Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #34

September 2020

Salvagene SARS-CoV-2 Task Force: How dangerous is SARS-CoV-2 in combination with the Influenza virus?

KEYNOTE

Dear Premium Customers,

The warnings are growing louder about a winter in which we not only have to contend with the risks posed by SARS-CoV-2 but also by influenza viruses. It is still not clear whether the viruses are mutually reinforcing.

As early as June, however, the infection specialists Edward Belongia and Michael Osterholm sounded an alert in the specialist journal Science that the world is about to enter uncharted waters. The fact is that we still don't know the answer to the above question.

Whenever a new virus appears, we not only have to observe how it spreads and what harm it causes to those who are infected, we also need to study the effect that the novel pathogen has on others that are already known to us, i.e. whether it makes the

outbreak of another disease more likely, and whether it tends to escalate it, make it less harmful or even suppress it.

When the AIDS virus first rampaged around the world, the hospitals were suddenly clogged with patients manifesting soft tissue sarcomas – the virus enabled these malignant tumors to grow more readily. However, pathogens may also cause a second infection to be less severe, e.g. relatively harmless common cold viruses ensured that the 2012 swine flu outbreak did not have as big an impact as feared.

In recent months, we have been closely monitoring the virus situation around the globe, especially the flu season in the southern hemisphere, as we have already reported in previous Keynotes. We feared the worst from an overlap between SARS-CoV-2 and influenza viruses: possibly severe double infections, but also that doctors' surgeries would be overwhelmed by a surge of flu and Covid sufferers. This would at least have helped us to learn about the consequences of a coincidence of SARS-CoV-2 and influenza. In this respect, however, our expectations have not been met, because the influenza season in Australia, South Africa and South America has failed to materialize. As we reported in our Keynote 27 last month, this is problematic insofar as relatively few samples have become available for the development of an influenza vaccine, and it is the reason why we expect this year's version to have a success rate of only about 50%. For example, our colleague Cheryl Cohen at the South African Institute of Communicable Diseases set up a study to see how patients fared when they were infected with both pathogens. In fact, there was only one patient whose results showed that he had both pathogens, so of course it was not possible to draw any scientific conclusions on that basis. Other regions in the southern hemisphere such as Australia and South America did not produce any significant results either. A handful of double infections have been reported from China and Iran, so all we can say at the moment is that there is no evidence of SARS-CoV-2 and influenza affecting each other one way or another.

We have also looked at the work done by a colleague at the Max Planck Institute for Infection Biology in Berlin and the Pasteur Institute in Paris. The research has only been published in draft form, and we are somewhat skeptical about its findings. The author claims to have shown on the basis of a purely mathematical model that the decrease in corona infections in Belgium, Norway, Italy and Spain over the spring months was not only due to the compulsory wearing of masks and the lockdown measures, but also to the fact that the influenza season in these countries was flattening out from March onwards. The mathematicians deduced that influenza increases the transmission rate of corona viruses by a factor of 2.5. The researchers suspect that influenza makes people more susceptible to corona. However, the work is a mathematical model and therefore not a biological explanation. The authors suppose that the influenza viruses cause more receptors to be formed on the cell surface to which the SARS-CoV-2 can attach itself. As we said above, we are rather skeptical about this because, conversely, the coronaviruses of the common cold also produce antibodies that we suspect will develop immunity to SARS-CoV-2.

So why should we even be afraid of the flu season if the social distancing and other measures in the southern hemisphere have helped to suppress influenza? Because the so-called “common” cold, which is spread by rhinoviruses, is currently rising significantly. And this suggests that social distancing does not affect all respiratory pathogens equally. Even if the flu viruses do not spread as much this year, the winter months are high season for infectious diseases. Because of the low temperatures, the viruses survive better, but people also travel more by bus and train and sit close together in restaurants and offices. The risk of infection is increased. It has repeatedly been shown that pathogens reinforce each other. Measles infections are known to increase susceptibility to other infections by blocking an important aspect of the immune response. Commenting on research done at the University Hospital of Jena Institute of Immunology, Thomas Kamradt, President of the German Society of Immunology, said that this effect can last for up to three

