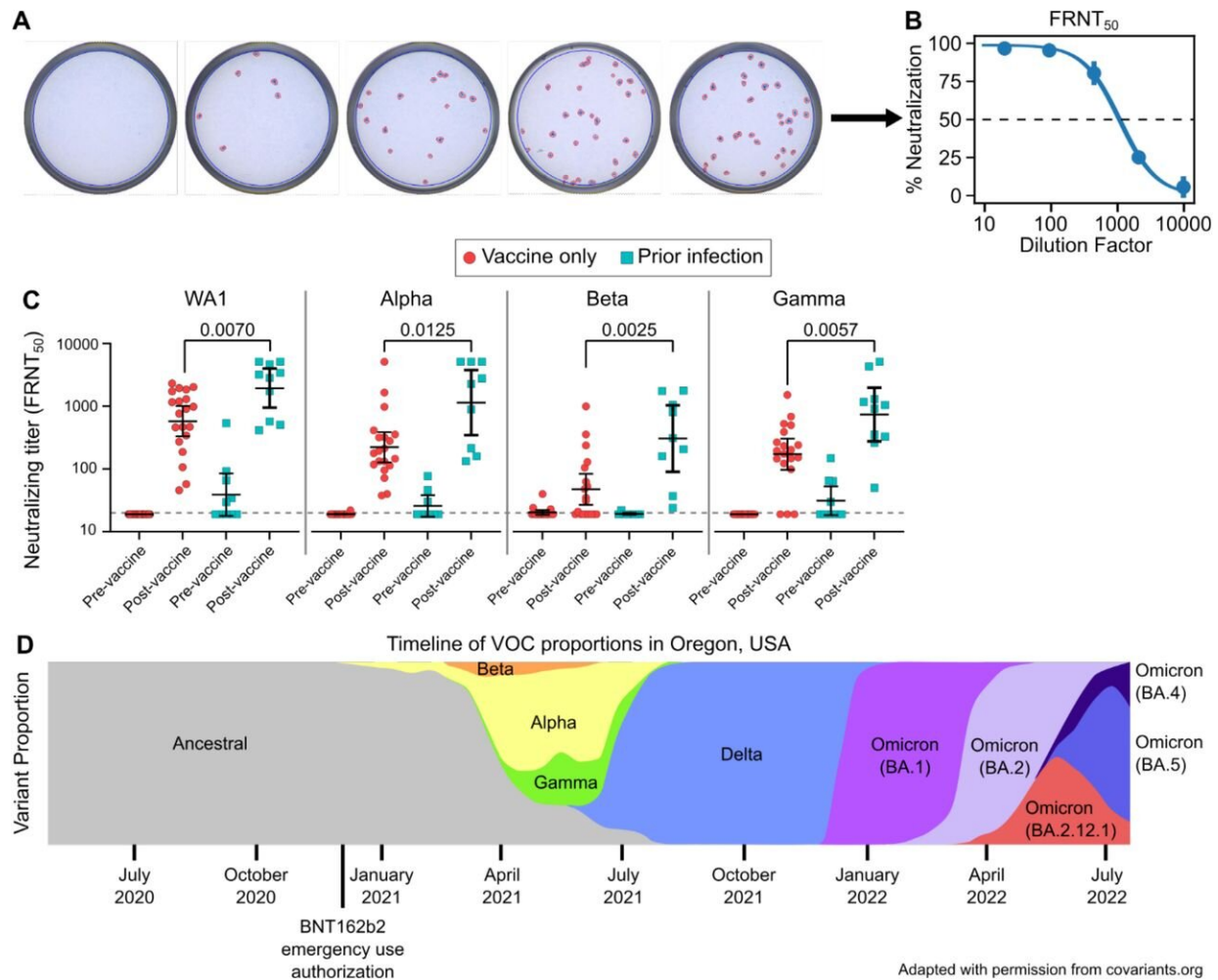


Researchers find immune response to COVID strengthens over time

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Longitudinal cohort of previously infected vaccinees shows improved variant neutralization compared to vaccination alone. Representative focus reduction neutralization test (FRNT) results showing wells infected with live SARS-CoV-2 with the addition of serially diluted serum which were stained and counted (A).

