High-performance antibodies to fight COVID-19

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American and Dutch researchers have just isolated from the blood of people who have cured extremely strong antibodies to COVID-19, capable of neutralizing the virus responsible for the disease at very low concentrations.

When our immune system is exposed to an infectious agent like the coronavirus SARS-CoV-2, certain white blood cells (B lymphocytes) will activate and start the production of antibodies intended to neutralize the virus.

This is a highly specialized response: each B cell clone will produce a different antibody, recognizing a specific region (epitope) of the virus, and it is for this reason that these antibodies are called monoclonals. Obviously, these monoclonal antibodies will not all have the same neutralization capacity: certain regions of the virus are less important for its biological activity, so that an antibody which interacts with one of these regions will have little impact on the infection.

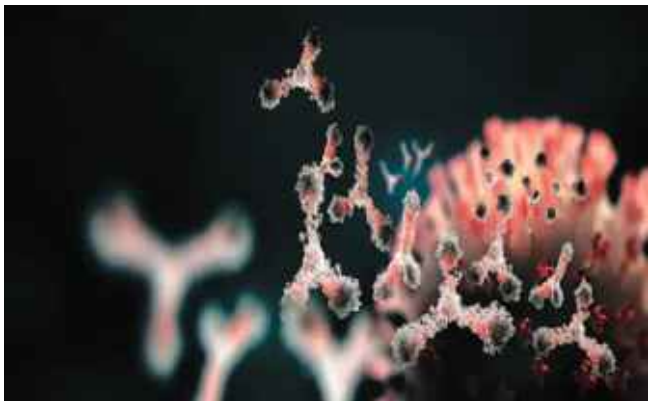
However, when an antibody specifically interacts with a domain of the virus that is absolutely essential for its activity, the neutralization potential by the antibody will be significantly greater and may allow elimination of the virus and lead to healing.

CRITICAL DOMAIN

Molecular analyzes of the structure of the coronavirus have shown that the region of the virus most important for its activity is located at the level of the external peaks, in particular a region called RBD (receptor binding domain) involved in the binding with the membrane protein ACE2 and which is absolutely essential for the entry of the virus into cells (1). It is therefore no coincidence that the blood of convalescent patients who have defeated COVID-19 shows the presence of monoclonal antibodies against this region of the virus (2).

According to recent results, some of these antibodies have an extraordinary affinity for the RBD portion of the coronavirus and can therefore neutralize the virus at very low concentrations (3). From the blood samples of patients who had been affected by COVID-19 and who had recovered, Dutch researchers managed to isolate 19 neutralizing antibodies directed against this RBD portion of the virus, including two which had remarkable neutralizing activity, with an interaction with the virus detected at concentrations as low as 7 nanograms (one millionth of a milligram or 0,000 000 001 g) per milliliter.

Such powerful anti-RBD antibodies (affinity of the order of ng/mL) were also obtained by a Californian group from the convalescent plasma of three different donors, and these antibodies protected the model animals (hamsters) exposed to very high amounts of SARS-CoV-2 (4). The detection of these high-performing antibodies in different individuals affected by COVID-19 therefore suggests that the immune response to the coronavirus presents similarities from one person to another and that these antibodies contribute to the cure of this disease.



UNITY IS STRENGTH

Evolutionary pressure means that viruses must constantly adapt to improve their chances of survival, for example by mutating portions of their genetic material to become resistant to antiviral drugs. One of the potential problems with monoclonal antibodies to the coronavirus is that a simple mutation of the virus in the region recognized by the antibody could completely abolish the neutralizing ability of the antibody and make it completely ineffective.

Researchers at Regeneron have recently shown that this problem can be overcome by using a mixture containing two antibodies directed against different regions of the coronavirus (5).

When the virus is exposed for a few generations of its reproductive cycle to antibodies, it does manage to slightly modify the structure of its RBD region and become completely resistant to each of the eight monoclonal antibodies developed by the researchers. On the other hand, when the virus faces a mixture of two antibodies which each recognize a distinct region of the RBD domain, it becomes unable to escape the pressure exerted by the cocktail of antibodies.

According to the authors, these monoclonal antibody cocktails may represent the future of antiviral therapy against COVID-19 pending the development of a vaccine. The clinical trials with the antibody cocktail developed by Regeneron which are about to start should answer this question.

(1) Lan J et coll. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature 2020; 581: 215-220.

(2) Ju B et coll. Human neutralizing antibodies elicited by SARS-CoV-2 infection. Nature (published online, May 26th 2020)

(3) Brouwer PJM et coll. Potent neutralizing antibodies from COVID-19 patients define multiple targets of vulnerability. Science (published online, June 15th 2020)

(4) Rogers TF et coll. Isolation of potent SARS-CoV-2 neutralizing antibodies and protection from disease in a small animal model. Science (published online, June 15th 2020)

(5) Baum A et coll. Antibody cocktail to SARS-CoV-2 spike protein prevents rapid mutational escape seen with individual antibodies. Science (published online, June 15th 2020)

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