years. It is interesting to note, however, that a vaccine that has no direct link to specific pathogens may also provide a solution. For example, there are vaccines which exhibit a contrary effect, such as the tuberculosis vaccine. The BCG vaccine is a live vaccine that contains attenuated pathogens. Some time ago, the authorities in Guinea-Bissau decided to check whether this vaccine really does prevent tuberculosis. The epidemiological evaluation then produced the very surprising conclusion that the vaccine not only protects against this particular lung disease, but also against other pathogens. Apparently, the innate immune system is activated so strongly that the individual is permanently more resistant to other infectious diseases. **In light of this realization, modeling the innate immune system becomes even more important, and that is why we have made it integral to the strategy for our Salvagene Covid-19 Immunization Program.**

This effect has also been described by scientists at Yale University. The team led by Ellen Foxman used the data from patients who were treated at Yale New Haven Hospital during the winter months of 2016-19 for symptoms of a respiratory infection. The results showed that, if rhinoviruses were present in the swab samples, no influenza viruses were found, even if both viruses were currently circulating in the population at large and the likelihood of a double infection could therefore be considered high. The rhinoviruses had activated the immune system to such an extent that the influenza viruses could not penetrate the cells. This was confirmed in the laboratory. When the team infected lung tissue with rhinoviruses, the influenza viruses had no chance. The effect lasted for at least five days.

Writing in The Lancet Microbe, Foxman and her colleagues conclude that this also provided the answer to a previously unsolved puzzle in epidemiology, namely the low level of infection during the 2010 swine flu pandemic, as we mentioned above. At that time, it was expected that H1N1 numbers would increase dramatically during the winter months in the northern hemisphere. But the opposite was the case, and there was no

increase in the infection curve. The established common cold viruses had caused the pandemic to develop in a far less dramatic way.

The protective effect can be explained by a system of non-specific body defense that arose early on in the evolutionary process – one that we have already written about on several previous occasions. If pathogens penetrate the body, special tissue hormones – so-called interferons – are released. They ensure that viruses cannot multiply or can only multiply very poorly in the tissue. To see how effective the interferon activation is, we epigenetically analyze and monitor the interferon receptor as a standard feature of our **Salvagene Covid-19 Immunization Program**. Appropriate measures are then taken to further optimize it.

As Leif Erik Sander at the Berlin Charité has pointed out, SARS-CoV-2 unfortunately seems able to switch off the interferon system. This is also the reason why we investigate certain parameters in the Salvagene Covid-19 Immunization Program, such as the epigenetic status and degree of methylation of the interferon receptor family. Initial studies have shown that, when the interferon system is switched off, Covid-19 patients who were hospitalized are also susceptible to infection with other pathogens. In a quarter to a third of cases, rhinoviruses or other cold viruses were found in addition to SARS-CoV-2.

But we believe that at least as dangerous as double infection with viruses are cases in which fungal and bacterial infections are also present. In most severe cases of Covid-19, we are also seeing bacterial and fungal infections in the lungs. Such co-infections also occur with other viral diseases, but in severe Covid-19 cases, it is as if the immune system has become paralyzed and is no longer able to combat the other pathogens.

So, what does all of this mean for the coming months?
From our perspective, it is crucial that the key weak points exploited by SARS-CoV-2 are closely monitored so that preventive action can be taken at an early stage. It has to be said that it is not clear at present what the implications of the onset of winter will be for the pandemic or for the situation in general. We can only hope that there will not be such a virulent influenza season as there was two years ago. At that time, hospitals in North America and in parts of Europe reached the limits of their capacity due to the influx of influenza patients alone, and at that time there was of course no Covid-19. But at least there is a vaccine against the influenza viruses. As we have already informed you, any decision on whether to be vaccinated has to be taken on an individual basis. We already sent out our recommendations to Premium customers a few weeks ago.

SALVAGENE HQ
Université Paris Sorbonne
125 Rue Saint-Jacques, 75005 Paris

SALVAGENE UK
52 Grosvenor Gardens • SW1W 0AU London UF
Tel: 0044 20 3287 0644

SALVAGENE USA
101 Avenue of the Americas, 8th floor • 10013 New York
Tel: +1 646 583 0370

info@salvagene.com • www.salvagene.com