NIH begins clinical trial of live, attenuated Zika vaccine

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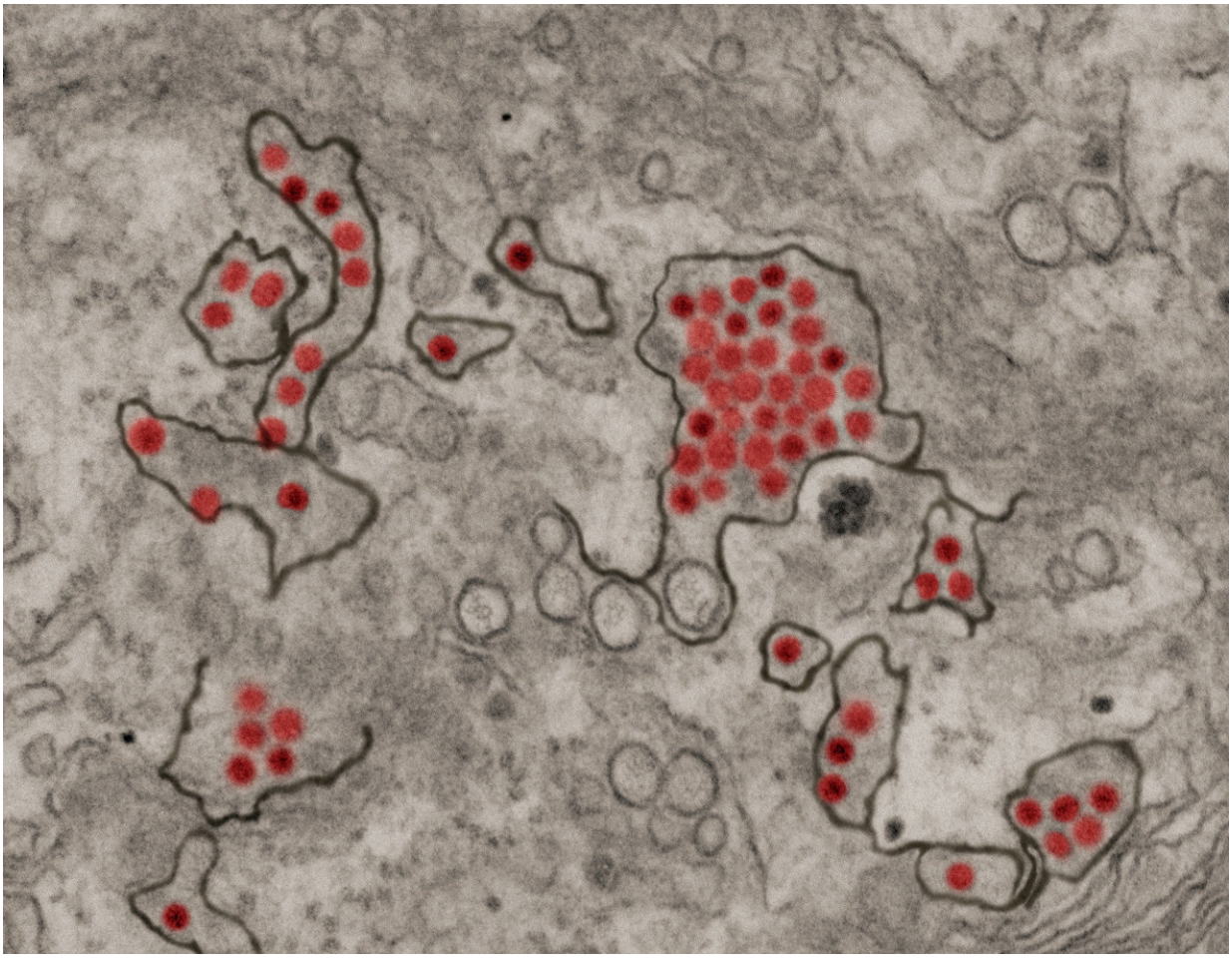

Zika virus particles (red) shown in African green monkey kidney cells. Credit: NIAID

Vaccinations have begun in a first-in-human trial of an experimental live, attenuated Zika virus vaccine developed by scientists at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. The trial will enroll a total of 28 healthy, non-pregnant adults ages 18 to 50 at the Johns Hopkins Bloomberg School of Public Health Center for Immunization Research in Baltimore, Maryland, and at the Vaccine Testing Center at the Larner College of Medicine at the University of Vermont in Burlington. NIAID is sponsoring the trial.

