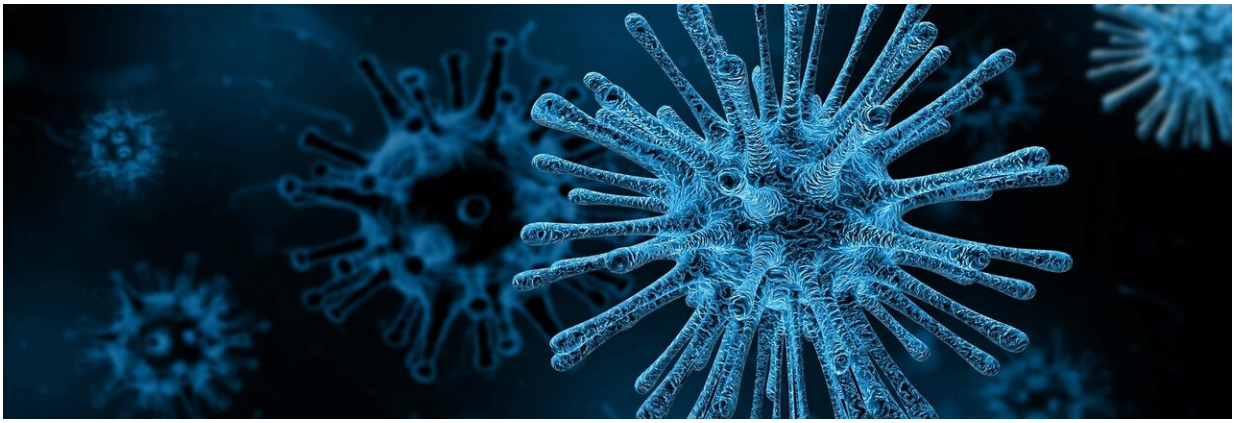
# New study finds immune cells can defend against multiple viruses

March 20 2020, by Brita Belli



Credit: CC0 Public Domain

An underlying virus does not stop the body's immune system from launching a strong defense against a second, newly introduced virus, according to a Yale-led study that appears in the March 9 online edition of the journal *PLOS Neglected Tropical Diseases*.

For the study, Yale researchers obtained blood samples from patients from India with dengue infection, working in partnership with investigators from The National Institute of Mental Health and NeuroSciences in India and their colleagues at Apollo Hospital in Bangalore. They then infected these samples with the Zika virus and measured the cells' immune response using advanced cell-profiling

technology. The researchers found that the underlying dengue infection did not stop the cells from launching a robust immune response against the newly introduced Zika virus.

"The message from our paper is that your innate immune system is ready to launch a very powerful response to a new pathogen," said Ruth Montgomery, professor of medicine and epidemiology and associate dean for scientific affairs, and the paper's lead author.

Montgomery and her team tested samples from both dengue patients and healthy controls from India and found that the underlying dengue infection did not impair new immune responses to the Zika virus. Specifically, researchers noted an increase in small proteins called cytokines, which are related to fighting off infection, in 36 individual cell subsets when Zika was introduced.

"Patients with acute dengue still had a strong immune response to the Zika virus," said Montgomery. "Their immune response was not diminished."

Both the dengue virus and Zika virus are mosquito-borne human pathogens that have caused significant public health concern across the globe. There are some 50-100 million estimated dengue infections, leading to fever, headaches, joint pain, and more severe shock syndrome; the Zika virus has been shown to be devastating to babies in utero, and has led to over 6,700 cases of deformities and neurological damage in newborns. Because the vectors for disease transmission are the same, certain regions are highly prone to both, including Brazil, which had a Zika epidemic in 2015. When the dengue samples were collected from India for the study, Zika was not yet a public health threat in that country. By 2018, that had changed, with 94 confirmed Zika cases, and widespread monitoring.

These findings provide a much more in-depth look at the body's response to viruses at the single-cell level, which Montgomery noted are consistent with existing literature. The research was part of a the HIPC consortium funded by the National Institutes of Health to better understand human immunology, infectious disease, and vaccination responses.

To measure immune response, she and her team used mass cytometry or CyTOF (Cytometry by Time-of-Flight), a state-of-the-art method for simultaneously revealing multiple components of the responses of distinct immune cell populations. Analysis of the results was done using SAUCIE, a novel deep-learning algorithm developed by a team in the lab of Smita Krishnaswamy, assistant professor of genetics and computer science at Yale. Montgomery, director of the Yale CyTOF facility, said Yale is at the forefront of advanced cell analysis, and one of the first academic medical centers with a CyTOF Imaging Mass Cytometer, which further extends its capabilities.

The findings can help guide scientists' understanding of all emerging infectious diseases, including coronavirus, something Montgomery's lab is now actively investigating.

"We are set up to investigate human immune cell response to viruses and have several collaborations currently underway to collect samples related to the coronavirus," Montgomery said. "We have containment facilities and excellent virologists at Yale, and there is a lot of activity right now," she added.

**More information:** Yujiao Zhao et al. Single cell immune profiling of dengue virus patients reveals intact immune responses to Zika virus with enrichment of innate immune signatures, *PLOS Neglected Tropical Diseases* (2020). DOI: 10.1371/journal.pntd.0008112

Provided by Yale University