Development of strategies for battle against COVID-19 (a mini-project)

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Abstract

Statement of the Problem: Despite of the key importance the immunity, the activated immune reaction, including by vaccines, could cause unwished effects, for instance in cases as allergies, auto-immune diseases and disorders, as well as cardio-vascular pathologies. Toxic side effects of the chemical anti-viral preparations should also be taken in consideration. So, the main goal is connected with suppression of the cellular penetration and/or replication of COVID-19, both *in vitro* and *in vivo*, by RNA-interference of respective viral genes with appropriate siRNAs.

Methodology & Theoretical Orientation: *In vitro*-incubated cells should be inoculated with viral strain with RNA-genome (if is possible, belonging to *Coronaviridae* family), which should then be treated with appropriate siRNAs against genes in the viral RNA-genome, necessary about viral penetration in the cell and/or viral replication. Subsequent evaluation on the *in vivo*-influence of the tested siRNAs on appropriate experimental animals, infected with the same RNA-viral strain, should further be performed.

Findings & Perspectives: Besides suppression of the virus penetration in the cell and/or its replication, adequate immunity should be supported. Possibility for production of antibodies and membrane receptor glycoproteins by non-lymphoid and non-myeloid cellular types. Because the so produced immunoglobulins/antibodies are out of the germinative centers, their functions should be controlled by low-molecular mass molecules as gangliosides. Further intra- and extra-cellular interactions between different biological molecules (protein-protein, protein-RNA, protein-DNA, protein-lipid, protein-carbohydrate, DNA-DNA, DNA-RNA, RNA-RNA, DNA-DNA, etc.), underlining these processes, should be performed. CRISPR/Cas systems as universal mechanisms, responsible about normal/non-malignant cellular differentiation, adequate immune reaction, but also of cellular ageing and death, should be investigated.

Conclusion & Significance: After performance of all steps described, evaluation on the *in vivo*-influence of the tested siRNAs on patients/volunteers with COVID-19 (in the first 24-48 hours post infection) could be performed.

The aim is to elucidate the kinetics of SARS-CoV-2 shedding in patients with Covid-19, depending on the severity of the disease, age and existing comorbidities (shedding in upper respiratory tracts – from the nose to the larynx – and lower respiratory tracts – from the windpipe to the alveoli, or at non-respiratory sites), and also to analyze the kinetics of the viral load at respiratory and non-respiratory sites in confirmed cases according to severity, age group and existing comorbidities. The project also intends to determine the correlation between the development of the viral load and infectivity, and to understand the kinetics of introducing a neutralizing humoral response (the body's production of antibodies to neutralize the virus).

This work is partly presented at

41st Global Summit and Expo on Vaccines & Immunology on May 11, 2021, Webinar