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AL18F LABELED NOTA-OCTREOTATE: LABELING AND IN VITRO CHARACTERIZATION

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BACKGROUND-AIM

Radiolabeled receptor binding peptides are being extensively utilized as radiopharmaceuticals. For PET imaging, Ga-68 labeled compounds have been widely used in recent years. Fluorine-18, however, has physical characteristics that would make it more appealing than Ga-68 for labeling of small peptides. It has a slightly longer half-life than Ga-68 that would allow preparation in remote facilities for later distribution to imaging centers and lower positron energy that yields better image resolution, particularly for preclinical imaging. We are currently working on labeling peptides with a recently described method based on the chelation of Aluminum ^{18}F-Fluoride (ALF) by 1,3,7-triazacyclononane-1,4,7-triacetic acid (NOTA). The method is being applied for the synthesis of ^{18}F-NOTA-Octreotate to target Somatostatin receptor 2 (SSTR2) overexpressing tumors.

METHODS

Conditions for labeling have been optimized by varying different parameters including type of buffer, reaction volume, reaction temperature, mass of peptide. Radio-HPLC was used to determine radiochemical yield. Saturation binding assays were performed in HEK-293 cells that have been stably transfected with the pcDNA3.1-HSSTR2 plasmid. ^{111}In-Octreoscan from commercially available kits for clinical use was tested in parallel as control.

RESULTS

Among the different labeling conditions tested the one that has given the most reproducible results with acceptable yields is use of a sodium acetate/gentisic acid buffer system, 20 µg of peptide, a starting activity of 40 mCi of ^{18}Fluoride, 80% ethanol and an incubation time of 15 min at 100 °C. These conditions yield a specific activity of ~0.5 mCi/µg (0.65 Ci/µmol) end of synthesis and radiochemical yield of 30 ± 5 %. The product is purified with an HLB cartridge. Saturation binding experiments with ALF-NOTATATE have shown very similar binding characteristics to ^{111}In Octreoscan in HEK 293 SSTR2 cells with Kd of 5.5 ± 2.9 nM (mean ± SE) and Bmax 5.5 ± 0.8 E5 sites/cell for the F18 labeled peptide and 10.2 ± 4.4 nM (mean ± SE) Bmax 4.9 ± 11.5 E5 sites/cell for the reference peptide.

CONCLUSION

The described procedure for labeling NOTATATE has reasonable yields and provides a labeled product that maintains high affinity binding for SSTR2. Further evaluation of ALF-NOTATATE in vitro and in animal models is ongoing. ALF-NOTATATE has great potential for future use of patients with neuroendocrine tumors.