

## **DESCRIPTION FOR GENERAL PUBLIC**

Despite many years of research, the problem of effective treatment of cancer is still not solved, and cancer annually causes death of about 8 million people in the world, including about 100,000 in Poland. Most of the currently used therapies are aggressive therapies, which side effects are felt by patients by long time after the end of therapy. Colorectal cancer is the third most commonly diagnosed malignant. Most often, colon cancer affects people who live in developed and developing countries. The factors that favor illness are: smoking, sedentary lifestyle, poor-fiber and rich-fat diet, old age, genetic predisposition and intestinal inflammatory diseases. Symptoms of the disease (problems with bowel movements, occurrence of blood stools) often manifest themselves in an advanced stage of the disease associated with the presence of distant metastases that prevent effective treatment. For this reason, less than 60% of diagnosed patients manage to survive.

Tumor suppression is made possible by the ability of the immune system to distinguish its own from foreign cells. Unfortunately, the ability of the immune system to effectively recognize cancer cells is often limited, among others due to the fact that cancer cells do not have antigens recognized by T lymphocytes and have common genotypic origin with normal cells. One of the receptors present on the surface of tumor cells, acting as a "hypnotic" of the immune system, is the CD47 receptor. Its original name is Integrin-Associated Protein (IAP) because the CD47 receptor was first isolated in a complex with  $\alpha\beta3$  integrin derived from the placenta and granulocytes. In the eighties of the last century, the spatial structure of the CD47 receptor was recognized due to the fact that its structure corresponded to the OA-3/OVTL3 antigen structure, typical for ovarian cancer. Then, for the first time, the CD47 receptor was identified as a cancer marker. It is now known that the CD47 receptor is a frequently occurring glycoprotein on the surface of various solid tumors, leukemias, lymphomas and gliomas. The CD47 receptor is the so-called "compatibility marker", which binds to the SIRP $\alpha$  receptor present on the surface of macrophages. The CD47-SIRP $\alpha$  complex formed in this way prevents the phagocytosis of tumor cells. One of the latest advances in the fight against cancer is immunotherapy, based on the effective diagnosis and removal of cancer cells from the patient's body. However, the hypothesis about the ability of the immune system to recognize specific antigens on the surface of cancer cells has been proposed by Sir Frank Macfarlane Burnet already more than 40 years ago. One of the most frequently chosen drugs are monoclonal antibodies. Currently, many research groups carry out research using the anti-CD47 antibody.

In order to enhance the therapeutic effect of the used antibody, we want to use a natural substance that causes the apoptosis of colon cancer cells and potentially stimulates macrophages to phagocytosis. By the way, we want to check whether the above substance is responsible for the immunogenic death of cancer cells. Immunogenic cell death is responsible for the activation of the immune system, which consists of several main stages, such as: release and presentation of tumor antigens by antigen presenting cells, T-cell activation by activated antigen presenting cells, T-cell migration into the tumor and killing tumor cells. Due to the low bioavailability, the substance will be encapsulated in liposomes.

**The aim of the project is to develop integrated immunotherapy of colorectal cancer, which will lead to activation of the immune system and phagocytosis of cancer cells. The project includes research on the survival of cancer cells, biochemical tests determining their physiological and phagocytosis state.**