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Review

COVID-19: Proposals for Therapy of Infection and Immunization against SARS-CoV-2 Virus

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Abstract

Therapy and development of vaccines in the context of the novel coronavirus (COVID-19) are of major interest. This communication describes examples (Date: 15.04.2020).

Keywords: COVID-19; SARS CoV-2; protein S; ACE 2; binding; kinds of therapy; tests; proposal for vaccine

Резюме

Терапията и разработването на ваксини в контекста на новия коронавирус (COVID-19) представляват голям интерес. Това съобщение описва примери (Дата: 15.04.2020 г.)

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 – functionally and structurally important properties of the virus. One should assume that this situation is also true for the novel coronavirus SARS-CoV-2.

One aspect should be considered: attachment of this virus to a human cell – according to published findings – 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 on the membrane of human cells (Li *et al*., 2005). The 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, whereby the virus is enabled to penetrate the epithelial cells of the airway and the parenchymal cells of the lung – the precondition for virus multiplication and infection with its disastrous consequences (Deutsche Apotheker Zeitung, 2020).

Recently, it has become evident that protein S, together with few other proteins of the virus, may become one of the key factors in coronavirus 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 (Penninger *et al*., 2020). His approach is to use soluble ACE 2, intended to block protein S by „covering“ the binding motif of this protein that is responsible for binding the virus stalks to membrane-integrated ACE 2 of the human cell. It has been reported that tests of this kind of therapy, undertaken in China, are underway (Deutsche Apotheker Zeitung, 2020). This approach is not development of a vaccine. Specific antibodies are not involved besides those that are developed in the infected human cells of sick people according to known mechanisms used by the human cells against „foreign“ invaders.

Another remarkable approach (Hoffmann *et al*., 2020) 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 serine 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 underway

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(Deutsche Apotheker Zeitung, 2020).

This approach is not vaccine development either, 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 motif of protein S with ACE 2 is the basis. The approach uses the potential of the human cells to identify „foreign" proteins and develop antibodies against them.

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

Proposal for the design: a (poly-) peptide simulating the exposed motif 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 (also in the case of Dr. Penninger´s approach a polypeptide has to be synthesized: the soluble ACE 2). It can be assumed that this (poly-) peptide is identified by the human body as „foreign", and that the human body develops antibodies against it. After this has happened, it can be expected that the tips of the spikes of incomimg coronaviruses are „identified" by the antibodies. The amount of antibodies should be sufficient to reach the majority of all spikes. The antibodies are intended to prevent the spikes from binding to ACE 2.

It might happen that a part of these (poly-) peptides bind to the membrane-integrated ACE 2 during the time period where the human cells 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 mutate 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 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 sick human bodies brought about by the contact with fully active SARS-CoV-2 identified as „foreign".

Appendix:

Antibodies are produced in the human body by specific kinds of cells after contact with „foreign" „antigens", e.g. proteins. These specific cells are B lymphocytes or plasma cells. In the context of the present article, these foreign antigens are SARS-CoV-2 viruses or components of them, e.g. protein S or (poly-)peptides simulating the domain/motif of protein S that can bind to the „receptor" of the human cell.

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