



People with vicious personalities cannot resist hurting others, even when it is not in their interests.

People do not necessarily behave rationally according to circumstances.

A metaphor for psycopaths, whose impulsive and vicious personalities often hurt the people they depend on.

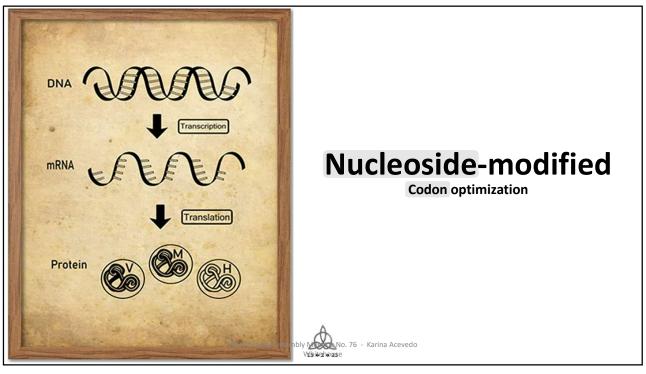
The scorpion **could not resist its natural urge to sting**, but it also chose to be honest about it to the frog ("certain charm and tragic dignity")

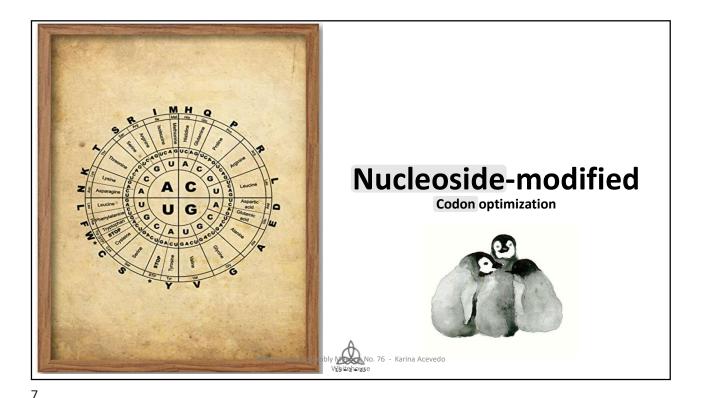


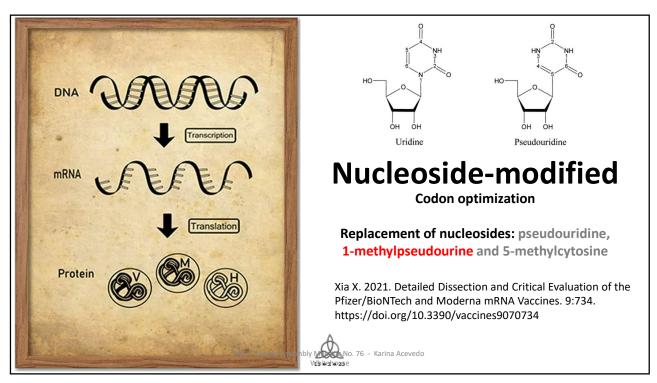


The impact of synthetic mRNA on health

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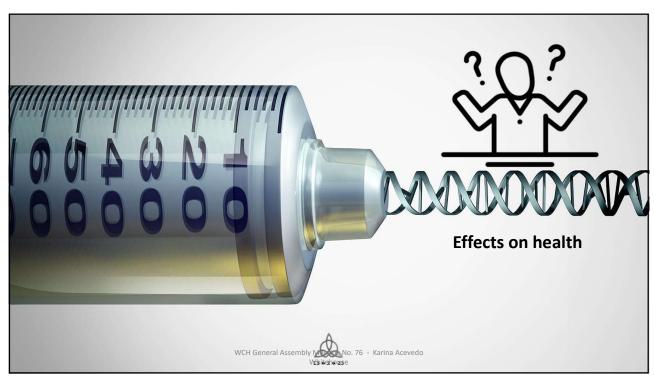
Nucleoside-modified

Codon optimization Replacement of nucleosides

Encased in LNP



C



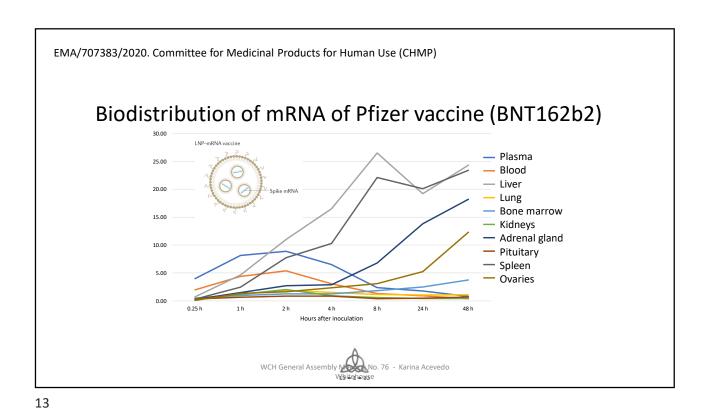


"High levels of safety"

