DESCRIPITION FOR THE GENERAL PUBLIC

Tumor development is dependent on reliable communication and interactions between tumor cells and other cellular components of a tumor microenvironment (TME). Exosomes are important element of the intercellular communication. They are membrane-derived nanovesicles of endocytic origin of about 30-200 nm which are released by all cell types into the extracellular space. Depending on the cell of origin, the exosome content varies greatly. Proteins, DNA and RNAs presented in the lumen of exosomes play a crucial role in exosomes biology. Exosomes have been described as critical mediators of several biological processes associated with tumor cell migration, modulation of cell functions as well as with induction of inflammation or suppression. Initially it was thought that exosomes secreted by tumor cells (TEx) could be an excellent source of cancer antigens. However, subsequent studies have shown that exosomes of tumor origin rather inhibit the anti-tumor response by providing suppressor molecules to cells. Nevertheless, due to their biocompatibility, stability and high ability to penetrate the tumor microenvironment and the fact that they are readily available source of tumor antigen, they are considered as a potent therapeutic tool.

The main objective of our project is to answer the question if modification of tumor-derived TEx content with anti-tumor molecules may revert their pro-tumor activity and raise their anti-tumor potential. Despite a growing amount of published research in field of modified exosomes in cancer therapies, proposed in the project modifications involving simultaneous introduction of selected pro-inflammatory cytokine and inhibitor of suppressive molecules have not been developed up to this time. In our investigations we are going to apply two methods of TEx modification: indirect *via* genetic modification of tumor cells secreting TEx and direct *via* electroporation. After optimization of protocol of modified TEx production and isolation, we will perform a detailed analysis of exosome content in order to follow changes occurring after introduction of anti-tumor factors and analysis of their immunomodulatory and angiogenic activity. The obtained data will be used to establish a novel protocols of antitumor immunotherapies with application of selected mTEx in the form of immune adjuvant tested in murine colon carcinoma and murine lung carcinoma models.

The results of the project will broaden our state of knowledge on the activity of modified tumor-derived exosomes and possibilities of their application in anti-tumor strategies. Moreover, the obtained data will be used to establish novel protocols for a highly specific immunotherapy with the use of modified TEx as an adjuvant increasing the ability of the host to induce specific anti-tumor response, which could be recommended for clinical applications. The project will also tighten the cooperation between leading Polish and foreign research centers and will contribute towards the dynamic development of Polish science and broadening of general knowledge in the field of experimental oncology and immunology.