Many types of cancer use camouflage allowing the escape of immune recognition and elimination. Immunotherapy, an innovative approach for cancer treatment, aims at restoring the immune system's natural ability to recognize and to eliminate cancer cells. In recent years, the therapy targeting immune checkpoints has achieved spectacular effects. Immune checkpoints in physiological conditions prevent the excessive activation of the immune system. Among the multiple immune checkpoints known by now, the interaction between PD-1 protein (Programmed Cell Death Receptor 1) and its partner, PD-L1, expressed on cancer cells' surface, is prominently involved in tumorigenesis and associated with poor prognosis in many types of cancer. PD-L1 protein occurs in physiological conditions on the "healthy" cells. However, cancer cells can use this protein as a mechanism of escape from immune system detection. That is why blocking PD-1/PD-L1 interaction, in many cases, allows for improved immune system activation and cancer elimination.

The anti-PD-1/PD-L1 therapy using monoclonal antibodies (mAbs) is currently the only effective treatment for various types of cancers, for example, breast, kidney, bladder, and melanoma. Taking into account the negative aspects of using mAbs, such as adverse side effects and high costs of therapies, the need for the development of new PD-1/PD-L1 complex inhibitors is justified. **It is worth to underline that development of anti-cancer therapies is limited due to a lack of appropriate tools enabling the study of the mechanisms of cancer cells elimination by the immune system in the presence of PD-1/PD-L1 interaction blockers.** Only one *in vitro* system, commercially available, has been described so far for this type of research. However, this model does not reflect the tumor microenvironment and allows only for the verification of specific activation of the immune system. The model does not provide any information about the biological effects with respect to cancer cell elimination.

Taking into consideration, the lack of available models able to verify the biological activity of PD-1/PD-L1 inhibitors, the aim of this project is to develop an innovative three-dimensional *in vitro* model for mechanistic studies of triggering the immune response by the tested compounds. Preliminary research has led to the selection of several types of human cancer cell lines that are characterized by the high level of the PD-L1 protein. In the project, we plan to obtain three-dimensional (3D) cultures of chosen cancer cell lines in the form of spheroids and hydrogel scaffolds. To generation the co-culture model, immune cells collected from healthy donors will be used. **We would like to develop the model which will reflect the *in vivo* tumor microenvironment.** Based on the collected information and gained expertise, we know how to provide a reliable interaction between cancer and immune cells in 3D co-culture. One of the procedures that we would like to utilize will allow for the examination of the process of cancer cells elimination by immune cells in the presence of PD-1/PD-L1 interaction blockers.

We believe that the project results will contribute to a better understanding of the mechanisms of the interaction between cancer cells and the immune system. The new 3D *in vitro* platform will also provide more reliable information about PD-1/PD-L1 inhibitors' mode of action during cancer cell recognition and will help to evaluate their potential in triggering the immune-mediated tumor elimination.