- Biodistribution
- Cellular uptake
- Translation rates
- Functional half-life
- Endosomal escape
- Inactivation kinetics
- Rates/duration of antigen expression
- · Interactions with sensors of foreign RNA
- Interactions with host genome

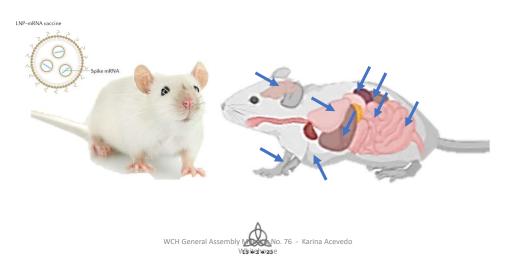
"We really do not know"





Bahl K. et al. 2017. Preclinical and Clinical Demonstration of Immunogenicity by mRNA Vaccines against H10N8 and H7N9 Influenza Viruses. Mol. Therapy 25:1316-1327. doi: 10.1016/j.ymthe.2017.03.035

Biodistribution of mRNA in vaccine prototype against Influenza





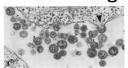
Zhang L. et al. 2021. Reverse-transcribed SARS-CoV-2 RNA can integrate into the genome of cultured human cells and can be expressed in patient-derived tissues. Proc. Nat. Acad. Sci. 118. https://doi.org/10.1073/pnas.2105968118

Evidence of viral subgenomic RNA integration into host genome

- Ebola virus
- Marburg virus
- Vesicular stomatitis virus
- Lymphocytic choriomeningitis virus

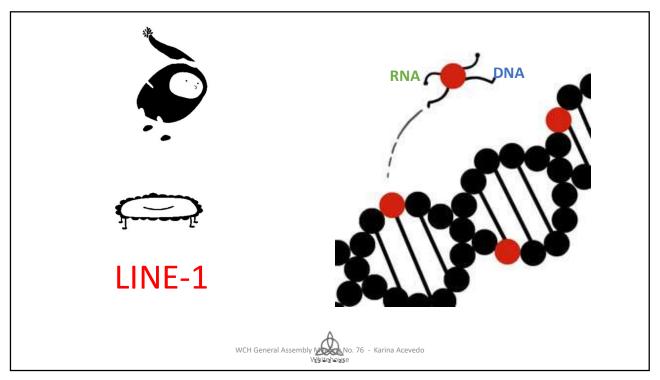


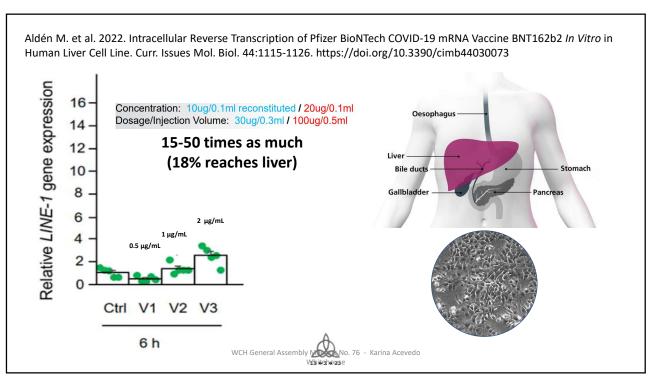


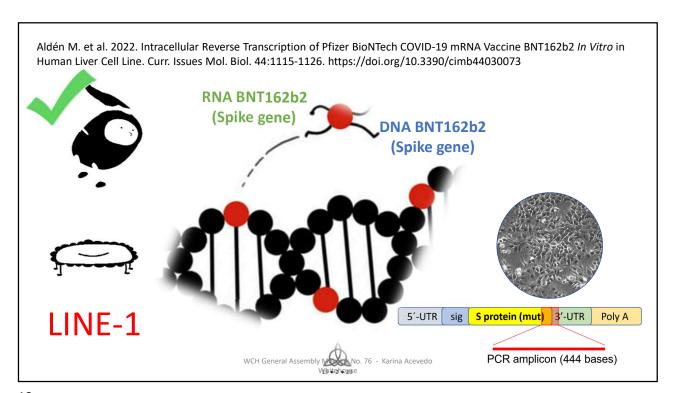


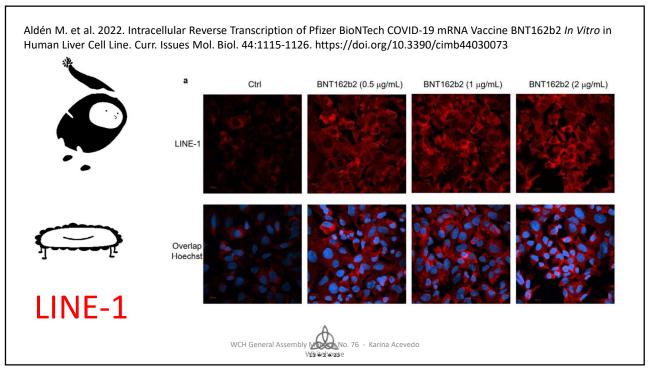
Activation of human retrotransposons (LINE-1)

