# Structural biology reveals new target to neutralize COVID-19

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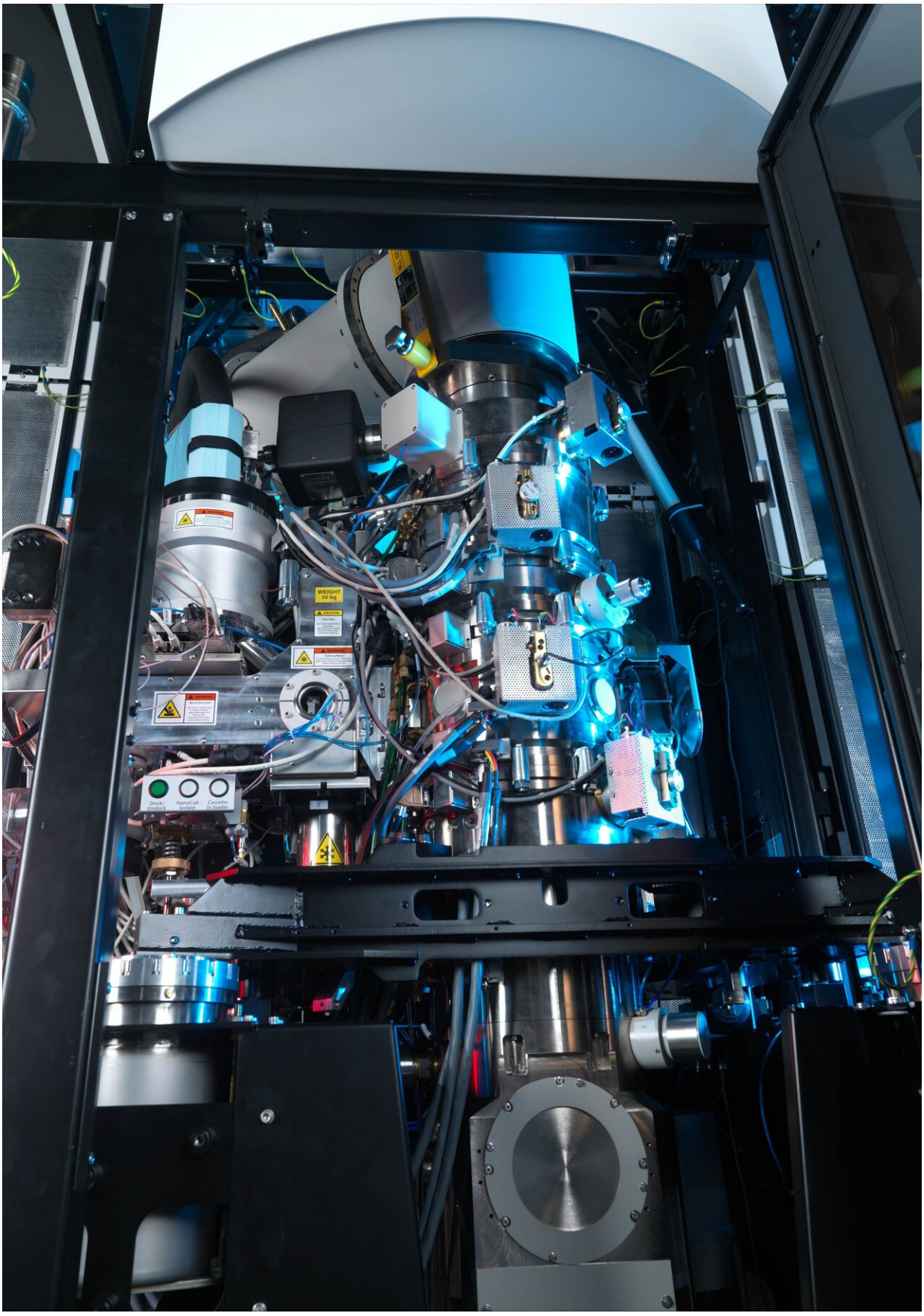
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One of the five Titan Krios cryo-electron microscopes used at eBIC for both single particle analysis and cryo-tomography at Diamond Light Source for the work on this paper. Credit: Diamond Light Source Ltd

An international team of researchers have discovered a new and highly conserved site on the SARS-CoV-2 virus that can be neutralized by a specific antibody. Previous studies have reported that antibodies that block the virus interaction with the human receptor (ACE2) have a significant neutralizing effect and can be used to save the lives of critically ill patients. However, this recent study published in *Nature Structural and Molecular Biology* describes a different target that can be bound in synergy with ACE2 blocking antibodies for a stronger neutralizing effect. Together, with a group at a hospital in Taiwan, the team using the Electron Bio Imaging Centre (eBIC) at the UK's national synchroton, Diamond Light Source, to identify antibodies from a convalescent patient that could create a real potential for a drug target.

Antibodies are part of the body's defense against infections. They are proteins that bind to pathogens such as viruses preventing them from coming into contact with human cells. Antibody therapies have shown promise in the treatment of COVID-19, especially for extremely ill patients. Antibodies harvested from people recovering from the disease can be injected into COVID-19 patients and can significantly reduce the severity of the disease and lessen the potential long term effects. There is also evidence that antibody therapy can prevent serious symptoms from developing when administered before an individual is infected.

Scientists were able to isolate an antibody named EY6A from a patient recovering from COVID-19. Subsequent structural biology studies

revealed that EY6A bound to a novel target on the SARS-CoV-2 virus and demonstrated a new way of preventing the spread of COVID-19. "This finding is valuable because it comes from a real patient who had the virus. And the discovery of this new target means that more effective combination therapies which attack the virus at different points are now possible," comments one of the authors Prof. Dave Stuart, Director of Life Sciences at Diamond Light Source and Joint Head of Structural Biology at University of Oxford.

"Increasing the number of target sites that can be blocked on SARS-CoV-2 also means there is a lower probability that mutations preventing the antibody binding will compromise treatments. Even if one binding site mutates and can no longer be neutralized, the second binding site can still prevent infection," he adds.

Diamond's research is centered on drug targets for COVID-19. The focus is mainly on the virus spikes, the receptor binding and the main protease. One specific part of its work, in conjunction with the University of Oxford, has been to look at these spikes on the outside of the virus.

Depending on their function, different binding sites for antibodies can be more or less prone to mutation. If the protein sequence is not important, a random mutation could change the structure meaning that antibodies can no longer bind, but the virus is still infective. One of the main concerns about using antibodies as therapy is that if it is used too much, it can force viruses to mutate and render the antibody treatment useless. In this new study, researchers found that the amino acid sequence of the newly discovered target is highly conserved, meaning it is the same in all of the viruses that have been sequenced so far. This means that the region is important, and changes will likely negatively affect the virus, making it a safer candidate for antibody therapy.

**More information:** Daming Zhou et al. Structural basis for the neutralization of SARS-CoV-2 by an antibody from a convalescent patient, *Nature Structural & Molecular Biology* (2020). DOI: 10.1038/s41594-020-0480-y

Provided by Diamond Light Source

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