

## Press Release

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### Press and Public Relations

Campus A2 3  
66123 Saarbrücken  
Tel.: +49 (0)681 302-2601  
[presse@uni-saarland.de](mailto:presse@uni-saarland.de)

### Editor

Friederike Meyer zu Tittingdorf  
Tel.: +49 (0)681 302-3610  
[presse.meyer@uni-saarland.de](mailto:presse.meyer@uni-saarland.de)

## How Covid-19 vaccinations activate the immune response in organ transplant recipients

*Additional T cell analyses give a better picture of immune response than pure antibody tests*

**When critically ill patients receive a donor organ, they have to take immune-suppressing medication for the rest of their lives. However, these immunosuppressants can also prevent a vaccine from triggering the desired response in the patient's immune system. Professor of Immunology Martina Sester and her team have recently shown that despite the weakened immune response in organ transplant recipients, the different Covid-19 vaccines mobilize the immune defences in these individuals in different ways and that the best immune response is achieved when these vaccines are used in combination. They were also able to demonstrate that antibody tests alone do not provide an adequate means of determining an immune response in this patient group, and that T cell analyses also have to be carried out. Their research results have now been published in the American Journal of Transplantation.**

A total of 400 subjects are currently being enrolled in the ongoing study, which is still ongoing. For the paper just published, the team analysed data from 110 individuals, all of whom had received two doses of a Covid-19 vaccine. Within this cohort there were 40 people who had either undergone a kidney, lung or liver transplant or had a donor heart and were being treated at the Saarland University Medical Center in Homburg. The remaining 70 subjects were individuals who were not taking any immunosuppressant drugs. 'A person who has had an organ transplant needs to take several drugs, each with a different type of immunosuppressive action, to prevent their body rejecting the donor organ. With autoimmune diseases, a single immunosuppressant is often sufficient, but even here the medication taken can reduce

the efficacy of a vaccine – something we know from earlier studies on flu vaccination programmes,’ says Martina Sester, Professor of Transplantation Immunology and the Immunology of Infectious Diseases at Saarland University.

To understand the result of Sester’s most recent study, it helps to know how the human body defends itself when infected with the SARS-CoV-2 virus and how vaccines support this process. When viruses enter the body, our immune system generates antibodies, which act in the blood and on the mucous membranes, such as those in our lungs. Antibodies essentially capture the virus and neutralize it. In the case of the SARS-CoV-2 virus, the antibodies bind to the spike proteins that protrude from the surface of the viral particles. ‘White blood cells known as “helper T cells” have a number of functions, including that of activating the production of antibodies. The role of the “killer T cells” is to destroy those cells that have become infected with the virus. The Covid-19 vaccines trigger these naturally occurring defence mechanisms, but they do this in different ways depending on the specific vaccine, and in the case of organ transplant recipients the intensity of the response can be significantly reduced,’ explains Professor Sester, whose team conducted the very extensive series of tests needed to determine the vaccine responses of their test subjects.

They not only recorded whether antibodies were formed, they also analysed how the different T cells were activated by the different vaccines. After the first jab, it could be shown that the mRNA vaccine from BioNTech/Pfizer was more effective in generating antibodies than the viral vector vaccine from AstraZeneca. The ranking was reversed when studying the formation of T cells, which were present in greater numbers after a shot of the vector-based vaccine. However, when patients who had received an organ transplant were studied, antibodies were detected only in about five percent of the patients who had received their first vaccine jab, whereas the corresponding figure was 80 percent in the control group. A more encouraging picture was found when the levels of T cells were examined, with T cells detected in around one quarter of the transplant patients. In the control group, it was above 80 percent.

‘Our study not only shows that the different Covid-19 vaccines act differently after administering the first dose, we also found that antibody tests alone are not an appropriate means of determining whether immunocompromised individuals have an adequate level of vaccine protection,’ says Martina Sester. ‘A similar picture was

observed after the second shot of vaccine, where we found that the immune response picture was significantly better if T cells were also taken into account rather than just relying on the antibody titre. After the second dose of vaccine, antibodies or T cells were observed in 71 percent of the immunocompromised patients. As we were able to examine transplant recipients who were given two doses of the same vaccine ('homologous vaccination') and transplant recipients who were administered two different types of Covid-19 vaccines ('heterologous vaccination'), we were able to confirm that combination vaccinations produced better results also for this group of immunocompromised patients,' says Sester.

In an earlier research project, whose results have been published in *Nature Medicine*, Professor Sester's team found that individuals with a healthy immune system who received AstraZeneca as their first dose and the BioNTech vaccine as their second shot showed a significantly stronger immune response than those who received the AstraZeneca vaccine on both occasions. Germany's Standing Committee on Vaccination (STIKO) has taken note of these results and now recommends a combination vaccination for adults, including those over the age of sixty. 'We are currently examining whether a mixed vaccine approach should be adopted when giving immunocompromised patients a third booster shot so that they can develop the broadest possible immune response,' explains Martina Sester. The organ transplant centres in Germany also plan to link up in order to share and exchange study data. Another question of interest is whether these findings could help other groups who may be at greater risk from Covid-19, such as people with Down's syndrome, as it could help them develop an improved immune response.

The ongoing study involving recipients of organ transplants received €80,000 in funding from the Saarland State Chancellery.

### Original publication:

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Further information:

[Department of Transplant and Infection Immunology](#)

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**Questions can be addressed to:**

Prof. Dr. Martina Sester

Department of Transplant and Infection Immunology

Tel.: +49 (0)681 162-3557

Email: [martina.sester@uks.eu](mailto:martina.sester@uks.eu)