Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #37

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In the center of the Salvagene Covid-19 Immunization Program: The interferons and their receptors -

KEYNOTE

How you can avoid SARS-CoV-2 damaging your body's own interferon system.

Dear Premium Customers,

In the first part of this Keynote thread, we discussed the role and functionality of interferons in relation to the pandemic. Their importance is apparent from the very many projects in this field taking place around the world.

Almost all of the leading epidemiologists have their own opinion on interferons, one of them being Christian Droosten, a colleague who is held in high esteem by our Salvagene SARS-CoV-2 Task Force. He describes interferons as the primary defense barrier and responsible for firing up and managing the antiviral status of the entire system.

We are at war with the virus, and interferon activity is of existential importance for the battle order of the defending forces. Without full functionality of the interferon system, the attackers will rapidly swarm over the "castle moat", and the

defenders will then have to deploy all the means they have left at their disposal. The SARS-CoV-2 virus is so successful by comparison with influenza, norovirus or other coronaviruses because of the way in which it weakens and eliminates interferons more or less effortlessly depending on the epigenetic condition of the system, thus leaving it virtually free to proliferate. As already described in Part 1, the sheer complexity of the interferon system has so far proved an insurmountable obstacle for the many worldwide projects aimed at producing interferon therapies. As is so often the case, the replication of hormone or hormone-like substances is very complex, and the production processes are likewise too complicated to be readily reproduced. This is the challenge for scientific research. Interferon in particular involves intensely complicated processes. As with other hormonal problems, the Salvagene strategy is always to support, optimize and stimulate the body's own procedures and thereby achieve much greater sustainability. We also consider this to be the correct approach to be applied in interferon therapy.

The debate about simultaneous infections with different viruses in the northern hemisphere has reached an advanced stage due to the upcoming flu season, and we have already discussed this matter in detail in Keynote 34. Here, the risk and the solution may go hand in hand. The decisive factor in the case of simultaneous infections of norovirus or influenza with SARS-CoV-2 is the sequence of infection. This is very much related to the interferons. In contrast to SARS-CoV-2, norovirus, influenza and other coronaviruses cause the interferon systems to become strongly activated and to initiate corresponding interferon production; this then remains at the disposal of the defense mechanisms for a certain length of time. So, for example, if an influenza infection occurs first, the interferons formed can exert a protective effect in the event of a subsequent SARS-CoV-2 infection which, as already described above, would otherwise deactivate the interferon system. Of course, this only works if the interferon system is active and well optimized, which is the aim of the Salvagene Covid-19 Immunization Program. If the sequence is reversed, we can expect the consequences to be fatal. If there

is a SARS-Cov-2 infection first and the influenza infection only comes afterwards, then the absence of interferons caused by the SARS-Cov-2 infection means that the influenza infection is likely to be even more severe.

As already described, coronavirus-based colds also produce antibodies, which can have a supplementary effect in a SARS-CoV-2 infection. It should be noted that, when a cold is triggered by corona, influenza or noroviruses, the antibodies (for coronaviruses) and interferons (for norovirus and influenza viruses) which are released have a protective effect in the event of a subsequent SARS-CoV-2 infection. During the coming season, it is important that the status of a virus is definitively diagnosed. A virus can normally be distinguished on the basis of symptoms exhibited, but in our opinion, it makes sense to diagnose virus status explicitly this year and, depending on the result, our recommendation is not to overtreat the illness, thereby allowing possible interferons and also corona antibodies to remain active.

The extent to which SARS-CoV-2 can damage or deactivate the body's own interferon system is clearly related to the epigenetic condition of the interferon receptor family. And this is the central diagnostic factor in our Salvagene Covid-19 Immunization Program and in our testing. What we can be sure of is that certain courses of action impair the interferon system in its functionality. These include the uncontrolled intake of medications and of the Covid-19 vitamin supplements that are currently somewhat in vogue. Taken in extremely high doses, they accelerate the methylation of the crucial interferon receptors and thus impair functionality.

