The race for remedies: Monoclonal antibodies, a weapon of choice in our war against COVID-19

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Antibodies are at the heart of our immune defense. These proteins play a fundamental role in the detection and neutralization of infectious agents. Our immune system has the incredible ability to generate hundreds of millions of different antibodies, a vast repertoire that is absolutely necessary to deal with the countless pathogens we will be exposed to in our lifetime.

Each of these millions of separate antibodies is produced by a single white blood cell (lymphocyte) line (called a clone), which is why these antibodies are called monoclonals.

When the lymphocytes are placed in the presence of an infectious agent, the coronavirus SARS-CoV-2 for example, a clone which produces an antibody recognizing a given molecular region of the virus (what is called an epitope) will preferably be selected from all the others to very specifically amplify the immune response to this virus. It's a bit like facial recognition, but on a molecular level.

In parallel, this lymphocyte clone producing the neutralizing monoclonal antibody will be kept to keep a memory of the infection and be immediately available to produce the antibody again in the event of another exposure to the virus (which is the principle of the vaccination).

IMMUNE RESPONSE

Recent studies on the effectiveness of the immune response to the coronavirus show that infection with the virus does cause the production of antibodies, although this varies considerably from person to person (1).

In addition, it has been observed that transfusion of plasma (liquid part of the blood containing, among others, antibodies) from convalescent patients who have survived COVID-19 to patients who have developed severe complications of the disease causes a marked improvement in their clinical condition (2). This suggests that this convalescent plasma contains one or more antibodies capable of specifically blocking the action of the virus.

- We can therefore consider the use of these plasmas as starting material to first identify the most active antibodies against the coronavirus and, subsequently, administer these antibodies to patients affected by COVID-19 to neutralize the infection.
- This is one such approach that has been used successfully to identify monoclonal antibodies capable of treating patients infected with the Ebola virus (see below).

BLOCK ENTRY OF VIRUS

Currently, the most interesting monoclonal antibodies against the coronavirus are those that target spikes in the surface molecular structure (spikes) present in the outer layer of the virus.

The interaction of certain proteins present in these peaks with the membrane protein ACE2 of human cells is absolutely essential to allow the virus to penetrate inside the cells and reproduce there, which suggests that the neutralization of this interaction using a monoclonal antibody could prevent and treat the infection.

Several scientists are currently trying to isolate monoclonal antibodies directed specifically against peaks of the virus from different convalescent plasmas, and preliminary results appear promising.

- For example, a group of Israeli scientists recently announced that they had purified a monoclonal antibody that specifically recognizes a peak protein in the coronavirus and blocks the entry of the virus into human cells.
- This is also the case for AbCellera biotech from Vancouver.
- We can therefore be optimistic about the chances that one or more monoclonal antibodies specific to this virus be identified in the coming months.
- Obviously, vaccination remains the best way to generate a production of antibodies against the coronavirus which will neutralize the virus as soon as it enters the body and prevent the development of the disease.
- Until a vaccine is available, however, the very high specificity of action of monoclonal antibodies means that this approach currently represents one of the best hopes for developing an effective treatment against COVID-19 in the short term.

THE EXAMPLE OF EBOLA

Ebola is arguably the best example of the power of monoclonal antibodies for the treatment of infectious diseases. Until recently, there was no treatment option for this terrifying viral infection, which can have a death rate of over 80%, compared to 1% for COVID-19. Recent studies have shown, however, that a monoclonal antibody isolated from the plasma of a survivor of the disease drastically reduces the mortality linked to the disease, just like a cocktail of three monoclonal antibodies developed by Regeneron and which could be approved by the FDA over the next few months.

(1) Long QX et coll. Antibody responses to SARS-CoV-2 in patients with COVID-19, Nature Medicine, (published online April 29th, 2020).

(2) Shen C et coll. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. JAMA, (published online March 27th, 2020).

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