Researchers have identified antibodies that may eliminate the need for repeated booster vaccinations

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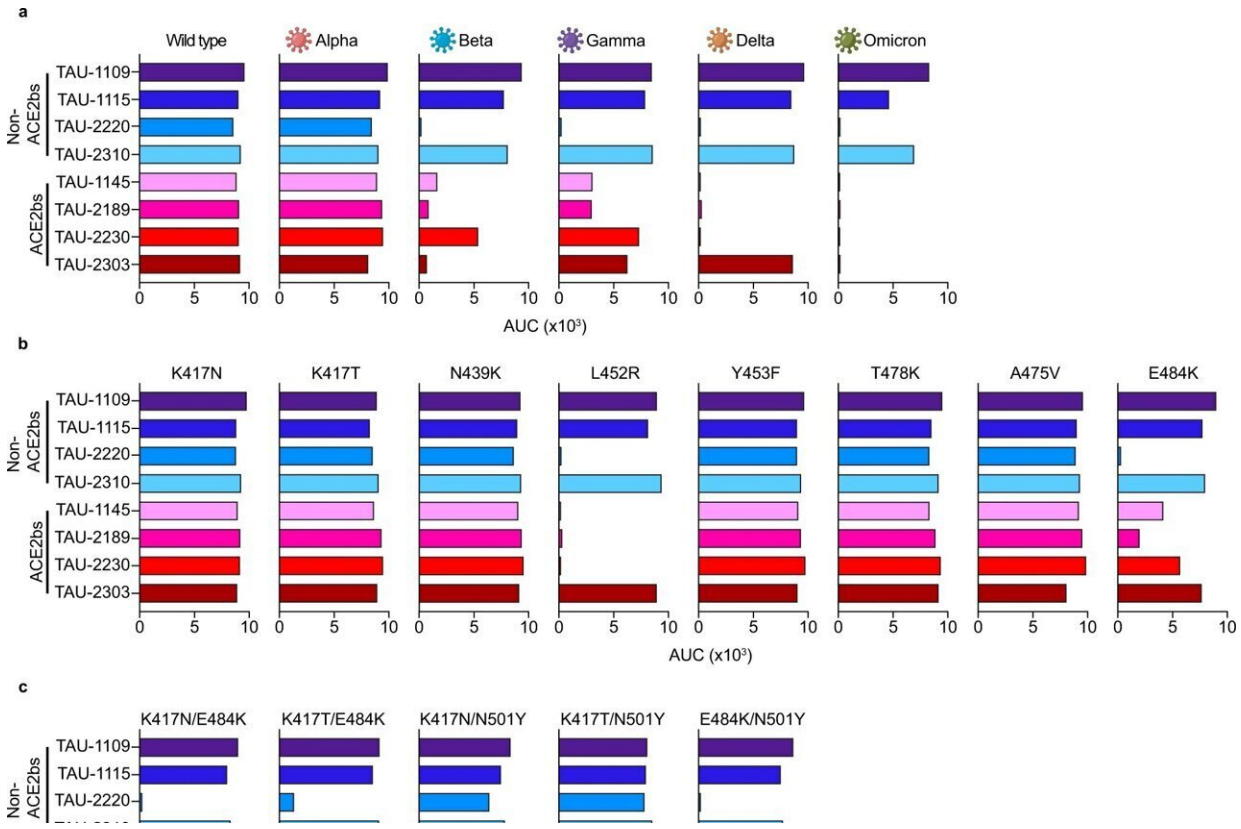

Antibody binding to the RBD of wild type and SARS-CoV-2 VOCs by ELISA. ACE2bs or non-ACE2bs antibodies are indicated to the left of each panel, a–d. For panels a–c, each graph represents antibody binding to wild type or VOC (a), single (b) or double (c) mutant RBD. AUC was calculated by GraphPad Prism. Each experiment was repeated at least three times (n ≥ 3). d Summary of the antibody binding affinity to each RBD generated in this study. Green color

indicates binding affinity of > 75%, orange of 25–75%, and yellow of
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A team of researchers from Tel Aviv University has demonstrated that antibodies isolated from the immune system of recovered COVID-19 patients are effective in neutralizing all known strains of the virus, including the delta and the omicron variants. According to the researchers, this discovery may eliminate the need for repeated booster vaccinations and strengthen the immune system of populations at risk.

