Vaccination protects against variants of the coronavirus

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Two recent studies show that the antibodies generated by COVID-19 vaccines retain the ability to neutralize the coronavirus variants that have appeared in recent months. On the other hand, it is observed that the accumulation of mutations by the virus tends to decrease this neutralization, which suggests that a periodic update of the vaccines could possibly be necessary to avoid a loss of clinical activity.

VARIANT DETECTION

The presence of the coronavirus can be detected very specifically in a sample (nasal swab, saliva) by a technique called "reverse transcription polymerase chain reaction" (RT-PCR). The virus's RNA is first copied into DNA using an enzyme (reverse transcriptase) and fragments of this DNA are subsequently amplified using sequences that specifically recognize certain regions unique to the virus (a bit like a molecular copier). The number of these fragments doubles with each amplification cycle (exponential of order 2), which makes it possible to generate measurable amounts of DNA very quickly, even from a very small amount of the starting material.

Detection of virus variants is generally slower because it requires sequencing all of the virus's genetic material to identify sites where mutations have been introduced. On the other hand, the development of RT-PCR kits capable of specifically amplifying the regions of the virus containing the mutations will considerably accelerate the detection of the variants responsible for the infection.

This precise identification of the coronavirus variants is important, because the Moderna and Pfizer vaccines which are currently being administered were produced using an RNA sequence present in the virus initially isolated in China, before the appearance of the variants recently identified in United Kingdom (UK) and South Africa (SA). These variants exhibit several mutations in the S protein located on the surface of the virus and which is the target of the neutralizing antibodies generated by these vaccines. Since these variants appear to be particularly contagious and are on their way to becoming the major forms of the virus in circulation, it is essential to determine whether the vaccines provide protection similar to that seen for the initial form of the virus.

NEUTRALIZE THE VARIANTS

Two studies recently published in *Nature* and *Nature Medicine* indicate that this is indeed the case, but that we must be on our guard, because the accumulation of mutations seems to favor the selection of variants that could possibly escape these antibodies.

In the first study (1), the researchers studied three variants containing one or more mutations in the S protein: 1) the N501Y variant (UK and SA), which increases the infectivity of the virus; 2) the Δ69/70 + N501Y + D614G (UK) variant and 3) the E484K + N501Y + D614G (SA) variant, one of the mutations (E484K) of which seems to confer the virus greater resistance to neutralizing antibodies.

Overall, the results obtained are quite reassuring: using sera from participants who had received two doses of the Pfizer vaccine in clinical trials as the source of antibodies, the researchers observed the same neutralizing capacity for the initial virus, or for its current variants. It should be noted in particular that the N501Y mutation, which is now spreading very rapidly, is as sensitive to the antibodies generated by the vaccine as the initial virus. On the other hand, the presence of the E484K mutation, present in the SA variant, seems to slightly reduce the neutralization activity of certain sera, in agreement with studies carried out with purified monoclonal antibodies (2).

In the other study, researchers looked at the ability to neutralize the coronavirus by antibodies from sera from volunteers who received Moderna or Pfizer's vaccine (3). In both cases, there is a slight decrease (1-3 times) in efficacy against the main variants of the virus currently circulating (E484K, N501Y and K417N), but it is likely that this drop in efficacy is not sufficient to abolish the protection offered by these two vaccines.

The researchers also showed that repeated exposure of the virus to neutralizing antibodies present in the sera of vaccinated people causes the appearance of the same mutations as those present in the current variants. It therefore seems that these variants are the result of an evolutionary pressure that favors the selection of mutations favoring an escape of the immune system by the virus. In practice, this means that the more time passes, the greater the likelihood that the virus will succeed in accumulating mutations that will allow it to escape the immune response generated by current vaccines. The best defense against virus variants is therefore to vaccinate as many people as possible as quickly as possible.

In the meantime, we must remain extremely vigilant and continue to monitor in detail the evolution of the virus and its impact on the immune response. As is done every year with influenza, it should now be considered that future mutations of the virus will eventually allow it to bypass the immunity offered by vaccination and will require adjustments to current vaccines. Fortunately, the messenger RNA platform on which these vaccines are based is very flexible and should allow rapid generation of these new vaccines when needed.

(1) Xie ,X. et al. Neutralization of SARS-CoV-2 spike 69/70 deletion, E484K and N501Y variants by BNT162b2 vaccine-elicited sera. Nature Medicine, (Online ahead of print, February 8th 2021)

(2) Baum, A. et al. Antibody cocktail to SARS-CoV-2 spike protein prevents rapid mutational escape seen with individual antibodies. Science 2020 ; 369 : 1014-1018.

(3) Wang Z et coll. mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants. Nature, (Online ahead of print, February 10th 2021)

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