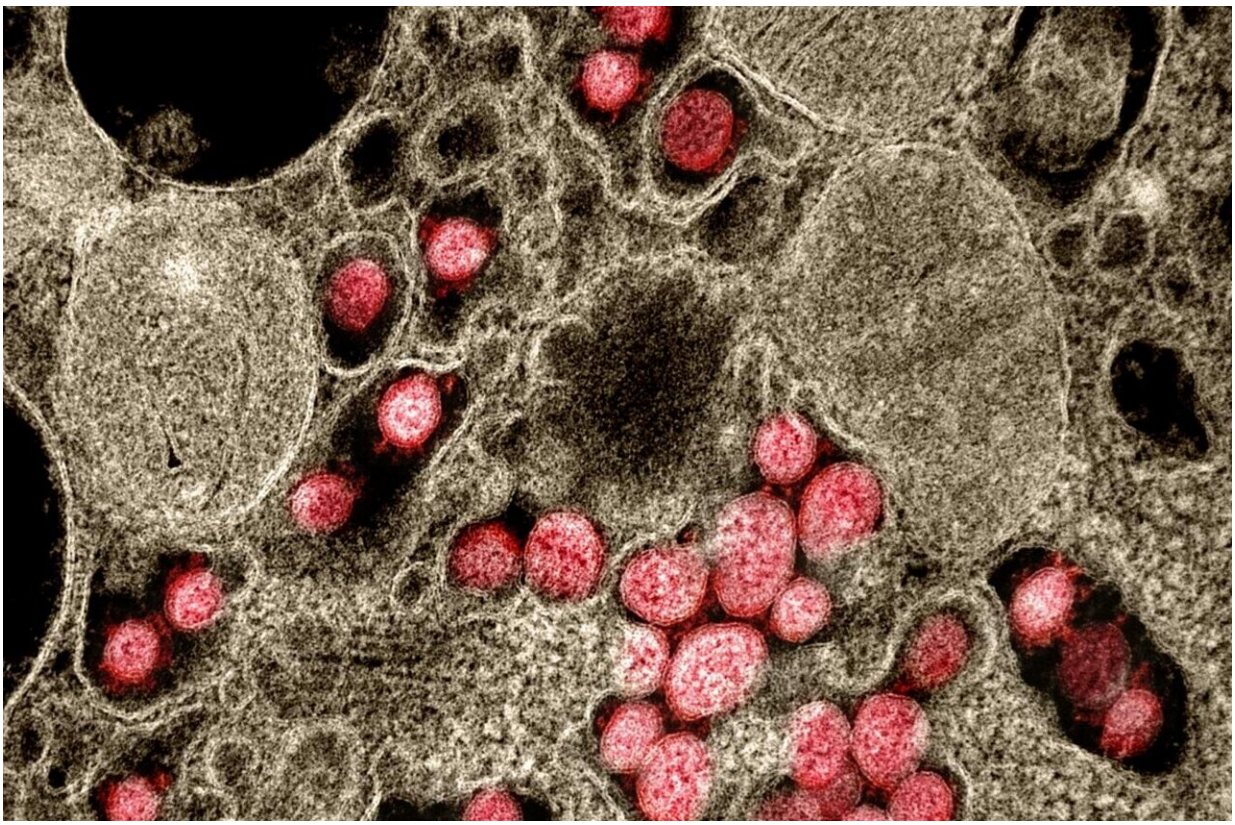
Antibodies that enhance SARS-CoV-2 infection—a possible factor for severe COVID-19

May 25 2021



Transmission electron micrograph of SARS-CoV-2 virus particles isolated from a patient. Credit: NIAID

