^{111}In-Tetrameric Plectin-1 targeting peptide (4(βAKTLLPTP-GGS(PEG5000))KKK-^{111}In-DOTA-βA-NH_2)

^{111}In-tPTP

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Chemical name:	^{111}In-Tetrameric Plectin-1 targeting peptide (4(βAKTLLPTP-GGS(PEG5000))KKK-^{111}In-DOTA-βA-NH_2)	
Abbreviated name:	^{111}In-tPTP	
Synonym:	^{111}In-Tetrameric Plectin-1 targeting peptide	
Agent category:	Peptide	
Target:	Plectin-1	
Target category:	Receptor	
Method of detection:	Single-photon emission computed tomography (SPECT), gamma imaging	
Source of signal\contrast:	^{111}In	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about Plectin-1.

Background

[PubMed]

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Patients with pancreatic ductal adenocarcinoma (PDAC) have a median survival of 6 months and a 5-year survival rate of only 3% (1). PDAC is an aggressive cancer with early metastasis in >80% of patients. Early detection would be particularly useful for monitoring people at high risk of developing pancreatic cancer. Plectin-1 was identified in 100% of tested PDAC lesions and 60% of tested preinvasive PanIN III lesions (2). Plectin-1, a cytoskeletal component, is not expressed in the normal pancreas, liver, lymph node, lung, or peritoneum in humans. Using phage display screenings, the linear peptide Lys-Thr-Leu-Leu-Pro-Thr-Pro (KTLLPTP) (Plectin-1–targeting peptide, PTP) (3) has been found to specifically bind to Plectin-1 (4, 5), a protein present both inside and on the membrane of human and mouse PDAC cells but only on the inside of normal pancreatic cells. Kelly et al. (3) conjugated PTP to Cy5.5-labeled cross-linked iron oxide particles (CLIO-Cy5.5) for imaging Plectin-1 expression in PDAC, which suggests that Plectin-1 can serve as a biomarker for PDAC. Bausch et al. (2) labeled a tetrameric PTP with ^{111}In (4(βAKTLLPTP-GGS(PEG5000))KKK-^{111}In-DOTA-βA-NH_2) (^{111}In-tPTP) for single-photon emission computed tomography (SPECT) imaging for primary and metastatic pancreatic tumors.

Related Resource Links:

- Chapters in MICAD (Plectin-1)
- Gene information in NCBI (Plectin-1).
- Articles in Online Mendelian Inheritance in Man (OMIM) (Plectin-1)

Synthesis

[PubMed]

4(βAKTLLPTP-GGS(PEG5000))KKK-DOTA-βA-NH_2 (tPTP) (100 μg) was incubated with 185 MBq (5 mCi) $^{111}InCl_3$ in ammonium acetate buffer (pH 4.5) for 15 min at 40°C (2). ^{111}In-tPTP was purified with column chromatography. The yield, radiochemical purity, and specific activity of ^{111}In-tPTP were not reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Competition binding assays were performed in Plectin-1–positive L3.6pl PDAC cells using ^{111}In-tPTP with tPTP. tPTP had a K_i value of 830 nM (2).

Animal Studies

Rodents

[PubMed]

Bausch et al. (2) performed *ex vivo* biodistribution studies in mice bearing orthotopically implanted L3.6pl (n = 10), Panc1 (n = 5), or AK134 (n = 8) PDAC tumor cells at 4 h after

injection of 37 MBq (1 mCi) ^{111}In-tPTP. Tumor accumulation of radioactivity was 2.0% injected dose per gram (ID/g), 1.8% ID/g, 1.5% ID/g, and 0.5% ID/g for L3.6pl, Panc1, AK134, and normal pancreas, respectively. Accumulation in these mice was highest in the kidney with 15%–22% ID/g, followed by the liver with 1.7%–2.6% ID/g. Immunohistochemistry of sections of the pancreas and peritoneum metastases confirmed the presence of Plectin-1–expressing tumor cells in the pancreas and peritoneum.

SPECT scanning clearly visualized the three tumors and the kidneys at 4 h after injection. SPECT scanning located metastases in the peritoneum of two mice, which were confirmed with autopsy. In a model of AK134 PDAC liver metastasis, SPECT/computed tomography scanning clearly identified tumor lesions in the liver, which were confirmed with autopsy.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

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