentiation of stem cells
- “The impact of SARS-CoV-2 Spike protein on cellular functions is of key interest”
- “searching for circulating Spike in plasma of COVID-19 patient might help in understanding unexpected adverse effects following COVID-19 mRNA vaccination”
- Conclusion: “SARS-CoV-2 S-protein, COVID-19 mRNA vaccines and SARS-CoV-2 infection might have dramatic effects of the hematopoietic compartment”
- Conclusion: “need of great attention on possible alteration of hematopoietic parameters following SARS-CoV-2 infection and/or COVID-19 vaccination”



- Spike protein production rises dramatically with increasing doses of Pfizer mRNA vaccine. This rise appears exponential.



- Increasing doses of Pfizer mRNA vaccine cause dramatic suppression of globulin gene expression in bone marrow stem cells

[Jul. 27, 2023 - Breda et al](#) - In vivo hematopoietic stem cell modification by mRNA delivery

- This paper was published in “Science”
- Summary: NIH funded authors injected LNPs/mRNA and delivered them to bone marrow stem cells where they conducted gene editing and “bone marrow transplantation”
- [The researchers developed two payloads](#): one that edited a mutation for sickle cell disease, and another that selectively killed hematopoietic stem cells, which would eliminate the need for chemotherapy before HSC transplantation.
- If the therapies can be successfully adapted to people, this approach “will actually make gene therapy affordable, not only to our patients but also to our health care system,” says [Hamideh Parhiz, a biotechnologist at the University of Pennsylvania](#), who co-led the research.
- The researchers designed the lipid nanoparticles to target HSCs using an antibody that binds to the protein CD117, which is found on these cells’ surface.
- After confirming that the nanoparticles were [breaking through](#) into about half of blood cells, they loaded the antibody-coated nanoparticles with an mRNA encoding a protein that induces cell death.
- Although the nanoparticles killed HSCs, the researchers discovered some off-target effects, so they added tiny bits of noncoding RNA that kept the protein from killing other cells. “That’s when we got success,” Parhiz says.
- In another experiment, the researchers stuffed their nanoparticles with an mRNA sequence that produces a gene editor when it enters the cell. The editor targets

- a mutation in hemoglobin causing sickle cell disease.
- The researchers tested the gene-editing nanoparticles on cells grown from samples taken from people with the disease. Reversing the mutation resulted in more than 95% of blood cells taking on a typical round shape rather than the sickle-like appearance characteristic of the disease.
 - Parhiz and her colleagues are working on fine-tuning the approach and testing it further in animals to get a better understanding of how efficiently it edits intended genes and how well it targets HSCs.
 - The study is “an impressive advance,” says [David R. Liu, a chemist and gene editing expert at the Broad Institute of MIT and Harvard](#). Though many steps remain before clinical testing, he says, the approach “could lay a foundation for the much broader availability of programmable therapeutic gene editing to treat a variety of genetic blood disorders”

“A step toward stem cell engineering in vivo”

- [Journal Intro](#): Hematopoietic stem cell (HSC) gene therapy provides lifelong and substantial benefits for several life-threatening inherited diseases, such as primary immunodeficiencies, storage disorders, and hemoglobinopathies.
- Currently, HSC gene therapy requires harvesting large numbers of a patient’s hematopoietic stem and progenitor cells (HSPCs), which undergo gene transfer or editing ex vivo. Before infusion, the cell product is qualified to ensure that it meets rigorous safety and efficacy standards, and the patient undergoes conditioning chemotherapy to deplete endogenous HSPCs and make space for the engineered cells to engraft in the bone marrow.
- However, the need for laborious manufacturing and the toxicity associated with the conditioning regimen limits the broad application of these treatments.
- On page 436 of this issue, Breda *et al.* provide a proof of principle of in vivo genetic engineering of HSPCs in the bone marrow of mice by leveraging transient delivery of mRNA through lipid nanoparticles (LNPs) functionally coupled to antibodies that target HSPCs.

[Jan. 22, 2023 - Puccetti et al](#) - Biodrug Delivery Systems: Do mRNA Lipid Nanoparticles Come of Age?

