

Covid-19: Are you prepared for your personal battle?

NEW!

Dear Premium Customers,

Many people become infected with Sars-CoV-2 without realizing it. Others become seriously ill – and some of them will die. How this might turn out for you personally depends on the efficiency of the various defense lines of your immune system and the countertactics used by the virus to multiply. Read here about the course your personal battle between the virus and the immune system might take.

Premium customers with a Covid-19 Risk Factor of less than 0.6 as calculated by our S.A.I.P. (Salvagene Artificial Intelligence Program) can read on without feeling unduly alarmed.

Maybe it starts with a harmless joke told by someone on the subway. The joke is topical – something about hoarding toilet

paper and noodles. Fellow passengers hoot with laughter. Tiny droplets loosen themselves from moist lips, floating invisibly through the air in the carriage. A person is standing a meter away, uninvolved in the conversation. A droplet lands on his cheek close to the corner of his mouth. Unsuspectingly, he wipes his hand across his face. And the deed is done. Despite the fact that he has been following all the hygiene guidelines for weeks. But as everyone knows, you cannot protect yourself 100%.

A few hundred viruses have entered his mouth, mingled with the saliva there and soon reached the oral mucosa. All of them are now almost at their destination. Their mission is to get inside the body and into the cells, to multiply and to spread. Evolution has designed them for no other purpose.

In an unprecedented flood of research, our own Covid-19 Task Force and thousands of scientists worldwide have been trying to find out as much as possible about novel coronavirus. They have been studying it in great detail to identify its potential vulnerabilities. They have analyzed its molecular structure, decoded its genes, observed it as it penetrates the cells. On the basis of their findings so far, we now understand a little better why Sars-CoV-2 is harmless for many but leads to a cruel death for others. And why this new strain of the coronavirus has succeeded in turning the world upside down in a very short time. What we have found out so far may help us to better understand the blitz campaign being waged by the virus and hopefully stop it in its tracks one day.

The virus has been in the mouth for some hours now. It drifts across the mucous membrane, looking for a target, a structure to which it can attach itself. Knobbly spikes protrude from the spherical virus, spikes which it will ultimately use to gain purchase. It glides along the cells in apparently leisurely fashion. Then suddenly its spikes snap into place: an ACE-2 molecule – an antenna by means of which the cell monitors blood pressure – gets hooked on the virus spikes. Human cells in the mouth, lungs and many other tissues are studded with these antennae. They fit

the spikes like a key to a lock. The virus has now taken hold. This close fusion is its recipe for success and is the reason why Sars-CoV-2 has triumphed around the world.

S.A.I.P. starts its calculations with the primary risk factors – IRRESPECTIVE of age. These include deficits in the area of cardiovascular health, e.g. diabetes, high blood pressure, arteriosclerosis and heightened Silent Inflammation levels, as well as all drugs that are taken regularly, e.g. ibuprofen or statins which increase the sensitivity of the ACE-2 receptors and affect coagulation factors. S.A.I.P. calculates the Covid-19 Risk Factor, logs all results and continues to calculate.

In the meantime, many more viruses have managed to attach themselves.

The unlucky passenger still has no inkling of what is going on in his mouth. Arriving home, he treats himself to a cold beer. What a satisfying fizz ...

The virus won't let go. It is attached to the cell, its spike locked on. But even though the key is already in the lock, it cannot yet enter the cell. It is unable to turn the key by itself, because of the security mechanism in place. The coronavirus must wait for assistance. Many molecules float past the cell – messenger substances, hormones, proteins. They float along the cell wall and glide over the surface of the virus, over its spikes. Nothing happens, the virus remains blocked.

Eventually, an enzyme called furin drifts past. Furin is common in human tissue, especially in the lungs and liver. Its presence there also explains symptoms such as liver failure, which has been observed in many of the severest cases in New York. This is another parameter for S.A.I.P. What is the current health status of the liver? How efficient are detoxification phases 1 and 2? And

what about the genetic predisposition of the detoxification genes? Why is this important?

Furin is there to activate proteins. It does this by splitting off parts of them. It is similar to the situation with a medical glass vial, one end of which has to be broken off before the content can be released. Furin does this automatically; it does not distinguish between friend and foe! So Furin unfortunately also unlocks the mechanism blocking the virus especially in lungs and liver because there are the most Furin enzymes. The way is now clear for the virus to enter the cell. It has reached its destination. The furin protein is coded by the appropriately named furin gene, which is an old acquaintance for Salvagene. It has been part of the epigenetics research activities at Salvagene for quite some time, long before the Sars-CoV-2 outbreak, and is currently part of a gene pool set up to determine whether there might be a genetic susceptibility to SARS-CoV-2. Should this be confirmed one day, S.A.I.P. would have further work to do.

Having finished his beer and enjoyed the evening, the subway traveler goes to bed. The night passes peacefully.

No matter whether we are awake or asleep, building blocks are constantly being produced and scrapped inside our cells. It is like a factory: orders are issued from the control center, the cell nucleus. What needs to be produced quickly? Where can production be cut back? The cell's internal machinery processes every order efficiently, decoding it and rapidly assembling amino acids and proteins.

