

Activation of the stimulator of interferon genes (STING) protein has recently emerged as potent anti-tumor therapeutic strategies. As a result of STING pathway activation, type I IFN production and antitumor immune response occur. There has been also observed massive infiltration of white blood cells – neutrophils. Tumor neutrophils seem to have diversified functions, depending on the microenvironment and stage of tumor development. They can be divided into N1 neutrophils which exhibit anti-tumor properties and N2 neutrophils which are considered as pro-tumor cells. There are evidence that neutrophils can achieve N1 features in the presence of type-1 interferons. However, it is unexplored whether STING activation transforms neutrophils into anti-tumor N1-like cells in the tumor microenvironment. Another type of immune cells, present in large numbers in the tumor, are macrophages. It has been proven that macrophages and neutrophils during infection exist in a cooperation. Neutrophils are the first cells that appear in an area of inflammation and then they enhance recruitment of macrophages and their polarization toward pro-inflammatory (M1) cells. In the tumors, M1 macrophages are considered as cells displaying anti-cancer properties. The aim of the project is to investigate the role of infiltrating neutrophils and their polarization status after STING protein stimulation in the tumor microenvironment.

In the project we are going to investigate whether tumor - infiltrating neutrophils after STING agonist administration exhibit N1-like anticancer features. We will also investigate the impact of tumor-associated neutrophils on the cancer cells and macrophages. We will conduct *ex vivo* and *in vivo* experiments.

We believe, that better understanding of the STING pathway activation in tumors microenvironment could find new more effective anticancer solutions.