

## COVID-19: Proposals of Therapy of Infection and of Immunization Against the Virus SARS-CoV-2

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### ABSTRACT

*Development of a so-far unknown kind of vaccine in context with the new Corona virus SARS-CoV-2 may be a topic of interest. This communication describes details.*

### Keywords

COVID-19, SARS-CoV-2, Protein S, ACE 2, Binding, Kinds of therapy, Tests, Proposal for vaccine.

Mutations in the genetic material of viruses are common and well known. They can be the reason why vaccines developed against a certain virus strain might not be effective against a mutated strain. Mutations can affect protein properties – e.g. sequences, protein folding, protein stability – of functionally and structurally important properties of the virus. One should assume that this situation is also true for the new Corona virus SARS-CoV-2.

One aspect should be considered: attachment of this virus to a human cell is brought about by the binding of a virus protein located at the tip of a "spike" (a Glycoprotein called Protein S), to „receptors“ exposed at the membrane of human cells [1]. This "receptor", called ACE 2, is an enzyme involved, besides other functions, in the regulation of blood pressure; it is a transmembrane protein. This is a misuse of a protein on the surface of the human cell by a virus, and it enables the virus to penetrate into the mucosal epithel cells of the airway and the mucosal parenchym cells of the lung – the precondition of virus multiplication and infection with its disastrous consequences [2].

Recently it became evident that protein S, together with few other proteins of the virus, may become one of the key factors in Corona virus research, especially regarding therapy and development of vaccines. One remarkable example is the work of Dr. Josef Penninger and his group, University of British Columbia, Vancouver [3]. His approach is to use soluble ACE 2, intended to

block protein S by "covering" the binding motive of this protein that is responsible for binding of the virus stalks to membrane-integrated ACE 2 of the human cell. It was reported that tests of this kind of therapy, undertaken in China, are under way [2]. This approach is not a development of a vaccine. Specific antibodies are not involved besides those that are developed in B lymphocytes of sick people according to the known mechanisms used against "foreign" invaders.

Another remarkable approach [4] has been described only recently. Protein S can only bind to ACE 2 when the protein S at the virus spike is "activated". This happens by a serin protease located in the human cell during contact of protein S with ACE 2. This protease can be inactivated by a clinically-proven protease inhibitor. This drug is available. Respective tests are under way [2].

Also this approach is not the development of a vaccine, but might be used for therapy.

The present communication describes an approach that may play an important role both for therapy and for the development of a vaccine. Also in this case, the interaction of a domain/a motive of protein S with ACE 2 is the basis. The approach uses the potential of the human B lymphocytes to identify "foreign" proteins and develop antibodies against them.

Few preconditions: ACE 2 does not undergo mutations; the structural organization of the domain/the motive of protein S in the virus stalk is not altered by mutation. If mutated, there would not be the proper fit to ACE 2.

Proposal for the design: a (poly-) peptide simulating the exposed motive of protein S located at the tip of the spike has to be developed (in fact, such a construct is already commercially available from jpt Innovative peptide Solutions in minor quantities) and injected as a kind of vaccine. It can be assumed that this (poly-) peptide is identified by the human B lymphocytes as “foreign“, and that antibodies against it are developed. After this has happened, it can be expected that the tips of the spikes of incoming Corona viruses are "identified" by the antibodies. The amount of antibodies should be sufficient to reach the majority of all spikes. The antibodies are intended to avoid binding of the spikes to ACE 2. At the same time, all processes belonging to the potential of the adaptive immune system regarding "foreign" invaders (SARS-CoV-2 virus) are started, and an immunological memory is established.

It might happen that a part of these (poly-) peptides bind to the membrane-integrated ACE 2 during the time period where the human B lymphocytes develop the antibodies. The balancing-out of the numerical ratio of ACE 2 integrated into the membrane of the human cell and the simulating (poly-) peptide would be a matter of tests. If the balance is shifted towards a surplus of (poly-) peptide, the efficiency of the development of antibodies could be higher; the chance of spikes of the virus to find a cell-bound ACE 2 would be reduced: the respective site on the ACE 2 would already be occupied due to the surplus of the (poly-) peptide.

### Conclusion

A comparison of Dr.Penninger’s approach with the approach described here shows significant differences: a kind of vaccine

described here initiates synthesis of respective antibodies directed against protein S as discussed above. The tip of the stalks, i.e. protein S, is not expected to be mutated as long as ACE 2 is not mutated. Both kinds of protein can be assumed to be constant. Therefore, it can be deduced that the (poly-) peptides used in the described approach should also be valid for mutant strains of SARS-CoV-2. This situation would mean that such a kind of vaccine could be used right away.

Another difference might be even more important. The approach described here would give rise to an immunization of healthy people. Application of Dr. Penninger’s approach would be restricted to the treatment of infected people (a therapy). Immunization would not be supported ; the only immunization would come from antibodies developed by the B lymphocytes of sick humans by the contact with fully active SARS-CoV-2 identified as “foreign“.

### References

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