Essentially, we can say that the old adage "the more the merrier" is completely wrong in this case; indeed, it could have fatal consequences. Not everything that may be right for treating Covid-19 once caught is also right for the prevention of the disease and for the optimization of our own immune status.

Especially in the case of Covid-19, the protocols developed for the prevention of disease and optimization of the immune system differ completely from Covid-19 therapies. The increase in vitaminosis in the USA is also the result of these uncontrolled preventive measures. They usually do more harm than good. Epigenetic and methylation analyses of interferon receptors produce a list of do's and don'ts which in turn generate targeted and individual measures. Here, it is crucial that we suppress the presentation of MHC-1 molecules on the surface of the affected cells. This is one of several mechanisms in addition to our own interferon system that can inhibit SARS-CoV-2.

There are corresponding receptors for messenger substances on the cell surface. Interferons are therefore not absorbed into the target cell, but send a signal through the cell membrane into the interior of the cell. The receptors on the cell surface are specific for the type of interferon. A group of receptors bind the various interferons of the alpha subtype interferon beta. The other type of receptor is specific to interferon Y. Almost all cells have interferon receptors – even tumor cells. All interferon receptors are composed of an extra-cellular N-terminal domain, a transmembrane part of the protein and an intracellular co-terminal domain through which the signal is transmitted into the cell. Similar to other cytokines, the signal is passed from one protein to the next by means of phosphorylation. The signal transmission cascades of type 1 interferons and type 2 interferons differ in a few details.

This signal transmission is measured by us. For example, our interferon activity analysis based on epigenetic and methylation status and the functionality of the entire system checks how well the receptor-dependent production of the MX protein works. This protein specifically blocks the replication of certain viruses such as influenza. Alongside the optimization of MX protein production and the optimization of the MHC-1 complex, we also seek to optimize translation and transcription. These are among the most important processes after a virus attack, without which neither the viral genome nor the viral envelope proteins can be

synthesized. So-called 2-5A synthetase is also one of the most important interferon-inducible cell proteins which are synthesized during a viral attack. This enzyme reacts to the presence of double-stranded DNA, which is normally not found in a cell.

The aim is to optimize the processes described here and at the same time reduce the virus's own defense measures against the interferons as far as possible. This is because viruses produce RNAs that prevent the activation of the cellular virus defense. The presence of numerous small double-stranded RNA molecules is a signal for the cell that viruses are multiplying within. Under these circumstances, for example, double-stranded (ds)RNA-dependent protein kinase is normally activated, which then stops the reproduction of the viruses in the cell. This activation can be undermined by SARS-CoV-2. For example, it synthesizes small, viral RNAs such as VAI which binds (ds)RNA-dependent protein kinase of the infected cell and thus prevents its activation by the viral (ds)RNA. SARS-CoV-2 also produces proteins that prevent the 2-5A synthetase described above. The conclusions we draw from this are as follows:

1. Interferons are the most important barrier, providing an effective, rapid and targeted immune response.
2. Weak interferon systems are reduced or inactivated by SARS-CoV-2 with the result that this virus spreads much more easily than other types of virus.
3. Without interferon activation, only reactive and strongly interventionist measures remain, such as vaccination and/or powerful drugs with much lower chances of success.
4. Due to the complexity of the issue, all interferon projects being pursued worldwide are currently still associated with strong side-effects and risks.
5. The most sustainable remedy in the meantime is the optimization of our own interferon system by epigenetic methylation analysis of the interferon receptors, regular monitoring and recommendations for optimization derived from this.

This is what we have been doing since May in the context of our Salvagene Covid-19 Immunization Program. And since the results of the regular monitoring and retests became available, we have been able to register a perceptible improvement in weakened interferon systems.

In case you missed the first part of our Interferon series, you can read it here.

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