Synthesis of novel hybrid nanomaterials based on fullerene scaffold for photodynamic therapy of cancer

Principal Investigator: Dominik Dreszer, MSc (University of Silesia in Katowice)

Pancreatic cancer is characterized by a very aggressive nature and is one of the most deadly cancers of the digestive system. The prognosis for this type of cancer is very low, with a 5-year survival rate of about 5% and has remained virtually unchanged for several decades. Most pancreatic tumors respond poorly to current therapeutic agents due to the highly desmoplastic and immunosuppressive tumor microenvironment. Traditional drug delivery methods have some limitations, such as poor water solubility, insufficient toxicity, unfavorable pharmacokinetics, and limited stability due to metabolic or enzymatic degradation. These obstacles can be alleviated by the use of appropriate nanoparticles, for example liposomes, polymers, iron oxides, gold or silver nanoparticles and carbon nanomaterials (fullerenes, nanotubes). One of the methods of cancer treatment is photodynamic therapy of cancer. It is a minimally invasive therapeutic method for the treatment of cancer and bacterial infections, which uses a non-toxic drug called a photosensitizer. After irradiation with electromagnetic radiation and in the presence of oxygen, the photosensitizer generates reactive oxygen species (singlet oxygen, anionic superoxide radical or hydroxyl radical) that induce the death of cancer cells. As one of the targeted methods, it is characterized by high selectivity towards cells affected by cancer, without damaging most of the healthy tissue surrounding the tumor.

The main objective of this project is to design and synthesise hybrid fullerene-phthalocyanine nanomaterials for use in photodynamic therapy of pancreatic cancer. In particular, two generations of fullerene nanotherapeutics will be developed based on different chemical modifications of the fullerene scaffold using the Bingel-Hirsch and Prato reactions. Subsequently, the formed fullerene-phthalocyanine hybrids will be dissolved in water by complexing with proteins (albumin or lysozyme) and cyclodextrins. It is also planned to attach the cRGDfK peptide to already complexed compounds as an inhibitor of integrin $\alpha V\beta 3$, which acts as a targeting peptide to increase the permeability of cancer cells to drugs in anti-angiogenic cancer therapy. We think that the described modifications of fullerene molecules with a phthalocyanine core will allow to increase the ability to generate reactive oxygen species and solubility in aqueous solutions. An increase in the efficiency and penetration capacity of photodynamic therapy using new substances with potentially better pharmacological properties would lead to an increase in the effectiveness of this method against cancer or bacterial infections.

In summary, the above-described project aims to obtain fullerene nanomaterials based on the phthalocyanine structure as potential photosensitizers for photodynamic therapy of cancer that can effectively induce cancer cell death with the help of reactive oxygen species.