Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #67

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Dear Premium Customers,

The alpha version of this monitoring program will be applied immediately to all retests for Premium clients at no extra charge.

One year ago, at the start of the pandemic, a lot of resources went into testing for antibodies alongside PCR tests, but the focus has since shifted away, not least because of the unreliability of antibody detection and the inadequacy of the tests that were available at the time.

As with antigen rapid tests, we consider this neglect to be highly unfortunate. That's why we at Salvagene began work in November on a project to record and monitor a comprehensive antibody profile. We have now come to the end of the first product phase and are introducing the more comprehensive monitoring version.

It makes a lot of sense at this stage of the pandemic, because the number of infections and the number of vaccinations taken together provide us with a very broad base, which gives us a lot more scope for recording the various SARS-CoV-2 antibodies. This is going to play a very important role in the coming months as the course of the pandemic remains unpredictable. On the one hand, there are countries that have high vaccination rates such as Chile where the rollout is well advanced but where infection rates remain stubbornly high. However, the Brazilian virus variant is predominant here, which complicates matters and undoes a lot of the good work. This is in contrast to countries such as Israel, where the picture is mixed, and the United Kingdom, where the situation is looking promising – although the penetration of the South African and Brazilian variants there has been limited to date.

We therefore need to emphasize that the direction taken by the pandemic will depend on the rate at which the virus mutates, which appears to have massively accelerated worldwide in recent weeks. We have to assume a connection between vaccines and escape mutations, especially when vaccine resistances form or vaccines have only weak efficacy. It is not yet possible to determine which way the wind is blowing.

The majority of mutations observed are suspected to be of the more infectious variety. However, there will also be mutations that turn out to be less injurious to health. This could be an indication that the entire mutation process is taking a turn towards becoming less of a threat. But either of these scenarios is entirely possible at the moment. As already reported on our Ticker service, a mutation has been detected for the first time in Brittany (France) which manages to escape detection by the current set of PCR tests.

We therefore estimate that it will most likely take another 1 - 1½ years before the global community wrests some sort of control over the situation. In the meantime, it is very possible that the Asian countries and the western industrialized countries will require significantly less in the way lockdown restrictions in the coming

months. But this depends entirely on which direction the mutation process takes.

Antibody monitoring will therefore play a valuable role in gauging not only the effectiveness of vaccination for our Premium clients but also the outcome of a survived infection in terms of quantitative and qualitative antibody production.
From this information, we will be able to assess the appropriateness as well timing of a booster jab. If a client is recovering from Covid, we will be able to assess whether the quality and quantity of antibodies generated in response to the disease are adequate or whether to recommend vaccination nonetheless.

The problem of reinfection is another important element in antibody monitoring. According to official statistics, reinfection is relatively rare and in almost cases results from exposure to a different mutant second time around. This leads us to believe that the rate of reinfection will rise next autumn and that it will tend to affect the over-50s. This is where the T-helper cell structure ultimately plays a crucial role, because in an older immune system the production of new T-cells is relatively weak and the already existing T-helper cells within the system produce a diffuse rather than targeted immune response.

All the data we collect is stored in our in-house AI system where we build up a status classification of the entire antibody profile. We then use this information to form an overall assessment of the immune response. It is important to note that antibodies are only part of the immune response – and indeed only part of the solution. As we have mentioned in previous Keynotes, the specific immune response consisting of T-helper, T-memory and natural killer cells, and in particular those of the CD4 and CD8 classification, is the main line of defense.

In addition to the range of better-known antibodies, there are so-called “nanobodies” which are being developed by our colleagues at the University Hospital in Bonn. These have the advantage of being more adept at penetrating the tissue, of being much smaller in size, easier to produce in larger quantities and capable of identifying different angles of attack on the virus. This approach can also prevent SARS-CoV-2 from evading the active substances in vaccines by means of mutation, which is ultimately the biggest challenge to vaccination in terms of long-term efficacy.

The multi-stage test procedure examines blood serum. We use an optimized chemiluminescence test that corresponds to the World Health Organization reference material First WHO International Standard for SARS-CoV-2 Immunoglobulin, and the result is given in BAU/ml, a standardized, international unit meaning Binding Antibody Units per milliliter. Calibration of the antibody tests to a common unit also facilitates the comparability of test results obtained with different serological essays. This serological test is based on SARS-CoV-2 spike protein in trimeric form, which mimics the native structure of the protein. It is thus excellently suited as a follow-up test after a Covid-19 vaccination. According to current scientific studies, the antibodies detected in this test are not only directed against individual epitopes but also, for example, towards the receptor-binding domain (RBD) of the spike. Multiple epitopes are detected, enabling us to record a broad antibody spectrum as the body’s own immune reaction.

Stage 2 of the test procedure has its origins in tropical medicine, an area in which highly sensitive and accurate antibody tests play an important role. This requires so-called “recombinant antigens” to be produced in advance. These are proteins that occur in a similar form inside or on the envelope of the SARS-CoV-2 virus and against which antibodies are formed in the event of an infection. The recombinant antigens are used to extract antibodies from blood samples submitted by our clients. The antigen-bound antibodies can then be bound to the surface by the patented process and made visible by a color reaction. This allows us to reliably detect even small amounts of Covid-specific antibodies,

and only gives a positive result if the individual really has survived an infection with SARS-CoV-2. In this context, it is particularly important to distinguish SARS-CoV-2 from infections with related coronaviruses. These occur naturally in countries all around the world and also cause respiratory diseases. The patented test procedure is exceptionally sensitive and therefore allows the selection of a small antigen that interacts only slightly with antibodies against the other coronaviruses. Any false-positive signals that occur can be intercepted and suppressed by the addition of so-called competitor proteins, which contain antibodies against other coronaviruses.

Our classification of antibodies goes far beyond the generally accepted categories. We distinguish five different classifications: Immunoglobulin M (IGM), which we measure because it shows when the antibodies were first produced – in other words, when the body first came into contact with the virus. This is measured as standard, of course. The four other categories are IGE, IGA, IGD and IGG. The latter plays a major role because the quality and quantity of the antibodies is recorded here.

We are able to perform several classifications of effectively neutralized antibodies, as not all antibodies are the same, nor even are neutralizing antibodies. They vary in effectiveness, and some are even suspected of causing damage in the so-called "Late-Covid Phase". This third stage of the disease is now narrowly defined by the Salvagene SARS-CoV-2 Task Force. It refers to the period when complications arise even after a negative PCR test. This comes at around three weeks after infection. The vast majority of hospital admissions are these late-covid cases, in which the patient's overactive immune response may even land them in the intensive care unit.

As we have said on many occasions before, the really serious damage in a severe course of disease is not triggered by the virus, but are the result of our body's own defense mechanisms going into overdrive. We would therefore remind our clients not to self-

medicate or consume supplements, because in severe cases, the immune response ultimately decides whether complications can be prevented or even whether they are triggered.

At this point, we would like to remind all Premium clients who are subscribed to our Covid-19 Immunization Program that we are able to optimize the four major areas of the immune response ourselves, namely the T-helper cells, the T-memory cells, the NK cells and the CD4 + CD8 classifications. In particular, by optimizing the interferon system, which is something the individual has so much influence over. All clients who have had an infection to date have produced relatively few antibodies and have simply been asymptomatic with regard to their well-modelled immune system, which can ultimately get by without a supply of antibodies.

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