DESCRIPTION FOR THE GENERAL PUBLIC

The role of the immune system is protection of the body from harmful factors such as bacteria, viruses, fungi and cancer cells. However, cancer cells are able to "hide" from the immune system, divide without stopping and not be recognized as foreign. Thus far, cancer treatment has mainly been based on chemotherapy, radiotherapy, surgery and combinations of the aforementioned methods. Unfortunately, in some types of cancer, none of these strategies is effective.

Over the past few years, immunotherapy has become the greatest hope of oncology. It is based on stimulating the immune system of patients and restoring it to normal activity, so that they can fight cancer cells effectively. One of the focuses of immunotherapy is the area of „immune checkpoints". These are receptors which are located on the surface of T-cells and which can, by interacting with their ligands, stimulate or inhibit the immune system. The co-inhibitory molecules include these receptor-ligand pairs: CTLA4-CD80/CD86, PD1-PD-L1/ PD-L2 and BTLA-HVEM.

Currently, monoclonal antibodies such as *Ipilimumab* (which blocks the interaction between CTLA4 and CD80/CD86) and *Nivolumab* and *Pembrolizumab* (which inhibit the binding of PD1 to PD-L1/PD-L2) are used in the treatment of some types of cancers. Clinical trials also include antibodies able to block BTLA-HVEM interactions. While antibodies prolong the life span of patients they also have many disadvantages, such as high toxicity and autoimmune reactions of the body. Monoclonal antibody therapies are also very expensive. It therefore seems reasonable to search for low molecular weight inhibitors of receptor-ligand complex formation that could be used in immunotherapy as drugs.

In the presented project we are going to focus on blocking the interaction between the BTLA and HVEM proteins. It has been proven that these proteins are overexpressed in some types of cancer, such as melanoma, gastric cancer and chronic lymphocytic leukemia. To design the inhibitors of BTLA-HVEM complex formation we are going to use other ligands which interact with the above-mentioned proteins, such as glycoprotein D (which binds to HVEM) and UL144 protein (which interacts with BTLA). The ability of compounds to interact with BTLA and HVEM proteins will be examined by affinity chromatography and enzyme-linked immunosorbent assay (ELISA). To check whether the designed compounds can inhibit the BTLA-HVEM complex formation, competitive ELISA tests and cell line assays will be performed. For the most promising inhibitors immunological reactivity and safety assessment will be determined.