Nanotechnology is an intensively developing field of science, which has recently become popular also in biology and medicine. Noble metal-based nanoparticles including palladium nanoparticles (Pd NPs) are increasingly the object of interest of scientists, because of their advantages, such as biocompatibility and stability. Considering the fact that these nanoparticles have cell-sensitizing properties for subsequent radiation-based anticancer therapy, they may find a potential application in supporting proton therapy.

Glioblastoma multiforme is rare, but a highly lethal primary malignant brain tumor, which occurs more often in children than adults. Due to the specificity of this cancer, surgical interventions are often ineffective. In turn, alternative combination therapy based on simultaneous administration of chemotherapy and the using of photon beam radiation therapy of brain, can be very troublesome for the patients. What can help us, is the proton therapy, in which protons are used for very precise irradiation of the tumor, allowing for more effective treatment and reduction of side effects. Noble metal nanoparticles have properties, which sensitize cancer cells to proton therapy, which may increase the effectiveness of anticancer therapy. So far, there have been reports in the literature about the application of gold, platinum, zirconium or hafnium nanoparticles as radiosensitizers in proton therapy, but no information was found on the potential use of palladium nanoparticles.

The goal of the project is to obtain Pd NPs with different morphology (shape and size) being potential radiosensitizers in proton therapy of glioblastoma. Investigating such various Pd NPs is important from the point of view of their subsequent *in vivo* testing in a mouse model, because penetration of the Pd NPs across the blood-brain barrier is determined by both morphology and surface modification of Pd NPs. The physicochemical characterization of Pd NPs will be determined by: transmission electron microscopy (TEM) to study the morphology of synthesized Pd NPs, selected area electron diffraction (SAED) and X-ray diffraction (XRD) to evaluate the crystal nanostructure and UV-Vis spectroscopy to define optical properties of Pd NPs. It is also planned to modify the Pd NPs with poly(ethylene glycol) (PEG) to reduce their toxicity and with glucose or chitosan to make higher uptake of such Pd NPs by glioblastoma cells in compare to normal brain cells.

Subsequently, cytotoxicity studies of the modified and unmodified Pd NPs against two glioblastoma cell lines (U118 and U251) using the MTS test will be carried out determining the optimal concentration Pd NPs, which does not cause a significant decrease in the cell survival. Next, the influence of the Pd NPs with pre-determined concentrations on the efficacy of glioblastoma proton beam irradiation will be assessed. The level of cell damage, as well as the chemical changes caused by Pd NPs and the proton beam, will be examined by clonogenic assay, flow cytometry, Raman- and infrared spectroscopies. Statistic methods, such as one-way analysis of variance (ANOVA), as well as chemometric methods: principal component analysis (PCA) and linear discriminant analysis (LDA) will be useful for spectra analyzing. Thanks to them we will get statistically significant information about the differences in chemical composition of cells before and after proton irradiation assisted- and non-assisted with Pd NPs. Additionally, using Nanolive 3D Cell Explorer-fluo microscope, it will be possible to determine the site of Pd NPs accumulation in the glioblastoma cells.

The described project is an interdisciplinary approach to combine biology and nanotechnology in order to find new potential radiosensitizers in proton therapy of glioblastoma.