ISOTOPE LABELLED FERRITIN - DEVELOPMENT OF AN ALTERNATIVE DRUG DELIVERY SYSTEM

Abstract for the general public

In recent years a dynamic expansion of nuclear medicine tomographic imaging techniques could be observed. The use of modern detectors, counts processing and analyzing systems enable measurements of even low radiotracer activity with higher resolution. I have chosen ferritin as an object of the interest because of the specific structure of this protein and is potential ability to bind various radioisotopes. Ferritins belong to a family of iron-binding proteins, occurring in almost all living organisms, the members of which vary in the form depending on the species and tissues of origin. In mammalian cells, ferritin is the main iron storage protein and regulates many biological functions. The wide and specific role of ferritin, related to its three-dimensional cage structure, iron storage ability and relatively effective transport in the mammalian tissues, makes it an ideal tool for diagnostics and therapy of different diseases, and especially, early detection of tumors using molecular imaging techniques. Ferritin is configured as a spherical polymer with a hollow core in the middle of the molecule, where the iron is stored. These properties of the ferritin molecule are similar to those of Au nanoparticles, which have been the subject of numerous studies in the last 10 years. Many researchers used ferritin as a nanoplatform for further modification because it is capable of docking molecules both inside and outside.

Despite the important role of ferritin, the application of this protein is limited by its size and biodistribution process. In this project I would like to verify three research hypotheses:

1. The structure of ferritin enables accumulation of a wide range of metallic radioisotopes, with sufficient efficiency to detect the modified protein with modern molecular imaging techniques, for example, single-photon emission computed tomography (SPECT).
2. Binding of isotopes does not affect the stability of ferritin in the specified range of activity, what minimizes the influence of radiolysis on the integrity of the protein, but still allows to detect its accumulation.
3. The applicability of the isotopes with longer half-life allows to monitor labelled ferritin biodistribution process in small animals.

In the project I plan to optimize two methods of labelling ferritin with radioisotopes: the indirect incorporation of radioactive atoms into a protein and iodination process. In my research I would like to examine the influence of temperature, the composition of the reaction mixture and the time of process on the labelling efficiency. Additionally, I would investigate methods of separating the desired compounds from the by-products. The obtained product will be characterized using analytical methods and the stability of radioconjugates will be verified both in storage and physiological conditions. The most promising molecules will be injected to healthy mice and the accumulation of the radioconjugates in animal body will be analyzed.

The expected result of the project is a protocol for labelling ferritin with radioisotopes and bioditribution monitoring of the produced compound, including the assessment of the efficiency of labelling and the obtainment of the highest specific activity. Effective and stable connection of radionuclides to the protein will be a great starting point for functionalization of this compound. The obtained results will constitute a benchmark for other scientists developing novel techniques for early diagnosis and treatment of cancer.