Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #79

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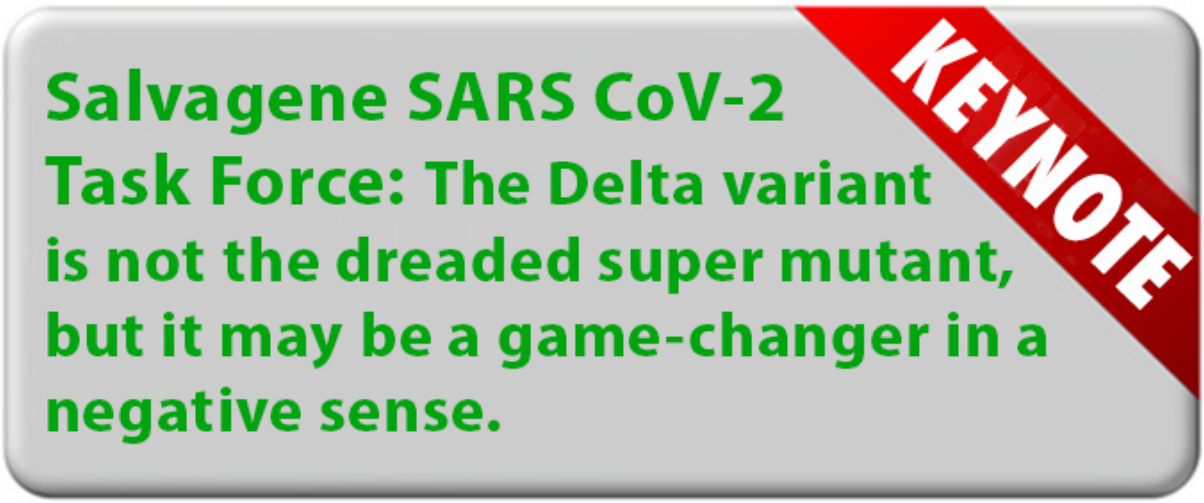

Dear Premium Customers,

In India, the Delta variant has been responsible for a sharp increase in the number of infections, illnesses and fatalities. The health system there is at breaking point. In the meantime, the Delta variant has also been discovered in other parts of the world, especially in the UK, which is a country where virus variants are monitored with exemplary thoroughness. It is expected that the Delta variant will supplant Alpha (B.1.1.7), which has been the most widespread variant so far. According to official data, Delta is currently present in nine out of ten samples sent for analysis.

In various parts of the UK, incidences are rising sharply again; the seven-day rate, which has long been around 20 new infections per

100,000, has recently risen to over 90. Mass testing has now been started in the north-west of England and the vaccination campaign has been stepped up.

Delta has twelve genetic changes in its spike protein compared to the original Wuhan strain discovered in December 2019. However, it has no changes at positions 501 or 484 of the receptor binding site, which we are closely monitoring here at Salvagene. These mutations have so far been detected on the Beta (South Africa B.1.3.5.1) and Gamma (Brazil P.1) virus variants and defined as escape mutations. In the case of the Delta variant, however, the relevant change is the L452R substitution in the spike protein. Initial experiments in the laboratory suggest that it significantly boosts binding to the ACE 2 receptors, making it more infectious on the one hand and more dangerous on the other. This means that the risk of infecting a person from the same household is 60% higher with Delta than with the previously dominant Alpha variant; in other words, it is much more easily transmissible. This is apparent not only from the increase in the number of cases but also from contact tracing. The percentage of infected contacts is higher at 12.5% than for persons infected with B.1.1.7 at 8.1%. Data from the UK also indicate that individuals who contract B.1617.2 are at greater risk of ending up in hospital than those who contract B.1.1.7. These statistics make it clear that Delta is not only more infectious, but also more dangerous.

In a study just published in the Lancet, medical experts looked at how effective the antibodies produced by vaccinated individuals are against the Delta variant. The good news is that everyone who received two doses of their particular vaccine developed antibodies against the spike protein of SARS-CoV-2. The bad news, however, is that these antibodies are clearly less able to neutralize the Delta variant than the wild-type virus by a factor of more than 5.8.

