Press release

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Antibody Formation after Vaccination with Different mRNA Vaccines and after COVID-19 Infection

A research team at the Paul-Ehrlich-Institut has compared the antibodies formed after vaccination with the COVID-19 Comirnaty vaccine from BioNTech/Pfizer – currently the most widely used in Germany – with those formed after vaccination with vaccine candidate CVnCoV (CureVac), which has been withdrawn from the authorisation process, and after COVID-19 infection. Specific antibody levels, neutralisation capacity, and binding ability of the antibodies vary considerably from person to person following vaccination with Comirnaty and after COVID-19 infection on the one hand, and following vaccination with CVnCoV on the other hand, which may help to explain the differing efficacy.

The mRNA vaccines consist of messenger RNA (mRNA), which is coated by lipid molecules. The mRNA contains the genetic information for the blueprint of the SARS-CoV-2 surface protein (spike protein). In some body cells, this genetic information is translated into spike protein and leads to immune response and to immune protection against COVID-19. Although the mRNA vaccine Comirnaty from BioNTech/Pfizer and the COVID-19 vaccine candidate CVnCoV from CureVac each encode a stabilised spike protein of SARS-CoV-2 as an antigen, they differ with regard to the type of mRNA. While the mRNA in Comirnaty is nucleotides (building blocks of RNA) modified by methylation, the mRNA of CVnCoV is not modified. Another difference is the amount of mRNA administered in the two vaccines. One vaccine dose of Comirnaty contains 30 µg mRNA, while a dose of CVnCoV contains 12 µg mRNA.

A research consortium led by Professor Eberhard Hildt, Head of the Virology Department at the Paul-Ehrlich-Institut, and scientists at Aachen University Hospital, the Robert Koch Institute, and the Main-Kinzig-Clinics examined the way the formation of protective antibodies against COVID-19 differs following vaccination with Comirnaty and various doses of CVnCoV, as well as following COVID-19 infection (convalescents). To this end, they examined blood sera (cell-free blood fluid without clotting factors) from healthcare workers vaccinated with Comirnaty, blood sera from participants of a phase I trial of Curevac’s COVID-19 vaccine candidate who had been vaccinated with 2, 4, 6, 8 or 12 µg of CvnCoV, and blood sera from persons in recovery (convalescent sera), which came from hospital patients. The blood sera were analysed by means of ELISA (enzyme-linked immunosorbent assay), an enzyme-linked immunological detection method, live virus neutralisation tests, surface plasmon resonance spectroscopy (SPR), and peptide arrays.

Most blood sera after vaccination with Comirnaty and from persons in recovery showed a higher titre of spike receptor binding domain (RBD)-specific antibodies and neutralising antibodies compared to those vaccinated with CVnCoV. Neutralising antibodies mostly bind directly to the RBD and thus prevent the virus from penetrating the human cell.

All blood sera analysed showed a reduction in binding and neutralising antibodies for the beta variant of Coronavirus SARS-CoV-2 (virus variant first detected in South Africa), which suggests somewhat lower efficacy. Furthermore, SPR analyses revealed that the blood sera after vaccination with CVnCoV showed a lower proportion of slowly dissociating antibodies. This means that the CVnCoV blood sera are less well able to obstruct the interaction between the spike protein of the virus and the ACE2 receptor, a portal of entry of the virus into somatic cells. It is true that most of the sera following vaccination with CVnCoV came from persons vaccinated with lower doses than the 12 µg RNA that was
ultimately selected in the phase 3 study. However, the published data from the phase I trial clearly indicate that the dose has little effect on the titre of spike-specific antibodies or on the neutralising capacity after the second vaccination.

The research team also investigated the significance of some important virus mutations (K417N, E484K, N501Y). Here, a clear difference was revealed between convalescent sera and sera induced by the vaccine: with the N501Y mutation in particular, which is found in the alpha, beta, and gamma variants of the virus, the scientists found a notable decrease in the binding of antibodies in the blood sera of the two vaccines.

Although the efficacy of an RNA vaccine depends on more parameters than just the serological, the lower antibody titre after vaccination with CVnCoV, the lower neutralising activity, and the lower affinity may contribute to the lesser efficacy of the CVnCoV vaccine.

The current study characterises the SARS-CoV-2 spike RBD-specific humoral immune response, i.e. the part of the immune response mediated by non-cellular components of the immune system, which is induced by two different mRNA vaccines and by convalescent sera. The analysis of these kinds of differences and the influence of viral variants provide important findings with regard to possible adaptations of vaccines to new viral variants.

Background – mRNA vaccines against COVID-19 in Europe

There are currently two mRNA vaccines against COVID-19 authorised for use in the European Union: Comirnaty from BioNTech/Pfizer and Spikevax from Moderna. The data on a third mRNA vaccine candidate, CVnCoV from CureVac, were reviewed by the Committee for Medicinal Products for Human Use (CHMP) at the European Medicines Agency (EMA) as part of a rolling review process. In October 2021 CureVac withdrew its application for review (rolling review). In phase 2b/3 of the trial, which is important for licensing, the vaccine candidate showed efficacy of 48 percent in preventing illness from COVID-19 of any severity. Although the emergence of new viral variants during the clinical trial may have affected the efficacy, it still showed lower efficacy compared to the licensed mRNA vaccines.

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