- “Although recent research has largely focused on advancing mRNA vaccines and large-scale manufacturing capabilities, the technology has also been used to develop various immunotherapies, gene editing strategies, and protein replacement therapies.”
- “Lipid nanoparticles (LNPs) have emerged as a very promising delivery method. However, when intravenously delivering LNPs, most of the cargo is trapped by the liver”
- Modifying the composition of the lipids in LNPs allows for the more specific delivery of the LNPs to some organs

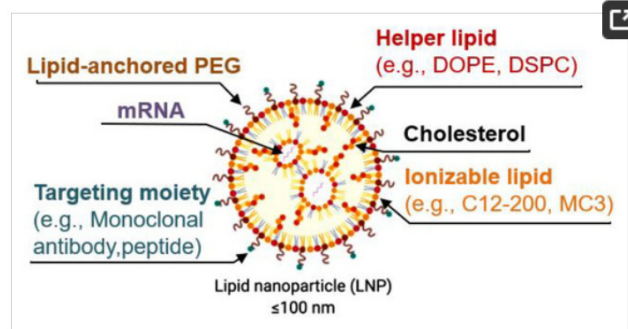


Figure 1. LNP formulation of mRNA. Components are mixed via chaotic mixing via microfluidic device. Interaction of lipid nanoparticle with the lipid bilayer of eukaryotic cells will then occur. Fusion merges the lipids of the nanoparticle with the ones in the cell membrane, ultimately releasing the contents of the nanoparticles inside the cell. Adsorption occurs when the nanoparticles are attracted to the cell membrane by electrostatic forces, ultimately promoting the release of the cargo inside. Lipid exchange happens when the lipids from the cell membrane and the ones from the nanoparticle switch. Endocytosis will then occur when the phagocyte cells engulf the nanoparticles. The inclusion of a targeting moiety—a target cell-specific biomimetic ligand meant to bind an appropriate acceptor on a cell type—is often referred to as nanoparticle surface “functionalization” or “decoration”, and it is meant to improve targeted delivery of the RNA cargo.

- “Messenger RNAs (mRNAs) present great potential as therapeutics for the treatment and prevention of a wide range of human pathologies, allowing for protein replacement, vaccination, cancer therapy, and genomic engineering”
- mRNA for vaccines: “Optimal vaccine targets can be quickly discovered through genetic sequencing, rapidly yielding templates for subsequent large-scale mRNA production. The rapid discovery process, synergistically paired with relatively inexpensive biomanufacturing costs for LNP formulations, have enabled mRNA vaccine candidates to reach clinical testing and receive regulatory authorization much faster than traditional vaccines.”
- Both Pfizer & Moderna mRNA vaccines “contain nucleoside-modified mRNAs that induce the membrane-bound expression of a perfusion-stabilized, full-length SARS-CoV-2 spike protein. In each case, the mRNA vaccines were formulated using LNPs for intramuscular injection. The rapid development and potent efficacy of these vaccines will serve as a strong benchmark for the advancement of future mRNA-based vaccines against a broad set of diseases.”
- “to increase the efficacy of mRNA-based vaccines, additional strategies such as self-amplifying mRNA vaccines are being developed.
- Self-amplifying mRNA vaccines use an engineered RNA virus genome in which the genes for the antigens of interest are inserted in place of those encoding the virus structural proteins while the genes for the virus RNA replication machinery are kept intact.
- In contrast to traditional mRNA-based vaccines, self-amplifying mRNA vaccines allow for the intracellular replication of antigen-encoding RNA, resulting in a higher level of antigen production that enhances vaccine efficacy.
- Self-amplifying mRNA vaccines show some difficulties compared with mRNA vaccines.
- They have a necessarily higher molecular size due to the presence of the viral-derived genes for the RNA replication machinery, which can also cause immunogenicity, thus limiting their potential repeated use
- Thus far, the self-amplifying mRNA vaccine platform has been applied against diverse viruses including influenza, Ebola, hepatitis C, rabies virus, *Toxoplasma gondii*, human cytomegalovirus, and HIV-1.
- mRNA for Gene Editing: “In addition to protein replacement and vaccines, more recently, the development of CRISPR (Clustered Regularly Interspaced Short

Palindromic Repeat) technology led to the application of mRNAs in gene editing and extended their use in pathologies requiring not only protein expression but also gene knockout”

