

'Natural immunity' from omicron is weak and limited, study finds

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In unvaccinated people, infection with the omicron variant of SARS-CoV-2 provides little long-term immunity against other variants, according to a new study by researchers at Gladstone Institutes and UC

San Francisco (UCSF), published today in the journal *Nature*.

In experiments using mice and blood samples from donors who were infected with omicron, the team found that the omicron variant induces only a weak immune response. In vaccinated individuals, this response—while weak—helped strengthen overall protection against a variety of COVID-19 strains. In those without prior vaccination, however, the immune response failed to confer broad, robust protection against other strains.

"In the unvaccinated population, an infection with omicron might be roughly equivalent to getting one shot of a vaccine," says Melanie Ott, MD, Ph.D., director of the Gladstone Institute of Virology and co-senior author of the new work. "It confers a little bit of protection against COVID-19, but it's not very broad."

"This research underscores the importance of staying current with your vaccinations, even if you have previously been infected with the omicron variant, as you are still likely vulnerable to re-infection," says co-senior author Jennifer Doudna, Ph.D., who is a senior investigator at Gladstone, a professor at UC Berkeley, founder of the Innovative Genomics Institute, and an investigator of the Howard Hughes Medical Institute.

A weaker infection

As the omicron variant of SARS-CoV-2 spread around the globe in late 2021 and early 2022, anecdotal evidence quickly mounted that it was causing less [severe symptoms](#) than delta and other variants of concern. However, scientists weren't initially sure why that was, or how a weaker infection might impact long-term immunity against COVID-19.

"When the omicron [variant](#) first emerged, a lot of people wondered whether it could essentially act as a vaccine for people who didn't want

to get vaccinated, eliciting a strong and broad-acting immune response," says Irene Chen, co-first author of the new study and graduate student in Ott's lab. Other first authors are Rahul Suryawanshi, Ph.D., a Gladstone staff research scientist, and Tongcui Ma, Ph.D., scientist in the Roan Lab at Gladstone.

To find the answer, the team of researchers first examined the effect of omicron in mice. Compared to an ancestral strain of SARS-CoV-2 and the [delta variant](#), omicron led to far fewer symptoms in the mice. However, the virus was detected in airway cells, albeit at lower levels. Similarly, omicron was able to infect isolated [human cells](#) but replicated less than other variants.

The team then characterized the immune response generated by omicron infections. In mice infected with omicron, despite the milder symptoms, the [immune system](#) still generated the T cells and antibodies typically seen in response to other viruses.

"We demonstrated in this study that the lower pathogenicity of omicron is not because the virus cannot take hold," says Nadia Roan, Ph.D., an associate investigator at Gladstone.

That leaves other reasons that might explain why omicron differs from other variants in terms of symptoms and immunity, including the lower replication seen with omicron or the types of antibodies that the immune system generates in response to the virus.

No cross-variant protection

To gauge how the [immune response](#) against omicron fared over time, the researchers collected [blood samples](#) from mice infected with the ancestral, delta, or omicron variants of SARS-CoV-2 and measured the ability of their immune cells and antibodies to recognize five different

viral variants—ancestral (WA1), alpha, beta, delta, and omicron.

Blood from uninfected animals was unable to neutralize any of the viruses—in other words, block the ability of any of the viruses to copy themselves. Samples from WA1-infected animals could neutralize alpha and, to a lesser degree, the beta and delta virus—but not omicron. Samples from delta-infected mice could neutralize delta, alpha and, to a lesser degree, the omicron and beta virus.

However, blood from omicron-infected mice could only neutralize the [omicron variant](#).

The team confirmed these results using blood from ten unvaccinated people who had been infected with omicron—their blood was not able to neutralize other variants. When they tested blood from 11 unvaccinated people who had been infected with delta, the samples could neutralize delta and, as had been seen in mice, the other variants to a lesser extent.

When they repeated the experiments with blood from vaccinated people, the results were different: vaccinated individuals with confirmed omicron or delta breakthrough infections all showed the ability to neutralize all the tested variants, conferring higher protection.

"When it comes to other variants that might evolve in the future, we can't predict exactly what would happen, but based on these results, I'd suspect that [unvaccinated people](#) who were infected with [omicron](#) will have very little protection," says Ott. "But on the contrary, vaccinated individuals are likely to be more broadly protected against future variants, especially if they had a breakthrough infection."

"Our results may be useful not only to inform individuals' decisions on vaccination, but also for the design of future COVID-19 vaccines that confer broad protection against many variants," says Charles Chiu, MD,

Ph.D., a professor of infectious diseases at UCSF and a co-senior author of the work.

The research was published in *Nature*.

More information: Rahul K. Suryawanshi et al, Limited cross-variant immunity from SARS-CoV-2 Omicron without vaccination, *Nature* (2022). [DOI: 10.1038/s41586-022-04865-0](https://doi.org/10.1038/s41586-022-04865-0)

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