



Publication in *Cell* Demonstrates Moderna's Zika mRNA Vaccine Prevents In Utero Transmission of Zika Virus in Mice, Protects Against Zika-Related Congenital Damage

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First Study to Show Protection from Zika Virus during Pregnancy

CAMBRIDGE, Mass., July 13, 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, today announced new data demonstrating that its Zika mRNA vaccine prevented Zika virus transmission from pregnant mice to their fetuses. The findings, which were [published](#) today in *Cell*, also demonstrated that Moderna's Zika mRNA vaccine protected the placenta and fetus from Zika virus-induced injury.

In the study, Moderna's Zika mRNA vaccine was evaluated in addition to a live-attenuated vaccine candidate developed by the University of Texas Medical Branch (UTMB). The research was conducted by scientists from the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), and Washington University School of Medicine and UTMB.

Children born to mothers infected with Zika can develop microcephaly, a severe disease characterized by abnormally small heads and severe neurologic disabilities. Zika infection is also strongly associated with Guillain-Barré Syndrome (GBS), an autoimmune disease that attacks the peripheral nervous system, leading to rapidly progressive and potentially life-threatening muscle weakness. GBS can lead to death caused by respiratory arrest if a patient is not ventilated. There are no treatment options or approved vaccines for the Zika virus or congenital Zika syndrome. This is the first study to establish vaccine protection from the Zika virus during pregnancy.

"We're highly encouraged by these preclinical findings demonstrating the ability of our mRNA vaccine to provide robust prevention of maternal transmission of Zika and protection against congenital defects," said Giuseppe Ciaramella, Ph.D., Chief Scientific Officer of Moderna's infectious disease-focused venture, Valera, and an author on the paper. "The threat to pregnant women and women who may be planning on getting pregnant remains a serious concern in certain regions of the U.S. and abroad. We look forward to further study of our Zika mRNA vaccine to prevent Zika infections, with the ultimate goal of improving outcomes for mothers, their children, and families in the U.S. and globally."

About the Zika mRNA Vaccine Findings

The study was designed to evaluate protection of fetuses during pregnancy in mice. Researchers gave a cohort of non-pregnant female mice (n=20) a 10 µg intramuscular (IM) injection of the Zika mRNA vaccine followed by a boost at 28 days. An additional cohort of non-pregnant mice (n=20) received placebo injections at the same time points. At day 49, the mice that received the mRNA vaccine produced high levels of neutralizing antibodies against Zika virus in their blood compared to placebo.

Both cohorts were then mated and infected with the Zika virus. After seven days, most fetuses in the vaccinated mice showed no evidence of having Zika virus transmitted to them from their pregnant mothers compared to placebo. In addition, vaccinated mice had significantly lower levels of Zika virus RNA in maternal, placental and fetal tissues compared to placebo-injected mice, resulting in protection against damage to the placenta and fetus. Specifically,

- Placenta and fetal heads from the placebo cohort showed high levels of viral RNA levels while corresponding tissues in mice immunized with Moderna's Zika mRNA vaccine showed marked virological protection (placenta, 200-fold mean reduction; fetal head, 13,000-fold mean reduction).
- 10 of 19 (53%) placentas and 11 of 19 (58%) fetal heads from mice who received Moderna's Zika mRNA vaccine had viral RNA levels at the limit of detection of the assay, suggesting virtually complete protection, and the remainder had substantially lower levels than those detected in samples from mice in the placebo cohort.
- Only three of 19 (16%) of placentas and 0 fetal heads from maternal mice immunized with Moderna's mRNA Zika vaccine were positive for the infectious virus compared to 21 of 23 (91%) of placentas and 10 of 23 (43%) fetal heads from placebo-vaccinated maternal mice.

The researchers repeated the experiment in order to determine the effects on fetal viability at birth, again comparing maternal mice who were vaccinated with Moderna's mRNA vaccine (n=14) and maternal mice who received placebo (n=14). None of the mice in the placebo group delivered pups at term due to extensive placental injury and fetal demise. In contrast, 100% of the fetuses from mice who received Moderna's mRNA vaccine were born without signs of damage, and the heads of newborn pups of mothers in this treatment group showed no measurable levels of viral RNA.

"These are very promising findings and, as the first study to demonstrate protection from Zika in the pregnancy setting, are an important development in our efforts to combat Zika virus," said Michael Diamond, M.D., Ph.D., Professor, Departments of Medicine, Molecular Microbiology, Pathology & Immunology, and Associate Director, Center for Human Immunology and Immunotherapy Program at Washington University School of Medicine, and a lead author on the *Cell* paper. "This type of collaboration, fusing the expertise of academia, government and industry, will be critical in order to speed advancement of novel vaccines like the mRNA vaccine and live-attenuated vaccine involved in this study."

Moderna's Zika mRNA vaccine, mRNA-1325, is currently in Phase 1/2 clinical study in healthy volunteers. The company's [pipeline](#) includes seven additional mRNA prophylactic vaccines, all of which address infectious diseases for which there currently are no approved vaccines.

In February 2017, a [paper](#) published in *Cell* demonstrated that Moderna's mRNA vaccine protected mice against Zika. In April 2017, Moderna [published](#) human data for its mRNA vaccine technology in *Molecular Therapy*, which showed that its first prophylactic vaccine candidate, mRNA-1440 -- an mRNA prophylactic vaccine against avian H10N8 influenza -- induced high levels of immunogenicity and was safe and well

tolerated.

About Moderna's Zika mRNA Vaccine

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 Zika mRNA vaccine encodes for viral antigenic proteins (Zika virus prM and E) associated with the Zika virus. The mRNA directs cells to produce and express the proteins on the cell surface, much like a native infections would do, but without the ability to cause disease. This is because no other viral proteins are present to enable the production of an infectious Zika virus.

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 Zika virus, and prevent infections in the event the vaccinated person is exposed to the actual virus in the future.

In 2016, Moderna received a funding award of up to \$125 million from 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), to accelerate development of its Zika mRNA vaccine. Moderna's preclinical work for mRNA-1325 was funded through a grant from the Defense Advanced Research Projects Agency ([DARPA](#)).

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 a new class of mRNA 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 diseases, cardiovascular disease and pulmonary disease, through proprietary development and collaborations with strategic partners.

Headquartered in Cambridge, Mass., privately held Moderna currently has strategic agreements with AstraZeneca, Merck, Alexion Pharmaceuticals 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.

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