Gold nanoparticles (AuNPs) have many properties that make them beneficial in anti-cancer therapy. They can enter the tumor using two pathways: passively through the mechanism of increased permeability and retention, and through the use of biomolecules that have an affinity to cancer cell receptors. One of these receptors is HER2. HER2 overexpression is reported to be found in 20-30% of breast tumors and 6-7% of ovarian tumors and plays a key role in patient prognosis. HER2-overexpressing cancers multiply very quickly and over time become resistant to standard therapy. For this reason, they have been selected as the target of our research.

In this project, we propose the use of radioactive mercury isotopes for the synthesis of radiopharmaceuticals administered directly to the tumors with HER2 overexpression, which would show high selectivity and toxicity towards cancer cells, without destroying healthy tissues. We plan to use very small (5 nm) gold nanoparticles coated with $^{197/197m}$Hg, with a targeting biomolecule - trastuzumab attached to the nanoparticle surface.

Trastuzumab is the best known antibody with an affinity to HER2 receptor. It shows very high internalization in the area close to the cell nucleus, which is crucial in the case of therapy with Auger electrons. Moreover, the use of AuNPs will significantly increase the specific activity of the obtained radiopharmaceutical, because many radioactive mercury atoms will be present on the AuNPs' surface.

^{197}Hg and ^{197m}Hg radionuclides as Auger electron emitters have nuclear properties favorable for medical applications. They can be used in the treatment of small tumors and micrometastases. However, their optimal effectiveness is achieved only after close binding to the DNA of cancer cells. Due to the short range, comparable to the cell size, Auger-electron-emitting radionuclide therapy has fewer side effects, even with higher radiation doses than for the therapy with β-emitters, which is now widely used in nuclear medicine.

The aim of the project is the synthesis of a radiopharmaceutical based on AuNPs with $^{197/197m}$Hg on their surface conjugated with trastuzumab and the biological studies on cancer cells with and without overexpression of the HER2 receptor.

This will be achieved through the implementation of four planned research tasks. Firstly, the method of $^{197/197m}$Hg reactor production will be developed. Then, the synthesis of 5 nm AuNPs covered with a monolayer of $^{197/197m}$Hg will be performed, and the conjugation with stabilizing PEG and biomolecule – trastuzumab will be done. Finally, biological studies will be performed on cancer cells that overexpress HER2 receptors. Receptor affinity (determination whether the specimen specifically binds to HER2 receptors), internalization (percentage of the specimen penetrating inside the cell), intercalation (mercury attachment to the DNA), and induction of DNA double-strand breaks by the obtained radiopharmaceutical will be tested.

The resulting potential radiopharmaceutical can be used in the treatment of small tumors and micrometastases with HER2 overexpression.

To our knowledge, this is the first study of the combination of AuNPs with $^{197/197m}$Hg radionuclides in therapeutic applications.