

## The synthesis of an $^{18}\text{F}$ -labeled luteinising hormone-releasing hormone receptor targeting peptide ligand

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*Abstract – Images from Positron Emission Tomography (PET) contain unique metabolic information that is not available from anatomical imaging techniques. PET scanning with the tracer  $^{18}\text{F}$ -fluoro-deoxyglucose (FDG), is widely used in clinical oncology and considered as a working horse of this area. However, high glucose uptake rates are not specific to tumors. To address this problem special focus has been laid on the labeling of larger biomolecules such as peptides. In this work we describe a radiosynthesis of a fluorine-labeled LHRH analogue, as a ligand for visualization of various tumors expressing LHRH receptors.*

*Keywords – Oncology, receptor specific interaction, peptide,  $^{18}\text{F}$*

### I. INTRODUCTION

PET offers a non-invasive, highly sensitive method for the diagnosis of various cancers. The fact that tumor cells metabolize glucose faster than normal cells generates an elevated level of FDG in the cancerous region. But this kind of accumulation is not a specific process. To overwhelm the drawback of the application of FDG the use of a carrier molecule with specific interaction for the tumor tissue was introduced. Peptides or differently labeled analogues can be considered ideal agents for these purposes. Malignant cells, which express receptors for peptide hormones, can be targeted with radiolabeled hormone analogs containing a peptide carrier linked to a prosthetic group. Receptors for luteinizing hormone-releasing hormone (LHRH) (1,2) were found on various cancer cell lines. Due to the relaying receptors, the positron emitting radionuclide sustaining peptide hormone analogues with high specificity become useful diagnostic tools for PET.

Recently, oxime formation between aminoxy- and carbonyl functionality has been proposed as a suitable methodology for labeling of cyclic RGD peptides, as well as analogs of octreotide (3,4). The method is suitable for labeling a big number of peptides in general.

### II. MATERIALS AND METHODS

The  $D$ -Lys<sup>6</sup> LHRH analogue was selected for carrier molecule, as a lead compound. The  $\epsilon$ -amino group of the Lys was modified with aminoxy acetic acid to embody the labeling. The synthesis of the peptide was carried out by solid phase peptide synthesis. 4-( $^{18}\text{F}$ )fluorobenzaldehyde served as a labeling prosthetic group. It was produced from 4-formyl- $N,N,N$ -trimethylanilinium triflate by means of aromatic nucleophile substitution, and the resulted material was

purified by solid phase extraction. The conjugation was performed of chemoselective oxime formation in aqueous media, and the conjugated peptide was purified by RP-HPLC. To assess the identity of the radiolabelled material, a  $^{19}\text{F}$ -labelled peptide analogue was co-eluted with the product, and the experiments revealed, that our material was identical with the proposed fluorine labeled peptide.

Biological assays: The receptor binding features of the conjugated peptide was assessed by radioreceptor binding studies. The fluorine labeled peptide was tested on LHRH receptor positive human pituitary and prostatic carcinoma samples. The affinity of the conjugated peptide was evaluated by ligand competition studies using [ $^{125}\text{I}$ ][ $D$ -Trp<sup>6</sup>]LH-RH as a radioligand. Our results demonstrated, that the conjugated LHRH analogue exhibited high affinity binding to human pituitary and prostate cancer samples expressing specific LHRH receptors.

### III. CONCLUSION

We have synthesized an  $^{18}\text{F}$ -labelled LHRH analogue with great radiochemical purity. The ligand displacement experiments indicated that our compound shows high affinity binding to the LHRH receptor positive human tumor samples, and this fact is indispensable for the PET based diagnostic. Since LHRH receptors are expressed on various human tumors, this type of ligand can be a useful tool for the non-invasive detection of these malignancies. Based on our results we intend to perform experiments on other types of human tumor models and we would like to develop a series of fluorine labeled LHRH ligands to evaluate the effect of the hydrophile/lipophile balance on the biodistribution by varying the prosthetic aldehyde groups.

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