New study boosts hopes for a broad vaccine to combat COVID-19 variants and future coronavirus outbreaks

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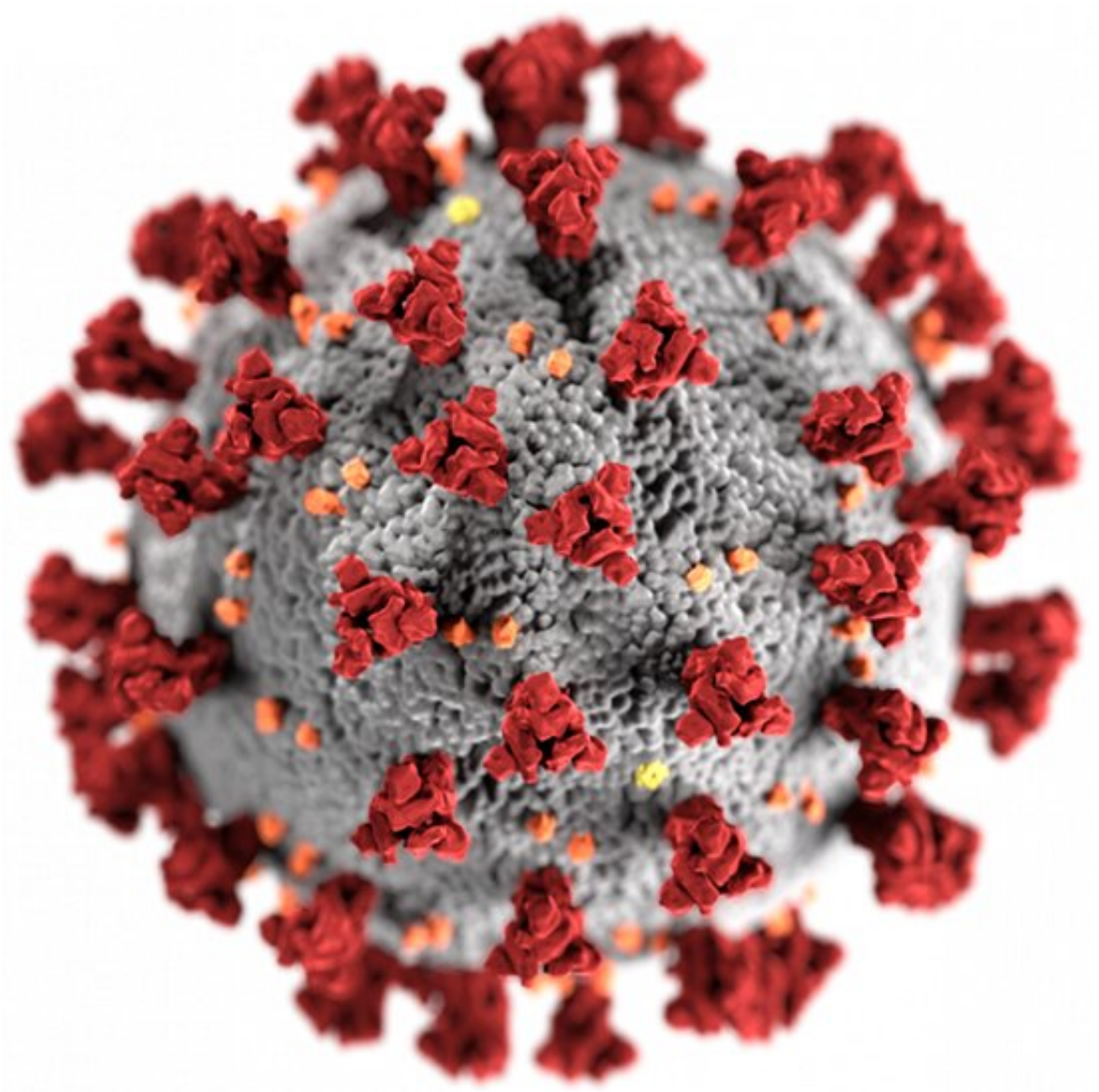

Image of the ultrastructural morphology exhibited by the 2019 Novel Coronavirus (2019-nCoV). Credit: CDC

Scientists from Duke-NUS Medical School and National Centre for Infectious Diseases (NCID) found that 2003 SARS survivors who have been vaccinated with the Pfizer-BioNTech mRNA vaccine produced highly potent functional antibodies that are capable of neutralizing not only all known SARS-CoV-2 variants of concerns (VOCs) but also other animal coronaviruses that have the potential to cause human infection. This finding, published in The New England Journal of Medicine, is the first time that such cross-neutralizing reactivity has been demonstrated in humans, and further boosts hopes of developing an effective and broad-spectrum next-generation vaccine against different coronaviruses.

