

A good immune response to the coronavirus

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Translated from Le Journal de Montréal, June 6th, 2020

Several recent articles report that the immune response to the coronavirus responsible for Covid-19 is very good and that one can therefore be optimistic about the chances of developing resistance to the disease naturally or through vaccination.

The immune system plays an essential role in protecting us from the countless pathogens present in the world in which we live. It should come as no surprise that the vast majority of viral infections induce the development of protective immunity (1).

The effectiveness and durability of this immune response can however vary significantly from one virus to another, and to know the degree of protection against a new virus (as is the case with the SARS-CoV-2 coronavirus current), it is therefore necessary to determine to what extent the viral agent can activate different parameters of the immune response.

PROTECTIVE ANTIBODIES

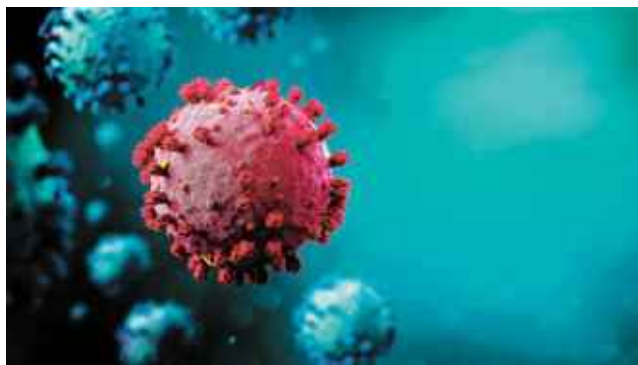
The first important parameter is of course the production of antibodies. These defense proteins produced by B lymphocytes help fight the infection by specifically binding to certain regions (epitopes) of the virus to prevent it from entering and reproducing in cells.

Data collected to date from patients who survived Covid-19 indicate that the infection has effectively produced neutralizing antibodies and that these inhibit the entry of the virus by blocking its interaction with the receptor ACE2. The reactivity of some of these antibodies is excellent and several teams are currently trying to produce them in large quantities to treat infected people (2). It also seems that these antibodies are produced even when the infection is mild and does not cause major symptoms: a study carried out by the Institut Pasteur with 160 people working in hospitals and having presented mild symptoms of Covid-19 showed the presence of antibodies in almost all (99%) of these people (3). These antibodies are also capable of neutralizing the virus, suggesting that they can protect patients from another future infection if this immune response is sustained.

This response time is not yet known, but the results obtained in non-human primates (rhesus macaques) are promising. Infection of monkeys with SARS-CoV-2 has been observed to elicit a strong immune response, characterized by the presence of several neutralizing antibodies. After successfully eliminating the virus and curing the disease (viral pneumonia), the monkeys re-exposed to the virus a few weeks later showed strong resistance to infection, indicating that the antibodies generated during the initial infection were still efficient (4).

SUPPORT FROM T LYMPHOCYTES

There is a lot of talk about antibodies, but another class of lymphocytes, CD4 (helper) and CD8 (killer) T cells, is also absolutely essential for



building long-term immune memory. These cells have several functions, one of which is to help clones of antibody-producing B cells to establish themselves in a sustainable manner so that they can be quickly reactivated in the event of future infection by the same infectious agent. The degree of activation of T cells therefore largely determines whether the immune response to a virus can be sustained over time.

The good news is that this appears to be the case for the current coronavirus: American researchers have shown that people who had been affected by Covid-19 produced CD4 lymphocytes recognizing the protein present in the external peaks of SARS-CoV-2, indicating an adequate immune response to the virus (5). This activation of T cells bodes well for the production of a Covid-19 vaccine because these cells greatly accelerate the production of antibodies essential for effective vaccination.

The researchers also observed that 30% to 50% of the population who were not infected with SARS-CoV-2 still produced T lymphocytes against the virus. This cross immune response is thought to be due to previous infections with other coronaviruses, including those responsible for the common cold, since these viruses have certain proteins similar to the current coronavirus. It would therefore seem that a significant portion of the population can fight SARS-CoV-2 thanks to this residual immunity from previous colds: even without antibodies, the killer T lymphocytes eliminate the infected cells and can therefore stop the infection.

Overall, it therefore seems that the immune response to the coronavirus is rapid, robust and involves all the cellular systems necessary for obtaining optimal immunity. There is therefore reason to be optimistic about the development of long-term natural immunity against this virus and, by the same token, about the potential to develop an effective vaccine against Covid-19.

- (1) Sallusto F et coll. From vaccines to memory and back. *Immunity* 2010; 33: 451-463.
- (2) Wu Y et coll. A noncompeting pair of human neutralizing antibodies block COVID-19 virus binding to its receptor ACE2. *Science*, published online May 13th, 2020.
- (3) Fafi-Kremer S et coll. Serologic responses to SARS-CoV-2 infection among hospital staff with mild disease in eastern France. *medRxiv*, published online May 22nd, 2020.
- (4) Chandrashekar A et coll. SARS-CoV-2 infection protects against rechallenge in rhesus macaques. *Science*, published online May 20th, 2020.
- (5) Grifoni A et coll. Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals. *Cell*, published online May 20th, 2020.