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„Towards safe anti-SARS-CoV-2 coronavirus vaccine - modifications of the spike protein leading to the elimination of ADE effect".

For centuries infectious diseases have had a significant impact on human societies. Immunoprophylaxis with a specific vaccine is one of the most important elements of combatting many infectious diseases. Rapid progress in scientific fields such as molecular biology, genetic engineering and virology contributed to the development of many vaccines against dangerous viral pathogens. Today many vaccines are administered to children and adults protecting whole populations against dangerous, or even deadly, diseases. Initially, two types of vaccines were used against viral diseases – killed virus vaccines or attenuated viral strains. With the development of molecular sciences, subunit vaccines based on recombinant viral proteins came into light. Therefore, the development of new vaccines or improvement of already existing antiviral vaccines is of paramount importance.

An outbreak of SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2 virus) virus that causes atypical pneumonia (COVID-19) started in December 2019 in Wuhan, China. The virus rapidly spread globally and on 11 March 2020, World Health Organization declared that COVID-19 can be characterized as a pandemic. The current epidemic situation excludes the possibility of rapid termination of COVID-19 morbidity, therefore extremely intensive efforts should be undertaken to develop an effective vaccine, which will allow to reduce and then eliminate the disease caused by this virus from the human population providing long-lasting immunity. Although six other coronaviruses have been isolated from humans before this ongoing pandemic (e.g. SARS-CoV and MERS), no anti-coronavirus vaccine has been approved for human use despite several preclinical and clinical studies. It is hypothesized that the antibody-dependent enhancement (ADE) of infection, when non-neutralizing antibodies produced during an infection or vaccination enhance the infectivity of the subsequent infection, can be the reason of potential vaccines failures. The ADE reaction also led to the withdrawal of the commercial vaccine against dengue virus produced by Sanofi in Asia. ADE effect has been observed for coronaviruses, including SARS-CoV and MERS (described in several publications in 2019 and 2020). It is therefore almost certain that this phenomenon occurs as well in case of SARS-CoV-2, genetically very similar to the SARS-CoV virus, and should be considered as the very serious factor in designing of anti-COVID-19 vaccines.

Highly glycosylated glycoprotein S (spike) of coronaviruses is the main neutralizing component of SARS-CoV-2, hence it represents a major target for therapeutic approaches. Since very little is known about the impact of glycans present in SARS-CoV-2 S protein on the formation and infectivity of viral particles, the following proposal aims to characterize the role of these glycans and their modifications on S protein production and maturation. In the presented project, we plan to carry out different modifications of glycoprotein S protein glycans leading to the elimination or at least reduction of ADE effect. Our goal is to carry out such modifications that will allow for the qualitative change of the S protein from a potential antigen with immunogenic properties to an effective vaccine. We hope that the knowledge obtained during this project will contribute to the improvement of the safety and effectiveness of future SARS-CoV-2 vaccines. Therefore, our prospective goal of the project is to propose a safe anti-SARS-CoV-2 virus-like particles (VLPs)-based vaccine made of modified S protein. VLPs can be defined as empty shells of viruses resembling authentic viruses but devoid of genetic material, so the virus cannot multiply. However, virus-like particles retain many properties of viruses – they can enter cells and provoke very strong immunological response of both types important for conferring protection: humoral and cellular response. We, at the Department of Recombinant Vaccines, Intercollegiate Faculty of Biotechnology University of Gdansk and Medical University of Gdansk, specialize in the construction of virus-like particles for many viruses with pathogenic potential. In our laboratory, advanced work is underway to eliminate the ADE effect of Zika virus vaccine. Our experience in this field can be directly transferred to the coronavirus SARS-CoV-2 vaccine.