

# COVID-19: Vaccination and infection found to trigger differential immune responses

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It was initially unclear how the immune system would react to infections with SARS-CoV-2 after a third vaccination. A team of scientists from the University Medical Center Göttingen (UMG), in collaboration with the University of Münster, has now investigated this question in the CoV-ADAPT study ("Humoral and cellular immune responses of the adaptive

immune system after vaccination or natural COVID infection").

The investigations on 213 study participants, all of them employees of the UMG, show that a third vaccination leads to a renewed improvement in the immune response.

The vaccination increases both the quantity and quality of antibodies as well as the cell-mediated immune response. The latter involves the activity of certain cells, so-called T cells, which are particularly relevant in the defense against [viral infections](#).

In the study participants who underwent a SARS-CoV-2 infection despite the third vaccination, an even greater increase in antibody quantity and quality was observed, but no further increase in the cell-mediated immune response.

"The results show that the responses of the [immune system](#) differ to a relevant extent in the vaccinated study participants with and without subsequent SARS-CoV-2 infection," says Dr. Moritz Schnelle, Managing Senior Physician in the Interdisciplinary UMG Laboratory and last author of the study. The results were [published](#) in the *Journal of Medical Virology* on October 3, 2023.

"Previous studies have shown that the number of antibodies decreases quite quickly after vaccination, while the cell-mediated immune response is maintained for longer. It is therefore possible that the boosted immunity after infection does not last very long. A further increase in the cellular immune response would also have been important for this, but we were unable to observe this," says Prof. Dr. Luise Erpenbeck, Professor at the Department of Dermatology at the University Hospital Münster (UKM) and also last author of the study.

In earlier study results, the team led by the two study directors Prof. Dr.

Erpenbeck and Dr. Schnelle has already been able to identify relevant differences in immune responses between the various SARS-CoV-2 [vaccine](#) combinations using the participants of the CoV-ADAPT study, which consists of over 400 UMG employees.

This has already led to two publications. The study, which started in 2021, is divided into several research phases.

## **The study**

Between March and June 2022, the researchers in Göttingen were able to recruit 213 of the original over 400 study participants for the third phase of the CoV-ADAPT study. People who were taking medication that suppresses or otherwise influences the immune system were excluded from the study.

Blood samples were taken from the study participants, all of whom were UMG employees, at an additional time point after the third vaccination.

Similar to the earlier blood tests, antibody quantity and quality as well as the activity of certain immune cells, known as T cells, were examined. In 62 of the 213 participants, a SARS-CoV-2 infection, also known as a breakthrough infection, occurred between the third vaccination and the new blood sample. 151 [test subjects](#) remained without infection.

The data show that a third vaccination leads to a renewed improvement in the virus-specific immune defense. It increases both the quantity and quality of antibodies as well as the cellular immune response.

In the 62 test subjects who underwent a SARS-CoV-2 infection despite the third vaccination, an even greater increase in antibody quantity and quality was observed as a result of the infection, but no further increase in the cell-mediated [immune response](#).

## Increased risk of breakthrough infections cannot be predicted

The team also wanted to find out why some people suffer a SARS-CoV-2 infection despite the vaccination, while others are spared. To do this, the Department of Medical Statistics at the UMG trained a machine learning model with the data from the study and the previously published CoV-ADAPT studies. However, despite the large data set, this model was not able to identify people with a higher risk of breakthrough [infection](#) based on the available information.

"An important contribution of this study is that even based on comprehensive immunological data over a long period of time, no prediction of breakthrough infections for individuals seems to be possible," said Dr. Sascha Dierks, Scientist in the Interdisciplinary UMG Laboratory and one of the two first authors.

"Other studies show that higher SARS-CoV-2 antibody levels are on average associated with a lower risk of SARS-CoV-2 breakthrough infections. However, our findings demonstrate that for individuals, the long-term SARS-CoV-2 immune status is not meaningful enough to make an accurate risk prediction on an individual level," adds Dr. Moritz Hollstein, Resident Physician in the Department of Dermatology, Venereology and Allergology at the UMG and also first author of the study. "Environmental factors probably play a greater role in identifying people at risk."

Scientists from the Institute of Clinical Chemistry and the Interdisciplinary UMG Laboratory, the Department of Dermatology, Venereology and Allergology, the Institute of Medical Microbiology and Virology and the Department of Medical Statistics at the UMG and the University of Münster worked closely together on this study.

All scientists agree that the CoV-ADAPT study contributes to a better understanding of immunological changes.

**More information:** Moritz M. Hollstein et al, Humoral and cellular immune responses in fully vaccinated individuals with or without SARS-CoV-2 breakthrough infection: Results from the CoV-ADAPT cohort, *Journal of Medical Virology* (2023). [DOI: 10.1002/jmv.29122](https://doi.org/10.1002/jmv.29122)

Provided by University of Göttingen

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