Research team develops new antibody test for COVID-19

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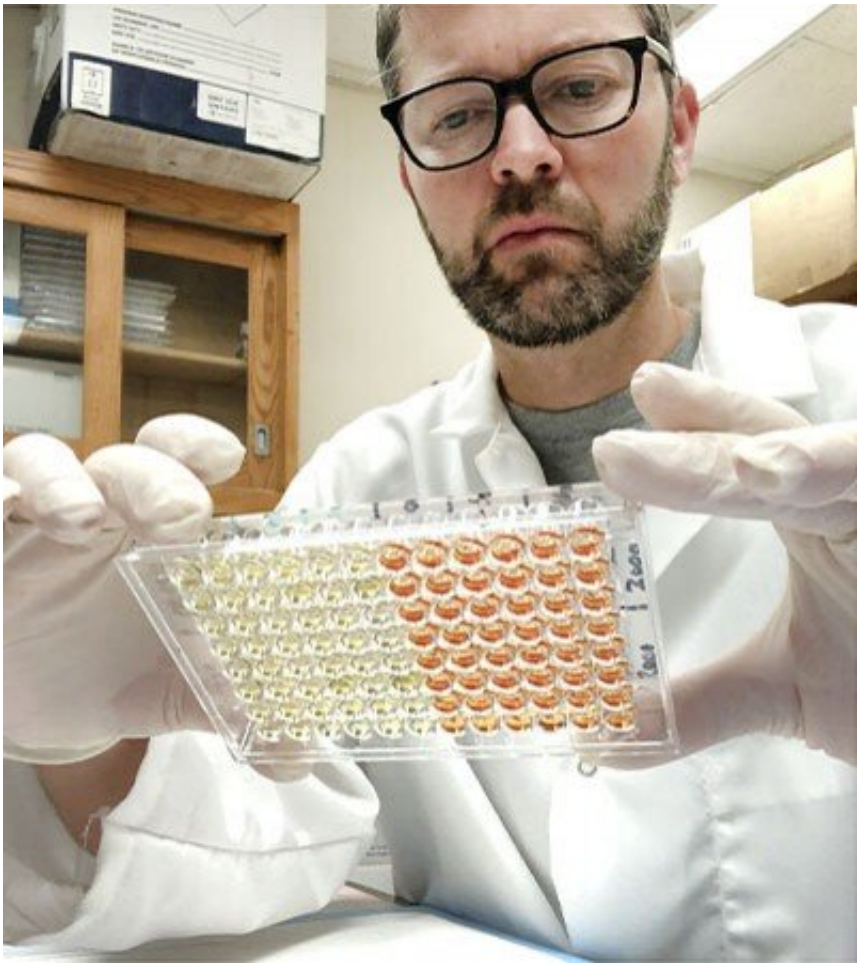

Biological anthropologist Thom McDade. Credit: Northwestern University

As antibody testing ramps up across the country, Northwestern University researchers have developed a new method for testing for

SARS-CoV-2 (the virus that causes COVID-19) antibodies. The method requires only a single drop of blood collected from a simple finger prick.

A team of scientists, including biological anthropologist Thomas McDade, together with pharmacologist Alexis Demonbreun and investigators Dr. Richard D'Aquila, Brian Mustanski and Dr. Elizabeth McNally, reported this new test in a paper on MedRxiv, the preprint server for health sciences.

Antibody tests are useful for determining prior exposure to a virus, like the one that causes COVID-19. But current approaches to antibody testing have significant limitations: Point-of-care tests using finger stick blood are qualitative and often inaccurate, while more precise lab-based tests require venous blood. The Northwestern team has developed an approach that combines the convenience of finger stick blood sampling in the home with the analytical rigor that can be applied in the lab.

"As the first waves of infection subside, antibody testing is necessary for ascertaining the true prevalence and mortality rate of infection and for evaluating how effective policies such as social distancing or closing schools and restaurants are working to prevent viral transmission," said McDade, professor of anthropology in the Weinberg College of Arts and Sciences and a faculty fellow with the University's Institute for Policy Research. He is the lead author of the paper.

