

Infection plus vaccination yields better antibodies against COVID-19 variants

December 7 2021, by Joanna Urban



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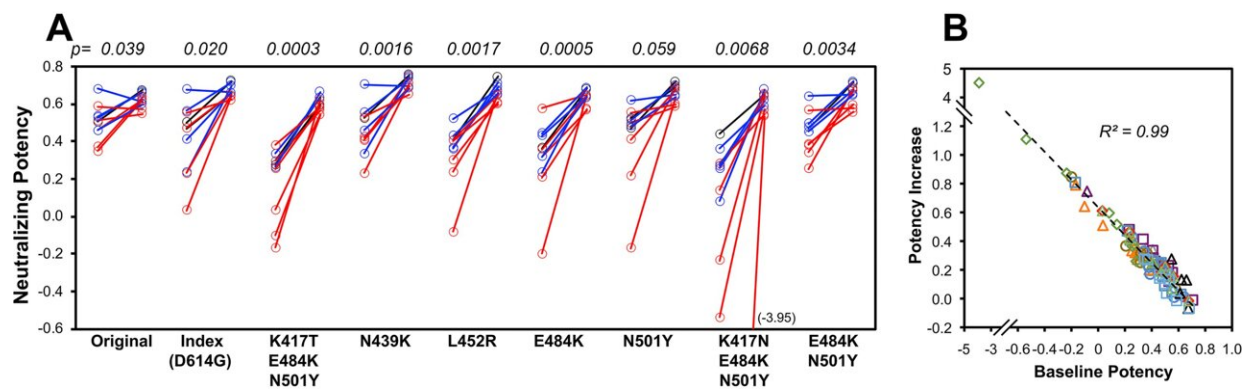
Antibodies against the SARS-CoV-2 spike protein produced by the immune system can help identify and fend off future infections, but not all antibodies are the same. People who either recovered from

COVID-19 early in the pandemic or received a current vaccine may not be able to fend off new and emerging variants.

But, this week in *mBio*, an open-access journal of the American Society for Microbiology, researchers report that the combination of the two can produce a more potent defense. According to the study, people who've had an infection and received a vaccine have high-quality [antibodies](#) that act against spike variants—and more effectively than either group alone.

"It shows that antibody quality can improve over time, and not just quantity," said immunologist and physician Otto Yang, M.D., at the David Geffen School of Medicine at the University of California Los Angeles. Finding the optimal mix of antibodies could help guide future preventive efforts. "It fits in to understanding what the optimal vaccination regimen is," said Yang, who led the new study.

The pandemic continues to propagate, in part, because as the coronavirus spike protein evolves—which helps the virus infiltrate a host cell—new variants emerge that help the infection spread more easily from person-to-person. As a result, antibodies that a person developed after an early infection or after vaccination may not adequately protect the body from these newer emerging variants.



Changes in SARS-CoV-2 spike variant neutralizing potency of antibodies after vaccination of persons with prior SARS-CoV-2 infection. For the 10 persons with prior COVID-19 described in the legend to Fig. 1, vaccination was initiated a mean of 353 days after symptom onset (range, 280 to 394 days), and serum neutralizing potency against each variant was determined after vaccination. (A) Potency against each variant is plotted consecutively for recent infection (18 to 45 days after the onset of symptoms; mean, 31 days) and postvaccination. Five persons received BNT162b2 (red), four persons received mRNA-1273 (blue), and one person received Ad26.COV2.S (black). The P values for comparisons between recent infection and postvaccination are given above each variant. (B) The changes in potencies against each variant are plotted against the initial potencies against each corresponding variant. Each symbol depicts the value for one variant. Credit: DOI: 10.1128/mBio.02656-21

An area of the spike protein called the receptor binding domain, or RBD, enables the virus to invade a host cell. This region is also a critical target for antibodies, but random mutations in the RBD mean it's an ever-changing target. In the new study, Yang and his colleagues compared anti-RBD antibodies in the blood of participants to the ability of the antibodies to neutralize the virus.

In uninfected patients who had received one of two COVID-19 vaccines, the researchers found antibodies that were less effective against mutations in the new variants (like Beta or Gamma) than they were against the original genetic sequence encoded in the vaccine. Similarly, when the researchers analyzed [blood samples](#) from people who'd been infected with the coronavirus before May 2020—before the first confirmation of variants—had reduced potency against newer variants compared to the original. These findings suggest that both mild infection and vaccination produce antibodies that still leave a person vulnerable to new variants.

But the results differed dramatically for individuals who'd been infected before May 2020 and, a year later, been vaccinated. In these prior-infected, vaccinated individuals, the researchers found antibodies that were unchanged in efficacy against the original sequence—but just as potent against new variants. Yang said those results align with similar findings by other groups, published earlier this year, that also show high-quality antibodies in people who'd been infected and vaccinated.

"We might have predicted that antibodies would continue to evolve and get better with multiple exposures," said Yang, "but we didn't expect it to happen that fast."

Studies like this one showing how antibodies change in quality could help researchers improve the implementation of vaccines and boosters—not only for COVID-19 but for the next pathogen that comes along, said Yang.

More information: F. Javier Ibarondo et al, Previous Infection Combined with Vaccination Produces Neutralizing Antibodies with Potency against SARS-CoV-2 Variants, *mBio* (2021). DOI: 10.1128/mBio.02656-21

Provided by American Society for Microbiology

Citation: Infection plus vaccination yields better antibodies against COVID-19 variants (2021, December 7) retrieved 15 June 2024 from <https://medicalxpress.com/news/2021-12-infection-vaccination-yields-antibodies-covid-.html>

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