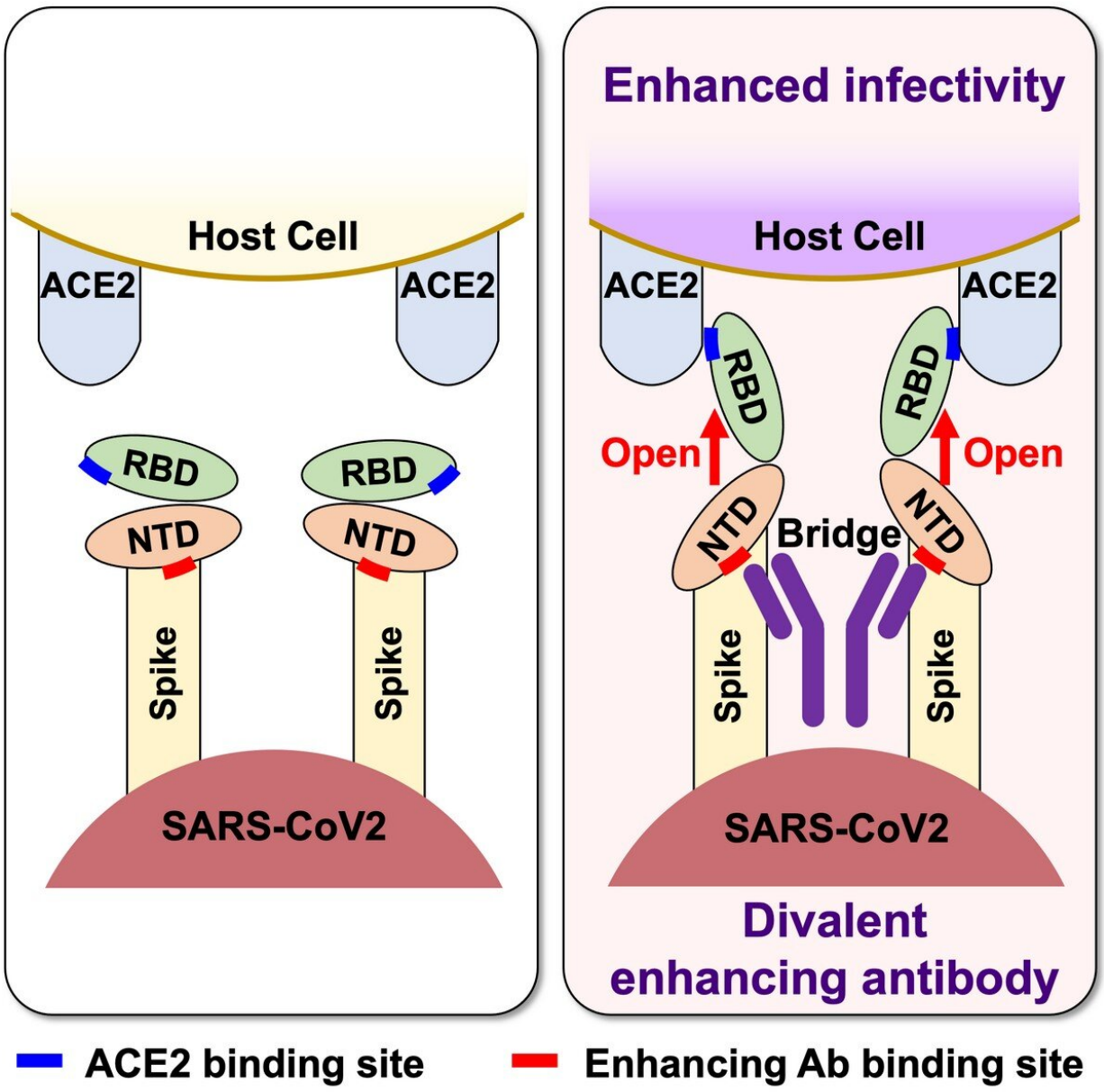
A research group from Osaka University led by Professor Hisashi Arase

and consisting of researchers from the Research Institute for Microbial Diseases, the Institute for Protein Research, the Immunology Frontier Research Center, the Center for Infectious Diseases, and the Graduate School of Medicine has discovered for the first time that both neutralizing antibodies that protect against infection as well as infection-enhancing antibodies that increase infectivity are produced after infection with SARS-CoV-2 by analyzing antibodies derived from COVID-19 patients.

Antibodies against the receptor binding site (RBD) of the SARS-CoV-2 spike protein play an important function as neutralizing antibodies that suppress SARS-CoV-2 infection by inhibiting its binding to the human receptor, ACE2. On the other hand, the function of antibodies against other sites of the spike protein was unknown.

"We found that when infection-enhancing antibodies bind to a specific site on the spike protein of SARS-CoV-2, the antibodies directly cause a conformational change in the spike protein, resulting in the increased infectivity of SARS-CoV-2. Neutralizing antibodies recognize the RBD, whereas infection-enhancing antibodies recognize specific sites of the N-terminal domain (NTD)," explains Professor Hisashi Arase. "Furthermore, the production of infection-enhancing antibodies attenuated the ability of neutralizing antibodies to prevent infection."

Higher production of infection-enhancing antibodies was found in patients with severe COVID-19. It was also found that non-infected individuals may have small amounts of infection-enhancing antibodies.



SARS-CoV-2 infectivity is enhanced upon antibody binding to NTD. Credit: Cell Press

Although the production of infection-enhancing antibodies may be involved in the development of severe disease, further analysis is required to ascertain whether they are actually involved in the

exacerbation of infection in the body.

By analyzing the antibody titer of infection-enhancing antibodies, it may be possible to check for people who are prone to severe disease. The results of this research are also important for the development of vaccines that do not induce the production of infection-enhancing antibodies.

"It is important to analyze not only neutralizing antibodies but also infection-enhancing antibodies. In the future, it may be necessary to develop vaccines that do not induce the production of infection-enhancing antibodies, because infection-enhancing antibodies may be more effective against mutant strains in which neutralizing antibodies are not sufficiently effective," says Professor Hisashi Arase.

More information: Yafei Liu et al, An infectivity-enhancing site on the SARS-CoV-2 spike protein targeted by antibodies, *Cell* (2021). DOI: 10.1016/j.cell.2021.05.032

Provided by Osaka University