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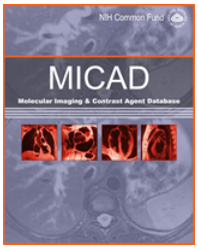

2-[18F]Fluoropropionyl-osteosarcoma–specific peptide-1 (ASGALSPSRLDT)

[18F]FP-OSP-1

Kam Leung, PhD[1]

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Chemical name:	2-[18F]Fluoropropionyl-osteosarcoma–specific peptide-1 (ASGALSPSRLDT)	
Abbreviated name:	[18F]FP-OSP-1	
Synonym:		
Agent Category:	Peptide	
Target:	Heparan sulfate proteoglycans (HSPG)	
Target Category:	Receptor	
Method of detection:	Positron emission tomography (PET)	
Source of signal / contrast:	18F	
Activation:	No	
Studies:	• *In vitro* • Rodents	Structure not available in PubChem.

Background

[PubMed]

Osteosarcoma typically affects adolescents and represents the most common primary bone tumor in childhood (1). Approximately 25% of osteosarcomas metastasize to the lung (2). Heparan sulfate proteoglycans (HSPGs) are glycoproteins that are glycosylated with two or three heparan sulfate polysaccharide chains. HSPGs are associated with the cell surface of cells (3). HSPGs play an important role in cell–cell and cell–extracellular matrix adhesion. Heparan sulfate binds to a variety of protein ligands (e.g., growth factors and interleukins) and regulates a wide variety of biological activities, including developmental processes, angiogenesis, blood coagulation, and tumor metastasis. HSPGs are overexpressed on a variety of tumor cells including osteosarcoma cells (4, 5). Sun et al. (6) identified a new 12-mer peptide (OSP-1, ASGALSPSRLDT) with the use of phage display screening against human osteosarcoma 143B cells with a high homology to the 17-28 amino acid residues of heparinase II/III. Heparinases bind and cleave cell-surface HSPGs. OSP-1 was radiolabeled with 4-nitrophenyl-2-[18F]fluoropropionic acid at the N-terminus to yield 2-[18F]fluoropropionyl-OSP-1 ([18F]FP-

Author Affiliation: 1 National Center for Biotechnology Information, NLM, NIH, Bethesda, MD; Email: micad@ncbi.nlm.nih.gov.

OSP-1), which was then evaluated for positron emission tomography (PET) imaging of tumor xenografts in mice.

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (HSPG).
- Articles in OMIM (HSPG)

Synthesis

[PubMed]

OSP-1 and its scrambled peptide OSP-S (DLPSRTSALASG) were prepared with solid-phase peptide synthesis (6). Peptide purity and molecular mass were confirmed with MALDI-TOF mass spectroscopy and electrospray ionization mass spectrometry. To label with ^{18}F, OSP-1 was incubated with 4-nitrophenyl-2-[^{18}F]fluoropropionic acid in dimethyl sulfoxide for 1 h at room temperature. [^{18}F]FP-OSP-1 was purified with high-performance liquid chromatography with a radiochemical yield of 20% at the end of purification. The specific activity was ~37 GBq/μmol (1 Ci/μmol). Radiochemical purity of the injected product was not reported. [^{18}F]FP-OSP-S was prepared similarly and had a similar radiochemical yield, radiochemical purity, and specific activity.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Studies of the cellular uptake and efflux of [^{18}F]FP-OSP-1 into 143B human osteosarcoma cell line (high HSPG expression), UM-SCC1 human neck and head squamous carcinoma cell line (low HSPG expression), and 293T human embryonic kidney cell line (low HSPG expression) cells were performed in culture (6). The accumulation was time-dependent with 0.4%, 0.2%, and 0.1% of the incubation dose in 143B, UM-SCC1, and 293T cells, respectively, after 60 min of incubation at 37°C. [^{18}F]FP-OSP-S exhibited little uptake in 143B cells. 143B cells retained ~50% of radioactivity after 60 min, whereas the radioactivity in UM-SCC1 and 293T cells was undetectable after 60 min. Immuofluorescence staining with anti-heparin/heparin sulfate antibody showed strong binding to 143B cells but not to UM-SCC1 or 293T cells. Preincubation of 143B cells with OSP-1 abrogated the antibody binding.

Animal Studies

Rodents

[PubMed]

Sun et al. (6) performed *ex vivo* biodistribution studies of [^{18}F]FP-OSP-1 (0.93 MBq (25 μCi)) at 2 h after intravenous injection in nude mice (n = 4/group) bearing 143B and UM-SCC1 xenografts. Tracer accumulation was significantly higher ($P < 0.05$) in 143B tumors (2.4 ± 0.1% injected dose per gram (ID/g)) than in UM-SCC1 tumors (1.2 ± 0.3% ID/g). The organ with the highest radioactivity was the intestine (1.3% ID/g). Accumulation in most normal organs was <1% ID/g. The radioactivity values in the blood and bone were 1% ID/g and 0.5% ID/g, respectively. Experiments with injection of [^{18}F]FP-OSP-S showed that [^{18}F]FP-OSP-S exhibited a significantly lower ($P < 0.05$) tracer accumulation in 143B tumors than [^{18}F]FP-OSP-1 (1.1% ID/g *versus* 2.5% ID/g). The tumor/muscle ratios were 3.49 ± 0.35 and 1.74 ± 0.05 for [^{18}F]FP-OSP-1 and [^{18}F]FP-OSP-S at 2 h, respectively ($P < 0.05$).

PET analysis was performed after intravenous injection of 3.7 MBq (100 μCi) [^{18}F]FP-OSP-1 or [^{18}F]FP-OSP-S in nude mice (n = 6/group) bearing 143B and UM-SCC1 xenografts (6). The 143B tumors were clearly visualized with high contrast compared with the UM-SCC1 tumors at 0.5–2 h after injection of [^{18}F]FP-OSP-1. Tumor accumulation was determined to be 1.43 ± 0.14% ID/g for 143B tumors and 0.75 ± 0.12% ID/g for UM-SCC1 tumors at 2 h after injection (P < 0.01). [^{18}F]FP-OSP-1 accumulation was three- to five-fold higher than [^{18}F]FP-OSP-S in 143B tumors at 0.5–2 h. The 143B tumor/muscle ratios were 3.77 ± 0.21 and 1.54 ± 0.18 for [^{18}F]FP-OSP-1 and [^{18}F]FP-OSP-S at 2 h, respectively (P < 0.05). The tumor/muscle ratios of [^{18}F]FP-OSP-S were similar in 143B and UM-SCC1 tumors.

Other Non-Primate Mammals

[PubMed]

No references are currently available.

Non-Human Primates

[PubMed]

No references are currently available.

Human Studies

[PubMed]

No references are currently available.

NIH Support

Intramural Research Program

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