Among the coronavirus family, one sub-group relies on the ACE2 molecule to enter human cells. Both SARS-CoV-1 and SARS-CoV-2 belong to this group as well as a number of coronaviruses circulating in animals such as bats, pangolins and civets. While the exact route of transmission remains unknown, these viruses have the potential to jump from animals to humans and could start the next pandemic. Collectively, this group of viruses is called sarbecovirus.

"We explored the possibility of inducing pan-sarbecovirus neutralizing antibodies that can block the common human ACE2-virus interaction, which will be protective not only against all known and unknown SARS-CoV-2 VOCs, but also future sarbecoviruses," said Dr Chee Wah Tan, Senior Research Fellow with Duke-NUS' Emerging Infectious Diseases (EID) program and co-first author of this study.

To test their hypothesis, researchers recruited eight people who recovered from SARS-CoV-1, which was responsible for the 2003

SARS epidemic, as well as ten healthy people and ten COVID-19 survivors. They then compared the immune response of the three groups before and after they were vaccinated with the SARS-CoV-2 vaccine. In particular, they wanted to understand whether the neutralizing antibodies developed in SARS-Vaccinated group could wipe out both SARS-CoV-1 and SARS-CoV-2 viruses as well as other sarbecoviruses, including potentially zoonotic sarbecoviruses that have been identified in bats and pangolins.

"Prior to vaccination, SARS-CoV-1 survivors had detectable neutralizing antibodies against SARS-CoV-1 but no or low-level anti-SARS-CoV-2 neutralizing antibodies. After receiving two doses of the mRNA vaccine, all displayed high levels of neutralizing antibodies against both SARS-CoV-1 and SARS-CoV-2," said Dr Wanni Chia, Research Fellow at the Duke-NUS EID' program and co-first author of this study. "Most importantly, they are the only group with a broad spectrum of neutralizing antibodies against ten sarbecoviruses that were chosen to be examined."

"Our study points to a novel strategy for the development of next-generation vaccines, which will not only help us control the current COVID-19 pandemic, but may also prevent or reduce the risk of future pandemics caused by related viruses," said Professor Wang Linfa from Duke-NUS EID program, who is the senior corresponding author of this study.

"Professor Wang's team made an astute serendipitous observation in an ongoing national multicentre immune monitoring study of COVID-19 vaccination called the Singapore COVID-19 Vaccine Immune Response and Protection Study (SCOPE), which is coordinated by NCID. As emerging variants of concern have already demonstrated some degree of immune evasion against the first-generation vaccines, this discovery has the potential to address that problem as the world continues COVID-19

vaccination to exit the pandemic. In addition, this can potentially act as a highly promising preventive vaccine against future coronavirus pandemics," said Associate Professor David Lye, Director, Infectious Disease Research and Training Office, NCID and joint corresponding author of the study.

The team conducted their investigation using an improved version of the surrogate virus neutralization test (sVNT) developed by Duke-NUS in early 2020. Prof Wang and his team invented the sVNT assay, trade named cPass[1], which has been granted Emergency Use Authorisation by the US FDA to determine SARS-CoV-2-specific neutralizing antibodies in human sera following infection or vaccination. Dr Tan and Dr Chia are part of Prof Wang's team and co-inventors of the sVNT. The improved multiplex sVNT allows simultaneous detection of neutralizing antibodies against different sarbecoviruses in a single tube, thus playing a pivotal role in studies like this that require accurate side-by-side comparison of neutralizing antibody levels against different viruses.

The team is currently conducting a proof-of-concept study to develop a third-generation vaccine against different coronaviruses (3GCoVax) as well as broad neutralizing antibodies for therapy and is looking to recruit individuals who recovered from SARS infection in 2003.

More information: Chee-Wah Tan et al, Pan-Sarbecovirus Neutralizing Antibodies in BNT162b2-Immunized SARS-CoV-1 Survivors, *New England Journal of Medicine* (2021). DOI: 10.1056/NEJMoa2108453

For those who would like to take part in ongoing studies, please contact scrn@ncid.sg.

Provided by Duke-NUS Medical School