Understanding Messenger RNA and Other SARS-CoV-2 Vaccines

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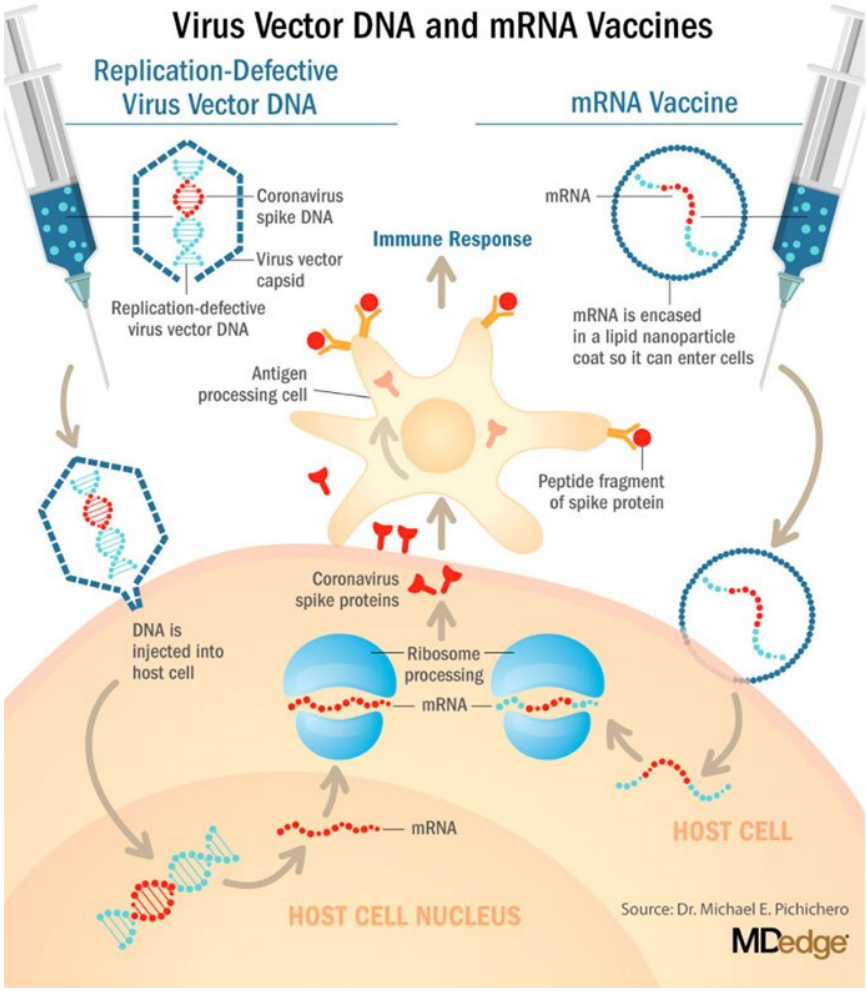
Editor's note: Find the latest COVID-19 news and guidance in

Medscape's Coronavirus Resource Center.

In mid-November, Pfizer/BioNTech were the first with surprising positive protection interim data for their coronavirus vaccine, BNT162b2. A week later, Moderna released interim efficacy results showing its coronavirus vaccine, mRNA-1273, also protected patients from developing SARS-CoV-2 infections. Both studies included mostly healthy adults. A diverse ethnic and racial vaccinated population was included. A reasonable number of persons aged over 65 years, and persons with stable compromising medical conditions were included. Adolescents aged 16 years and over were included. Younger adolescents have been vaccinated or such studies are in the planning or early implementation stage as 2020 came to a close.



These are new and revolutionary vaccines, although the ability to inject mRNA into animals dates back to 1990, technological advances today make it a reality.[1] Traditional vaccines typically involve injection with antigens such as purified proteins or polysaccharides or inactivated/attenuated viruses. mRNA vaccines work differently. They do not contain antigens. Instead, they contain a blueprint for the antigen in the form of genetic material, mRNA. In the case of Pfizer's and Moderna's vaccines, the mRNA provides the genetic information to synthesize the spike protein that the SARS-CoV-2 virus uses to attach to and infect human cells. Each type of vaccine is packaged in proprietary lipid nanoparticles to protect the mRNA from rapid degradation, and the nanoparticles serve as an adjuvant to attract immune cells to the site of injection. (The properties of the respective lipid nanoparticle packaging may be the factor that impacts storage requirements discussed below.) When injected into muscle (myocyte), the lipid nanoparticles containing the mRNA inside are taken into muscle cells, where the cytoplasmic ribosomes detect and decode the mRNA resulting in the production of the spike protein antigen. It should be noted that the mRNA does not enter the nucleus, where the genetic information (DNA) of a cell is located, and can't be reproduced or integrated into the DNA. The antigen is exported to the myocyte cell surface where the immune system's antigen presenting cells detect the protein, ingest it, and take it to regional lymph nodes where interactions with T cells and B cells results in antibodies, T cell–mediated immunity, and generation of immune memory T cells and B cells. A particular subset of T cells – cytotoxic or killer T cells – destroy cells that have been infected by a pathogen. The SARS-CoV-2 mRNA vaccine from Pfizer was reported to induce powerful cytotoxic T-cell responses. Results for Moderna's vaccine had not been reported at the time this column was prepared, but I anticipate the same positive results.

The revolutionary aspect of mRNA vaccines is the speed at which they can be designed and produced. This is why they lead the pack among the SARS-CoV-2 vaccine candidates and why the National Institute of Allergy and Infectious Diseases provided financial, technical, and/or clinical support. Indeed, once the amino acid sequence of a protein can be determined (a relatively easy task these days) it's straightforward to synthesize mRNA in the lab – and it can be done incredibly fast. It is reported that the mRNA code for the vaccine by Moderna was made in 2 days and production development was completed in about 2 months.[2]