Novel vaccine approach proves powerful against Zika virus

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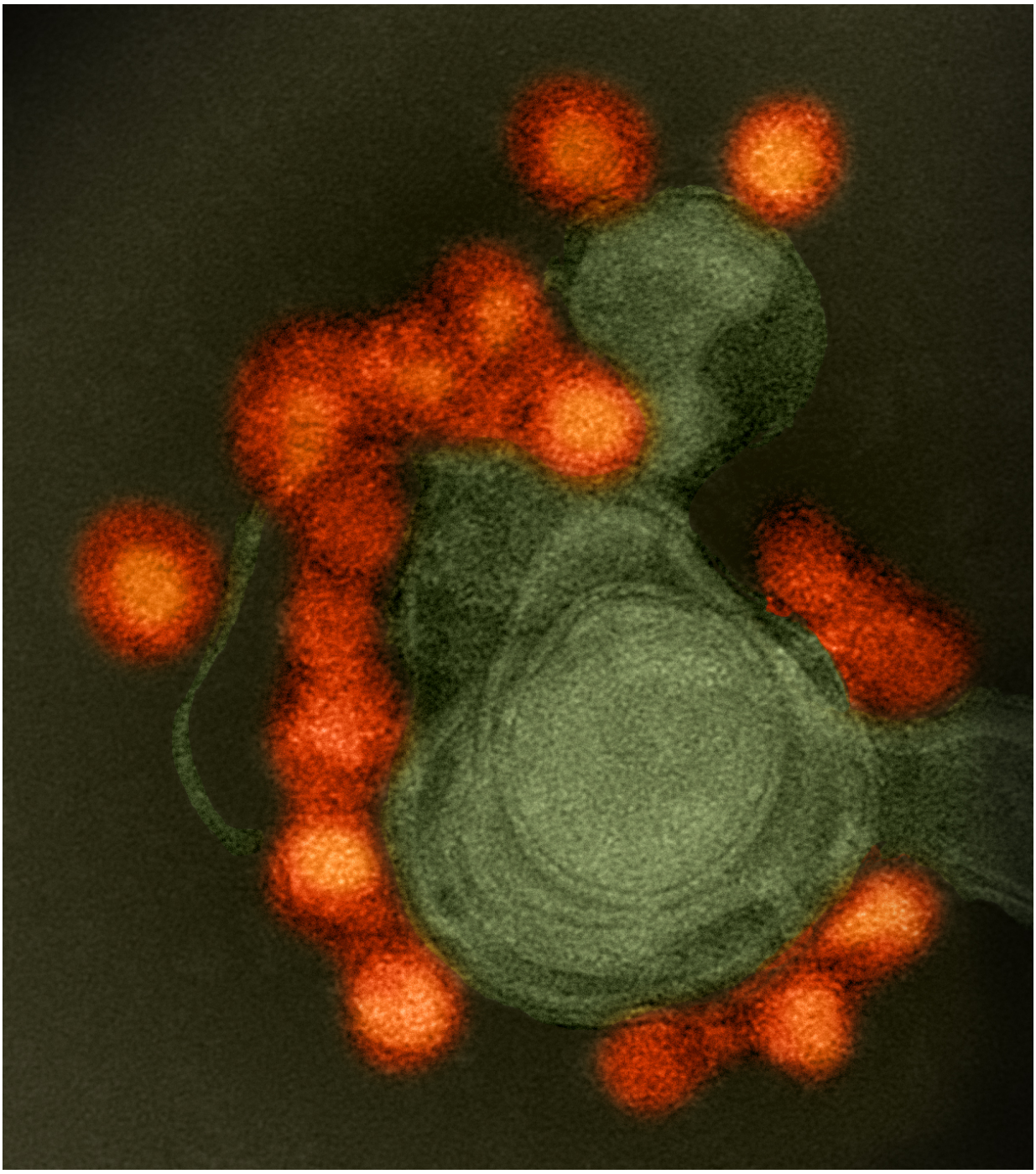

Transmission electron microscope image of negative-stained, Fortaleza-strain Zika virus (red), isolated from a microcephaly case in Brazil. The virus is associated with cellular membranes in the center. Credit: NIAID

A uniquely designed experimental vaccine against Zika virus has proven powerful in mice, new research has found.

