INDIUM-111 RADIOLABELLED PEPTIDE FOR THERANOSTICS OF ER POSITIVE TUMOURS

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Introduction: Estrogen Receptor (ER) expression is considered one of the most important biomarkers in breast cancer. The current treatment of the ER positive breast cancer involves specific hormone therapy to inhibit the ER signaling. Despite the recent therapeutic advances, many patients still become resistant to the endocrine treatment and develop metastasis by mechanisms that are not fully understood [1] [2].

In the last years there has been evidence that in addition to the classical genomic action, the ER is also involved in non-genomic responses that have proliferative and anti-apoptotic effects in cancer cells. The interaction between ER-‥and the Src kinase that occurs upon stimulation by estradiol is known to elicit an acute signaling pathway that leads to increased DNA synthesis. To block this association a six amino acid ER-mimicking peptide, pY-pep (Ac-Leu-pTyr-Asp-Leu-Leu-NH_2) was described [3].

Objectives: The simultaneous emission of gamma-rays and Auger electrons makes Indium-111 (^{111}In) a relevant radionuclide for both imaging and therapy. Taking advantage of these properties we aimed to obtain a potential theranostic agent based on the pY-pep.

Methods: The peptide was synthesized and conjugated to two different bifunctional chelating agents (DOTA and DTPA) by solid phase synthesis and purified by RP-HPLC. The conjugates were radiolabelled with ^{111}In and the radiochemical purity was assessed by ITLC and HPLC. The *in vitro* stability of the radioconjugates was assessed in PBS (pH=7.4), in the presence of excess of apo-transferrin, and in human serum at 37ºC at different time points until 48 hours.

Results: ^{111}In-complexes were obtained with labelling efficiencies higher than 95% at low ligand concentrations. The structure of the complexes was assessed by HPLC comparison with the analogous cold In-complexes characterized by ESI-MS. The HPLC analysis showed that the radioactive complexes are stable in PBS and in the presence of excess of apo-transferrin up to 48 hours. However, the two conjugates demonstrated to be unstable in human blood serum.

Conclusions: The pY-pep was successfully conjugated to two different bifunctional chelating agents and the conjugates were radiolabelled with ^{111}In with high radiochemical yield and purity. The radioactive conjugates demonstrated to be stable in PBS (pH 7.4) and in the presence of excess of apo-transferrin. Further cell and animal studies are currently underway.

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