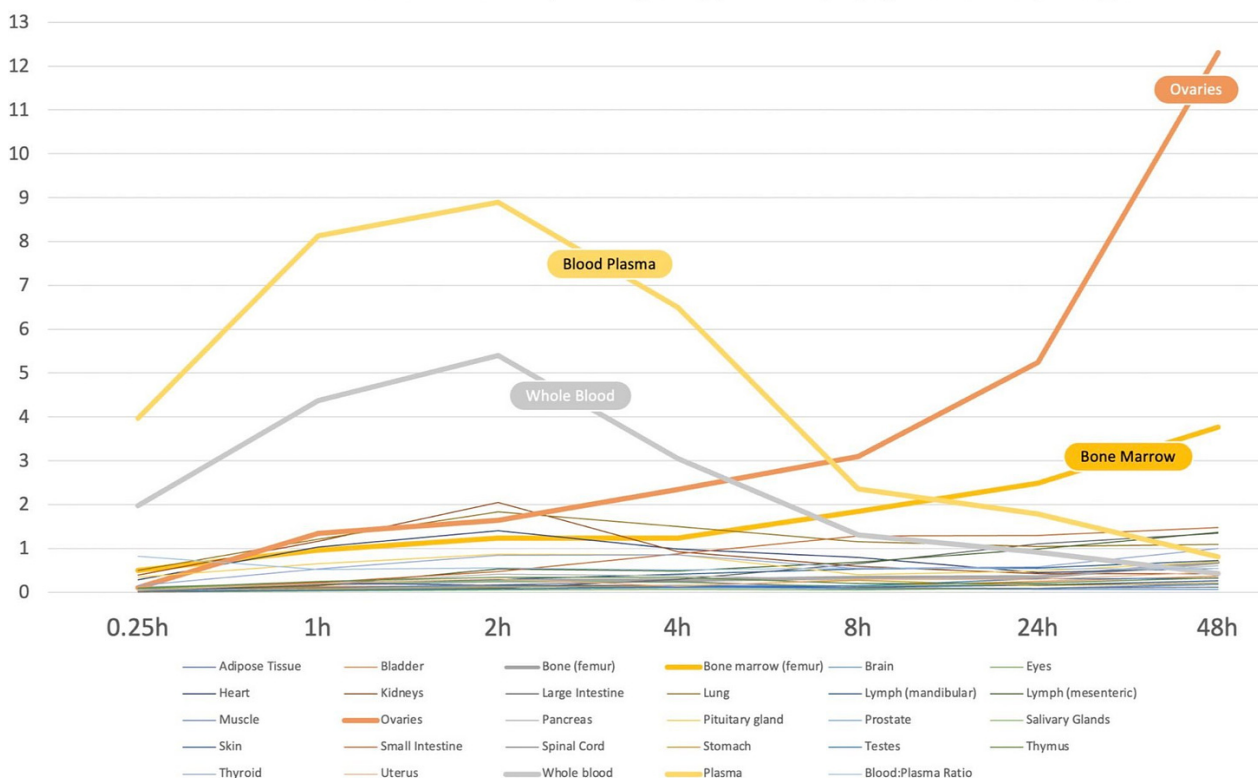
My Take...

We know from the Japan biodistribution study obtained by Virologist Dr. Byram Bridle, that Pfizer COVID-19 mRNA vaccine accumulates in the bone marrow.

Organ bio-distribution study: post-vaccination total lipid concentrations, mL

Pfizer mRNA Vaccine BNT162, PF-07302048

Obtained under Freedom of Information - Japanese Regulator (Byrum Bridle) <https://files.catbox.moe/0vvcjmj.pdf>



2.6.5.5B. PHARMACOKINETICS: ORGAN DISTRIBUTION CONTINUED

Test Article: [³H]-Labelled LNP-mRNA formulation containing ALC-0315 and ALC-0159
Report Number: 185350

Species (Strain): Rat (Wistar Han)
Sex/Number of Animals: Male and female/3 animals/sex/timepoint (21 animals/sex total for the 50 µg dose)
Feeding Condition: Fed ad libitum
Method of Administration: Intramuscular injection
Dose: 50 µg [³H]-08-A01-C0 (lot # NC-0552-1)
Number of Doses: 1
Detection: Radioactivity quantitation using liquid scintillation counting
Sampling Time (hour): 0.25, 1, 2, 4, 8, 24, and 48 hours post-injection

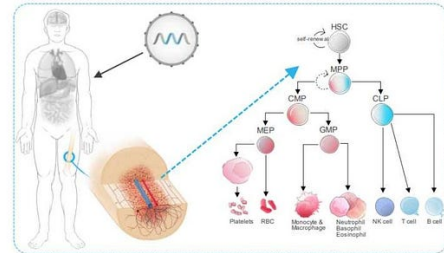
Sample	Mean total lipid concentration (µg lipid equivalent/g (or mL) (males and females combined))							% of administered dose (males and females combined)						
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h
Adipose tissue	0.057	0.100	0.126	0.128	0.093	0.084	0.181	--	--	--	--	--	--	--
Adrenal glands	0.271	1.48	2.72	2.89	6.80	13.8	18.2	0.001	0.007	0.010	0.015	0.035	0.066	0.106
Bladder	0.041	0.130	0.146	0.167	0.148	0.247	0.365	0.000	0.001	0.001	0.001	0.001	0.002	0.002
Bone (femur)	0.091	0.195	0.266	0.276	0.340	0.342	0.687	--	--	--	--	--	--	--
Bone marrow (femur)	0.479	0.960	1.24	1.24	1.84	2.49	3.77	--	--	--	--	--	--	--
Brain	0.045	0.100	0.138	0.115	0.073	0.069	0.068	0.007	0.013	0.020	0.016	0.011	0.010	0.009
Eyes	0.010	0.035	0.052	0.067	0.059	0.091	0.112	0.000	0.001	0.001	0.002	0.002	0.002	0.003
Heart	0.282	1.03	1.40	0.987	0.790	0.451	0.546	0.018	0.056	0.084	0.060	0.042	0.027	0.030
Injection site	128	394	311	338	213	195	165	19.9	52.6	31.6	28.4	21.9	29.1	24.6
Kidneys	0.391	1.16	2.05	0.924	0.590	0.426	0.425	0.050	0.124	0.211	0.109	0.075	0.054	0.057
Large intestine	0.013	0.048	0.093	0.287	0.649	1.10	1.34	0.008	0.025	0.065	0.192	0.405	0.692	0.762
Liver	0.737	4.63	11.0	16.5	26.5	19.2	24.3	0.602	2.87	7.33	11.9	18.1	15.4	16.2
Lung	0.492	1.21	1.83	1.50	1.15	1.04	1.09	0.052	0.101	0.178	0.169	0.122	0.101	0.101

