New lab test clarifies the potential protective effects of COVID-19 antibodies

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Cong Zeng and Jack Evans were first authors of a paper describing a new assay that detects neutralizing antibodies against SARS-CoV-2. Credit: The Ohio State University

Knowing you have developed antibodies against the SARS-CoV-2 virus after recovering from COVID-19 doesn't tell you everything about your immunity. The levels and even types of antibodies can differ among patients, and those differences can influence whether a person is protected against being reinfected.

Scientists at The Ohio State University have developed a new lab testing procedure for the detection of antibodies against SARS-CoV-2 that gives results more quickly than existing assays and specifically identifies so-called "neutralizing" antibodies—those that protect by blocking infection of cells.

"With many assays currently in use, we can detect antibodies, but that doesn't tell us if they're neutralizing antibodies. We only know the level of antibodies someone has," said Shan-Lu Liu, professor in the Ohio State College of Veterinary Medicine's Department of Veterinary Biosciences and the senior author of a new journal article describing the assay.

"Some antibodies might be protective, some might not be protective, and some might even enhance infection—we know with this type of coronavirus and some other viruses, some antibodies can even do harm," he said. "Our assay examines whether antibodies are potentially protective, which means they prevent a patient from reinfection and block viral replication. That's the outcome of infection that we want people to have."

In analyses of blood samples from several different populations that had tested positive for COVID-19, the researchers found with this new assay that, overall, ICU patients had produced the highest concentration of neutralizing antibodies, and convalescent plasma donors and health care workers had the lowest antibody levels.

"So the more severe the disease, the higher the antibody levels produced. And what this tells us is there is a wide spectrum of different antibody levels after infection," said Liu, also an investigator in the Center for Retrovirus Research and co-director of the Viruses and Emerging Pathogens Program in Ohio State's Infectious Diseases Institute. "We're in a pandemic now, but eventually we'll be able to see not just how many people were infected, but also the outcome. Our assay could be used to tell whether antibodies have been developed in individuals who have had contacts with SARS-CoV-2."

The research is published online in the journal *JCI Insight*.

Liu and colleagues developed what is called a "pseudotype" virus neutralizing antibody assay, in which an HIV vector and core is coated with the SARS-CoV-2 spike protein to detect antibodies against the coronavirus. The team applied a new approach by selecting a different form of light-producing enzyme that can be detected conveniently in culture media containing the virus-infected cells. That choice saved several steps, and

time, in the detection process without losing accuracy and sensitivity to the target virus.

Co-first authors Cong Zeng, a postdoctoral researcher, and Jack Evans, a student in the molecular, cellular and developmental biology graduate program, completed the majority of the work to develop the assay.

With the new analytical tool in hand, scientists in the College of Veterinary Medicine collaborated with Gerard Lozanski and others in the College of Medicine to analyze 221 patient blood samples to validate the effectiveness of the assay and verify that the detection test could be scaled up for widespread screening.

The samples were derived from 104 hospitalized COVID-19 patients, 49 of whom were in intensive care; 42 health care professionals who had tested positive for COVID-19; 38 convalescent plasma donors (recovered patients who donated plasma for potential therapeutic use in very sick COVID-19 patients); and 37 control samples from patients who had been hospitalized with respiratory conditions before September 2019.

Results showed that, in general, hospitalized patients—and ICU patients in particular—had the highest concentrations, or titers, of neutralizing antibodies in their systems. However, over 14% of those who had been hospitalized had no or very low levels of antibodies.

Of the health care professionals, 40% were negative for neutralizing antibodies and 36% had low concentrations. And more than half of the convalescent blood donors had concentrations of antibodies that were too low to qualify them as donors for treatment of COVID-19 patients, Liu said.

The assay detected no SARS-CoV-2 antibodies in the samples from people who had been sick with other types of respiratory diseases.

The test accuracy was further validated by verifying in a lab setting that the antibodies detected in the COVID-19 patient blood samples did in fact neutralize the authentic SARS-CoV-2 virus.

It won't be long before the assay is put to a larger test. The effectiveness, sensitivity and specificity of the assay were important factors in Ohio State's successful application for a $10 million National Cancer Institute grant awarded last month for studies of the long-term impact of COVID-19 on first responders, health care workers and the general population. Two of the co-authors on the JCI Insights paper will be co-principal investigators of the first-responders study: Eugene Oltz, chair of microbial infection and immunity in the College of Medicine, and Linda Saif, Distinguished University Professor in the College of Veterinary Medicine's Department of Veterinary Preventive Medicine and the Food Animal Health Research Program in the College of Food, Agricultural and Environmental Sciences.

"We will use this assay to conduct a serological study of first responders in Columbus, among others," Liu said.

Additional applications could include screening for protective qualities in lab-manufactured monoclonal antibodies designed for therapeutic purposes and neutralizing antibody production in vaccine candidates.

Patent applications have been filed covering the assay and its use in a variety of applications. Inventors named on the applications are Liu, Zeng, Evans, and co-authors Panke Qu and Yi Min Zheng.

"We are pleased to have developed a neutralization assay which provides a sensitive, specific and simple method for determining the neutralizing antibody titers in patient serum or plasma with results being achieved in 24 hours—without requiring access to a biosafety level-3 facility," Liu said.

"We'd like to make it widely available as quickly as possible because we think it's a rapid and simple system compared to other systems."

More information: Cong Zeng et al, Neutralizing antibody against SARS-CoV-2 spike in COVID-19 patients, health care workers and convalescent plasma donors, *JCI Insight* (2020). DOI:

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