

## Antibodies to dengue may alter course of Zika virus infection

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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



Scientists at Emory Vaccine Center, in collaboration with investigators from Thailand, have found that people infected with dengue virus develop antibodies that cross-react with Zika virus.

Some of these <u>antibodies</u> have the potential to neutralize Zika <u>virus</u> - possibly providing immune protection. At the same time, in laboratory experiments, antibodies against dengue could enhance Zika virus infection of human cells.

The results are scheduled for publication on Monday, June 27 in PNAS.

Zika virus is similar genetically to <u>dengue virus</u> and part of the same flavivirus family. They are both transmitted by Aedes mosquitos. Dengue is endemic in several countries currently experiencing Zika outbreak, leading to proposals that pre-existing dengue immunity is influencing the severity of the Zika epidemic.

"There are really two sides of the coin here: both cross-neutralization and antibody-dependent enhancement," says Jens Wrammert, PhD, assistant professor of pediatrics (infectious diseases) at Emory University School of Medicine and Emory Vaccine Center. "We find antibody-mediated enhancement of infection with cells in the laboratory, but we have yet to clarify what effects these antibodies have on the outcome of infection in humans."

"Zika immune responses and disease severity may be different in dengueendemic areas, or among dengue-experienced vs dengue-naïve groups. These factors must be taken into account when doing Zika vaccine or other clinical studies."

There are four strains of dengue virus, and infection with one strain does not lead to long-lasting immunity against the other three. In fact, secondary infection with a different strain can increase the risk of



developing a more severe illness, called dengue hemorrhagic fever.

This is thought to happen through "antibody-dependent enhancement": pre-existing antibodies to the first strain, unable to stop the secondary infection, instead bind to <u>immune cells</u> and help the new strain infect them.

Emory scientists found that a similar phenomenon occurs with Zika. Antibodies obtained from nine dengue-infected patients at Siriraj Hospital in Bangkok - both during acute infection and after recovery could help Zika virus (a strain isolated in 2015 from Puerto Rico) infect immune cells in cell culture.

"It will be important to know whether anti-dengue antibodies facilitate Zika virus penetrating the placental barrier and allowing access to the developing fetus," says co-author Mehul Suthar, PhD, assistant professor of pediatrics (infectious disease) at Emory University School of Medicine and Emory Vaccine Center.

Since 2012, a handful of cases of Zika have been reported in Thailand, ("sporadic transmission" according to the World Health Organization), but not at the numbers seen in South America or the Caribbean.

The co-first authors of the paper are Emory graduate students Lalita Priyamvada and Kendra Quicke. They tested serum samples from the Thai patients and also isolated antibody genes from plasmablasts, the immune cells responsible for pumping out antibodies.

All the serum samples tested were able to cross-react with Zika, both by binding and by neutralization. Nearly half the dengue-reactive monoclonal antibodies isolated bound to samples of Zika proteins. A bright spot for the future is that the team has identified potent Zika neutralizing antibodies.



"Determining what part of the virus the various neutralizing antibodies target could help with design of vaccines or antibody-based therapies," Wrammert says.

Wrammert and Suthar are planning to examine immune responses in returning travelers who experienced Zika <u>infection</u> in collaboration with co-author Mark Mulligan, MD, director of the Hope Clinic of Emory Vaccine Center.

**More information:** Human antibody responses after dengue virus infection are highly cross-reactive to Zika virus, *PNAS*, <u>www.pnas.org/cgi/doi/10.1073/pnas.1607931113</u>

Related paper on dengue immunology: jvi.asm.org/content/early/2016 ... VI.03203-15.abstract

Provided by Emory University

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