Neutralization efficacy of antibodies against omicron variants BA.1 and BA.2 declines quickly

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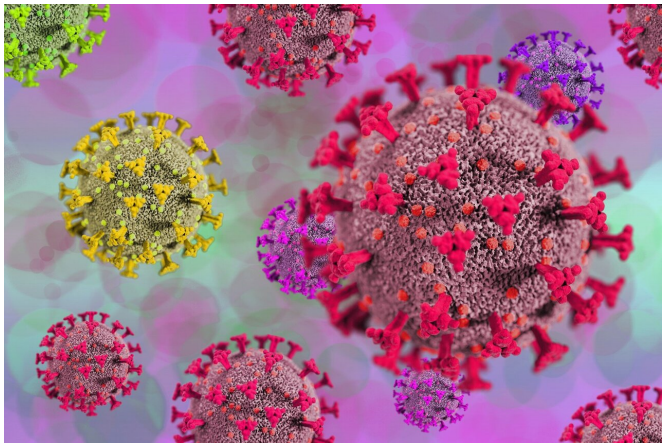

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The omicron variant of the SARS-CoV-2 virus was first detected in South Africa in November 2021. The high level of infectiousness of the virus and its ability to quickly spawn additional variants has also been observed in Germany: Since January 2022 the omicron variant BA.1 has dominated here, followed in subsequent months by the variant BA.2. In the meantime, the virus has mutated further, and since June the variants BA.4 and BA.5 have superseded their predecessors.

This poses major challenges for the immune system of the human body: antibodies are formed in the course of a SARS-CoV-2 infection and these attach themselves to the surface structures of the virus, thus preventing it from penetrating human cells. The viral spike protein plays the key role here.

In the omicron variants, this has changed in more than 50 sites compared to the first SARS-CoV-2 virus identified in Wuhan. The consequence: the antibodies formed after an infection or a vaccination do not recognize the variants as efficiently. This is why despite having overcome an infection, people can again become infected with a new SARS-CoV-2 variant, or there are breakthrough infections. However, how good the immunity response is to an infection depends on more than just antibodies.

Researchers in Frankfurt headed by Marek Widera and Professor Sandra Ciesek from the Institute for Medical Virology at the University Hospital of the Goethe University Frankfurt have now examined how long the antibodies present in blood after a vaccination or recovery from an infection were still able to neutralize the virus variants omicron BA.1 and BA.2.

To this end, they collected blood samples from people who had been vaccinated twice or three times (booster shot), placed the liquid blood component (blood serum), which contains antibodies, together with SARS-CoV-2 viruses on cultivated cells and observed how many of the cells became infected. Furthermore, in each case they ascertained the quantity of antibodies in the samples that recognized the spike protein.

The result: six months after the second vaccination, the tested sera practically had no neutralizing effect on the omicron variants BA.1 and BA.2. The effect of a booster vaccination declined rapidly: although the sera still provided very good protection shortly after the booster vaccination, three months later the protective effect was merely very weak, with the effect that the tested sera were no longer capable of neutralizing the two virus variants.

"This is due to the fact that the antibody titer in serum—the amount of antibodies, so to speak—after a vaccination or infection declines in the course of time," explains Widera. "Because the antibodies

have a significantly lower ability to recognize newer virus variants, a lower level of antibodies is then no longer sufficient to neutralize the virus variants and prevent an infection of the cells in a cell culture. However, the data from this study does not allow any conclusions to be drawn regarding protection against the seriousness of the course of the disease." The decisive factor for the immune function is not just the antibody titer, but also the cellular immune response, which was not examined in this study, Widera adds.

These results are particularly problematic for the use of monoclonal antibodies, which are administered to patients with a compromised immune system as a precautionary measure, for example, says Professor Sandra Ciesek.

Ciesek is the Director of the Institute for Medical Virology at the University Hospital Frankfurt and the senior author of the study. She explains that "as an example we studied three such monoclonal antibodies in laboratory experiments and saw that their efficacy is very heavily dependent on the virus variant. So that we are able to protect vulnerable patients with such preparations, it is absolutely essential to also test in patients the extent to which such antibodies can neutralize the virus variants that are currently prevalent, therefore."

Admittedly, the virus variants BA.1 and BA.2 examined in the study are no longer dominant in Germany in the meantime, adds the virologist. "Our study shows, however, that we cannot afford to let up in adapting our protective measures in line with the genetic changes in the SARS-CoV-2 virus, at present to the omicron variants BA.4 und BA.5."

The research was published in *eBioMedicine*.

More information: Alexander Wilhelm et al, Limited neutralisation of the SARS-CoV-2 Omicron subvariants BA.1 and BA.2 by convalescent and vaccine serum and monoclonal antibodies, *eBioMedicine* (2022). DOI: 10.1016/j.ebiom.2022.104158

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