Phase 2 Zika vaccine trial begins in US, Central and South America

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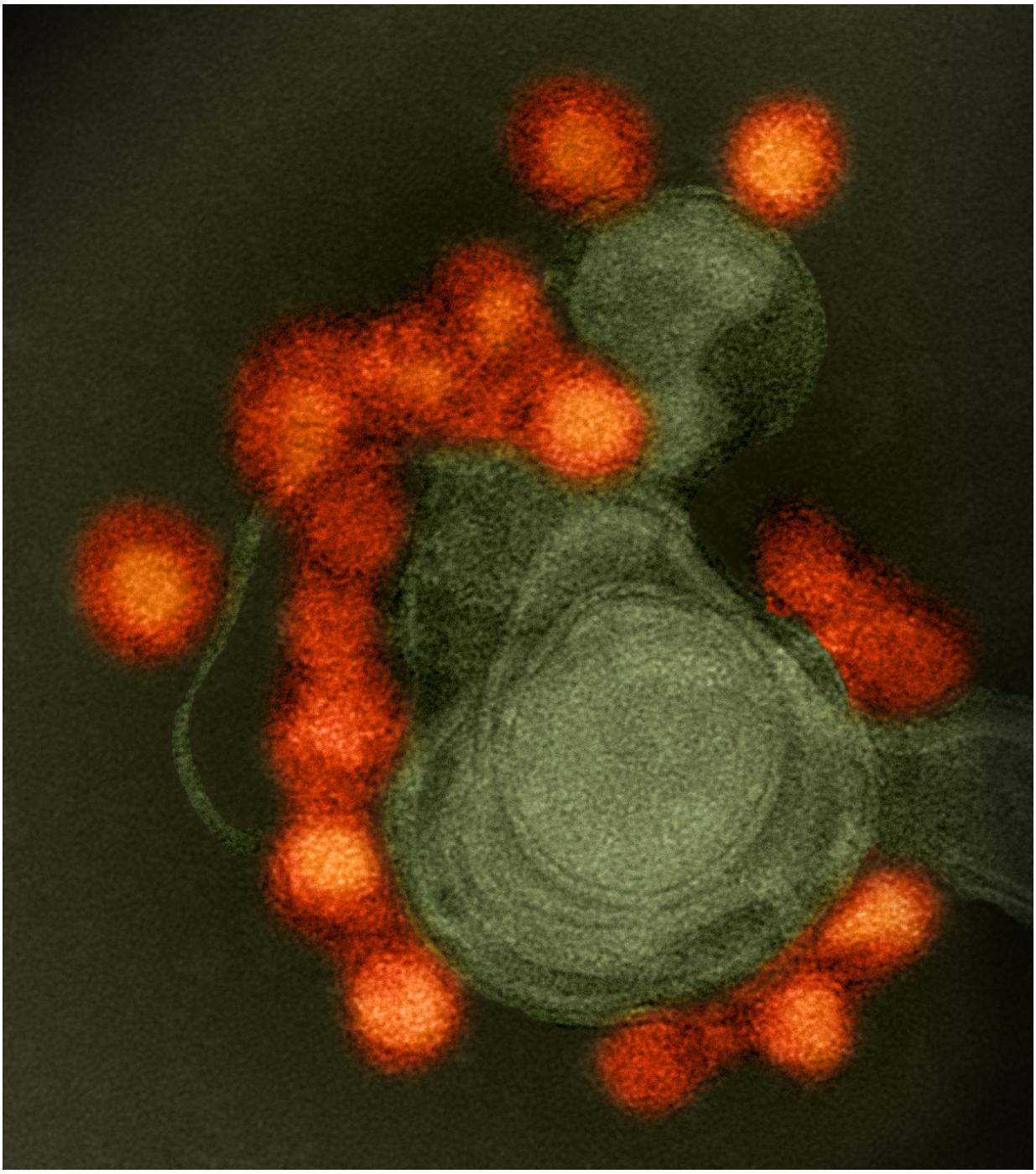

Transmission electron microscope image of negative-stained, Fortaleza-strain Zika virus (red), isolated from a microcephaly case in Brazil. The virus is associated with cellular membranes in the center. Credit: NIAID

Vaccinations have begun in a multi-site Phase 2/2b clinical trial testing an experimental DNA vaccine designed to protect against disease caused by Zika infection. The vaccine was developed by government scientists at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH). NIAID is leading the trial, which aims to enroll at least 2,490 healthy participants in areas of confirmed or potential active mosquito-transmitted Zika infection, including the continental United States and Puerto Rico, Brazil, Peru, Costa Rica, Panama and Mexico. The two-part trial, called VRC 705, further evaluates the vaccine's safety and ability to stimulate an immune response in participants, and assesses the optimal dose for administration. It also will attempt to determine if the vaccine can effectively prevent disease caused by Zika infection.