Although most people experience a mild illness or no symptoms when infected with Zika virus, babies born to women infected with Zika virus during pregnancy may have birth defects and/or develop health problems in their early years.

Zika virus is primarily transmitted to humans by the bite of an infected mosquito or can be transmitted through sex. As a result, the Centers for Disease Control and Prevention (CDC) advises that pregnant women should not travel to areas with risk of Zika. CDC also recommends that partners of pregnant women and couples considering pregnancy should know pregnancy risks and take certain precautions. The U.S. Zika Pregnancy and Infant Registry has recorded the number of pregnant women with laboratory evidence of possible Zika virus infection since 2015. As of July 17, 2018, the registry had recorded 2474 pregnancies in states and the District of Columbia and 4900 pregnancies in U.S. territories and freely associated states.

"Zika virus infection remains a significant threat to pregnant women and their developing fetuses, and we can expect to see periodic outbreaks and cases in areas where *Aedes aegypti* mosquitoes thrive," said NIAID Director Anthony S. Fauci, M.D. "NIAID remains committed to developing safe and effective Zika vaccines, and we are pleased to begin clinical testing of a live attenuated candidate." No licensed vaccines for

Zika virus infection are currently available; however, several are in various stages of development.

Stephen Whitehead, Ph.D., of NIAID's Laboratory of Viral Diseases, led the efforts to develop the experimental vaccine, known as rZIKV/D4?30-713. The laboratory used genetic engineering techniques to create a chimeric virus, made by combining genes from multiple viruses. The chimeric virus consists of a dengue virus type 4 backbone (dengue is caused by any of four related viruses, termed serotypes) that expresses Zika virus surface proteins. The chimeric virus is live but attenuated, or weakened, so it cannot cause disease in recipients. When injected into the body, the weakened virus should prompt an immune response. The Phase 1 clinical trial will analyze this response in participants and assess the safety of the experimental vaccine, which showed promise in earlier tests in rhesus macaques (monkeys). Charles River Laboratories, in Malvern Pennsylvania, manufactured the vaccine candidate for the Phase 1 clinical trial.

Dr. Whitehead also has developed a live, attenuated dengue vaccine candidate called TV003 designed to elicit antibodies against all four dengue virus serotypes. The experimental vaccine is currently under evaluation in a Phase 3 clinical trial conducted in Brazil by the Butantan Institute. Dr. Whitehead plans to develop a single vaccine that would protect against both Zika and dengue viruses. According to the CDC, dengue is endemic in at least 100 countries in Asia, the Pacific, the Americas, Africa and the Caribbean. Zika virus has been found to circulate in many of these same areas. Once the Zika vaccine candidate proves safe in Phase 1 clinical testing, Dr. Whitehead plans to add the Zika component to the tetravalent dengue vaccine candidate and evaluate the new pentavalent candidate in a Phase 1 clinical trial.

Anna Durbin, M.D., professor of International Health at the Johns Hopkins Bloomberg School of Public Health and part of the university's

Center for Immunization Research, is leading the Phase 1 clinical trial of the monovalent Zika vaccine candidate. Kristen Pierce, M.D., associate professor at the Larner College of Medicine at the University of Vermont, is a co-investigator.

Interested volunteers who test positive for a prior flavivirus infection (such as Zika, dengue, or yellow fever) will be excluded from the trial to ensure that any antibodies detected in blood samples are related to the experimental vaccine alone. All participants will be randomly assigned to receive a single subcutaneous dose of the experimental vaccine (20 participants) or a placebo (eight participants). Neither the participants nor the investigators will know who is receiving the experimental vaccine.

After the vaccination, participants will receive a diary card to record their temperature at home at certain timepoints. During the following 6 months, they will return to the clinic periodically for physical examinations and to provide blood and other samples. Investigators will test the blood samples to see if participants are developing antibodies in response to the experimental vaccine.

Dr. Durbin expects that the trial will take up to one year to complete. For more information, visit ClinicalTrials.gov and search identifier NCT03611946.

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