A tumor is a tissue in which extensive regions of low oxygen concentration are observed. The concentration of oxygen in the tumor varies between 1 and 2%. In the healthy tissue however, the oxygen concentration ranges from 4.5% to 9.5%. The difference results from the construction of tumor vasculature. Cancer blood vessels are twisted, leaky, often terminated blindly. Such a design contributes to disturbed blood flow with odds of hemostasis. It leads to the abnormal oxygen delivery to the tumor tissue. Thus, the low oxygen tension in the tumor may be the target of anti-cancer therapy.

The aim of the project is to design and test a new polymeric nanocarrier (polymersome) loaded with two different anticancer agents: agonist of STING protein - cGAMP and doxorubicin. The first one (cGAMP) will activate the immune system to fight effectively against cancer cells and the second one will be a chemotherapeutic (doxorubicin). Both of the drugs will be specifically released in the regions of low oxygen concentrations (hypoxia regions) in the tumor. Such a kind of polymersomes have not been reported, yet.

Such a specific drugs delivery to the tumor regions of hypoxia will allow to avoid two major limitations of anticancer drugs application: (i) the need of the direct administration of the drug into the tumor and (ii) high overall toxicity. There are many drugs that need direct intratumoral administration what limits their use in the treatment of hard-to-reach tumors. In addition, the systemic use of chemotherapeutic agents is often associated with high toxicity not only for cancer cells but also for healthy tissues.

As a part of the project, we will synthesize and test the properties of polymeric carriers (polymersomes) that accumulate in the tumor tissue and specifically release drugs in hypoxia regions. Both, on tumor and normal cell lines, specific drug release in low oxygen environment will be examined. The effectiveness of specific drug releases in the tumor tissue on the mouse model of melanoma (skin cancer) and mouse breast cancer will be investigated. We will also assess the efficacy of tumor growth inhibition with the use of drug-loaded polymersomes.

The planned project will allow to assess the therapeutic potential of new nanocarriers that deliver selected drugs to the regions of low oxygen concentration in the tumors. Such an innovative therapeutic approach will enable more effective treatment of hard-to-reach tumors and reduce the high toxicity of clinically used anti-cancer drugs.