

Radiotherapy (RT) represents a standard treatment for more than half of all cancer patients and is leading therapeutic strategy for prostate cancer (PCa) and a major curative treatment for head and neck squamous cell carcinoma (HNSCC). Although the majority of cancer patients will respond to RT, some patients may not benefit from applied treatment due to developed radioresistance and may experience disease recurrence, ultimately resulting in therapeutic failure. 20 - 30% of patients with prostate cancer and 40 - 50% of HNSCC patients will show signs of recurrence within 5 years after treatment. Therefore, there is a need for the introduction of a safe and effective method to improve effectiveness of RT and to minimize the risk of radioresistance development and tumor recurrence. One of the methods to improve the effectiveness of radiotherapy is the use of a radiosensitizers. A radiosensitizer may be a non-toxic compound that is placed within the tumor and activated by visible light generated during clinical beam irradiation. Such a compound is called a photosensitizer (PS). PS activation by light of a given wavelength leads to the formation of highly toxic particles (reactive oxygen species) that kill cancer cells, cause damage to tumor blood vessels, and activate the immune system. These assumptions are the basis of a therapy called photodynamic therapy (PDT). Therefore, combination of RT and PDT should induce cells damage on different targets (DNA and cell membranes) and should significantly increase cancer cells destruction.

The aim of the project is to verify whether the use of PSs during clinical beam irradiation increases the effectiveness of radiotherapy.

During RT the light to induce PDT can be generated in two ways: 1) through Cherenkov radiation (produce by photon that travels faster than the speed of light through a medium thereby generating UV light) - RECA; 2) through nanometer-sized particles (called nanoscintillators) that convert X-ray radiation photons to visible photons (UV light) – X-PDT. In the project we will use drugs already used in the clinic (ketoprofen, lomefloxacin, doxycycline, 8-methoxypsoralen), with proven phototoxic effects and anti-cancer properties and investigate whether they can serve as PS in RECA or X-PDT therapies. We will examine if selected drugs generate cytotoxic reactive oxygen species and enhance RT-induced cancer cells death. Phototoxic potential of the tested drugs will be assessed against radioresistant head and neck squamous cell carcinoma and prostate cancer. Furthermore, we will verify if radioresistant cells subjected to tested therapeutic regimen will be more sensitive to chemotherapy standardly used in the clinic and if small-molecule inhibitors that target the survival pathways of cancer cells will increase the effectiveness of tested therapy that combine RT and PDT. The research hypothesis will be verified on mouse models of human HNSCC and PCa. The potential to trigger anti-cancer immune response and the role of immune cells in the investigated therapeutic regimen will be determined in immunocompetent mouse models of HNSCC and PCa.

The project is innovative. Its aim is to develop a novel method of sensitizing cancer cells to radiotherapy using drugs with photosensitizing potential available in the clinic, which can significantly increase the effectiveness of radiotherapy in radiotherapy-resistant head and neck and prostate tumors.