Hope for the development of a vaccine against all coronaviruses

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A fascinating study reports that giving COVID-19 vaccines to people who were infected with SARS-CoV-1 in 2002 generates very large amounts of antibodies against several types of coronaviruses. These surprising results pave the way for the biochemical development of vaccines capable of neutralizing several coronaviruses.

In just 20 years, we have had to deal with three major epidemics of infectious diseases caused by zoonotic coronaviruses (of animal origin), namely SARS in 2002-2003, Middle East Respiratory Syndrome (MERS) in 2012 and COVID-19 since December 2019.

While the impact of the first two epidemics was relatively small globally, the high number of deaths and the huge economic losses caused by Covid-19 show how seriously the threat posed by these viruses must be taken.

Fortunately, we are fortunate to have several extraordinarily effective vaccines developed in record time that have contained the epidemic and saved countless lives.

However, the recent emergence of highly infectious variants (Delta, in particular) capable of partially escaping the immune response generated by these vaccines shows that we must now think about the development of second generation vaccines, not only capable of neutralizing all current and future variants, but also coronaviruses which are already endemic in fauna (in bats, in particular) and which can at any time acquire the capacity to infect humans and to cause devastating epidemics.

Cross reaction

To assess the immune cross-reaction between different types of coronaviruses, a team of researchers had the brilliant idea of administering one of the current messenger RNA-based vaccines (Pfizer) to a group of people who had contracted and survived its infection with another type of coronavirus, SARS-CoV-1 of 2002 (1).

To their surprise, the vaccination of these individuals elicited a very strong immune response against a broad spectrum of coronaviruses, including of course the original SARS-CoV-1 and SARS-CoV-2, but also the variants. alpha, beta and delta of SARS-CoV-2, a bat coronavirus (RaTG131), two pangolin coronaviruses (GD-112 and GX-P5L12) and two bat coronaviruses related to SARS-CoV-1 (WIV1 and RsSHC01413).

In other words, in those people who had previously been infected with SARS-CoV-1, there remains, even after twenty years, an immune memory against a region of the virus which is also present in SARS-CoV-2 and other coronaviruses, and this memory can be quickly reactivated by the anti-Covid-19 vaccine.

Block virus entry

The coronaviruses tested in the study are all sarbecoviruses, a subgenus of beta-coronaviruses that use the ACE2 receptor as a gateway into cells. It is therefore likely that the antibodies capable of neutralizing a wide range of these sarbecoviruses, as identified in this study, exert their action by blocking this interaction.

In this sense, it is interesting to note that a very detailed biochemical analysis of several sarbecoviruses has shown that the binding of these viruses to the ACE2 receptor involves a constant molecular region very conserved from an evolutionary point of view, essential to maintain the spatial organization governing the interaction with the receptor (2).

It is therefore possible that the immune cross-reaction observed in the study reflects the activation of certain clones of antibodies specifically targeting those molecular domains (called epitopes) more common to these different types of viruses, much like a master key. different types of locks.

The precise identification of these regions could therefore pave the way for the design of vaccines recognizing a wide range of coronaviruses, capable of neutralizing not only the variants of the current coronavirus, but also preventing the outbreak of future epidemics caused by other coronaviruses, currently present in a latent state in the animal world.

Biochemistry is at war declared against these viruses!

(1) Tan CW et al. Pan-Sarbecovirus neutralizing antibodies in BNT162b2-immunized SARS-CoV-1 survivors. N. Engl. J. Med., (Published online, August 18th, 2021)

(2) Starr TN et al. Deep mutational scanning of SARS-CoV-2 receptor binding domain reveals constraints on folding and ACE2 binding. Cell 2020; 182: 1295-1310.e20.

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