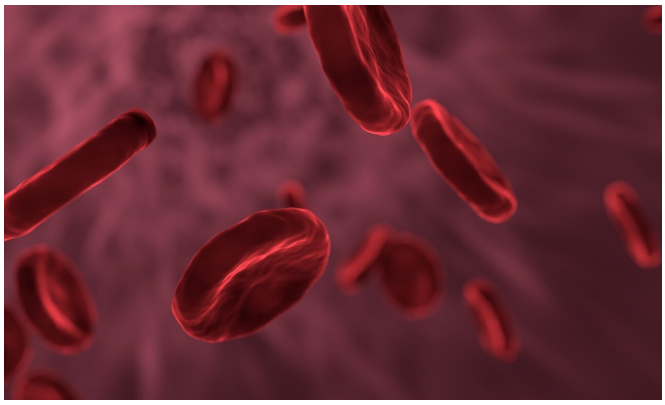
Study identifies antibodies that block alphaviruses

25 September 2020, by Bill Snyder



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Researchers at Vanderbilt University Medical Center have identified antibodies that, in animals, block infection by alphaviruses, which can cause chronic and debilitating joint pain and arthritis and are an increasing global health concern.

The findings, published in the journal *Cell Host & Microbe*, could lead to potential broad-based therapies or a vaccine to prevent infection by this family of primarily tropical, mosquito-transmitted viruses.

"Mosquito-borne viruses are constantly causing infections around the world, and alphaviruses have proven their ability to cause major epidemics," said James Crowe Jr., MD, the paper's corresponding author and director of the Vanderbilt Vaccine Center (VVC). "We were excited to find antibodies that could be developed for prevention or treatment of multiple alphaviruses."

Alphaviruses with exotic-sounding names like chikungunya, Mayaro, Ross River, Sagiyama, Getah and O'nyong'nyong can cause rash, fever and, most prominently, joint pain that can persist for years.

From Africa, Asia and the Pacific Islands to South and Central America and the Caribbean, these viruses infect thousands of people every year, yet there is no licensed treatment or vaccine to combat them.

VVC researchers have developed techniques for rapidly isolating clones of white blood cells called B cells that produce antibodies targeting specific viral proteins. In the laboratory, these "monoclonal" antibodies are then comprehensively examined to identify rare antibodies with a laser-like focus for finding—and neutralizing—a specific virus.

Using these techniques, the researchers have generated human monoclonal antibodies against a wide range of pathogenic viruses including Ebola, HIV (which causes AIDS), dengue, norovirus, respiratory syncytial virus (RSV) – and chikungunya, which in recent years has spread from Africa to India and Southeast Asia.

Crowe and his colleagues have pioneered the rational design of neutralizing antibody treatments and vaccines. Some of them, including a potential treatment for chikungunya infection, have progressed to clinical trials.

In the current study, the researchers identified cross-reactive antibodies produced by B cells isolated from the blood of people who had a prior history of infection with chikungunya or Ross River virus (RRV), which is endemic to Australia and the Pacific Islands.

They found that the antibodies attack a common antigenic site shared by chikungunya, RRV and other alphaviruses. Researchers recently have discovered a receptor on certain cells in the body that binds the alphavirus antigen, enabling the virus to enter the cells and spread.

One of these antibodies, RRV-12, by targeting the viral antigen, prevented attachment to the receptor,

effectively neutralizing a broad range of alphaviruses. The researchers found that in alphavirus-infected mice, RRV-12 reduced the amount of virus in body tissues and prevented serious illness.

These findings imply that RRV-12 may be a possible therapy against multiple alphaviruses in humans and could inform the design of a universal alphavirus vaccine, they concluded.

More information: Laura A. Powell et al. Human mAbs Broadly Protect against Arthritogenic Alphaviruses by Recognizing Conserved Elements of the Mxra8 Receptor-Binding Site, *Cell Host & Microbe* (2020). DOI: 10.1016/j.chom.2020.07.008

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