23. THE SIGNIFICANCE OF SARS-COV-2 S GLYCOPROTEIN FOR MEMBRANE FUSION

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Introduction. The emergence of severe acute respiratory syndrome coronavirus (SARS-CoV-2) presents significant social, economic and political challenges worldwide. The severity of coronavirus infections depends on virus-mediated tissue damage as well as the antiviral immune inflammation, which are influenced by viral tropism, infectivity, virus spread, and specificity of host responses, all of which are majorly regulated by the SARS-CoV-2 glycoproteins, especially Spike (S) glycoprotein.

Aim of study. Glycoproteins are ubiquitously distributed and play a major role in various biological processes such as cell-cell interaction, immune recognition, cell signaling, cell proliferation and differentiation.

Methods and materials. In obtaining the main results, several researches published from 2019 until 2022 have been reviewed, using 15 bibliographic sources, which include virtual libraries, like PubMed, HINARI and Medscape.

Results. Coronaviruses have a simple protein composition. While there is some variation among different members, a basic set of four protein species universally occurs: the nucleocapsid protein (N), the spike glycoprotein (S), a small membrane protein (SM), and the membrane glycoprotein (M). The pathogenic SARS-CoV-2 enters human target cells via its viral transmembrane S glycoprotein, which is synthesized as a single 1273 amino acid polypeptide chain on the rough ER, and consequently has been trimming to monomers. In result, are obtained three main topological domains, parts of the structure of S glycoprotein, namely the head, stalk, and cytoplasmic tail-playing key roles in membrane fusion of the virus. In the trans-Golgi, the SARS-CoV-2 S glycoprotein is proteolytically cleaved by cellular furin or furin-like proteases at the S1/S2 cleavage, yielding a surface subunit S1 and S2. The S1 subunit facilitates attachment of the virus while the S2 subunit facilitates fusion of the viral and human cellular membranes. Like in other coronaviruses, S glycoprotein mediates attachment to the host receptors, using angiotensin-converting enzyme 2 (ACE2) receptor and/or dendritic cell-specific intercellular adhesion molecule-3-grabbing non-integrin 1 (DC-SIGNR) as the dominant mechanism of cell entry. The hemagglutinin-esterase (HE) is the fifth additional structural protein, which is present in a subset of β-coronaviruses, acting as the classical glycan-binding lectin and receptor-degrading enzyme.

Conclusion. It is widely accepted that the S protein of SARS-CoV-2 is a most promising immunogen for producing protective immunity, becoming a therapeutic target in treatment of SARS-CoV-2. However, it is likely that the S protein has evolved to perform its functions while evading host neutralizing antibody responses and thus should be engineered to ensure an optimal immune response. The immunogen design strategies described are based on the wealth of the SARS-CoV-2 S glycoprotein research related to its biosynthesis, structure, function, antigenicity as well as immunogenicity will likely contribute to the ultimate success of safe and efficacious vaccines against SARS-CoV-2/COVID-19.