Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #29

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Salvagene SARS-CoV-2 Task Force: Fears of a cytokine storm resulting from a future C-19 vaccination

KEYNOTE

Dear Premium Customers,

An incorrectly formulated vaccine can significantly exacerbate the harm done by the virus.

Many cytokines are part of our innate immune system (which is separate and distinct from our adaptive immune system). Unfortunately, SARS viruses are particularly adept at interacting with the innate immune system, which is what makes SARS-CoV-2 such a potentially deadly pathogen. Normally, infected individuals do not die from the virus itself, but from a cytokine storm, as we have already touched on in several previous keynotes and podcasts. This is what makes the development of vaccines in this area so risky. Not only the virus but also the vaccine designed to counteract it can trigger a fatal signal chain. There is, however, a problem: so that the vaccines can be approved and made available more quickly, authorities around the world are tempted to bypass trials on humans that might show up these undesired effects. Instead, developers are asked

to base their findings on other evidence that can be obtained more quickly. But is that wise?

For this very reason, we are highly skeptical about so-called "quick-fix" projects in vaccine development. This is an area in which shortcuts should definitely not be taken. Multiple safety thresholds have been laid down between the conceptual stage for a vaccine and its first injection in humans. The new formulas are first tested in cell cultures, then they undergo experiments in animals to show that they can reliably trigger immune reactions and that their ingredients are well tolerated. At the very end of the animal trials comes a so-called "challenge": the animals are first vaccinated and then infected with the corresponding pathogens. From this point on, the rest is usually just a formality. With SARS, however, it suddenly got serious: in 2008, when researchers in Japan caused freshly vaccinated mice to inhale the viruses, some of these animals very quickly manifested signs of distress.

Autopsies revealed that the mice which had died did indeed have hardly any viruses in their lungs – the antibodies formed after vaccination had presumably fended them off. The same phenomenon is currently being demonstrated in vaccination projects worldwide. Nevertheless, there was extensive inflammation and a proliferation of defender cells was observed. Just as in a SARS infection, the walls of the alveoli were thickly swollen and the subjects could hardly breathe. The problem was that the vaccination contained viral components which must have given the immune system such a fright that it went completely haywire upon coming into contact with the relevant virus. At that time, a total of 14 vaccines failed due to the severe reaction.

Coronaviruses are notorious for their ability to cross over between the mammalian species and for creating surprisingly different effects. Because of the urgent need for vaccines in the current pandemic, we believe that extensive pretesting should be done with as many animal species as possible – and certainly not

restricting ourselves to the customary mice. Among the shortcuts we are seeing is the omission of these vital challenge tests. Time is of the essence. We are conferring with institutions such as the US regulatory authority NIAD, and its German equivalent, the Paul Ehrlich Institute, which have argued in favor of shortening the process.

But in our conversations with these authorities, we sense that there are indeed concerns about such shortcuts. In Germany, for example, the proposed solution is that the challenge tests on laboratory animals are carried out in parallel with vaccination of humans. For this to proceed, other additional conditions must be fulfilled before the human tests receive approval. Here, determining the markers of the cytokine profile is crucial to detection of a harmful polarization of the immune system caused by a vaccine, and according to the Paul Ehrlich Institute, this is an essential part of the study design. Such investigations should be integrated into a study, first in animal experiments, and only later in humans.

The decisive additional condition is the determination of the cytokine profile – which we have already been recording and monitoring regularly over recent weeks for all our Premium clients as part of the Salvagene Covid-19 Immunization Program – so that we will be able to compare this profile with different vaccine profiles and the different approaches they take. This is one of the decisive factors in making an individual and considered recommendation on Covid-19 vaccination to our clients.

What we seek to establish are the most minute changes in the cytokines. **This is also the reason why we regularly check the cytokine receptors as part of our Salvagene C-19 Immunization Program**. Why do we do this? There are a whole range of cytokines. Some of them stimulate immune cells while others suppress them. For a balanced vaccination response – and this is absolutely vital for a successful outcome – both types of

cytokine must be present, but neither must be allowed to get the upper hand.

The SARS virus has four different proteins on its envelope. Two of them were instrumental in the failure of previous vaccination projects. One of them is the well-known SPIKE protein. It is by far the largest protein on the surface of the virus, the component that attaches itself to the host cells and the protein that is now present in most vaccine models. Because the spikes stick out so far, there can be no perfectly matched antibodies without them. The failure of vaccines with SARS proteins can be explained by what the antibodies do: They can have an infection-enhancing effect. Antibodies are V-shaped structures. In the case of good antibodies, the foot fits the virus surface like a plaster cast on the original – indentation for indentation. This allows them to smother the virus – the feet at the bottom, the arms above and equipped with a tight, sticky layer that renders the pathogen non-functional.

However, it has long been known just how harmful badly fitting antibodies can be, in which case the feet of the antibodies formed by the first infection do not fit well with the viruses of the second wave. They do not bind. As we already mentioned in March, it is possible that the symptoms of a second infection may be significantly worse, and we continue to assume that this may apply, although not in all cases. Because the virus has an alternative – a binding site suitable for the arms. But there is a nasty twist to all of this. As soon as the foot of the antibody is on the outside, certain immune cells react to this signal, direct the viruses marked as unorthodox to their interior and replicate them there. The infected cells then begin to release large quantities of pro-inflammatory signal substances – **a cytokine storm develops, exactly the effect that we at Salvagene want to prevent**. In most of the experimental setups in the vaccine projects known to us, the cytokine profiles do not show the risk. But the matter can probably only be clarified once and for all in animal experiments at the challenge stage. The regulatory authorities are conscious of precisely this risk, which ultimately

has to be weighed against delay in making the vaccine generally available.

There is a lively debate among infectiologists about how this situation will develop. The key question is, how does SARS-CoV-2 behave when antibodies are a poor match? Similar observations can also be made in cases of survived infection. We assume that recently survived coronavirus-based infections may offer additional protection, but may equally trigger a flood of inflammatory substances if antibodies are poorly fitting.

Based on the current state of scientific knowledge, we assume that the Covid-19 pathogen may be able enter the body more easily as a result of vaccination because of poorly bound antibodies, but there is no general agreement on whether the virus really wants to do this. Individuals who have already been vaccinated can only hope for the best of luck.

Consequently, we do not intend to issue any general recommendation in favor of a Covid-19 vaccination for the moment. The current state of knowledge can be found in our Salvagene C-19 Vaccine and Medication Advisor on our website. We will only make individual recommendations on the basis of each Premium client's personal results while taking into account the compatibility of their individual health status with the available vaccine profiles.

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