

Tumors, in particular pancreatic tumors, are characterized by strong hypoxia. This condition is called hypoxia and very often its presence in the tumor is associated with its resistance to treatment and malignancy. To counteract hypoxia, the temperature of the tissue can be increased, causing for example increase of the flow in the blood vessels. As a result, the perfusion of tumor tissue increases and can lead to temporary increase in tumor oxygenation. To achieve the hyperthermia effect of the tumor gold nanorods, with high affinity to the tumor, can be used. Then, the tissue is exposed to irradiation at a wavelength of 808 nm (light energy is absorbed by nanorods and can be deposited in tumor tissue as a thermal energy). Additionally in this project, gemcitabine will be added to the gold nanorods, which is a chemotherapy drug used as a gold standard in the treatment of human pancreatic cancer. Thus, in addition to thermal effects in the tissue, we will obtain the effect of chemotherapy in the same time window. As a result of such as double combination therapy, it will be possible to obtain a number of effects in tumor tissue for example: the chemotherapeutic will accumulate more efficiently in the tumor tissue than without the addition of hyperthermia, immune system will be stimulated, cancer cells will die as a result of high temperature and the presence of a chemotherapeutic agent and tumor vasculature will be affected which should lead to changes of tumor hypoxia. This last effect, associated with the increase in oxygenation of the tumor tissue, is associated with the formation of "therapeutic window". Therapeutic window is a special time after the treatment of a cancer, in which the use of additional treatment will be much more effective - there will be a synergy effect of individual elements of the three-combined therapy (chemotherapy-hyperthermia and radiotherapy). One of the aims of the project is to evaluate how to use the effects of hyperthermia using a new derivative of gold nanorods to multiply the effectiveness of radiotherapy.

As a result of this project, it will be possible to assess the biological effects of near infrared light induced hyperthermia and gold nanorods combined with chemotherapy (gemcitabine) and the optimization of such therapy with radiotherapy. In the course of such combination therapy, hypoxia of tumors growing in mice will be examined in a special way (by Electron Paramagnetic Resonance Imaging and Ultrasound Doppler and Contrast modes). As a result, molecular mechanisms related to hypoxia, angiogenesis and tumor perfusion will be examined.