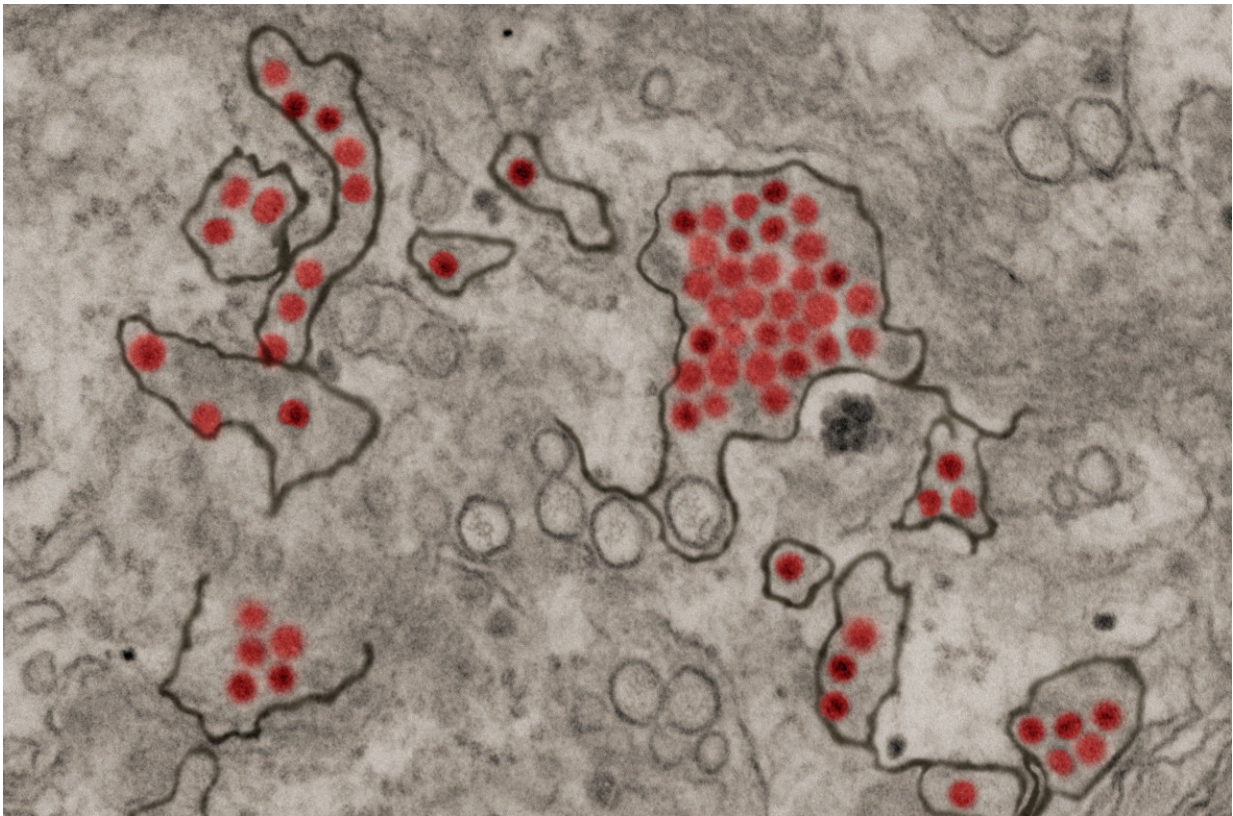


Unusual type of antibody shows ultrapotent activity against Zika

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

An unusual type of antibody that even at miniscule levels neutralizes the Zika virus and renders the virus infection undetectable in preclinical

models has been identified by a team led by Weill Cornell Medicine, New York-Presbyterian and National Institutes of Health (NIH) investigators.

Because Zika can cause [birth defects](#) when passed from a pregnant person to their fetus, this discovery could lead to the development of therapies to protect babies from the potentially devastating effects of this disease.

