

### **The reasons for choosing the research topic:**

Despite some successes in the field of prevention and treatment of cancer, malignancies continue to pose a growing problem in the current world. Therefore, new methods to combat these deadly diseases are being searched for. One such modern methods is an **adoptive cancer immunotherapy**, which has been gaining an increasing interest in recent years. This strategy uses the effector cells of the immune system. The real breakthrough occurred following development of **chimeric antigen receptor (CAR)** technology, which provides to the effector cells the ability to accurately recognize and kill cancer cells, while preserving satisfactory tolerance to healthy cells in the body. This allows for the potential use of this technology in almost all types of cancer.

After the success of CAR-based adoptive therapies against leukemias and lymphomas, the search continues for new therapeutic targets for this kind of strategy. What is also being sought for are the methods of improving the efficacy of CAR-based therapies, especially against the solid tumors. It is being achieved, among others, by combining the CAR-based therapies with antibodies that target the immunosuppressive abilities (so called 'immune checkpoints') of cancer. Despite the noticeable effectiveness, the use of such antibodies is associated with the risk of serious side effects, including deaths due to complications of this therapy. The cause is a poor selectivity of these antibodies and their adverse effects towards healthy tissues. It is therefore necessary to develop new therapeutic strategies in this regard.

### **The aim of the project:**

The main objective of the project is an assessment of the effectiveness and selectivity of a new adoptive therapy using receptor CAR against one of the molecules that inhibit the antitumor activity of the immune system. This method can become more effective and safer alternative compared to the use of antibodies against immune checkpoints.

### **Implementation of the project:**

In the current project, we have plan the implementation of four Research Objectives. In Objective 1, we plan to evaluate what methods can provide the satisfactory level the presence of CAR receptor on the immune effector cells (T lymphocytes and NK cells). In Objective 2, we will assess the effectiveness of the effector cells with a new CAR receptor against cells of various cancers, mainly derived from breast cancer and lymphoma. Objective 3 aims at initial examination if we can precisely aim the cells with the new CAR receptor only against cancer cells and tumor-associated stromal cells, and not healthy tissues. In Objective 4, we will assess the effectiveness of the effector cells with a new CAR receptor in animal models.

### **Expected results:**

In the present project, we apply a modern CAR technology to provide evidence for experimental efficacy and safety of the elimination of tumor cells and tumor-associated stromal cells, which show the expression of a protein that is critical for the evasion of the tumor from the immune system and immunotherapies. The results of this project can impose a direct impact on improving the effectiveness and safety of the immunotherapeutic strategies used in modern Oncology.