Representative focus reduction neutralization curve showing the average neutralization of duplicates as a percent of no serum controls and fit to a dose-response curve to find the 50% neutralizing titer (FRNT₅₀) (B). Live virus FRNT₅₀ measurements against original SARS-CoV-2 (WA1) and the Alpha, Beta, and Gamma variants before and after vaccination (C). Timeline depicting the prevalence of impactful variants in the study location, Oregon, USA (D). Vaccine-only participants are represented by red circles and hybrid immune participants by cyan squares. Error bars represent the geometric mean with 95% confidence intervals. P values in C show the result of Mann-Whitney U tests. All P values are two-tailed and 0.05 was considered significant. For panel C, n=20 for the vaccine only group and n=10 for the prior infection group. Credit: *medRxiv* (2023). DOI: 10.1101/2023.01.02.23284120

Immunity from COVID-19 appears to gather strength with more time between vaccination and infection, a new laboratory study from researchers at Oregon Health & Science University suggests. The findings carry implications for vaccine recommendations as the pandemic transitions to an endemic state.

Researchers measured the antibody response in blood samples for a group of people who gained so-called "hybrid immunity" through two means: either vaccination followed by a [breakthrough infection](#), or by getting vaccinated after contracting COVID-19. They measured the immune response in [blood samples](#) of 96 generally healthy OHSU employees and found that the immune response was uniformly stronger the longer the time period between vaccination and infection. The longest interval measured was 404 days.

Their findings suggest that [vaccine](#) boosters should be spaced no more frequently than a year apart, at least among healthy people.

"Longer intervals between natural infection and vaccination appear to

strengthen immune response for otherwise healthy people," said co-senior author Fikadu Tafesse, Ph.D., associate professor of molecular microbiology and immunology in the OHSU School of Medicine.

The study comes as an [advisory panel](#) for the Food and Drug Administration is due to meet Thursday, Jan. 26, to consider the nation's COVID-19 vaccine strategy going forward.

Published in the *Journal for Clinical Investigation Insight*, the new research is the latest in a series of laboratory discoveries by OHSU scientists revealing a pattern of strengthened immune response through hybrid immunity. Their findings suggest that the magnitude, potency and breadth of hybrid immune response all increased with a longer time period between exposure to the virus—whether through vaccination or natural infection.

This likely is related to the body's immune response maturing over time, said co-senior author Marcel Curlin, M.D., associate professor of medicine ([infectious diseases](#)) in the OHSU School of Medicine and medical director of OHSU Occupational Health.

"The [immune system](#) is learning," Curlin said. "If you're going to amplify a response, what this study tells us is that you might want to boost that response after a longer period of learning rather than early after exposure."

Further, the research team found that it didn't matter whether someone developed hybrid immunity by getting vaccinated after contracting COVID-19 or after a breakthrough infection following vaccination. Both groups developed an equally potent immune response.

The findings suggest long-lasting potency of so-called "memory cells," the B cells that recognize an invading virus and generate protein

antibodies to neutralize the virus and its many variants. The authors write that an ever-growing pool of people who have contracted the SARS-CoV-2 virus stand to benefit from vaccination, even if they've delayed it until now.

Relying on natural [infection](#) alone is a bad idea, "given the risks of severe illness, long-term complications, and death," the authors write.

The researchers say the findings are the latest to point toward the virus evolving to an endemic state.

"Our results point to a future where inevitable vaccine breakthrough infections would be expected to help build a reservoir of population-level immunity that can help blunt future waves and reduce the opportunity for further viral evolution," they write.

The researchers cautioned that the [immune response](#) was measured in relatively healthy people, and boosters may be advisable on a more frequent basis among vulnerable people who are older or are immunocompromised.

More information: Timothy A. Bates et al, The time between vaccination and infection impacts immunity against SARS-CoV-2 variants, *medRxiv* (2023). [DOI: 10.1101/2023.01.02.23284120](https://doi.org/10.1101/2023.01.02.23284120)

Timothy A. Bates et al, An extended interval between vaccination and infection enhances hybrid immunity against SARS-CoV-2 variants, *JCI Insight* (2023). DOI: 10.1172/jci.insight.165265 , insight.jci.org/articles/view/165265

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