

## **Antibodies that enhance SARS-CoV-2 infection**

### **—A possible factor for severe COVID-19—**

Primary Keyword: Medicine/Health

Additional Keywords: Infectious/Emerging Diseases, Virology, Microbiology

A research group led by Hisashi Arase (IFReC/RIMD/the Center for Infectious Diseases, Osaka University) discovered 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.

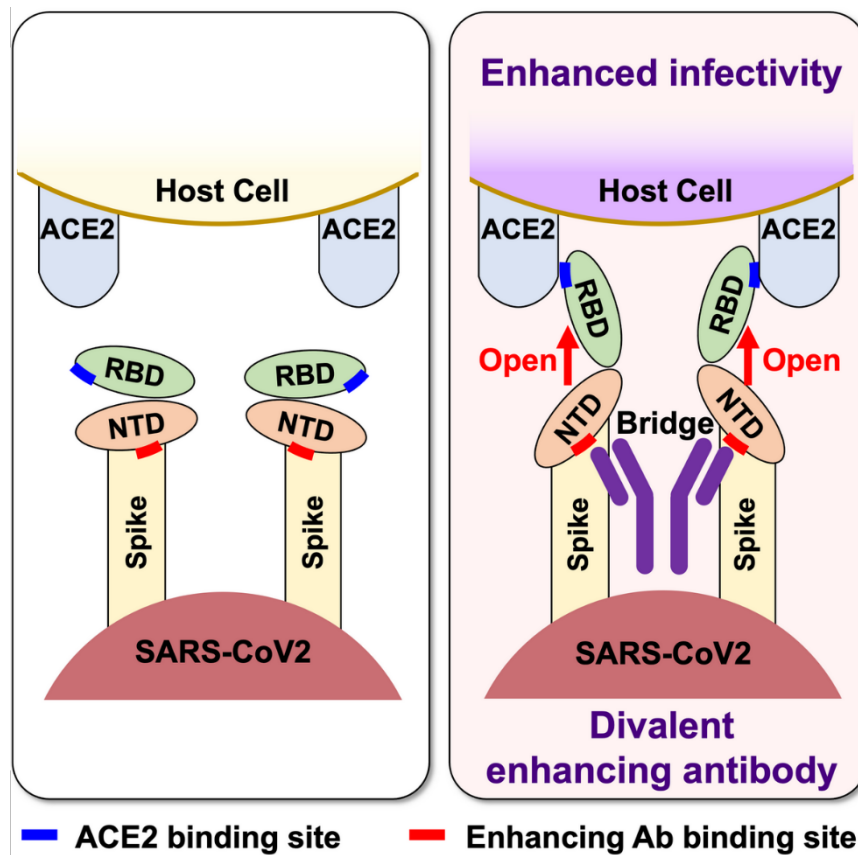
“We found that when infection-enhancing antibodies bind to a specific site on the spike protein of SARS-CoV-2, the antibodies directly cause a conformational change in the spike protein, resulting in the increased infectivity of SARS-CoV-2. Neutralizing antibodies recognize the RBD, whereas infection-enhancing 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.

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.



SARS-CoV-2 infectivity is enhanced upon antibody binding to NTD. (credit: Osaka University)

**Summary:** Osaka University researchers found that infection with SARS-CoV-2 produces not only neutralizing antibodies that prevent infection, but also infection-enhancing antibodies. They demonstrated that the infection-enhancing antibodies enhance the infectivity of SARS-CoV-2 by modulating the conformation of spike protein of SARS-CoV-2. Furthermore, the infection-enhancing antibodies attenuated the ability of neutralizing antibodies to prevent infection. Their findings will help to develop vaccines that do not induce the production of infection-enhancing antibodies.

- **Journal:** *Cell*
- **Title:** “An infectivity-enhancing site on the SARS-CoV-2 spike protein targeted by antibodies”
- **Authors:** Yafei Liu, Wai Tuck Soh, Jun-ichi Kishikawa, Mika Hirose, Emi E. Nakayama, Songling Li, Miwa Sasai, Tatsuya Suzuki, Asa Tada, Akemi Arakawa, Sumiko Matsuoka, Kanako Akamatsu, Makoto Matsuda, Chikako Ono, Shiho Torii, Kazuki Kishida, Hui Jin, Wataru Nakai, Noriko Arase, Atsushi Nakagawa, Maki Matsumoto, Yukoh Nakazaki, Yasuhiro Shindo, Masako Kohyama, Keisuke Tomii, Koichiro Ohmura, Shiro Ohshima, Toru Okamoto, Masahiro Yamamoto, Hironori Nakagami, Yoshiharu Matsuura Atsushi Nakagawa, Takayuki Kato, Masato Okada, Daron M. Standley, Tatsuo Shioda, Hisashi Arase