Most people with Zika infection have either no or only mild symptoms, such as fever, rash, joint pain and conjunctivitis (red eyes). However, when Zika infection occurs during pregnancy, the pregnant woman can pass the virus to her fetus, which can result in a range of fetal defects known collectively as congenital Zika syndrome. Currently there is no licensed vaccine to prevent disease caused by Zika infection, which is mainly transmitted via the bite of infected *Aedes aegypti* mosquitoes but also can be transmitted sexually.

"We are pleased to have advanced rapidly one of NIAID's experimental Zika vaccines into this next stage of testing in volunteers. We expect this study will yield valuable insight into the vaccine's safety and ability to prevent disease caused by Zika infection," said NIAID Director Anthony S. Fauci, M.D. "A safe and effective Zika vaccine is urgently needed to prevent the often-devastating birth defects that can result from Zika virus infection during pregnancy. Evidence also is accumulating that Zika can cause a variety of health problems in adults as well. This trial marks a significant milestone in our efforts to develop countermeasures for a pandemic in progress."

Scientists at NIAID's Vaccine Research Center (VRC) developed the NIAID Zika virus investigational DNA vaccine. It entered early-stage human testing in 2016 following extensive testing in animal models. Initial findings indicate the vaccine is safe and able to induce a neutralizing antibody response against Zika virus. The Phase 2/2b trial aims to gain more safety and immune response data and determine if this immune response protects against disease caused by natural Zika infection.

The Zika vaccine platform is based on a strategy VRC scientists used previously to develop a West Nile virus vaccine candidate. The Zika vaccine candidate being tested in this study contains a small circular piece of DNA called a plasmid into which scientists have inserted genes that encode two proteins found on the surface of the Zika virus. Once injected into muscle, the encoded proteins assemble into particles that mimic Zika virus and trigger the body's immune system to respond. The vaccine does not contain infectious material, so it cannot cause Zika infection.

The trial is being led by protocol co-chairs Julie E. Ledgerwood, D.O., chief of VRC's Clinical Trials Program, and Grace L. Chen, M.D., deputy chief of the same program.

The trial consists of two studies: part A and part B. Part A will build on ongoing Phase 1 trials to further evaluate the vaccine's safety and ability to stimulate an immune response, specifically in populations where Zika could be endemic. It will also help determine the optimal dose and injection sites for administration. Part A will enroll 90 healthy men and non-pregnant women ages 18-35 years at three sites in Houston, Miami and San Juan, Puerto Rico. All participants will receive the investigational vaccine intramuscularly at three separate clinic visits each four weeks apart. Participants will be randomly assigned to receive either a standard dose or a high dose of the investigational vaccine at all

three visits, and will be followed for about 32 weeks total.

Part B of the trial will enroll at least 2,400 healthy men and non-pregnant women ages 15-35 years. This part of the trial aims to determine if the vaccine can effectively protect against Zika-related disease when someone is naturally exposed to the virus. Sites will include the three locations from part A (Houston, Miami and San Juan) as well as two additional sites in San Juan, two sites in Costa Rica, and one site each in Peru, Brazil, Panama and Mexico. Additional sites might be added in the future. Participants will be randomly assigned to receive either the investigational vaccine or a placebo at three separate clinic visits each four weeks apart. The trial is double-blind, meaning neither the study investigators nor the participants will know who receives the investigational vaccine.

Part B participants will be followed for nearly two years, during which time they will undergo assessments for adverse events and symptoms of Zika infection. Trial participants in both parts will be counseled on how to protect against Zika infection. Investigators will compare the rates of confirmed cases of Zika in the placebo group and the vaccinated group to determine if the investigational vaccine protects against disease caused by Zika infection.

Each site will have a principal investigator responsible for ensuring daily review of safety data as they become available. A protocol safety review team that includes the protocol chairs and other medical officers at NIAID will review safety data reports weekly. The NIAID Intramural Data and Safety Monitoring Board will also review cumulative study data at least twice per year. The study is currently expected to be completed by 2019.

Provided by NIH/National Institute of Allergy and Infectious Diseases