Rapid COVID-19 test detects neutralising antibodies with high specificity and sensitivity

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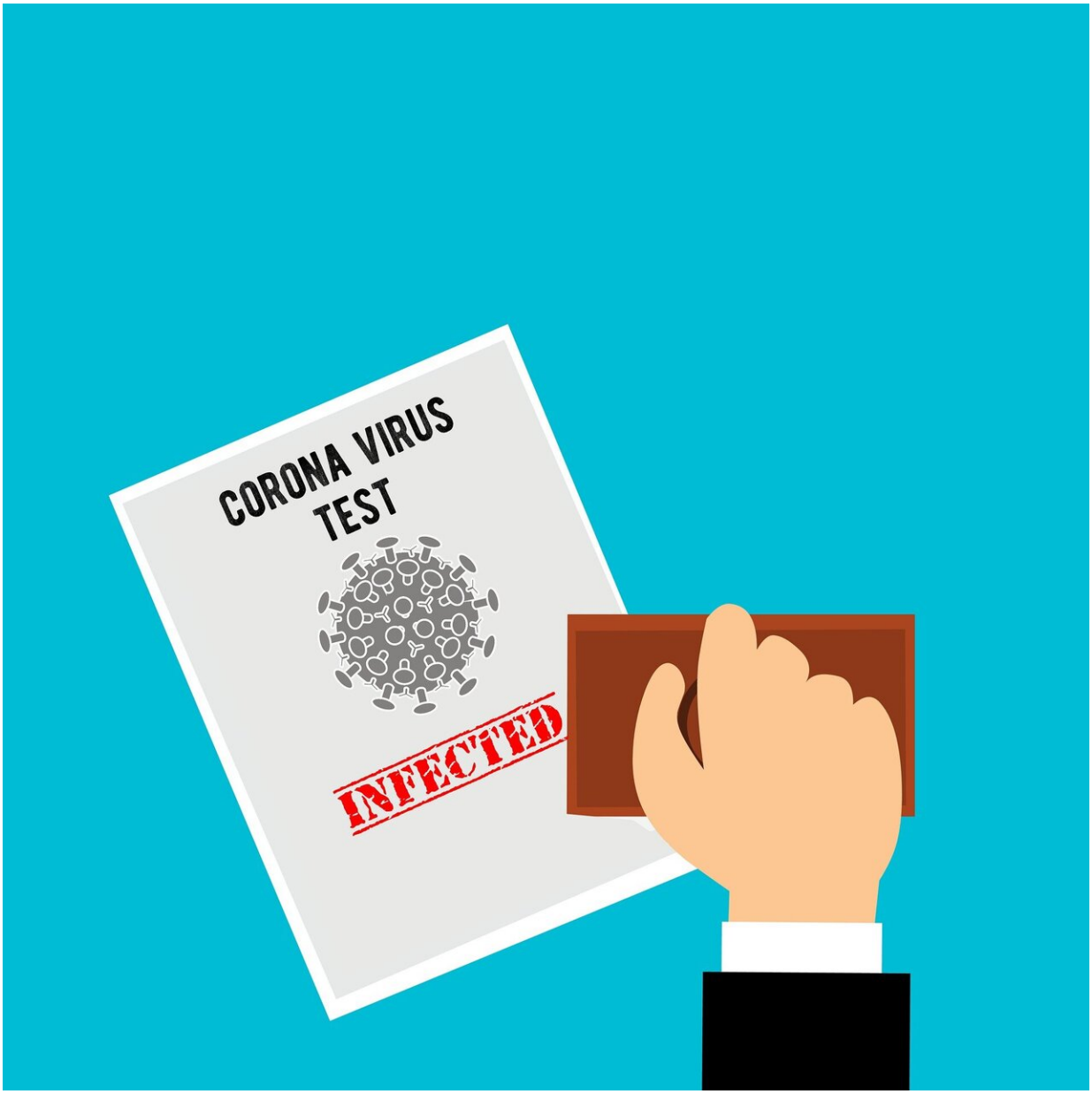

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As the current COVID-19 pandemic continues to adversely impact communities and economies across the world, efficiency in testing for the infection and antibodies is vital. A unique and rapid SARS-CoV-2 surrogate virus neutralization test (sVNT), developed in Singapore, may be the much-needed boost to current COVID-19 investigations to determine infection rate, herd immunity, predicted humoral protection, and vaccine efficacy during clinical trials.

