Comirnaty®

Pfizer-BioNTech's COVID-19 Vaccine

The discovery of a new way to stabilize coronavirus spike (S) proteins back in 2016 by National Institute of Allergy and Infectious Diseases (NIAID) inventors and their collaborators became a critical piece in Comirnaty®, colloquially known as the Pfizer vaccine.

Discovery

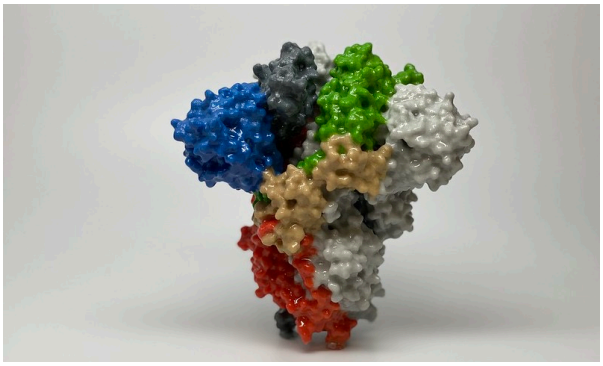
Dr. Barney Graham, former Deputy Director of the Vaccine Research Center, and his team used cryogenic electron microscopy to capture images of HKU1 proteins. From these images, the team was able to determine the structure of HKU1 S proteins in their prefusion form. They used this structure to guide their work to engineer the S protein with the goal of stabilizing the spike in its prefusion conformation. They discovered that adding two prolines, or rigid amino acids, to a specific location in HKU1's S protein, would stabilize the protein in its prefusion form. The team called this the "2P" mutation and the entire mutated S protein, "S2P." This finding suggested that the 2P mutation could stabilize the S protein of any coronavirus.

Role and Impact of Tech Transfer

Despite little commercial interest in coronavirus during the time of the discovery, the VRC team had the steadfast support of NIAID's Technology Transfer and Intellectual Property Office (TTIPO) in patenting and licensing the technology. TTIPO played a crucial role not only in ensuring the protection of this government-owned discovery, but also in serving as a broker to the dozens of commercial entities that were interested in licensing the technology.

TTIPO provided critical support to the team of inventors throughout the patenting and licensing process. The inventors first approached TTIPO when they crystallized the S protein of HKU1. TTIPO recognized that a patent application describing the HKU1 S protein structure would have limited utility but encouraged the VRC team to report its progress in applying their protein engineering expertise to modify the S protein and improve its usefulness in a vaccine. After stabilizing the S proteins for HKU1 and MERS using the 2P mutation, the inventors reported the invention to TTIPO.

> *Comirnaty wouldn't be possible without the support of NIAID's Technology Transfer and Intellectual Property Office. They really had to work hard to bring it all together.*
>
> - Dr. Barney Graham



3D print of a spike protein on the surface of SARS-CoV-2

Soon thereafter, TTIPO filed a patent application in October 2016 titled Prefusion Coronavirus Spike Proteins and Their Use (US Application 62/412,703).

By 2017, when TTIPO filed a follow-on application under the Patent Cooperation Treaty (PCT Application US2017/058370), the team had used the same approach in multiple coronaviruses. TTIPO hypothesized that, because the approach worked in every one of the 11 coronaviruses the VRC team tried, it should be possible to obtain patent claims for the use of the 2P mutation to stabilize any coronavirus. And so, they did. The patent describe es its technology as applicable to all coronaviruses.

Soon after China notified the World Health Organization (WHO) in December 2019 about a pneumonia cluster in Wuhan, TTIPO saw a flood of interest from commercial entities interested in licensing the technology for vaccine and diagnostic development. TTIPO managed relationships with dozens of commercial partners and provide the legal infrastructure to quickly license the technology to several companies. Availability of the NIH-developed prefusion S protein technology, has

- Contributed to the development of a COVID-19 vaccine in less than 12 months, the fastest on record and subsequently the first FDA-approved and most widely administered COVID-19 vaccine
- Enabled the development of the four vaccines available in the United States
- Helped boost the global supply of vaccines through WHO's COVID-19 Technology Access Pool
- Spurred innovation in vaccine research and development for other viruses.