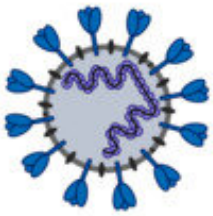
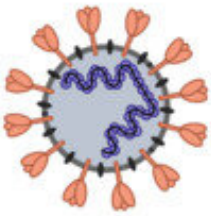
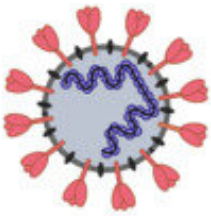
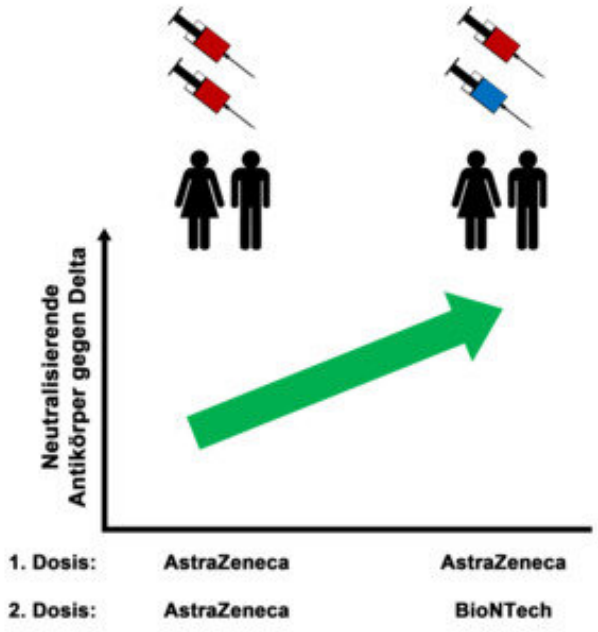
Delta and Delta Plus evade the antibody response

October 18 2021

A)

	Ursprungsvirus	Delta-Variante	Delta Plus-Variante
			
Wichtige Mutationen im Hüllprotein „Spike“:	---	L452R, T478K, P681R	K417N, L452R, T478K, P681
Eintritt in menschliche Lungen- und Darmzellen:	Normal	Erhöht	Erhöht
Fähigkeit Wirtszellen zu verschmelzen:	Normal	Erhöht	Erhöht
Wirksamkeit von therapeutischen Antikörpern:	Normal (4 von 4 wirksam)	Reduziert (3 von 4 wirksam)	Stark reduziert (2 von 4 wirksam)
Neutralisation durch Antikörper im Blut genesener oder geimpfter Personen:	Normal	Reduziert (Faktor 2-6)	Reduziert (Faktor 2-6)

B)



Properties of SARS-CoV-2 Delta and Delta Plus variants and efficacy of protection by different vaccination strategies. A) Summary of special properties of SARS-CoV-2 Delta and Delta Plus variants compared to the virus circulating to the beginning of the pandemic (wildtype virus). B) Heterologous vaccination with Oxford-AstraZeneca's vector-based vaccine and BioNTech-Pfizer's mRNA-based vaccine Induces the production of more neutralizing antibodies against the Delta variant than homologous (two-shot) vaccination with Oxford-AstraZeneca. Credit: Markus Hoffmann

The emergence of new SARS-CoV-2 variants that can spread rapidly and undermine vaccine-induced immunity threatens the end of the COVID-19 pandemic. The delta variant (B.1.617.2) emerged in India and subsequently spread globally within a short time period. Also in Germany, almost all recent infections are due to this variant. In addition to Delta, so-called Delta Plus sub-variants have been observed, which carry additional mutations that may make them more dangerous. A research team led by Stefan Pöhlmann and Markus Hoffmann from the German Primate Center—Leibniz Institute for Primate Research in Göttingen and colleagues from the Hannover Medical School, the University of Göttingen Medical Center and the Friedrich-Alexander University of Erlangen-Nürnberg have investigated why the Delta variant spreads so efficiently and whether Delta Plus viruses are more dangerous. They were able to show that Delta and Delta Plus infect lung cells with higher efficiency than the original virus. In addition, one of four antibodies used to treat COVID-19 was not effective against Delta, and Delta Plus was even resistant against two therapeutic antibodies. Similarly, antibodies generated upon vaccination with the BioNTech-Pfizer and Oxford-AstraZeneca vaccines were also less effective against Delta and Delta Plus compared to the original virus. Delta and Delta Plus, on the other hand, were comparably inhibited, suggesting that Delta Plus may not pose a greater risk to vaccinated persons than Delta.