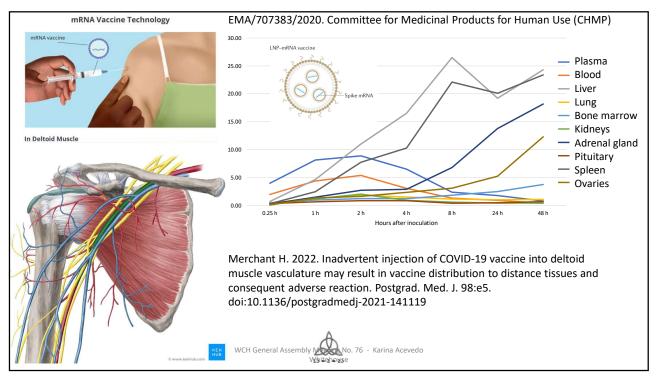


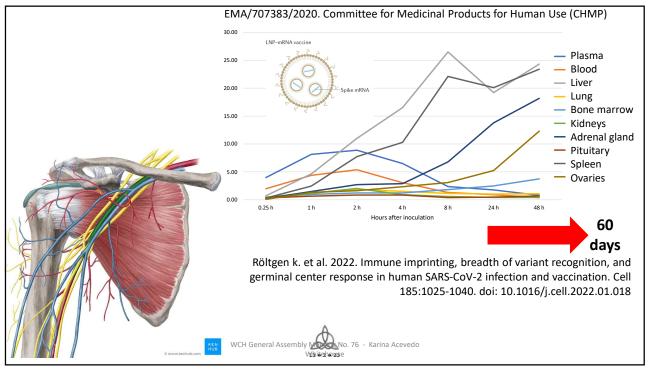












Merchant H. 2022. Comment on Aldén et al. Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 *In Vitro* in Human Liver Cell Line. Curr. Issues Mol. Biol. 44:1661-1663. doi: 10.3390/cimb44040113

In vitro in hepatic cancer cell line

#

In vivo in healthy human

mRNA concentration that reaches liver is likely to be lower than used in study

We really do not know this

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Merchant H. 2022. Comment on Aldén et al. Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 *In Vitro* in Human Liver Cell Line. Curr. Issues Mol. Biol. 44:1661-1663. doi: 10.3390/cimb44040113

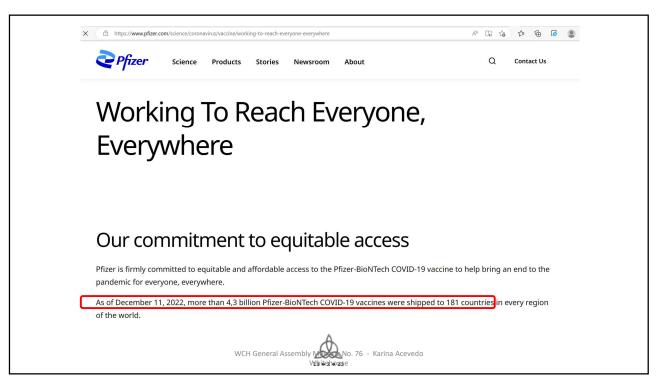
The in vitro data presented by Aldén et al. [1] without any in vivo validation in an appropriate animal model (for instance, the transgenic Fischer 344 Big Blue® rats in vivo mutation assay) can lead to misleading inferences. The current findings from Aldén et al. [1] may be detrimental to public confidence in mRNA therapeutics in general if not proven in vivo.