In research published Nov. 18 in *Cell*, the investigators isolated an ultrapotent immunoglobulin M (IgM) antibody—a five-armed immune protein that latches onto the virus—using blood cells taken from pregnant people infected with Zika. In experiments with mice, they determined that the antibody not only protected the animals from otherwise lethal infections, but also suppressed the virus to the point that it could not be detected in their blood.

Zika is currently circulating at low levels in many tropical countries, but that will inevitably change, according to co-senior author Dr. Sallie Permar, the Nancy C. Paduano Professor in Pediatrics and chair of pediatrics at Weill Cornell Medicine and pediatrician-in-chief at New York-Presbyterian/Weill Cornell Medical Center and New York-Presbyterian Komansky Children's Hospital. Dr. Mattia Bonsignori, chief of the Translational Immunobiology Unit of the Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases (NIAID), part of NIH, is a co-senior author.

"The important thing is that we've got to be ready for another outbreak of Zika," Dr. Permar said.

At this point, doctors have no approved vaccines or treatments to offer patients. With further research, this antibody has the potential to help fill that gap, according to Dr. Permar. "There are two potential ways it could

be used: To quickly reduce levels of Zika in the blood of pregnant people who have become infected, or as a preventative measure given to those at risk of contracting the virus during an outbreak."

Transmitted by infected *Aedes aegypti* mosquitoes, the Zika virus usually causes a mild illness in adults. However, Zika [virus infection](#) in pregnant people can cause severe birth defects, including abnormally small heads and brain damage in their babies.

During a Zika outbreak that began in 2015, researchers in Brazil, led by co-authors Dr. Reynaldo Dietze, of Global Health and Tropical Medicine and the Federal University of Espírito Santo, and Dr. Camila Giuberti, also of the Federal University of Espírito Santo, collected blood samples from pregnant people who had infections. The team decided to focus on those who were infected with Zika, but had given birth to babies that appeared healthy, because they suspected these patients might harbor antibodies capable of preventing the congenital infection.

One of these patients gave birth to an apparently healthy baby even after having Zika detectable in their blood for nearly two months, an unusually long period. The laboratory teams, led by first author Dr. Tulika Singh, a former graduate student at Duke University Medical Center where Dr. Permar's lab was located for part of this study and now a postdoctoral fellow at the University of California, Berkeley, found that their B cells produced an IgM antibody with a potent ability to prevent viral particles from invading cells.

The identity of this antibody, called DH1017.IgM, surprised the investigators because it belongs to a typically weaker, less mature type of antibody that is produced early in an infection. However, in this case, the potent function of this antibody depended on it being an IgM antibody. When the collaborators examined its [molecular structure](#) when binding to the virus, they found that multiple arms could latch onto a viral

particle simultaneously. The findings suggest that IgM antibodies might be especially effective to protect against Zika virus and possibly other viruses, the authors suggest.

To develop the antibody into a therapy, the researchers plan to begin testing its safety and how effectively it can prevent transmission to a fetus in additional preclinical models. Recalling how pregnant people were left out of COVID-19 vaccine trials, Dr. Permar emphasized that when [human studies](#) for new preventive or therapeutic treatments are done for Zika, they must be included.

"Pregnant people are the exact population that needs vaccines or immunotherapies for Zika," she said. "It's crucial to get anti-Zika vaccines and therapies that are safe in pregnancy rolled out as soon as there is evidence of an outbreak."

More information: Mattia Bonsignori, A Zika virus-specific IgM elicited in pregnancy exhibits ultrapotent neutralization, *Cell* (2022). DOI: [10.1016/j.cell.2022.10.023](https://doi.org/10.1016/j.cell.2022.10.023). [www.cell.com/cell/fulltext/S0092-8674\(22\)01369-1](https://www.cell.com/cell/fulltext/S0092-8674(22)01369-1)

Provided by Weill Cornell Medical College

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