Novel tricyclic glycomimetics as DC-SIGN receptor ligands

The ongoing coronavirus pandemic (Covid-19), caused by an infectious respiratory disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), entails intensive scientific research work in area of antiviral drugs and vaccines. In this context of glycomimetics (compounds that mimic the structure and activity of carbohydrates), due to their unique properties (*e.g.* affinity, stability and bioavailability), are very promising drug candidates.

In the living organisms glycomimetics can interact with lectins, which are carbohydrate-binding glycoproteins. Among lectins, DC-SIGN (***D***endritic ***C***ell-***S***pecific ***I***ntercellular adhesion molecule-3-***G***rabbing ***N***on-integrin), a receptor generously expressed on Dendritic Cells, play essential roles in innate immunity. This type of lectin is the port function for pathogens (*e.g.* SARS-CoV, SARS-CoV-2, HIV, human norovirus, influenza A virus, ZIKA-virus, *etc.*). Therefore, DC-SIGN is undoubtedly a very promising research goal in the context of shaping the immune response. And the development of effective DC-SIGN receptor antagonists is highy desirable.

The main goal of the project is to create effective DC-SIGN receptor ligands that can be used as antivirus drugs. This goal will be carried out by:

1. A virtual screen of a large library of tricyclic carbohydrate derivatives.

2. Synthesis and characterization of selected compounds.

3. Research of the interactions of synthesized glycomimetics with a DC-Sign receptor.

The project combines theoretical calculations, organic synthesis and biophysical investigations. To predict the binging ability of the compounds, we will use protein-ligand docking software. Ligands with a predicted high affinity will be synthesized and selected for experimental evaluation. The synthetic part, the most labor-intensive, will include the development of a general and efficient method for obtaining new DC-SIGN receptor ligands, using simple monosaccharides as substrates (glucose, mannose, galactose).

Research on the interaction of synthesized glycomimetics with DC-SIGN protein will be carried out using a nuclear magnetic resonance and isothermal titration calorimetry. The obtained results will allow to determine the impact of structural factors on the complexing properties of the investigated compounds. After developing effective monovalent ligands, multivalent ligands of DC-SIGN receptor will be synthesized and investigated. In conclusion, basic knowledge in the field of glycomimetic chemistry will be extended during the implementation of the project. In addition, the obtained molecules may have practical use as potential antiviral drugs.