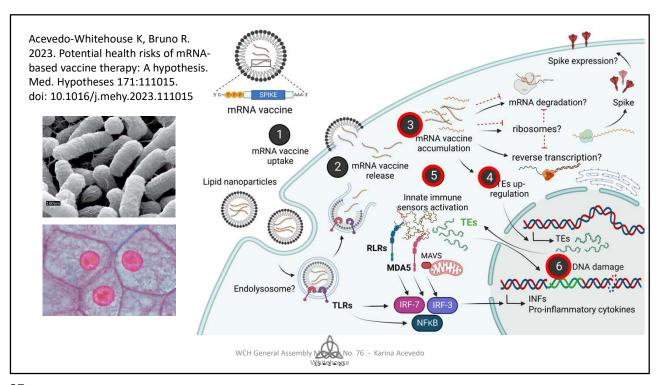
Aldén M. et al. 2022. Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 *In Vitro* in Human Liver Cell Line. Curr. Issues Mol. Biol. 44:1115-1126. https://doi.org/10.3390/cimb44030073

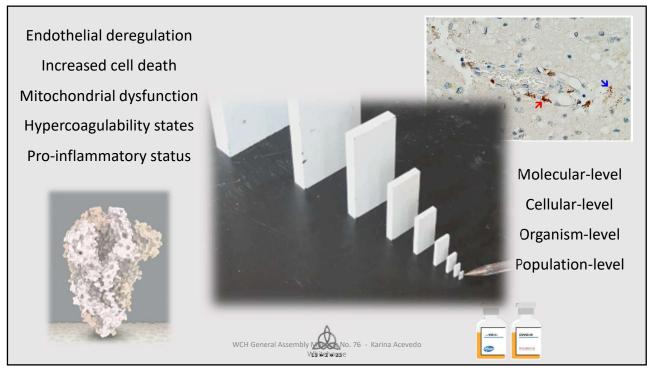
In the current study, we employed a human liver cell line for in vitro investigation. It is worth investigating if the liver cells also present the vaccine-derived SARS-CoV-2 spike protein, which could potentially make the liver cells targets for previously primed spike protein reactive cytotoxic T cells. There has been case reports on individuals who developed autoimmune hepatitis [39] after BNT162b2 vaccination. To obtain better understanding of the potential effects of BNT162b2 on liver function, in vivo models are desired for future studies.

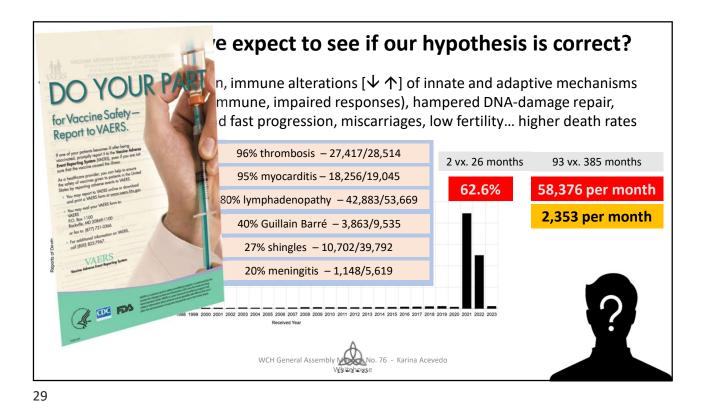


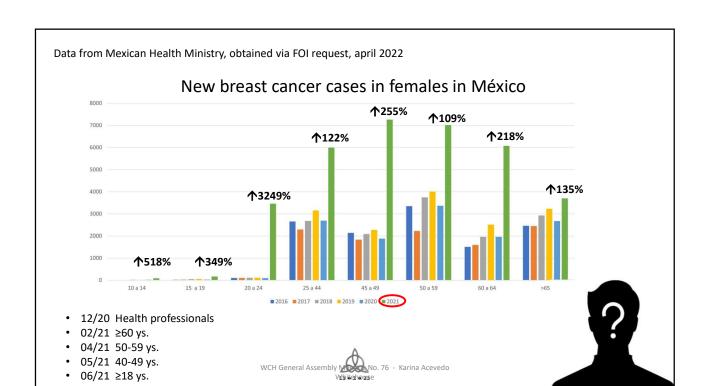




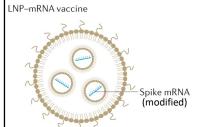








Would the same be expected for SARS-CoV-2 infections?









· Immune regulation is different between infected and injected

Gray-Gaillard SL et al. 2022. Molecularly distinct memory CD4+ T cells are induced by SARS-CoV-2 infection and mRNA vaccination. Preprint doi: 10.1101/2022.11.15.516351

Ivanova EN et al. 2021. SARS-CoV-2 mRNA vaccine elicits a potent adaptive immune response in the absence of IFN-mediated inflammation observed in COVID-19. Preprint doi: 10.1101/2021.04.20.21255677

Sureshchandra S et al. 2021. Single-cell profiling of T and B cell repertoires following SARS-CoV-2 mRNA vaccine. JCI Insight 6:e153201. doi: 10.1172/jci.insight.153201

Seneff S. et al. 2022. Innate immune suppression by SARS-CoV-2 mRNA vaccinations: The role of G-quadruplexes, exosomes, and MicroRNAs. Food Chem. Toxicol 164:113008. https://doi.org/10.1016/j.fct.2022.113008

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