Researchers find an antibody that targets omicron and other SARS-CoV-2 variants

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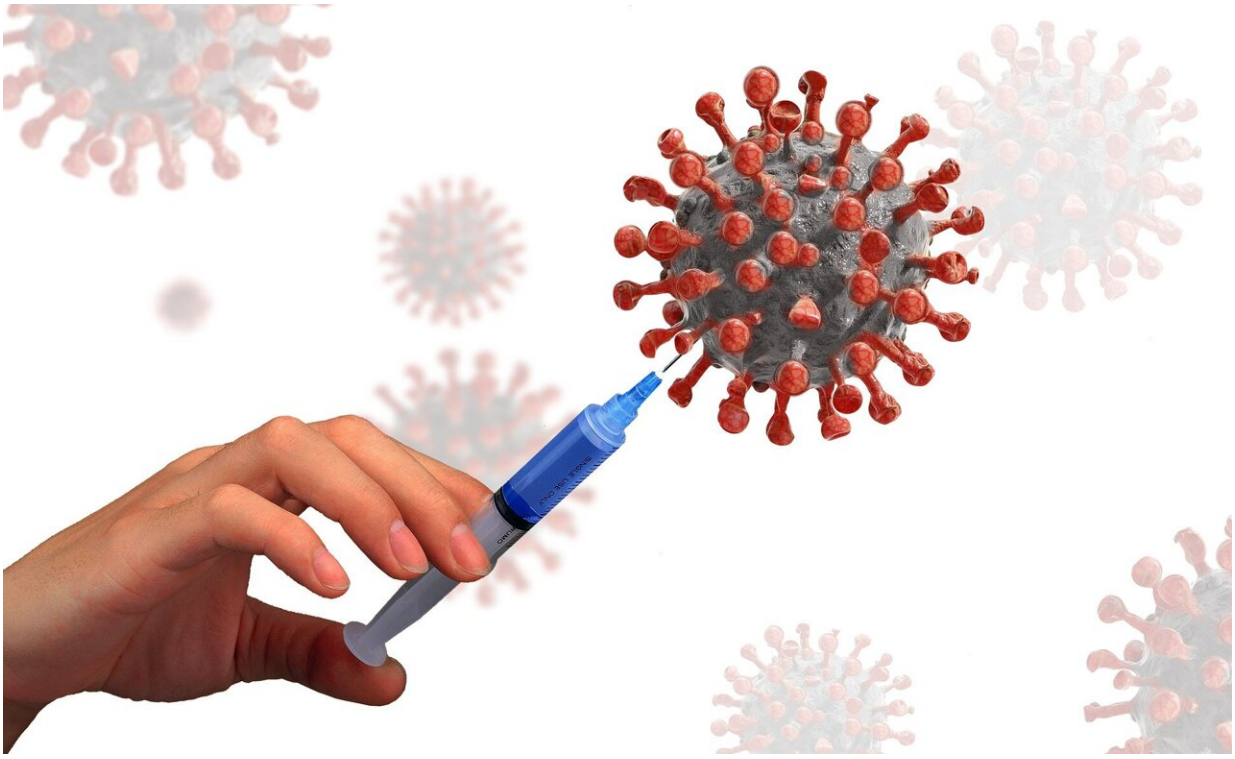

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A team led by researchers at Weill Cornell Medicine, the University of Wisconsin-Madison; Scripps Research and the University of Chicago has identified an antibody that appears to block infection by all dominant variants of the virus that causes COVID-19, including Omicron, the most recent. Their discovery could lead to more potent vaccines and new

antibody-based treatments.

In a study published March 6 in the *Journal of Clinical Investigation*, senior author Dr. Patrick Wilson, the Anne E. Dyson Professor of Pediatric Research and a member of the Gale and Ira Drukier Institute for Children's Health at Weill Cornell Medicine, and his colleagues tested antibodies derived from patient blood samples against successive versions of the virus that emerged during the pandemic. One of these proteins, dubbed S728-1157, proved highly effective at neutralizing not only older variants but also seven subtypes of Omicron.

"The pandemic is over, but the virus is around for the long haul. If not well controlled, it could cause annual epidemics," Dr. Wilson said. "This antibody and the insight it provides could help us avoid yearly surges of COVID-19 or if there is another coronavirus pandemic."

As it replicates in the cells of those it infects, the SARS-CoV-2 virus, which causes COVID-19, acquires new mutations. These changes are raw material for new variants, some of which have the capacity to partially evade vaccines and antibody-based treatments developed to fight the original virus. While many variants have arisen, only some have had the potential to significantly impact infections globally. These include Omicron, which first appeared in November 2021. As of mid-March, one of its subtypes, known as XBB.1.5, has predominated in the United States.

Early in the pandemic, before the variants emerged, Dr. Maria Lucia Madariaga, an assistant professor of surgery at the University of Chicago, collected blood samples from people recovering from COVID-19. As part of the response to the virus, the immune system generates proteins known as antibodies that latch onto specific parts of the virus, blocking its ability to infect a cell and martialing the immune system to destroy it.

Dr. Wilson's group analyzed antibody-producing cells from these samples to find those that latched on to the virus's spike protein, which it uses to get into human cells. Co-first author Dr. Siriruk Changrob, an instructor of immunology in pediatrics in his lab, tested the antibodies they found against 12 variants of SARS-CoV-2, including the original version of the virus.

One antibody, called S728-1157, stood out for its ability to interfere with Omicron. In experiments with hamsters, their colleagues at the University of Wisconsin-Madison School of Veterinary Medicine found treatment with this antibody reduced, or abolished, the amount of the original, Delta or Omicron virus in the animals' nose and lungs. (They are currently testing it against XBB.1.5.) Other collaborators at Scripps Research analyzed the structure of the antibody bound to the spike to understand where it bound and why Omicron's mutations didn't interfere.

Their results suggest that S728-1157 could become the basis for a much-needed alternative to conventional antibody-based treatments. The arrival of variants, particularly Omicron, has rendered many of these therapies, known as monoclonal antibodies, ineffective.

The research could also guide the design of new vaccines that rely on the spike protein to stimulate the production of antibodies. The team found the configuration of the spike matters. Specifically, the immune system produces more broadly effective antibodies like S728-1157 when it encounters spikes in an open conformation like the one they would assume to attack a cell. The current mRNA-based vaccines, especially Omicron-based, however, tend to produce more closed spikes.

"The take home message here is that the next generation of vaccines should try to stabilize the spike in a more open position," Dr. Changrob said.

More information: Site of vulnerability on SARS-CoV-2 spike induces broadly protective antibody to antigenically distinct Omicron subvariants, *Journal of Clinical Investigation* (2023).

Provided by Weill Cornell Medical College