A team led by researchers at The Ohio State University has developed and tested a vaccine that employs an uncommon two-pronged approach to fighting the virus, which is spread by mosquitos and is most serious for pregnant women and their fetuses.

The single-dose vaccine, carrying the genes for two or three Zika proteins, proved effective in triggering an immune response that prevented later infection by Zika virus, according to the study, which appears in the journal *Nature Communications*.

"In this study, the vaccine was potent, safe and highly effective, at least in the short term. There's a long way to go, but we think this is a promising candidate for a human vaccine," said Jianrong Li, an Ohio State professor of veterinary biosciences who led the study and developed the vaccine platform.

Babies born to Zika-infected mothers are sometimes born with a birth defect called microcephaly. Other complications include miscarriage, stillbirth and other birth defects. Research also suggests that a small percentage of people infected with the virus can contract Guillain-Barre syndrome, which affects the nervous system.

There's no vaccine available currently—though some are in clinical trials—and the only protection against Zika are preventative measures such as insect repellant, staying indoors and wearing long sleeves and pants.

Shan-Lu Liu, a study co-author and director of Ohio State's Viruses and Emerging Pathogens Program, said the experimental vaccine holds particular promise because it appears to afford an adequate immune

response with one dose. In hard-to-reach and resource-poor areas, that becomes especially valuable, he said.

When this study began, the Ohio State team wondered if a novel approach to vaccination might prove effective against the virus—one in which they targeted a protective immune response by expressing two or three Zika proteins.

As a vehicle for the Zika proteins, they looked to vesicular stomatitis virus, or VSV, which is a foot-and-mouth disease in cattle. The weakened form of the virus is harmless in humans and mice. VSV has been used in other vaccines, including a successful Ebola vaccine which has been used in preventing outbreaks in humans in Africa.

"It's a good platform for human vaccines, because people don't have any antibodies against it and that allows VSV to successfully transport the vaccine without being stopped by the immune system," said study co-author Mark Peeples, a pediatrics professor at Ohio State and researcher at Nationwide Children's Hospital in Columbus.

In general, vaccines work by delivering harmless amounts of the target virus proteins to the bloodstream, allowing the body to build up immune responses that will provide protection in the event of subsequent exposure to the virus. Li's work has been focused on weakening VSV so that it doesn't cause any problems and then inserting genes from other viruses to make powerful vaccines, said Peeples, who first encouraged Li to consider applying his vaccine platform to Zika.

In the experimental vaccine, VSV acts as a vehicle to deliver the genes for two or three key proteins from the Zika virus, carrying them into the mouse and expressing them inside some of the cells in the mouse so that the immune system could respond and build up a defense against Zika.

"The addition of NS1 protein is an innovative approach for a vaccine—it's a protein that is made after the Zika virus infects a cell. It's what this bug uses to replicate itself once it's inside the host," said Prosper Boyaka, a study co-author and Ohio State professor of veterinary biosciences.

The study included experiments in mice with severely compromised immune systems—a necessary step to make sure that mice could get sick after infection with Zika virus. When the vaccinated mice were exposed to Zika virus, their weak immune systems fought it off swiftly and efficiently, convincing the research team that their design had worked.

Without using the immunocompromised animals, the researchers would not have known how safe and effective the vaccine was, Peeples said.

The early success with this vaccine has encouraged this team to use the same approach to fight other related viruses, including Dengue fever, the researchers said.

The researchers also looked at the response to a vaccine with just the unique NS1 gene inserted into VSV and for the first time established that it offered partial protection all on its own, confirming its value in the vaccine, Boyaka said.

"We are very excited to find that VSV-based Zika vaccine is highly promising in both immunocompetent and immunocompromised mice", said Anzhong Li, who is the first author of the paper and a graduate student in Jianrong Li's laboratory. Anzhong Li recently presented these findings at a scientific conference in Italy.

"Really, the next big question is 'Will this be protective in humans?' " Peeples said.

Provided by The Ohio State University