



Moderna Announces Publication in Molecular Therapy Characterizing Potent Immune Response Generated by Its mRNA Prophylactic Vaccines

September 26, 2017

Research led by Karolinska Institutet describes how Moderna's vaccines target key antigen-presenting cells, leading to both B cell and T cell responses

Cambridge, Mass., September 26, 2017—Moderna Therapeutics, a clinical stage biotechnology company that is pioneering messenger RNA (mRNA) therapeutics and vaccines to create a new generation of transformative medicines for patients, announced a new [publication](#) in *Molecular Therapy* that provides mechanistic insights about its mRNA prophylactic vaccines. The research, led by Professor Karin Loré, Ph.D., and her [group](#) at the Karolinska Institutet in Stockholm, Sweden, characterizes how Moderna's vaccines target key antigen-presenting cells, leading to both B cell and T cell activation, which yields a potent immune response.

The study utilized a research version of Moderna's influenza H10N8 vaccine, which encodes for the viral antigenic protein hemagglutinin (HA) encapsulated in lipid nanoparticles (LNPs). In the study, the H10N8 vaccine induced protective titers of HA antibody, as well as CD4+ T cell responses, after intramuscular or intradermal injection into non-human primates (NHPs). Two types of cells, monocytes at the injection site, and dendritic cells in the draining lymph nodes, primarily expressed and presented HA to the immune system and upregulated key co-stimulatory receptors, CD80 and CD86. The vaccine also led to the upregulation of type 1 interferon (IFN)-inducible genes, including MXI and CXCL10. This innate immune activation resulted in the priming of H10-specific CD4+ T cells in the lymph nodes. The vaccine's ability to induce both innate immunity and antigen production by antigen-presenting cells generates a potent vaccine-specific immune response.

"There is a growing body of data demonstrating the robust immune response generated by mRNA vaccines. We designed this study to shed light on the mechanistic underpinnings of this novel and hugely promising vaccine technology," said Professor Karin Loré, Ph.D., principal investigator and corresponding author on the paper. "These data increase our understanding of how mRNA vaccines target key antigen-presenting cells to generate vaccine-specific T cell and B cell responses. We now know which cells are translating the mRNA, and we understand the cellular activation of target cells. We look forward to seeing the continued progress of mRNA vaccines in the clinic as a novel approach for addressing persistent and emerging unmet needs in the infectious disease space."

A Phase 1 clinical study of Moderna's H10N8 vaccine (mRNA-1440) in healthy volunteers has been completed, with subjects continuing to be followed for safety monitoring. In April 2017, Moderna [published](#) positive interim data from a 100 µg intramuscular (IM) cohort from the Phase 1 study demonstrating mRNA-1440 induced high levels of immunogenicity, and was safe and well tolerated.

"We are very pleased to have collaborated with Dr. Loré and her highly respected immunology research team at Karolinska on this important study. As pioneers of mRNA vaccines, it's incumbent upon us to advance a deeper understanding of the fundamental mechanisms by which they are working to generate immunity and prevent infectious diseases," said Giuseppe Ciaramella, Ph.D., Chief Scientific Officer, Infectious Diseases at Moderna, and a senior author on the paper. "Given the software-like nature of our medicines, these findings should translate across our vaccine platform. We look forward to publishing additional mechanism of action insights as we continue to advance our ambitious pipeline of prophylactic vaccines."

Moderna's development pipeline [currently](#) comprises 16 development candidates (DCs) across infectious diseases, immuno-oncology, cardiovascular diseases and rare liver diseases. Nine of these DCs are prophylactic vaccines – including monovalent, multivalent and multi-pathogen vaccines. There are Phase 1 studies currently underway for five of these vaccines.

About Moderna's mRNA Prophylactic Vaccines

Messenger RNA (mRNA) plays a fundamental role in human biology, directing protein production in cells. When used as a drug, mRNA can direct cells to produce therapeutic proteins (mRNA therapeutics) to fight disease or antigenic proteins (mRNA vaccines) to prevent disease.

Moderna's mRNA vaccines encode for viral antigenic proteins associated with viruses. The mRNA directs cells to produce and express the proteins, much like a native infection would do, but without the ability to cause disease.

As a result, the immune system recognizes the antigenic proteins as foreign to the body and produces antibodies that have the potential to neutralize the virus and to prevent infections in the event the vaccinated person is exposed to the actual virus in the future.

About Moderna Therapeutics

Moderna is a clinical stage pioneer of messenger RNA (mRNA) therapeutics and vaccines, an entirely new drug technology that directs the body's cells to produce intracellular or secreted proteins. With its breakthrough platform, Moderna is developing mRNA vaccines and therapeutics as a new class of medicines for a wide range of diseases and conditions, in many cases by addressing currently undruggable targets. Moderna is developing its innovative mRNA medicines for infectious diseases, cancer (immuno-oncology), rare liver diseases, cardiovascular diseases and pulmonary diseases, through proprietary development and collaborations with strategic partners.

Headquartered in Cambridge, Mass., privately held Moderna currently has strategic agreements with AstraZeneca, Merck and Vertex Pharmaceuticals, as well as the Defense Advanced Research Projects Agency (DARPA), an agency of the U.S. Department of Defense; the Biomedical Advanced Research and Development Authority (BARDA), a division of the Office of the Assistant Secretary for Preparedness and Response (ASPR) within the U.S. Department of Health and Human Services (HHS); and the Bill & Melinda Gates Foundation. To learn more, visit www.modernatx.com.

Moderna Contacts:

Media:

Liz Melone

617-256-6622

liz.melone@modernatx.com

Investors:

Lorence Kim

617-209-5849

lorence.kim@modernatx.com