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103Pd/103mRh in-vivo generator for Auger electron targeted therapy

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In recent years the application of Auger emitters for cancer targeted therapy has got great attention. Current clinically useful systemic radiation therapies are mainly based on β- radiation emitters. However, the tissue range of low energy β- particles is about several hundred cells length that is not optimal for treatment of small-size tumors [1]. Tissue range of α particles is only around several cells length (40 – 100 μm), what in combination with their high linear energy transfer (LET≈100keV/μm) results in high radiocytotoxicity. However, this therapeutic approach cannot be used widely due to the low availability of α-emitters [2]. Auger electrons are similar to high-LET particles, like α particles, and can induce considerable cell damage. Furthermore, compared to α and β- radiation, Auger emitters remain of low toxicity while travelling in blood or bone marrow but become highly efficient when incorporated into DNA of target cells. Hence, Auger radiotherapy is considered a promising field for targeting small tumors such as metastases [3]. Since most of the energy released by Auger electrons is deposited in close proximity from the decay site, the successful use of Auger emitters in therapy requires their precise delivery to a sensitive organelles in the cells [4]. We propose new idea to deliver the Auger emitter 103mRh to the cell nucleus by using an in-vivo 103Pd/103mRh generator conjugate. Synthesized trastuzumab or inhibitor of PSMA radiobiocojugates labeled with 103Pd (t1/2 = 16.99 d) will transport the radionuclide to the cytoplasm in the perinuclear area. As a result of nuclear decay, 103mRh (t1/2=56 min) will be released and in the form of 103Rh_aq^(3+) will penetrate the nuclear membrane and bind to the DNA inducing cytotoxic effect. In the first step, we synthesized Au nanoparticles, which were covered with a layer of metallic Pd. Next, using PEG linker, we attached monoclonal trastuzumab to the core-shell nanoparticles. The preliminary studies of cytotoxicity of non-radioactive Au@Pd nanoparticles and Au@Pd-trastuzumab bioconjugates were performed.

References

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