For those who have received only one vaccine dose, the effect was even more worrying. 21% did not neutralize the wild type very effectively. For Alpha it was 50% and for Beta (i.e. South Africa) it

was as much as 75%. The antibodies produced by a single dose were to all intents and purposes ineffective against the Delta variant in 80% of cases. These findings are clearly at variance with the report issued by Public Health England in which it was stated on a purely empirical basis and without any clinical evidence having been gathered that double vaccination could prevent 96% of hospitalizations. We are deeply skeptical of this claim.

Another study from England with a much better design shows that effectiveness against the Delta variants is clearly reduced, with a single dose of an mRNA or vector-based vaccine protecting against a symptomatic course of the disease in only 34% of cases. By comparison, a single jab protects in 51% of cases caused by the Alpha variant. Efficacy is thus clearly reduced by the new variant. After two doses of an mRNA vaccine, protection against Delta is 88%, slightly lower than the 93% efficacy rate for Alpha. The equivalent rate for two doses of the AstraZeneca vector vaccine is 60% protection against symptomatic disease with Delta and 66% with Alpha. The UK government has already responded by postponing the lifting of all restrictions, originally planned for 21st June, by four weeks. This change was of the utmost urgency, as Prime Minister Johnson announced it immediately after the G7 summit. What has been dubbed "Freedom Day" has now been postponed to 19th July.

The UK is once again at the focus of our attention because, in the western world at least, it is "Delta land" par excellence and, at the same time, it is a leader in the field of gene sequencing. It therefore makes sense for other countries to closely observe what is happening there. The current scenario is also absolutely fascinating for us as scientists. Infections have increased in the UK by 64% in the last few weeks. In the worst-affected areas, cases are even doubling every week. The link between infections and hospital admissions has weakened, but it has not been broken. The number of people in intensive care units is also growing again. According to Public Health England, 91% of new cases are now caused by the Delta variant. Our prediction has been validated, and the race between mutations and vaccination is vividly illustrated here once

again. How quickly can the vaccination program be implemented? How well will the vaccines work? And how soon will the next mutation emerge?
What is still unclear are the numbers of Delta patients admitted to hospital who had been vaccinated. At the moment, we have three different figures which range between five and twelve percent, so we cannot say that the vaccines are forming a solid wall of defense against these mutations so far. We endorse the four criteria laid down by the UK for mapping the way out of the crisis.
1) the progress made by the vaccination campaign
2) the efficacy of the vaccines
3) the burden on the health system and
4) the risk posed by new mutations.

We predict that the fourth criterion will be the most challenging worldwide.

Looking carefully at the mutations observed in the Delta variant, it is clear that this is definitely not the dreaded super mutant that would ultimately render the entire vaccination strategy futile. It is only a foretaste of what may lie ahead.

Even in other countries that already have a high vaccination rate, such as Chile, the infection rate continues to rise, although the Delta variant has not yet made an appearance there. In Chile, they are still struggling to control the P1 variant. Due to the non-homogeneous vaccination regime in the country, where mRNA- and vector-based vaccines are being administered alongside protein vaccines from China, it is not yet possible to make a definitive comparison of their effectiveness against P1. Ultimately, we have to conclude that, even with a high vaccination rate, a reduction in the number of infections is nowhere in sight, especially as winter is now beginning in Chile.

In Israel, another country that we are observing closely, the vaccination strategy has paid off so far. However, gene sequencing there shows that the Alpha variant still has a monopoly. It remains

to be seen whether further mutations will be introduced into the country.

In Moscow, which has taken on the status of “Delta city”, the rate of infection is also soaring and the number of patients requiring artificial respiration in intensive care units has risen sharply.

We are working on the assumption that the antibodies triggered by the vaccines currently in use are therefore less effective. It is possible that, with an overall higher antibody volume, Class 1 of the neutralizing antibodies (i.e. those with the highest efficacy) will also increase and consequently be more effective against the Delta variant. Here at Salvagene, we measure these levels every three months for our Premium clients.

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