On May 27, 2021, Moderna’s Fourth Annual Science Day, Moderna boasted about their

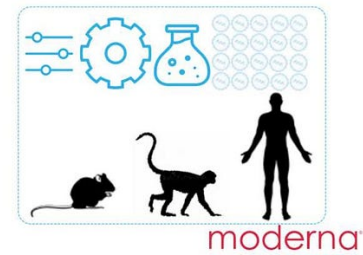
ability to deliver mRNA to the bone marrow, causing “long term modulation of all hematopoietic lineages” on page 113 of a document that is now impossible to find ([click here](#)):

Summary

- We have established in vivo mRNA delivery to the bone marrow, leading to HSPC transfection and long-term modulation of all hematopoietic lineages



- Different LNP formulations and repeat dosing can enhance transfection of mouse and NHP bone marrow HSPC, as well as human HSPC in humanized-mouse model systems



Slide 113

Key points from Zurlo et al paper:

- Pfizer COVID-19 mRNA vaccine accumulates in the bone marrow and can inhibit the growth & suppress the differentiation of bone marrow stem cells
- Pfizer spike protein can drastically alter gene expression in stem cells
- Pfizer spike protein can increase expression of pro-inflammatory genes
- spike protein production in bone marrow stem cells increases dramatically with increasing mRNA dose (looks exponential)
- authors conclude: “Pfizer spike protein might have dramatic effects on the hematopoietic compartment”

Key points from Breda et al and Puccetti et al papers:

- LNPs/mRNA can be delivered to bone marrow stem cells where they conduct gene editing and bone marrow transplantation
- LNPs can be modified via a surface “decoration” to improve targeted delivery of mRNA cargo
- mRNA can be encoded with a protein that induces bone marrow cell death
- mRNA can also be encoded with sequence that produces a “gene editor” when it enters the cell
- LNP/mRNA is repeatedly referred to as “gene therapy” and a platform for “genetic engineering” including “gene editing strategies”.

My Concerns...

- All these recent papers downplay the dangers of the LNP/mRNA platform and completely ignore the millions of COVID-19 mRNA vaccine injuries & deaths, pretending they are not happening as they push forward
- COVID-19 mRNA vaccines are being referred to as a “resounding success” even

though they are a complete failure.

- Pfizer COVID-19 mRNA vaccine messes with bone marrow stem cells, affects their growth and differentiation, the clinical implications of which we don't understand. Can this lead to turbo cancers such as leukemias?
- Pfizer COVID-19 mRNA vaccine alters gene expression in bone marrow stem cells the clinical implications of which we don't understand.
- Spike protein production in stem cells is not linear - slightly more mRNA can lead to exponentially higher spike protein production - may partly explain severity of COVID-19 mRNA vaccine injuries in someone who may have received only slightly higher concentration of mRNA in their vaccine dose.
- LNP/mRNA is a gene therapy, and a platform for "genetic engineering" including "gene editing strategies".
- Slight modification of LNP's external "decoration" can drastically impact where LNPs get delivered. Researchers are already playing with these modifications.
- LNP/mRNA technology is being combined with CRISPR tech for gene editing.
- researchers are playing with "self-amplifying mRNA", which means that the mRNA will now be able to replicate itself within YOUR cells so you get exponentially higher levels of spike protein produced to "improve vaccine efficacy". As if we all need EVEN MORE spike protein.

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Dr. William Makis is a Canadian physician with expertise in Radiology, Oncology and Immunology. Governor General's Medal, University of Toronto Scholar. Author of 100+ peer-reviewed medical publications.

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