Finally, it was found that individuals vaccinated first with Oxford-AstraZeneca and then with BioNTech-Pfizer had significantly more antibodies that inhibited Delta than individuals vaccinated twice with Oxford-AstraZeneca. The combination of two vaccines may thus induce a particularly strong immune protection against SARS-CoV-2 variants *(The Lancet, Cell Reports, Cellular & Molecular Immunology).*

At present, more than 99 percent of SARS coronavirus 2 infections caused in Germany are due to the Delta variant, according to the Robert Koch Institute. Using cell culture experiments, a team of researchers led by Stefan Pöhlmann and Markus Hoffmann was able to show that Delta is better at entering lung cells compared to the original virus (the virus that circulated during the early phase of the pandemic). In addition, Delta is better at fusing infected lung cells with uninfected cells. "It is conceivable that by fusing cells in the respiratory tract, the Delta variant may spread more efficiently and induce more damage. This could contribute to a more severe course of COVID-19," assumes Arora Prerna, scientist at the German Primate Center and first author of two studies specifically focusing on the Delta and Delta Plus variants.

Monoclonal antibodies are used to treat COVID-19. These antibodies are proteins that are produced by genetic engineering. Unlike our immune system, which produces a large number of different antibodies against pathogens during infection, only individual antibodies or combinations of them are used for COVID-19 therapy. The team led by Stefan Pöhlmann and Markus Hoffmann studied four of these antibodies. They found that Delta is resistant against the antibody bamlanivimab, while Delta Plus is resistant against two antibodies, bamlanivimab and etesevimab, which are used in combination for treatment of COVID-19 patients.

Delta and Delta Plus were less well inhibited (neutralized) by antibodies from infected and vaccinated individuals as compared to the original

virus and this likely contributed to the rapid spread of Delta. A direct comparison of Delta and Delta Plus showed that both viruses were comparably neutralized. "This means that vaccination likely confers comparable protection against Delta and Delta Plus, and that Delta Plus is not significantly more dangerous than Delta," says Stefan Pöhlmann. BioNTech-Pfizer's vaccine is the most widely used vaccine in Europe, followed by Oxford-AstraZeneca's vaccine. Due to very rare side effects following vaccination with Oxford-AstraZeneca, it is recommended in Germany and other countries that BioNTech-Pfizer is used for the second vaccination shot in people who have already received a first shot with Oxford-AstraZeneca. This strategy is referred to as heterologous vaccination. "Our studies show that heterologous vaccination induces significantly more neutralizing antibodies to Delta than two vaccination shots with Oxford-AstraZeneca. Individuals who have received such a heterologous vaccination may have a very good immune protection against Delta and Delta Plus," says Markus Hoffmann.

"Our results are consistent with the observation that vaccination efficiently protects against development of severe disease after infection with the Delta variant, but frequently fails to completely suppress infection. In light of the efficient protection against severe disease, the goal continues to be a high vaccination rate. This can prevent the health care system from being overwhelmed in case of increased spread of Delta and closely related viruses during the winter months," says Stefan Pöhlmann.

More information: Georg MN Behrens et al, SARS-CoV-2 delta variant neutralisation after heterologous ChAdOx1-S/BNT162b2 vaccination, *The Lancet* (2021). DOI: 10.1016/S0140-6736(21)01891-2

Prerna Arora et al, B.1.617.2 enters and fuses lung cells with increased efficiency and evades antibodies induced by infection and vaccination, *Cell Reports* (2021). DOI: 10.1016/j.celrep.2021.109825

Prerna Arora et al, Delta variant (B.1.617.2) sublineages do not show increased neutralization resistance, *Cellular & Molecular Immunology* (2021). DOI: 10.1038/s41423-021-00772-y