The research was led by Dr. Natalia Freund and doctoral students Michael Mor and Ruofan Lee of the Departmentof Clinical Microbiology and Immunology at the Sackler Faculty of Medicine. The study was conducted in collaboration with Dr. Ben Croker of the University of California San Diego. Prof. Ye Xiang of Tsinghua University in Beijing. Prof. Meital Gal-Tanamy and Dr. Moshe Dessau of Bar-Ilan University also took part in the study. The study was published in *Communications Biology*.

The present study is a continuation of a preliminary study conducted in October 2020, at the height of the COVID-19 crisis. At that time, Dr. Freund and her colleagues sequenced all the B immune system cells from the blood of people who had recovered from the original COVID strain in Israel, and isolated nine antibodies that the patients produced. The researchers now found that some of these antibodies are very effective in neutralizing the new coronavirus variants, delta and omicron.

Dr. Freund says that "in the previous study, we showed that the various antibodies that are formed in response to infection with the original virus are directed against different sites of the virus. The most effective antibodies were those that bound to the virus's 'spike' protein, in the

same place where the spike binds the cellular receptor ACE2. Of course, we were not the only ones to isolate these antibodies, and the global health system made extensive use of them until the arrival of the different variants of the coronavirus, which in fact rendered most of those antibodies useless."

"In the current study, we proved that two other antibodies, TAU-1109 and TAU-2310, which bind the viral spike protein in a different area from the region where most of the antibodies were concentrated until now (and were therefore less effective in neutralizing the original strain) are actually very effective in neutralizing the delta and omicron variants. According to our findings, the effectiveness of the first antibody, TAU-1109, in neutralizing the omicron strain is 92%, and in neutralizing the delta strain, 90%. The second antibody, TAU-2310, neutralizes the omicron variant with an efficacy of 84%, and the delta variant with an efficacy of 97%."

According to Dr. Freund, the surprising effectiveness of these antibodies might be related to the evolution of the virus: "The infectivity of the virus increased with each variant because each time, it changed the amino acid sequence of the part of the spike protein that binds to the ACE2 receptor, thereby increasing its infectivity and at the same time evading the natural antibodies that were created following vaccinations. In contrast, the antibodies TAU-1109 and TAU-2310 don't bind to the ACE2 receptor binding site, but to another region of the spike protein—an area of the viral spike that for some reason does not undergo many mutations—and they are therefore effective in neutralizing more viral variants. These findings emerged as we tested all the known COVID strains to date."

The two antibodies, cloned in Dr. Freund's laboratory at Tel Aviv University, were sent for tests to check their effectiveness against live viruses in laboratory cultures at the University of California San Diego,

and against pseudoviruses in the laboratories of the Faculty of Medicine of Bar-Ilan University in the Galilee; the results were identical and equally encouraging in both tests.

Dr. Freund believes that the antibodies can bring about a real revolution in the fight against COVID-19: "We need to look at the COVID-19 pandemic in the context of previous disease outbreaks that humankind has witnessed. People who were vaccinated against smallpox at birth and who today are 50 years old still have antibodies, so they are probably protected, at least partially, from the monkeypox virus that we have recently been hearing about. Unfortunately, this is not the case with the coronavirus."

"For reasons we still don't yet fully understand, the level of antibodies against COVID-19 declines significantly after three months, which is why we see people getting infected again and again, even after being vaccinated three times. In our view, targeted treatment with antibodies and their delivery to the body in high concentrations can serve as an effective substitute for repeated boosters, especially for at-risk populations and those with weakened immune systems. COVID-19 infection can cause serious illness, and we know that providing antibodies in the first days following infection can stop the spread of the virus. It is therefore possible that by using effective antibody treatment, we will not have to provide booster doses to the entire population every time there is a new variant."

More information: Ruofan Li et al, Conformational flexibility in neutralization of SARS-CoV-2 by naturally elicited anti-SARS-CoV-2 antibodies, *Communications Biology* (2022). DOI: 10.1038/s42003-022-03739-5

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