nature

[insideview]

moderna

Profile Feature as seen in *Nature* 30 August 2018

REWRITING CELLULAR SOFTWARE TO MAKE MEDICINE IN THE BODY

A conversation with **Tal Zaks, MD**, Chief Medical Officer of Moderna

Moderna is using messenger RNA (mRNA) to develop a new class of medicines, from therapeutics to vaccines, in the areas of infectious diseases, immuno-oncology, rare diseases, and cardiovascular conditions. The company, which started in 2011, has 21 candidates in its development pipeline, nine in phase I clinical trials and one in and phase II, and has recently opened a state-of-the-art manufacturing plant.

How is Moderna creating new drug candidates?
We're using mRNA, which we think of as the software of life. It encodes the critical instructions from DNA that direct cells in the body to make proteins to prevent or fight disease. We are working to invent a new class of medicines that use mRNA to deliver these instructions so a patient's body can make vaccines to protect against viruses, or therapeutics that can fix or replace proteins that are functioning incorrectly.

What sort of drugs can be made this way?
We have a program in phase II that is being developed for heart disease by our partner AstraZeneca. Here, a protein called vascular endothelial growth factor (VEGF) is injected into the hearts of patients after a heart attack, with the goal of improving cardiac regeneration and specifically re-growing the vessels critical for blood flow.

Many of our phase I programs in the clinic are infectious disease vaccines. We have demonstrated that our mRNA platform is able to achieve immunogenicity in several vaccines. One of our vaccines, against cytomegalovirus, is actually a combination of six different mRNAs, which come together to form a multi-protein complex that can be recognized by the immune system. We believe our platform is uniquely suited for developing these types of complex vaccines, which, so far, have been difficult to create using traditional vaccine development approaches.

What other diseases might your technology treat?
We are also developing cancer vaccines and have two programs in partnership with Merck. One is a personalized cancer therapy where we make a unique vaccine for every patient. The other is a vaccine targeting KRAS, one of the most common oncogenes, and long considered the biggest undruggable target in the field of cancer.

We also have several rare disease programs in our pipeline. One area of focus here is our work to develop potential therapeutics for metabolic disorders, such as methylmalonic acidemia (MMA), and propionic acidemia (PA). There are no effective treatments for either of these diseases. Children with MMA and PA suffer from repeated metabolic crises because their cells are missing one enzyme. What we're trying to do is use mRNA to provide the missing information, so that patients can produce the missing enzyme within their own cells. This has not been historically possible with enzyme replacement therapy because it is very difficult for enzymes injected into the blood to get into cells, but we think we may be able do this with an mRNA-based technology.

WE MAY BE ABLE TO EDUCATE THE PATIENT'S IMMUNE SYSTEM BETTER AGAINST THEIR OWN CANCER.

How does mRNA allow you to go after cancer?
mRNA is uniquely suited as a T cell vaccine because it expresses antigens from within the cell. It is possible that by better understanding the mutations that the immune system can see, we may actually be able to educate the patient's immune system better against their own cancer. Using a different approach, we can try to educate the immune system to recognize cancer by injecting mRNA encoding for immunological stimulants (cytokines) directly into tumors in order to overcome the immunosuppression caused by the cancer cells.

Why are you pursuing such a wide range of diseases?
All of our development candidates share the same fundamental building blocks, so if we are able to determine that a candidate can work in a given disease area, we expect it may work in related diseases. This gives us the ability to explore an array of potential medicines and vaccines to bring into the clinic. Our platform allows us to accelerate drug development in a way that we believe is different than other biotechs, giving us a unique opportunity to rapidly identify promising development candidates and translate these innovations into potential new medicines.

How does this technology affect the cost and speed of drug development?
It allows us to use the same process, and the same physical infrastructure, but simply change the sequence that goes into the process. For example, the mRNA production for VEGF and the vaccine against cytomegalovirus use the same fundamental process. These shared attributes should allow Moderna to gain significant efficiencies.

moderna

Moderna is continuing to build its team of physician-scientists to lead drug development for our mRNA-based programs in Rare Disease, Oncology, Vaccines, and other emerging therapeutic areas.

These leaders will report to the Chief Medical Officer and have responsibility for development programs, including creating clinical development plans, designing clinical studies, writing protocols and working in close collaboration with Moderna's internal clinical research and platform organizations and strategic collaborators.

Moderna is a leader in the discovery and development of messenger RNA (mRNA) therapeutics and vaccines, an entirely new class of medicines that directs the body's cells to produce intracellular or secreted proteins that can have a therapeutic or preventive benefit for both patients and healthy individuals. Moderna is creating mRNA medicines for a wide range of diseases and conditions, in many cases by addressing currently undruggable targets or underserved areas of medical need.

For more information on opportunities to join Moderna, please visit us at:
www.modernatx.com/careers

www.modernatx.com

moderna

SPRINGER NATURE