Currently, most viral testing has relied on polymerase chain reaction (PCR) analysis of nasal swabs to detect the presence of the virus. Serological testing, also known as antibody testing, serves a different and complementary function, detecting the presence of the IgM and IgG antibodies against SARS-CoV-2 in blood samples from previously exposed individuals.

"Tests for IgG can be used to screen for prior exposure, regardless of

whether a person had symptoms," McDade said. "IgG levels increase approximately 14 days after infection and remain detectable in blood for several months, and possibly years."

Gaps in testing

The research team realized early in the pandemic that there were important gaps in the current approach to antibody testing. They quickly assembled a unique team with complimentary expertise. Since testing materials—for all types of testing—have been in short supply, the team manufactured key reagents. Investigators worked in parallel on Northwestern's Evanston and Chicago campuses to expedite development and ensure the test performed equally well in the hands of multiple researchers. The team next built a scalable test so that it can be more broadly used in the community.

According to McNally, director of the Center for Genetic Medicine at Northwestern University Feinberg School of Medicine, "Widespread serological testing is essential for figuring out how the virus is spreading in the community, but it is very hard to screen large numbers of people when the tests require people to come to a health care provider."

Developing field-friendly methods

The team's testing approach builds on McDade's pioneering work to develop field-friendly dried blood spot (DBS) methods in which drops of whole blood collected from a simple finger stick are stored on special filter paper, where it dries. He has developed DBS methods for multiple biomarkers of inflammation and immune function, and many of those methods have been incorporated into large, population-based studies over the past 15 years. This approach overcomes the logistical challenges associated with venous blood collection and facilitates the collection of

blood samples in non-clinical settings at low cost.

The team developed two DBS-based protocols for SARS-CoV-2 IgG antibodies. In both, enzyme-linked immunosorbent assay (ELISA) was optimized to detect SARS-CoV-2 IgG antibodies against the receptor-binding domain (RBD) of the spike protein, which sits on the surface of the virus and is important for facilitating entry into our cells and initiating infection.

"The RBD is a section of the spike protein that is very 'immunogenic'—that is, it elicits a strong reaction from our immune system, including the production of antibodies specific to the RBD. We can, therefore, measure antibodies against RBD as an indicator of prior exposure with a high degree of sensitivity and specificity," McDade said.

In the lab, the researchers take segments of RBD that have been manufactured to match viral RBD and attach it to the bottom of small wells in 96-well plates. When they add a blood sample, if RBD antibodies are present, they will be "captured" by the RBD that is stuck to the plate. They can then implement some additional procedures to quantify the level of RBD antibody in the sample.

"We found that the results from serum perfectly mirrored those from the blood spots," said Demonbreun, an assistant professor of pharmacology at Feinberg.

Promoting widespread screening

McDade said DBS sampling has several benefits that will promote more widespread screening.

"It is inexpensive, relatively painless and people can collect their own blood and send samples to the lab through the regular mail," McDade

said. "By not requiring people to come into the clinic to have their blood drawn, we conserve clinical resources, keep people safe at home during shelter-in-place and greatly increase the potential reach of antibody testing."

The team's future plans for testing are two-fold. "We are testing more samples so we can more formally evaluate the sensitivity and specificity of our antibody test," McDade said. "Second, we are building a web-based platform to roll out antibody testing across Chicago. We are fortunate at Northwestern to have investigators like Brian Mustanski and Richard D'Aquila who have experience working with communities in Chicago studying viral infections."

They are among numerous researchers at Northwestern working on the front lines of the coronavirus crisis.

"Enzyme immunoassay for SARS-COV-2 antibodies in dried blood spot samples: A minimally invasive approach to facilitate community- and population-based screening" is available as a MedRxiv preprint.

More information: Thomas W McDade et al. Enzyme immunoassay for SARS-CoV-2 antibodies in dried blood spot samples: A minimally-invasive approach to facilitate community- and population-based screening, (2020). DOI: 10.1101/2020.04.28.20081844

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