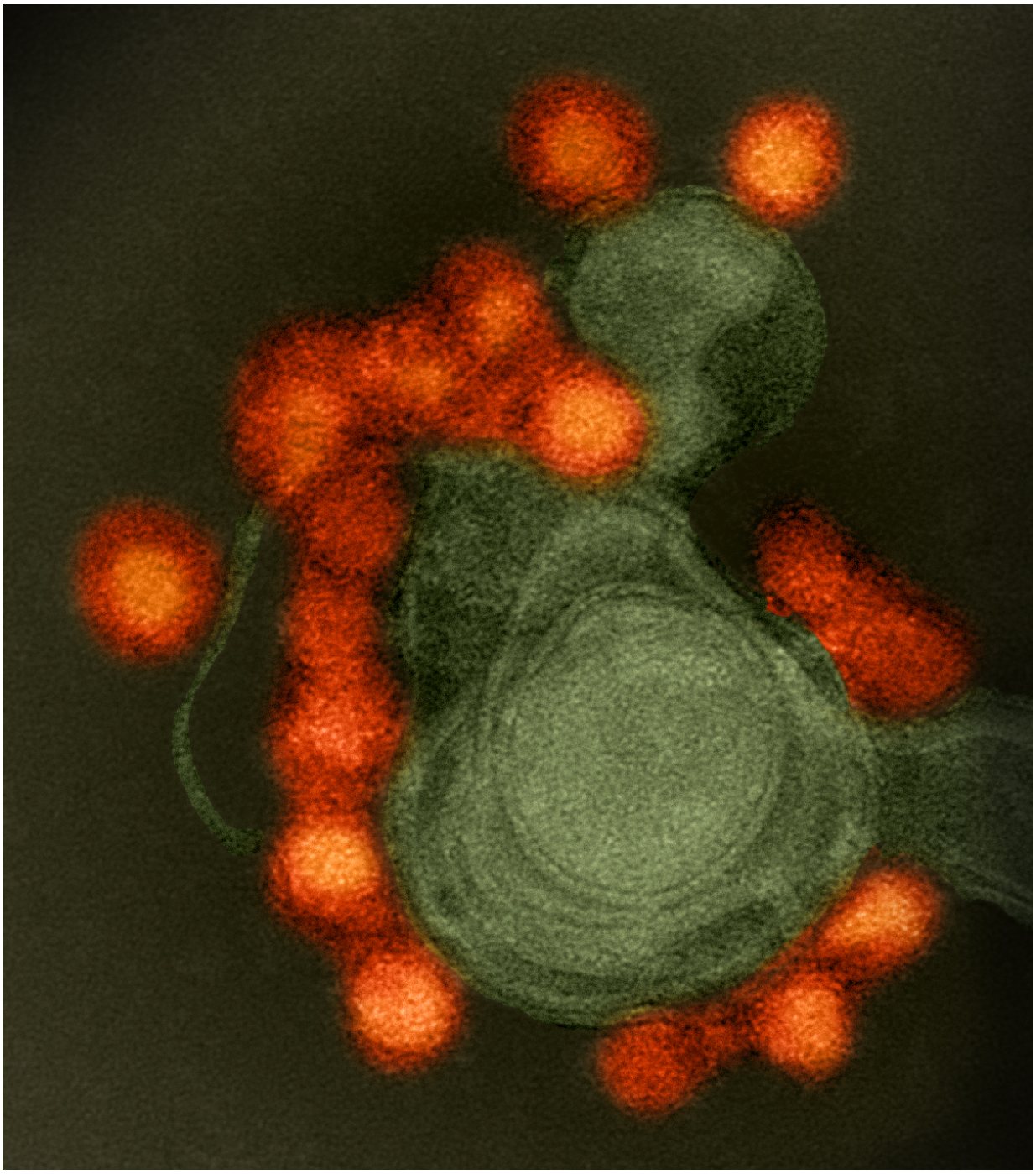
Antibody 'cocktail' can prevent Zika infection but is not effective for treatment of fetuses

April 26 2018



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 "cocktail" of monoclonal antibodies that can prevent Zika virus (ZIKV) infection in primates was not effective for treatment of fetuses, according to a new collaborative study led by a University of Miami Miller School of Medicine research team.

"We observed that ZIKV isolated from pregnant women in Rio de Janeiro also causes fetal infection in pregnant macaques. Unfortunately, we were unable to stop the transmission of virus to the fetus with an antibody cocktail therapy," said Diogo Magnani, Ph.D., associate scientist in the Department of Pathology and first author of the study, "Fetal Demise and Failed Antibody Therapy During Zika Virus Infection of Pregnant Macaques," published recently in the journal *Nature Communications*.

"One of the implications of the study is that preventing infection of the mother may be easier than finding a therapy for the fetus," said senior author David Watkins, Ph.D., professor and vice chair for research. "It also indicates that testing for ZIKV in mothers might not show whether or not the fetus was infected."

The team of researchers is now working on engineering the antibodies to redirect the therapies to the fetus.

Miller School co-authors of the study included Ronald C. Desrosiers, Ph.D., professor of pathology and director of research faculty development; Michael J. Ricciardi, Varian K. Bailey, Lucas Gonzalez-Nieto, Martin J. Gutman, Núria Pedreño-Lopez, Jaclyn M. Kwal, and Mauricio A. Martins, Ph.D., all in the Department of Pathology; as well as Christine L. Curry, M.D., Ph.D., assistant professor of obstetrics and gynecology; and Pascal J. Goldschmidt-Clermont, M.D., professor of medicine.

In the collaborative study, pregnant rhesus macaques were infected with

ZIKV from a patient in Rio de Janeiro, Brazil, where a high rate of fetal development complications was observed. The virus used in the studies was isolated by Dr. Myrna Bonaldo at FIOCRUZ in Rio de Janeiro.

The infection resulted in the virus crossing into the amniotic fluid, resulting in fetal deaths. The researchers found there were no mutations of the virus or other factors implicated in those outcomes.

"We treated three ZIKV-infected pregnant macaques with a cocktail of ZIKV- neutralizing human monoclonal antibodies," said Magnani. "While the antibody therapy was effective in clearing the virus from the mothers' blood, it was not sufficient to clear ZIKV from the amniotic fluid. Antibodies might not cross the placenta in sufficient concentrations to block the virus. Therefore, specific therapies will have to be developed in order to stop mother-to-fetus transmission and treat infected fetuses."

Leading the effort to engineer the antibodies to redirect the therapies to the fetus, Magnani is the principal investigator for a U.S. Department of Defense "Discovery Award" grant on "A Fetus-Targeted Antibody Therapy to Prevent Zika Virus Infection During Pregnancy."

More information: Diogo M. Magnani et al. Fetal demise and failed antibody therapy during Zika virus infection of pregnant macaques, *Nature Communications* (2018). DOI: 10.1038/s41467-018-04056-4

Provided by University of Miami Leonard M. Miller School of Medicine