According to a study published in *Nature Biotechnology,* the sVNT is capable of detecting the functional neutralizing antibodies (NAbs) that can block the binding of the coronavirus spike protein to the angiotensin-converting enzyme 2 (ACE2) host receptor, which mimics the virus-host interaction.

The sVNT was developed by scientists from Duke-NUS Medical School, in close collaboration with National Center for Infectious Diseases (NCID), Agency for Science, Technology and Research (A*STAR)'s Institute of Molecular and Cell Biology (IMCB) Singapore, and GenScript Biotech. The scientists in Singapore and China validated the test across two patient cohorts, with a sample size of 250 from China and 375 from Singapore, achieving 99-100% specificity and 95-100% sensitivity.

"The sVNT kit can detect functional NAbs in an hour and differentiate them with binding antibodies (BAbs), without the need for live virus or a biocontainment facility. It also has the ability to detect total receptor binding domain (RBD)-targeting neutralizing antibodies in patient

samples, in contrast to most SARS-CoV-2 antibody tests published or marketed, which are isotype-specific. This makes the sVNT accessible to the broader community for both research and clinical applications," said Professor Wang Linfa, Director of Duke-NUS' Emerging Infectious Diseases program. Prof Wang is considered among the most recognized international experts on emerging zoonotic viruses and is currently serving on multiple WHO committees on COVID-19.

Infection or immunity to the virus is diagnosed by the presence of NAbs in a patient's blood sample, which would block the RBD–ACE2 interaction. At this critical moment of the international response to the COVID-19 outbreak, there is an urgent need for a robust serological test that detects NAbs, for accurate assessment of infection prevalence and protective immunity at the individual and population level. Antibody tests, such as the conventional virus neutralization test (cVNT) and the pseudovirus-based virus neutralization test (pVNT), remain the only platforms for detecting NAbs. However, both require live viruses and cells, highly skilled operators, and days to obtain results. Other assays, such as the enzyme-linked immunosorbent assay (ELISA) detect Babs but are unable to differentiate between BAbs and NAbs.

The sVNT can also measure NAbs from different animals in a species-independent manner. It can therefore be a powerful tool to investigate the role of animals in the transmission of COVID-19 from natural reservoirs to intermediate hosts.

"It is an increasingly critical clinical question about what proportion of patients with COVID-19 develop antibodies to COVID-19, how long it lasts, and whether antibodies protect patients from reinfection. Neutralizing antibody is the gold-standard serological platform to determine this. Unfortunately, the conventional virus neutralization assay is laborious, time-consuming and requires Biosafety Level 3 for COVID-19. The sVNT developed by Prof Wang, in collaboration with

the national COVID-19 PROTECT study, makes it accessible to all hospital laboratories, and is a great advance in COVID-19 serological assays," said Associate Professor David Lye, Director, Infectious Disease Research and Training Office (IDRTO), and Senior Consultant, NCID.

Dr. Sidney Yee, CEO of A*STAR's Diagnostics Development Hub, said, "Due to the SARS outbreak in 2003, researchers in Singapore have gained important insights into that virus, which shares some similarities with SARS-Cov-2. A*STAR supported the clinical tests in this collaboration with Duke-NUS by sharing data drawn from our research experience in SARS. We are happy to have contributed to the validation of this innovative test, which will be instrumental in our fight against the global pandemic."

Mr David Martz, Vice President of New Product Management, Life Sciences Group, at GenScript, said: "We are very pleased that Prof Wang's work has come to fruition. This is great news for scientists researching herd immunity and vaccine efficacy as they will now have access to this innovative research tool to accurately determine the level of neutralizing antibodies in a population. We believe the test will shed new light on the current plaguing mysteries of COVID-19."

The sVNT kit is commercialized by GenScript and offered worldwide under the brand cPass for research use only. GenScript has also filed for Emergency Use Authorisation with the US Food and Drug Administration and this filing is currently under review.

More information: Chee Wah Tan et al. A SARS-CoV-2 surrogate virus neutralization test based on antibody-mediated blockage of ACE2–spike protein–protein interaction, *Nature Biotechnology* (2020). DOI: 10.1038/s41587-020-0631-z

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