The reasons for choosing the research topic:

B-cell non-Hodgkin lymphoma (NHL) and acute lymphoblastic leukemia (ALL) are the most commonly diagnosed hematologic malignancies in the Western world. Despite considerable progress in their management, they still constitute a challenge for modern oncology. In recent years, immunotherapy has emerged as a potent weapon against cancer. In particular, one strategy governed the attention of the researchers and the medical society. This strategy- the so-called adoptive cell transfer – relies on the patient's own genetically modified T cells or NK cells that express chimeric antigen receptors (CARs). CAR receptors enable specific recognition of proteins present on the surface of tumor cells. This recognition triggers their cytotoxic response, which consequently leads to the elimination of tumor cells. To date, a remarkable breakthrough has been made in the treatment of ALL with CAR-T cells recognizing CD19 antigen, with remissions reaching up to 90% in some of these cases. Nevertheless, an increasing number of reports on the resistance to CD19-CAR therapies stimulate research aimed at identifying novel druggable targets. One of the mechanisms of resistance to CD19 CAR depends on the downregulation of CD19 molecule in the cell membrane.

The aim of the project:

In this project, we aim at characterizing the phenotypic changes in tumor cells due to loss of CD19 antigen.

Implementation of the project:

Within the project, we plan to address four scientific tasks: 1. Creation of CD19 antigen knockout neoplastic B-cells 2. Investigation of the impact of CD19 antigen knockout on the functions of neoplastic B-cells 3. Characterization of the phenotype of CD19 knockout neoplastic B-cells 4. Identification of the antibody and scFv fragment recognizing selected surface molecule in neoplastic B-cells as a basis for further construction of CAR.

Expected results:

We anticipate that the successful completion of the project will shed new light on the hitherto unknown biological role of CD19 antigen and will help to delineate the perspectives for the treatment of the patients refractory to CD19-CAR T immunotherapies.