The tumors are complex formation composed of a variety of cells. The main cellular population is made of transformed, cancer cells but as a part of these, there is always a plethora of infiltrating untransformed normal cells. The cellular composition of the tumor microenvironment can shape therapeutic responses, particularly through the effect of infiltrating immune cells.

In recent years we have seen the unprecedented clinical success of immune therapies e.g. checkpoint inhibitors and T lymphocytes with chimeric antigen receptors. However, many cancer patients exhibit resistance to immunotherapies which is caused by the unfavorable, immunosuppressive tumor microenvironment, particularly by macrophages, monocytes, and suppressive dendritic cells. Activation and reprogramming of these intratumoral myeloid cells might enable effective immune responses against cancer e.g. by checkpoint inhibitors.

The project aims to investigate the optimal mechanism that can activate macrophages, to facilitate anticancer response. We plan to achieve this by stimulation physiological proinflammatory signaling pathways that are normally triggered by pathogens during infection. For that, we will trigger immuno-activatory pathways TLR or STING in intratumoral macrophages to reprogram their function from pro- to anti-tumor activity. We will use liposomal formulations of compounds that activate TLRs or STING signaling pathway. Our research will be done in tissue culture of primary and cancer cell lines as well as in mouse cancer models. Finally, we will examine the efficiency of delivering the above compounds to phagocytes and changes in activation of intra-tumor macrophages, which will allow inhibition of tumor growth in vivo.