Experimental COVID-19 vaccine provides mutation-resistant T cell protection in mice

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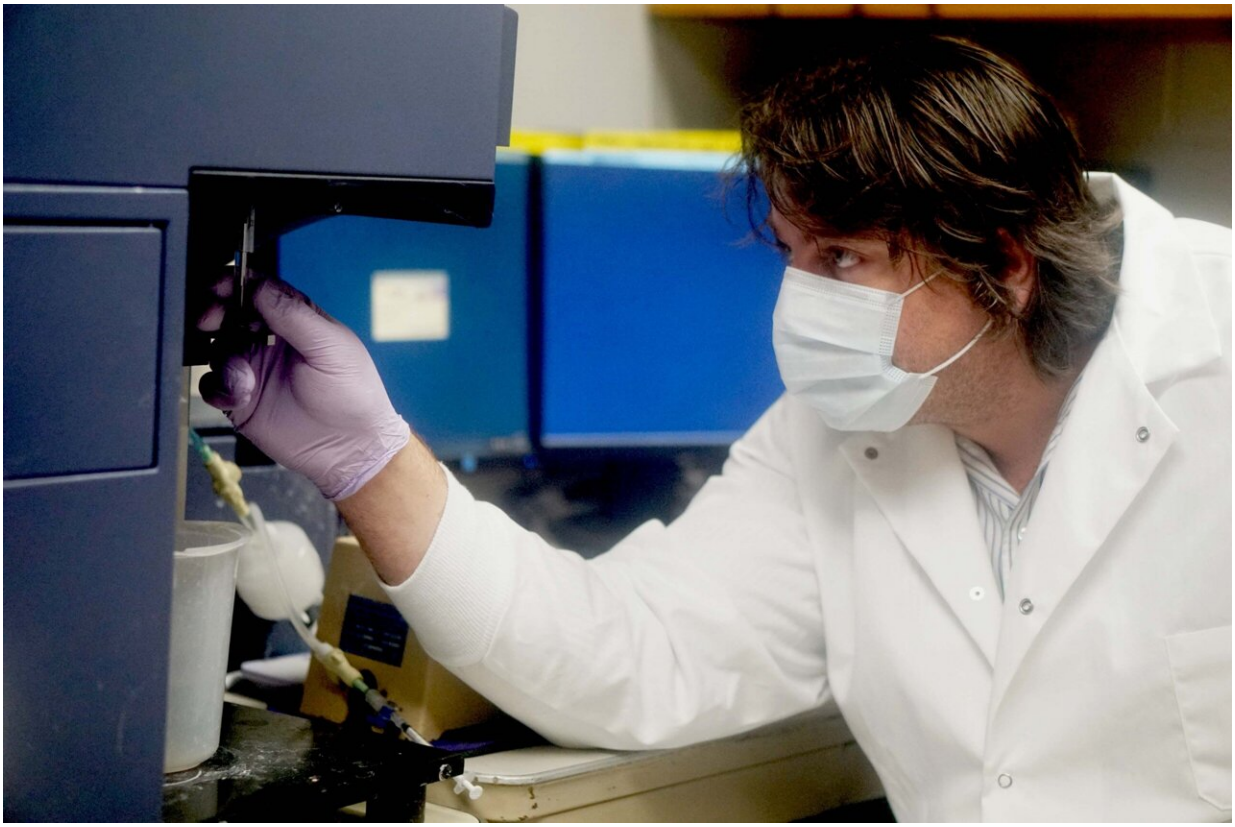

Brock Kingstad-Bakke, a scientist in the UW School of Veterinary Medicine. Credit: School of Veterinary Medicine

A second line of defense—the immune system's T cells—may offer protection from COVID-19 even when vaccine-induced antibodies no

longer can, according to new research out of the University of Wisconsin School of Veterinary Medicine.

The researchers discovered that a new, protein-based vaccine against the original version of the COVID-19 virus was able to teach mouse T cells how to recognize and kill cells infected with new, mutated versions of the virus. This T cell protection worked even when antibodies lost their ability to recognize and neutralize mutated SARS-CoV-2, the virus that causes COVID-19.

"Antibodies prevent COVID-19 infection, but if new variants escape these antibodies, T cells are there to provide a second line of protection," explains lead scientist Marulasiddappa Suresh, a professor of immunology and associate dean for research at the School of Veterinary Medicine.

The study, published in the *Proceedings of the National Academy of Sciences* on May 13, investigates the role of T cells, a specialized type of white blood cell, in defending against COVID-19 when antibodies fail.

When you receive a COVID-19 vaccine, your body learns to produce antibodies, proteins in the immune system that bind to and neutralize SARS-CoV-2. These antibodies circulate in the blood stream and protect you from illness by patrolling the nostrils, airways and lungs and wiping out the virus before it can cause infection or disease.

However, as SARS-CoV-2 mutates, these highly specific antibodies are less able to recognize new viral variants—especially if the changes occur on the virus's spike protein, where the vaccine's antibodies bind. This was especially apparent during the recent wave of the SARS-CoV-2 omicron variant, which has a staggering 37 mutations on its spike protein, making it more able to evade antibodies targeting the original virus's spike protein.

"The biggest problem right now is that none of our current COVID-19 vaccines give complete protection against infection from emerging variants, especially the omicron sublineages BA.1 and BA.2," Suresh says.

That's where T cells can help. Killer T cells aid the immune system by hunting and eliminating "virus factories"—infected cells, says Suresh. So, when antibodies cannot neutralize the virus prior to infection, T cells can clear it quickly, causing mild or no noticeable symptoms.

With this information in hand, the UW–Madison research team, co-led by Suresh and professor of pathobiological sciences Jorge Osorio and assisted by scientist Brock Kingstad-Bakke and doctoral student Woojong Lee, explored how T cells and antibodies can work to prevent COVID-19 infection altogether.

The researchers developed an experimental protein-based vaccine containing the unmutated version of the spike protein from the original SARS-CoV-2 virus. This vaccine was also designed to elicit a strong T cell response to the viral spike protein, allowing the lab to test the extent to which T cells can protect against COVID-19 infection in the presence and absence of virus neutralizing antibodies.

After injecting mice models with their vaccine, researchers then exposed them to two SARS-CoV-2 variants and tested their susceptibility to infection under different conditions.

While vaccine-stimulated antibodies were unable to neutralize the mutated SARS-CoV-2 variants, mice were still immune to COVID-19 caused by the mutated viruses, due to action by T cells that were induced by the vaccine.

Unlike antibodies, T cells are able to detect unfamiliar strains of virus

because the viral fragment that they recognize does not change considerably from one variant to the next.

This work has important implications for future T cell-based vaccines that could provide broad protection against emerging SARS-CoV-2 variants. The experimental vaccine is protein-based and designed to evoke a strong T cell response, differentiating it from currently available mRNA vaccines.

Now, the Suresh lab is studying how exactly T cells defend against SARS-CoV-2 and whether commercially available COVID-19 vaccines may induce these same mechanisms of T cell immunity to protect against emerging variants when the virus dodges established antibodies.

"I see the next generation of vaccines being able to provide immunity to current and future COVID-19 variants by stimulating both broadly-neutralizing antibodies and T cell immunity," Suresh says.

More information: Brock Kingstad-Bakke et al, Vaccine-induced systemic and mucosal T cell immunity to SARS-CoV-2 viral variants, *Proceedings of the National Academy of Sciences* (2022). DOI: 10.1073/pnas.2118312119

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