The reasons for attempting the research topic:

In recent years, dynamic development of cancer immunotherapeutic strategies has been observed. Immunotherapy acts by stimulation of the body's immune system to eliminate cancer cells. Despite numerous attempts and successes in this field, immunotherapy still encounters many obstacles in the effective elimination of cancer cells. One of the reasons for the failure of therapeutic strategies is the unfavorable, immunosuppressive microenvironment (TME) in the tumor. Indeed, the TME components exert deleterious and inhibitory effects on trafficking, infiltration, and effector functions of immune cells. Therefore, the profound analysis of the immunosuppressive microenvironment in the tumor accompanied by the development of new, effective therapeutic strategies eliminating specific TME components may contribute to harnessing the full potential of immunotherapy.

Project goal:

The aim of the project is to develop approaches that, by targeting TME, improve the antitumor activity of selected immunotherapies. We hypothesize that the elimination of cells present in the tumor microenvironment, for instance, tumor-associated macrophages (TAMs), may increase the effectiveness of the immune response against cancer cells.

Description of research:

Within the project, we plan to study the influence of TME on the activity of immune cells, to analyze the immunosuppressive factors affecting effector cells' functions, and determine the molecular mechanisms responsible for this immunosuppression. Using this knowledge, we will design and implement a new strategy, based on the effector T cells modified with chimeric antigen receptors (CARs), for the elimination of TME. We will evaluate the influence of this TME-eliminating strategy on the antitumor activity of selected immunotherapies in both *in vitro* and *in vivo* models. The studies will be conducted in collaboration with leading research centers in Poland and abroad.

Substantial results expected:

We believe that the results of this project will not only provide us with a better understanding of the TME immunosuppressive function but also will help to identify and evaluate the therapeutic potential of targeting TME in order to support tumor cells' immune surveillance. We also believe that our research may contribute to improving the effectiveness of immune-based therapies in cancer patients. To the best of our knowledge, this topic has not been studied in detail so far, and the results of this project may be of great importance for the basic studies in immunology and immuno-oncology.