

mRNA vaccines: How decades of basic science research delivered a vaccine quickly when it was urgently needed in 2020

Nearly 70 years ago, in 1953, the double-helix structure of DNA was first described, opening doors to understand how living cells divide and reproduce themselves so faithfully. Further investigation showed how DNA serves to manufacture proteins, the molecules which provide structure and function in cells. As it turns out, there is an intermediate step between DNA code and the building of proteins: DNA is first *transcribed* ("written") as a strand of messenger RNA (mRNA). mRNA is then *translated* into a chain of amino acids to become a protein. This is the *Central Dogma of Molecular Biology*.

Ever since this process was understood, research has been directed to use this information to improve human health. For decades now, many proteins - such as insulin, human growth hormone, and erythropoietin - have been produced in pharmaceutical labs and used to treat human disease. More recently, *proteins* such as antibodies to fight cancer and certain autoimmune diseases have been manufactured and given to patients. All of these proteins must be injected or given intravenously, however, which makes delivery difficult. The challenge has been to develop a strategy that would direct some of a patient's own cells to make the needed protein. *This is what has driven the interest in developing mRNA treatment techniques.*

Research into mRNA delivery systems has been going on for the past 30 years. Then, in 2013, it was discovered that specific segments of mRNA could be packaged in tiny lipid particles. That way, when delivered into the tissue of a recipient, the mRNA would be taken up by certain tissue cells and produce the specific protein encoded by that mRNA. When this protein was recognized by the immune system, antibodies would be produced directed to that specific protein. Over the past 7 years, the effectiveness and safety of this process has been evaluated.

In January of 2020, the novel coronavirus that brought us COVID-19 appeared on the scene. Right then, 18 months ago, there was a great need for a specific vaccine to protect people from this new pathogen. The long years of basic research and of development and testing of mRNA vaccines had arrived at a crucial time in human history. A vaccine was needed as the COVID-19 pandemic swept across the United States and around the world. Because of the ongoing research into mRNA delivery systems, a vaccine could be manufactured, tested for effectiveness and safety and delivered much more quickly than previously possible, using older techniques.

Fortunately, vaccination allows patients to generate specific antibodies to the coronavirus spike protein to protect against this latest viral threat, which has killed over 600,000 Americans in the past year. The challenge now is to move beyond misunderstanding and to deliver vaccinations, protecting not only the individuals who receive them, but also those with whom they come into contact.