## The reasons for attempting the research topic

In recent years, dynamic development of cancer immunotherapeutic strategies has been observed. Immunotherapy acts by stimulating the body's immune system to eliminate cancer cells. Cancer immunotherapy comes in a variety of forms, including targeted monoclonal antibodies that already constitute key treatment options for patients with various hematological malignancies and adoptive cell transfer of genetically modified cells. Direct mechanisms of antitumor activity of immunotherapies rely on the destruction of tumor cells by the disintegration of the tumor cell membrane. This process can be mediated by either a cell-mediated cytotoxic activity of effector cells or activation of the complement system.

Despite numerous attempts and successes in this field, immunotherapy still encounters many obstacles in the effective elimination of cancer cells. Therefore, exploring novel fundamental networks involved in the development of resistance to immunotherapeutic agents becomes a pressing subject in modern immunooncology.

## **Project goal**

The aim of the project is to better understand the network, organization, and regulation of the antitumor immune response. Specifically, we aim to discover and understand the functional regulatory circuits between cell-mediated and complement-dependent antitumor immunity, and to clarify the underlying mechanisms.

## **Description of research**

Within the project, we will establish several tumor models resistant to cellular-based immunotherapies and will thoroughly characterize these cells. We will also validate our hypothesis in primary material from patients resistant to immunotherapies currently used in the clinics. Using the knowledge gained during project implementation, we will design o novel immunotherapeutic strategy and validate its antitumor activity in both in vitro and in vivo models. The studies will be conducted in collaboration with leading research centers in Poland and abroad.

## **Expected results**

Altogether, the expected outcome of the project is to better understand the network, organization, and regulation of the antitumor immune response. We anticipate that the results of the project may not only shed new light on the hitherto unknown mechanism of regulation of antitumor immune response but also may expand the existing knowledge and grant the formulation of new foundations in tumor immunology. Understanding in detail the crosstalk between the tumor and immune system is one of the main challenges for oncological research in order to design new and more efficient immunotherapies. Therefore, we strongly believe that by achieving the goals of our proposal, we will make a significant step forward in the development of cutting-edge immunotherapeutic strategies.