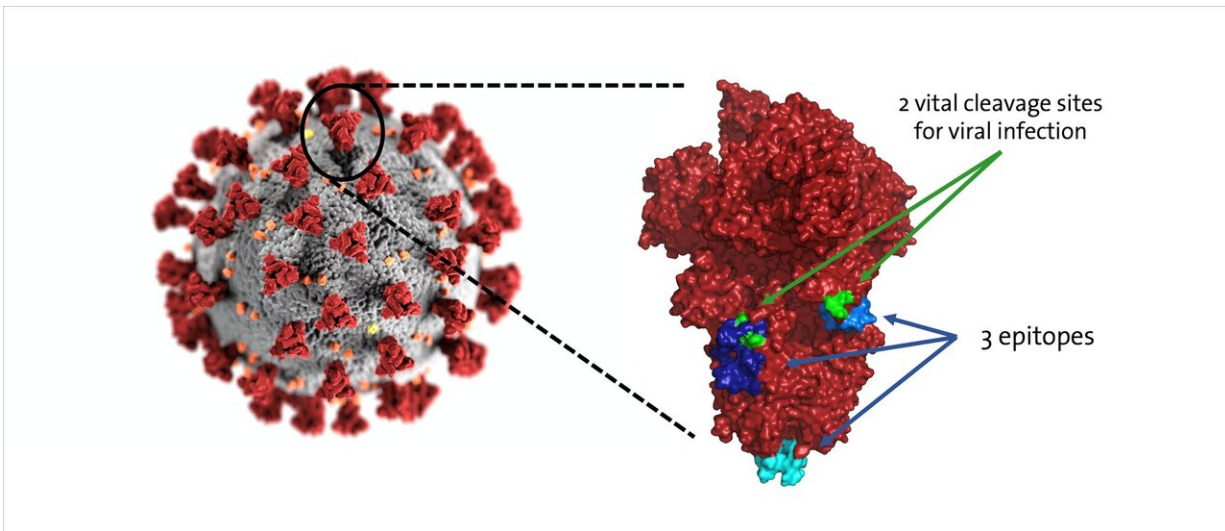


Two potential chinks in the coronavirus's armour

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Localisation of the three dominant binding sites of human antibodies on the coronavirus responsible for COVID-19. Credit: UNIGE

Serological tests can be used to ascertain whether an individual has developed antibodies against the coronavirus responsible for COVID-19. These tests, however, do not provide information about the precise part of the virus that the antibodies bind onto—an essential piece of information that determines the ability of the human immune system to neutralize the pathogen and stamp out the infection. Scientists from the University of Geneva and Geneva University Hospitals (HUG) have identified three of the targets (linear epitopes) most often selected by the

antibodies from a group of patients who have had COVID-19. As the scientists report in an article deposited on MedRxiv (an archive for preprints devoted to medical research), two of these epitopes are involved in the process used by the virus to release its genetic material into human cells. The identification of such very specific targets is of great importance for developing effective vaccines and treatments, especially if they prove to be neutralizing (which is not yet known).

"The [human body](#) continuously produces highly-diverse antibodies in random fashion," begins Nicolas Winssinger, a professor in the Department of Organic Chemistry in UNIGE's Faculty of Sciences. "There are trillions of them, all different, and they wait for a possible invader to attach themselves to and mark a target to be destroyed by the immune system. When a new pathogen, such as SARS-CoV-2, occurs, some of these antibodies have the ability to bind to it and trigger an effective immune system response. But not everyone selects the same antibodies and, as a result, not everyone develops the same immune response."

The current COVID-19 epidemic is distinguished by the highly-diverse range of responses to the coronavirus. Some people are asymptomatic, while others suffer from severe, or even fatal symptoms.

Binding site

To gain a better understanding of this diversity, the teams led by Professor Winssinger and Vuilleumier, a professor in UNIGE's Department of Medicine and head physician at the Laboratory Medicine Division at HUG, attempted to find out which antibodies are preferentially selected among people who have had COVID-19, focusing on the precise parts of the infectious agent they bind onto. The specific target of the antibodies is called the epitope.

Twelve patients took part in the study, with the results confirming that the responses are far from uniform. The only common element shared by all by the participants was that they generated antibodies targeting the spikes that cover the surface of the coronavirus and to which they owe their name. But they bind at very different sites on this large proteins. Nevertheless, the scientists identified three areas that were most frequently selected. And two of them correspond to binding sites that are essential for special proteins (proteases), which allow the coronavirus to merge with the cell membrane and release its genetic material inside its prey.

Top or bottom of the spike?

"We were surprised by this result," explains Professor Winssinger. "Until now, most of the work in this area has focused on the upper part of the spike, which we know enables the coronavirus to bind to the target cell. The fusion of the virus with the cell is only the second stage but in reality it is more critical."

In fact, binding to a cell does not yet ensure that the virus can merge with it. In addition, the problem with the upper part of the spike is that it is not necessarily an ideal target for a drug or vaccine, and can even be dangerous. Studies on monkeys infected with SARS-CoV1—the virus responsible for the 2003 epidemic and part of the same family of coronaviruses—showed that antibodies attaching at this site do not always prevent viruses from binding to their target cells. This earlier research also demonstrated that they redirect them to other types of [cells](#), causing the onset of secondary diseases (ADE: antibody-dependent enhancement of diseases).

The two epitopes identified by the Geneva-based authors, meanwhile, are involved in a very different process, meaning they could offer a more promising—and less risky—alternative in the quest for a new

treatment or vaccine. But before that can happen, the neutralizing power of the corresponding [antibodies](#) needs to be assessed.

More information: Lluc Farrera et al. Identification of immunodominant linear epitopes from SARS-CoV-2 patient plasma, (2020). [DOI: 10.1101/2020.06.15.20131391](https://doi.org/10.1101/2020.06.15.20131391)

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