DESCRIPTION FOR THE GENERAL PUBLIC

Over the last decade the number of death due to cancer significantly increased, despite the rapid progress in diagnosis of even small, early stage of cancerous transformations. In some type of advances tumors, like breast and prostate cancers percent cure is still low. Currently, surgery, next external radiotherapy, and chemotherapy and immunotherapy are the most common therapy options. Unfortunately, therapeutic effects of cytostatic drugs are usually hindered by serious side-effects due to their toxic influence on healthy tissues. Moreover, many types of cancer cells show inherited or acquired resistance to the administered drugs including monoclonal antibodies and ionizing radiation. In the last decades, there has been great emphasis on "targeted therapies" that are designed to kill cancerous cells selectively, leaving the healthy tissue unaffected. One of such therapy is the targeted radionuclide therapy (TRT) in which cancer cells are killed with help of corpuscular radiation emitted by radionuclides conjugated to biological molecules, which recognize and bind to the surface of specific cancer cells. The specificity of binding is effected by recognizing of matching the surface receptors or other proteins overexpressed by cancer cells. Such selective mechanism of radiation delivering minimizes toxicity to the surrounding normal tissues. Depending on the tumor size and location, the choice of proper type of radiation is the critical factor for cancer treatment. In the case of small tumors and cancer metastasis treatment spectacular therapeutic results are achieved recently with use of the targeting molecules labeled with the emitters of short distance corpuscular radiation like α and Auger electron particles.

In the case of Auger electron therapy, the barrier to the wider application of this method is the necessity to transport the radioisotope inside the cell nucleus. This is a very difficult task because we need to construct a radiopharmaceutical that first finds cancer cells and then places the radioisotope in the cell nucleus near the DNA strand. Paper published this year opens new perspectives in Auger electron therapy. It showed that in some cancer cells having high concentration of H_2O_2, like in hepatocellular carcinoma (HepG2) oxidation of 2.5 nm platinum nanoparticles takes place and Pt^{2+} ions released from PtNPs are transported to cell nucleus and attached to DNA. Our idea presented in the project is to obtain radioactive platinum nanoparticles by their synthesis from ^{193m}Pt or ^{195m}Pt radioisotopes, which are very effective emitters of Auger electrons. Folic acid or trastuzumab molecules will be attached to the surface of nanoparticles, which will transport the radioactive platinum nanoparticles to the interior of liver, breast or ovarian cancer cells where is significantly higher H_2O_2 concentrations than in healthy cells. The radioactive platinum nanoparticles will dissolve and the released ^{193m}Pt or ^{195m}Pt cations will pass through the cell nucleus membrane and attach to the DNA, destroying the cancer cells. The system we propose here will allow the delivery of large $^{193m/195m}$Pt activities into the cell and achieve their intercalation into the DNA after release $^{193m/195m}Pt^{2+}$ cations, which should cause lethal double-strand breaks. Therefore, this system should meet the criteria that are necessary for effective Auger electron therapy.

The proposed project will be carried out at the Centre of Nuclear Chemistry and Radiochemistry of the Institute of Nuclear Chemistry and Technology (INCT) in Warsaw. Part of the proposed project related to the production of Auger electrons emitting platinum radionuclides ^{193m}Pt and ^{195m}Pt will be realized in cooperation with the National Center for Nuclear Research (Świerk, Poland), and two foreign nuclear centers Nuclear Research Institute Rež (near Prague, Czech Republic) and GIP Arronax (Nantes, France). Some of biological studies will be performed in cooperation with Department of Biochemistry and Molecular Biology, Centre of Postgraduate Medical Education, Warsaw. *In ovo* tests on chicken embryos will be performed in cooperation with Warsaw University of Life Sciences.

The application of radioactive platinum nanoparticles containing ^{193m}Pt or ^{195m}Pt isotopes allows to achieve a large therapeutic effect on difficult-to-treat breast, ovarian and liver cancers. It should also be noted that the toxicity of our drug to healthy tissues will be negligible in contrast to radio- and chemotherapy.