The virus now muscles in on this activity – and covertly takes over command. It hijacks the internal machinery which is now forced to serve the will of the interloper: Copy me, multiply me! The cell machinery obeys. It produces what the virus demands: viruses, thousands of new viruses. Within hours, a single virus can make 20,000 copies.

The virus now has millions of copies, the replication process is running like clockwork. The newly created viruses begin to leave the cell and force their way through the tissue in search of new cells. Each virus is driven by only one objective: reproduction, dissemination.

Five days have passed, and when the commuter wakes up, he is surprised to find that he has a headache. There is a rough, scratching sensation in his throat. His initial reaction is to sink back into the pillows, but then he pulls himself together. He makes his way to the subway and goes to work. Another day goes by. His colleagues persuade him to join them at the pub. The next day he starts coughing.

The virus overwhelms cell after cell. At first, it seems unstoppable, but in fact it has a strong enemy and adversary – our immune system. The immune system is battle-tested and well equipped. It has a huge arsenal of cells, an army that sends out special platoons, patrols, surveillance units and killing squads. In hundreds of thousands of years of evolution, the immune system has learned a lot. The many foreign bodies that gain entry with every breath we take are its daily business. Calmly and resolutely, it faces up to the new enemy.

However, the serenity of the immune system soon begins to waver when it is already burdened with allergy, immune suppression, heavy medication, incorrect supplementation, a weak microbiome, the active epigenetic status of inflammation genes or pregnancy. This also applies in the case of oxidative stress experienced by young, otherwise “healthy” athletes, as a number of severe Covid-19 cases in Italy and Spain have shown.

In the circumstances described above, S.A.I.P. calculates additional potential complications in the further course of the disease, which contribute to raising the Covid-19 Risk Factor. This is because they make an adequate response to the virus more and more problematic.

Right at the beginning, the immune system fires up the standard defense program. Minutes after the virus has invaded the cells of the oral mucosa, specialized guards are on the scene – macrophages, granulocytes and natural killer cells. They recognize the infected cells, envelop them and destroy them together with their intruders. They also send out messenger substances that activate the next stage of the immune system: special cells capture virus particles, examine them for their characteristic, unalterable features. They are looking for the fingerprint that the virus also leaves on the surface of the infected cells. Salvagene regularly tests at the premium program to see how well this complex interaction works by means of the regulatory T-helper cells. The results obtained are the basis for the optimization of your immune response, which needs to be kept in shape to meet the current threat. S.A.I.P. recalculates to see whether the immune system responded: a) too quickly; b) too slowly; c) for too short a period or even worse too long; d) with too many antibodies; e) with too few antibodies; f) with the right antibodies. There are a lot of parameters for S.A.I.P. to work with.

Meanwhile, the immune system's guardian cells report in to the nearest control center, a lymph node where other cells review the findings. Antibodies are produced – templates, molecular forms that are the exact negative of the viral fingerprint. These are released into the tissue, finding their way to infected cells, marking them, attaching themselves to free-roaming viruses and bundling them together for neutralization.

The immune system continues to fire away, releasing messenger substances, cytokines and chemokines which reinforce the defense, reporting their activity, marking and killing the enemy. T-killer cells – the soldiers of the immune system – are sent out. They sally forth, searching for infected cells and destroying them. The attack comes from all sides.

S.A.I.P. now works to identify the next risk areas: What are the current micronutrient levels? Are there vitamin deficiencies or, potentially worse, excesses? If not already done, zinc and vitamin C must be supplied immediately via the mucous membranes (NB: not in capsule form, as metabolism via the liver can be counterproductive). The most important inflammation inhibitors for individuals in whom they have proved to be effective now get to work. They will be determined by a simulated inflammation inhibitor test, performed as standard also by Salvagene. This test have to be done regularly, because results can change by time. These inhibitors are the immune system modelers, important for an adequate response to the attack. Without them, the fever can get out of control, shooting up with fatal consequences. S.A.I.P. gets calculating again to see whether these inhibitors are doing their job.

For most individuals, the nightmare comes to an end after a few days or hours. S.A.I.P. sets this as a benchmark with a Covid-19 Risk Factor of 1.0. Anyone having a Covid-19 Risk Factor of less than 1.0 can now also read on relatively reassured.

Our unlucky commuter feels ill – very ill – and takes to his bed. Every time he coughs, his chest and lungs hurt. He shivers and retreats under the bed covers. His hands and feet are freezing cold. The thermometer is showing a temperature of 39.7°C.

The immune system is working at full blast, with everything happening in parallel. It dispatches the messenger substances to all tissues, even to the brain. It demands more heat, because it is able to work faster at 39°C than at 37°C. Orders are issued to the circulatory system: if less blood flows through the fine blood vessels in the hands and feet, the blood stays warmer. Hands and feet are not as important now as the fight going on inside the body. Orders also go to the muscles to contract and release thermal energy: the body temperature rises.

