

New study suggests two paths toward 'super immunity' to COVID-19

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New laboratory research from Oregon Health & Science University reveals more than one path toward robust immunity from COVID-19.

A new study finds that two forms of immunity—[breakthrough infections](#) following vaccination or natural [infection](#) followed by vaccination—provide roughly equal levels of enhanced immune protection.

The new study published online today in the journal *Science Immunology*.

"It makes no difference whether you get infected-and-then-vaccinated, or if you get vaccinated-and-then-a-breakthrough infection," said co-senior author Fikadu Tafesse, Ph.D., assistant professor of molecular microbiology and immunology in the OHSU School of Medicine. "In either case, you will get a really, really robust immune response—amazingly high."

The research follows an OHSU study published in December that described extremely high levels of immune response following breakthrough infections—so-called "super immunity." That study was the first to use multiple live SARS-CoV-2 variants to measure cross-neutralization of blood serum from breakthrough cases.

The new study found that it doesn't matter whether someone gets a breakthrough infection or gets vaccinated after a natural infection. In both cases, the immune response measured in blood serum revealed antibodies that were equally more abundant and more potent—at least 10 times more potent—than immunity generated by vaccination alone.

The study was done before the emergence of the omicron variant, but researchers expect the hybrid immune responses would be similar with the new highly transmissible variant.

"The likelihood of getting breakthrough infections is high because there is so much virus around us right now," Tafesse said. "But we position

ourselves better by getting vaccinated. And if the virus comes, we'll get a milder case and end up with this super immunity."

Researchers recruited a total of 104 people, all OHSU employees who were vaccinated by the Pfizer vaccine, and then carefully divided them into three groups: 42 who were vaccinated with no infection, 31 who were vaccinated after an infection, and 31 who had breakthrough infections following vaccination. Controlling for age, sex and time from vaccination and infection, the researchers drew [blood samples](#) from each participant and exposed the samples to three variants of the live SARS-CoV-2 virus in a Biosafety Level 3 lab on OHSU's Marquam Hill campus.

They found both of the groups with "hybrid immunity" generated greater levels of immunity compared with the group that was vaccinated with no infection.

A path toward endemic COVID

With the wildly contagious omicron variant now circulating across the globe, the new findings suggest each new breakthrough infection potentially brings the pandemic closer to the end.

"I would expect at this point many vaccinated people are going to wind up with breakthrough infections—and hence a form of hybrid immunity," said senior co-author Bill Messer, M.D., Ph.D., assistant professor of molecular microbiology and immunology and medicine (infectious diseases) in the OHSU School of Medicine

Over time, the virus will run into an ever-expanding pool of human immunity.

OHSU scientists say they haven't tested multiple rounds of natural

infection, although many people will likely find themselves in that category given that millions of people in the United States and around the world remain entirely unvaccinated. With the spread of the highly contagious omicron variant, many unvaccinated people who were previously infected are likely to confront the virus again.

For that group, previous research reveals a much more variable level of immune response than vaccination, Messer said.

"I can guarantee that such immunity will be variable, with some people getting equivalent immunity to vaccination, but most will not," he said. "And there is no way, short of laboratory testing, to know who gets what immunity. Vaccination makes it much more likely to be assured of a good immune response."

Senior co-author Marcel Curlin, M.D., agreed.

"Immunity from natural infection alone is variable. Some people produce a strong response and others do not," said Curlin, associate professor of medicine (infectious diseases) in the OHSU School of Medicine and director of OHSU Occupational Health. "But vaccination *combined* with immunity from infection almost always provides very strong responses.

"These results together with our previous work point to a time when SARS-CoV-2 may become a mostly mild endemic infection like a seasonal respiratory tract infection instead of a worldwide pandemic."

More information: Timothy A. Bates et al, Vaccination before or after SARS-CoV-2 infection leads to robust humoral response and antibodies that effectively neutralize variants, *Science Immunology* (2022). [DOI: 10.1126/sciimmunol.abn8014](https://doi.org/10.1126/sciimmunol.abn8014)

Timothy A. Bates et al, Neutralization of SARS-CoV-2 variants by convalescent and BNT162b2 vaccinated serum, *Nature Communications* (2021). [DOI: 10.1038/s41467-021-25479-6](https://doi.org/10.1038/s41467-021-25479-6)

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