

## Individual SARS-CoV-2 neutralizing antibody immunity lasts from days to decades

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Scientists from Duke-NUS Medical School, the National Center for Infectious Diseases (NCID) and the Agency for Science, Technology and Research (A\*STAR) Infectious Diseases Labs found that antibodies against SARS-CoV-2 wane at different rates, lasting for mere days in some individuals, while remaining present in others for decades. The study, published in *The Lancet Microbe*, shows that the severity of the infection could be a deciding factor in having longer-lasting antibodies. Individuals with low levels of neutralizing antibodies may still be protected from COVID-19 if they have a robust T-cell immunity.

The team followed 164 COVID-19 patients in Singapore for six to nine months, analyzing their blood for neutralizing <u>antibodies</u> against SARS-CoV-2, T cells and <u>immune system</u> signaling molecules. They then used this data to establish a machine learning algorithm to predict the trajectories of peoples' neutralizing antibodies over time.

"The key message from this study is that the longevity of functional neutralizing antibodies against SARS-CoV-2 can vary greatly and it is important to monitor this at an individual level. This work may have implications for immunity longevity after vaccination, which will be part of our follow-up studies," said Professor Wang Linfa, from Duke-NUS' Emerging Infectious Diseases (EID) Program, a corresponding author of the study.

The team was able to categorize people into five groups depending on how long their antibodies lasted. The first group, who never developed detectable neutralizing antibodies also called the 'negative' group, comprised 11.6 percent of the patients in the study. The 'rapid waning' group (26.8 percent) had varying early levels of antibodies that waned quickly. The 'slow waning' group (29 percent) tested mostly positive for antibodies at six months. The 'persistent' group (31.7 percent) showed little change in their antibody levels up to 180 days and, finally, the 'delayed response' group (1.8 percent) showed a marked rise in neutralizing antibodies during late convalescence.

While this study focused on determining the levels of neutralizing antibodies, which are part of the body's comprehensive immune defense system, the other important aspect of an effective immune defense is T-cell immunity. The study found that the patients tested, including those from the 'negative group', displayed sustained T-cell immunity six months after initial infection. This shows that individuals may still be protected if they have a robust T-cell immunity when the neutralizing antibody level is low.

"Our study examines neutralizing antibodies which are important in protection from COVID-19. We found that antibodies against SARS-CoV-2 wane in different people at different rates. This emphasizes



the importance of public health and social measures in ongoing pandemic outbreak response. However, the presence of T-cell immunity provides hope of longer-term protection which will require more studies and time for epidemiological and clinical evidence to confirm," said Associate Professor David Lye, Director, Infectious Disease Research and Training Office, NCID, also a corresponding author of the study.

"This study reminds us that we all react differently to infection and that various people mount different protective immune responses. Understanding the basis of these differences will help build better vaccines," added Professor Laurent Renia, Executive Director, A\*STAR Infectious Diseases Labs.

The findings are important as policy makers design vaccination programs and pandemic exit strategies. The rate of antibody waning suggests re-infection may occur in subsequent waves of infection. Also, if immunity provided via vaccinations wanes like naturally-produced antibodies, then annual vaccine administration could be necessary to prevent future outbreaks of COVID-19. Further research will be needed to clarify this as vaccine programs are rolled out.

**More information:** Wan Ni Chia, et al. Multifaceted dynamics of SARS-CoV-2 neutralising antibody responses predicts a wide range of immunity longevity from days to decades. *The Lancet* Microbe. doi.org/10.1016/S2666-5247(21)00025-2

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