The battle inside the tissues continues over several days until the immune system eventually triumphs. The viruses are eliminated, and the body's defense system recalls its troops. Cell and virus debris is eliminated via the body's usual waste disposal methods. 98,5% of Salvagene clients who had their Covid-19 Risk Factor calculated by the end of March would be in this scenario and can now await the cytokine storm with some degree of composure.

Because the virus is not always sent packing so readily. It has managed to penetrate into the deeper airways, namely the lungs. The immune system sends out even more killers, antibodies, T-cells and other helpers, to get rid of the viruses and the infected cells. The tiny air sacs at the end of the bronchi – the alveoli – are filling up with dead cells and viruses and becoming clogged up. Where oxygen was until now able to get into the blood through a thin layer of cells is now coated with mucus.

Our commuter's cough is getting worse, the pain in his lungs does not subside. He feels drained of energy. He would like to make himself a hot drink, but he is too weak and can hardly get out of bed. Everything hurts – his head, skin and joints. The fever simply refuses to subside. His heart beats faster, fluttering like a small, frightened bird in his chest. And the air, the air is getting short. THE CYTOKINE STORM HAS ARRIVED! This is the likely course of the disease for individuals with a Covid-19 Risk Factor greater than 2.5.

S.A.I.P. extrapolates in particular on the basis of the following factors:

- *excessive responses from the immune system in the past*
- *autoimmune diseases*
- *immunosuppressive events*
- *certain medications, especially cancer treatments (including historic), in particular rituximab*

- *past cytokine storms (e.g. triggered by Lyme Disease) are stored and activate new ones much faster, which is one reason why there have been younger casualties*
- *lingering infections*
- *undiagnosed bacterial infections*
- *no record of pneumococcal vaccination*
- *Lungs and liver disease*

Cytokines are proteins that regulate the growth and differentiation of cells. They are a group of peptides that primarily initiate or regulate the proliferation and differentiation of target cells. Some cytokines are consequently designated growth factors, while others, which play an important role in immunological reactions and in inflammatory processes, are designated mediators. There are essentially five main groups of cytokines: interferons, interleukins, colony-stimulating factors (CSFs), tumor necrosis factors (TNFs) and chemokines.

In the course of an immune reaction, cytokines are formed to allow further immune cells to migrate to the site of inflammation and activate them, whereupon they also form cytokines to enhance the immune response. In a cytokine storm, leukocytes are activated to such an extent that the immune response does not automatically calm down, as would normally happen when the antigen is no longer present.

A cytokine storm leads to the formation of various cytokines, radicals and clotting factors and the accumulation of immune cells at the site of inflammation. This can impair the functioning of a tissue, potentially to the point of organ failure.

The symptoms of a cytokine storm include fever, swelling, redness, fatigue and nausea, which in severe forms can be life-threatening. During a cytokine storm, high concentrations of the cytokines IL-6 and IL-8 and the chemokines CCL2, CCL5, CXCL10 and CXCL9 are produced.

S.A.I.P. keeps on calculating. The more data the system has, the more accurate will be its forecast. AND SAIP IS CALCULATING ALSO THE PHARMACO GENETIC PROFIL WHICH IS ALSO A STANDART SALVAGENE TEST TO FIND THE BEST OPTIONS FOR A POSSIBLE MEDICATION FOR THIS SITUATION. CHLOROQUINE AND HOW MUCH? OR BETTER AVIGAN?

The lung cells are now overwhelmed, not only by the viruses that are trying to multiply inside them but also by the messengers sent by the immune defense with the purpose of eradicating the virus; in doing so, they overshoot the mark and actually attack healthy tissue. As the battle rages inside the tissue, inflammation develops. Cancer medication such as rituximab whips the cytokine storm up into a hurricane. Bacteria are now able to penetrate more easily and further aggravate the situation. As the blood vessels become porous, viruses penetrate small fissures, entering the veins and arteries via which they are transported into the organs. Everywhere along the way, they penetrate cells, poison the liver and attack the heart muscle. They infect, multiply and keep on infecting. As fluid from the blood vessels seeps into the tissue, blood pressure starts to drop. The organs are screaming for oxygen, while the heart races to keep up. The organs fail.

Silence.

And what about the survivors? The individuals in whom the immune system has prevailed, with the virus having been eliminated after a few days, sometimes after three or four weeks? It is possible that they have acquired immunity for a while. As of 3rd April 2020, nobody on this planet really knows for sure.

Conceivably (though with our current level of knowledge less likely), they may be more susceptible in the case of a second infection due to the phenomenon of ADE, short for Antibody Dependent Enhancement (see Keynote 12 as updated on 3rd April 2020). Our hope is that an existing drug can be discovered by genetic A.I. analysis that will inhibit the replication ability of the virus. Some promising candidates have been identified in Japan, Germany and Israel. We are closely monitoring them, as they are currently our best chance, in contrast to vaccination which will take much longer to develop and make widely available. The immune system would then have enough time to study the signature of the virus. If it enters the body again, the defense army will give it short shrift. Quickly, efficiently and without complications.

In the meantime, it is important for us to get our immune system in good shape and to permanently eliminate weaknesses. The survivors get back up again. They were sick – some more than others. But now the daily routine can resume. Now people can laugh again, in the subway and in the pub.

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