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The history of mRNA vaccine

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Keywords: Messenger RNA, Vaccine, Virus.

Received: 18 April 2021

Revised date: 10 May 2021

Accepted: 02 June 2021

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Is messenger RNA (mRNA) vaccine a novel idea? Not completely true. These vaccines, although not commercially available, have been tested on humans. They have been used to combat viruses like Zika, Ebola, and Influenza in the past, albeit in trials [1,2]. This technique has been used to target cancer cells [3] and other genetic disorders as well although this has been limited to the *in vivo* studies.

But can you imagine that this miracle discovery, that could potentially save billions of lives, was actually a career dead end for the scientist Katalin Karikó in 1990. A Hungarian scientist who discovered the power of mRNA to fight disease but failed to garner backers in term of funding as most scientists regarded it as too far-fetched of an idea. As a consequence, in 1995, she was demoted from her academic post at the University of Pennsylvania. She also suffered from cancer the same year. But, still decided to carry on perusing the idea of mRNA manipulation [4].

The idea worked well in theory. The power of mRNA would be used to trick the body into making any desired protein, but the problem was that this synthetic mRNA when administered into the body would be quickly taken up by the scavenger cells and destroyed by the immune system before it had the chance to produce any protein. It took 15 years for Karikó and Weissman to modify the mRNA nucleotides into a sequence that would not trigger the body's immune system against it. The results were published in 2005 but remained unnoticed for a few years until they were picked up by the scientist who has now helped Moderna to design their vaccine, but it was a bumpy road. The young scientist, Derrick Rossi at Harvard Medical School, USA, first had the

idea of using this tweaked mRNA to make adult cells act like embryonic stem cells [5]. He succeeded in his endeavors in 2009. This work of his, led to the discovery of mRNA as the source of vaccine and drug delivery, and the rest as they say is a history [6,7].

The unique and ground breaking and potentially future Nobel prize winning idea of Kariko' and Weissman was the incorporation of pseudouridine (a naturally occurring modified nucleotide) into mRNA which helped make it non-immunogenic with increased translational capacity and biological stability. As we know that mRNA is made up of four nucleotide triphosphates: adenine, cytosine, guanine, and uridine. In their research, they modified all the four nucleotides and separately tested them *in vivo*. The result was that the pseudo uridine containing mRNA vector translated well *in vivo* and when injected in mice did not elicit high levels of TNF- α and INF- α [8].

So dear readers and future scientists, remember no idea is too far-fetched if you have the conviction. Follow Dr. Karikó's example, don't give up, keep doing research and you might change the world!

Conflict of interest

None to declare.

Grant Support & financial disclosure

None to disclose.

Ethical approval

Not applicable.

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