New study charts the complexity of SARS-CoV-2 neutralization

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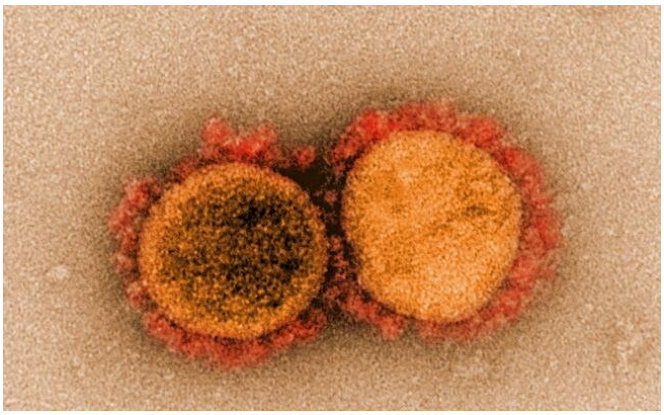

Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: NIAID

In the absence of effective treatments for COVID-19, many countries have approved the therapeutic use of blood plasma from recovering patients because it contains antibodies against the coronavirus. But not every type of antibody can neutralize the virus and render it noninfectious. New research published this week in *mSphere*, an open-access journal of the American Society for Microbiology, explores variation in virus neutralization capabilities, which can vary widely by type of antibody.

"What we need for plasma therapy is not only high levels of antibodies but also high neutralization capability," said virologist Michael Schindler, Ph.D, at University Hospital Tübingen, in Germany.

The researchers analyzed COVID-19 antibodies in the blood of 49 people with asymptomatic or mild cases, then tested those antibodies on human cell lines infected with the virus for neutralization capabilities. In agreement with other studies, they found that in the vast majority of cases (88%) infected individuals mounted a robust SARS-CoV-2-specific antibody response that neutralizes the virus. Furthermore, neutralization correlated strongly with the abundance of antibodies against the receptor-binding domain of coronavirus's S protein.

But that wasn't the entire story, Schindler said. Only 6 patients produced antibodies in sufficient amounts to neutralize virus at high serum dilutions. Four patients in the study who showed symptoms and tested positive for infection didn't develop antibodies specific to SARS-CoV-2 at all. Another 4 patients developed fairly high antibody levels, Schindler said, but poorly neutralized the virus in the experiments on human cell lines.

"It shows that we cannot generalize assumptions about the antibodies," said virologist Natalia Ruetalo, Ph.D, also at University Hospital Tübingen. Ruetalo, first author of the study, added that not everyone has the same immune response.

The findings suggest that some proportion of patients mount an immune response that doesn't lead to a neutralizing effect, Ruetalo said. "Those people may remain below some threshold of protective immunity and eventually get re-infected," she said.

In subsequent experiments, the researchers used an assay to quantify levels of antibodies from other coronaviruses in the serum of patients. They correlated those results to the ability of the sera to neutralize the COVID-19 coronavirus. They found, surprisingly, an association with antibodies against coronavirus 229E, which can cause the common cold. Antibodies produced during an infection with the cold likely aren't sufficient to protect a person against COVID-19, Schindler said, but they may help the body neutralize the virus.

The new work highlights the complexity of trying to use antibodies as evidence of immune protection,

but without measuring neutralization, Schindler said. His group is now conducting similar experiments to identify which antibodies may neutralize variants of SARS-CoV-2 that have emerged in South Africa and elsewhere.?

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