Double antibody against SARS-CoV-2 prevents therapy-resistant variants

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An international consortium that includes researchers at Karolinska Institutet has developed a double antibody that targets two sites of the SARS-CoV-2 virus, thereby preventing the virus from mutating to resist

the therapy. A study published in the scientific journal *Nature* shows that the antibody potently neutralizes SARS-CoV-2 and its variants and protects against COVID-19 in mice.

Antibody-based immunotherapy has already been shown to be effective against COVID-19 but faces two main obstacles; it needs to work against the circulating viral variants and it must prevent formation of new variants that can rapidly ensue via a mechanism similar to that leading to antibiotic resistant bacteria. The consortium solved the problem by joining two natural antibodies into a single artificial molecule, called 'bispecific antibody," that targets two independent viral sites simultaneously.

Stay one step ahead of the virus

Pre-clinical trials showed that this bispecific antibody potently neutralizes SARS-CoV-2 and its variants, including the recent UK variant circulating in Sweden and Europe with increased spread. In contrast to antibodies that target only one viral site, the bispecific antibody prevents the virus from changing its structure to evade therapy.

"The coronavirus is mutating, and it will continue to mutate, so we need treatments that can keep up with these changes and work effectively on all variants of the virus. This antibody means we can stay one step ahead of the virus," says Qiang Pan-Hammarström, professor at the Department of Biosciences and Nutrition, Karolinska Institutet, co-author of the study and the scientific coordinator of the consortium.

A single injection of the bispecific antibody provided protection against the disease in mice. The antibody effectively reduced viral burden in the lungs and mitigated inflammation typical of COVID-19. The antibody is an ideal candidate for human clinical trials, with good chances of employment both for prevention and treatment of COVID-19, according

to the researchers.

An ongoing need for medicines

"The fact that some people will not respond to vaccines and that it might take several years for the whole world to be vaccinated against COVID-19, means there will be an ongoing need for medicines that can protect us from or treat the disease," says Qiang Pan-Hammarström.

Though bispecific antibodies are gaining popularity in the treatment of certain cancers (where one part of an antibody might bind to a tumor cell and the other to an immune cell), the researchers are the first to produce a human bispecific antibody against SARS-CoV-2.

The bispecific antibody was developed within the research consortium ATAC, funded last year by the European Commission in response to the COVID-19 pandemic and coordinated by Karolinska Institutet. Other members include the Institute for Research in Biomedicine (IRB; Bellinzona, Switzerland, affiliated to the Università della Svizzera italiana (USI)), Policlinico San Matteo in Pavia (Italy), Technische Universitaet Braunschweig (Germany) and the Joint Research Centre of the European Commission. Collaboration with Rockefeller University and the Czech Academy of Science was instrumental to prove the bispecific efficacy. See the scientific article for information about patents and potential conflicts of interest.

More information: Raoul De Gasparo et al. Bispecific IgG neutralizes SARS-CoV-2 variants and prevents escape in mice, *Nature* (2021). DOI: 10.1038/s41586-021-03461-y

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