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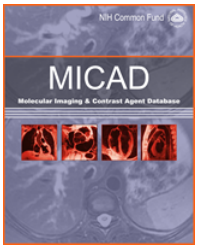

^{124}I-Anti–prostate stem-cell antigen back-mutated 2B3 diabody

^{124}I-bm2B3-Db8

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Chemical name:	^{124}I-Anti–prostate stem-cell antigen back-mutated 2B3 diabody	
Abbreviated name:	^{124}I-bm2B3-Db8	
Synonym:		
Agent category:	Antibody	
Target:	Prostate stem-cell antigen (PSCA)	
Target category:	Antigen	
Method of detection:	Positron emission tomography (PET)	
Source of signal:	^{124}I	
Activation:	No	
Studies:	• *In Vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about PSCA.

Background

[PubMed]

Prostate stem-cell antigen (PSCA) is a cell-surface protein (123 amino acids) that is expressed in normal prostate tissue and overexpressed in prostate cancer tissues (1). PSCA expression is detected in >80% of patients with local disease, including high expression in bone metastases (2). Elevated levels of PSCA are correlated with increased tumor stage, grade, and androgen independence (3). PSCA overexpression is also observed in bladder and pancreatic cancers (4).

The anti-PSCA murine monoclonal antibody (mAb) 1G8 has been shown to have anti-tumor activity (5). A humanized version of the 1G8 mAb (hu1G8) has been radiolabeled as ^{124}I-hu1G8 for tumor imaging in mice (6). However, it took ~1 week to observe an enhanced target/background ratio with positron emission tomography (PET) because of the slow kinetics of the mAb. A hu1G8 minibody fragment (2B3), a dimer of scFvs-C_H3 with a linker composed of 18 amino acids (molecular weight, ~80 kDa), has been developed and labeled as ^{124}I-2B3 minibody for tumor-targeting studies (7). To create a stable, rapidly clearing antibody

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fragment, the parental 2B3 diabody (p2B3-Db) (molecular weight, 55 kDa) was mutated back to the original mouse residues to produce a high-affinity, back-mutated diabody with a linker of 8 amino acids (bm2B3-Db8) (8). ^{124}I-p2B3-Db8 and ^{124}I-bm2B3-Db8 were evaluated for tumor imaging.

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (PSCA)
- Articles in OMIM

Synthesis

[PubMed]

The p2B3-Db8 and bm2B3-Db8 diabodies were labeled with [^{124}I]sodium iodide by the Iodogen method (8). ^{124}I-p2B3-Db8 and ^{124}I-bm2B3-Db8 were purified with gel filtration, and each labeled diabody exhibited a specific activity of ~5.6 MBq/nmol (0.15 mCi/nmol).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

With the use of PSCA competition assays, binding affinity (K_d) values were found to be 5.4 nM for p2B3-Db8, 1.9 nM for bm2B3-Db8, and 46 nM for 2B3 minibody (8).

Animal Studies

Rodents

[PubMed]

Leyton et al. (8) performed biodistribution studies with ^{124}I-p2B3-Db8 and ^{124}I-bm2B3-Db8 (~0.6 nmol/mouse) in nude mice bearing xenografts of the LAPC-9 (PSCA-positive) and PC-3 (PSCA-negative) tumor cell lines. The ^{124}I-bm2B3-Db8 uptake in the LAPC tumors was 1.02 ± 0.2% injected dose per gram (% ID/g) at 20 h after injection, whereas the uptake in the PC-3 tumors was 0.51 ± 0.1% ID/g. Accumulation of radioactivity in the lung, liver, spleen, and kidney was lower than in the LAPC-9 tumor. Accumulation in the thyroid and stomach was not reported. The tumor/blood and tumor/control tumor ratios were 1.2 and 2.0, respectively. On the other hand, the ^{124}I-p2B3-Db8 uptake was 0.57 ± 0.2% ID/g in the LAPC tumors and 0.34 ± 0.2% ID/g in the PC-3 tumors. The tumor/blood and tumor/control tumor ratios were 0.7 and 1.7, respectively. The tumor accumulation of ^{124}I-bm2B3-Db8 was lower than that of ^{124}I-2B3 minibody in the same tumor model as reported previously (7). PET imaging with ^{124}I-bm2B3-Db8 visualized the LAPC-9 tumor as early as 4 h after injection with a higher contrast at 12 h. No blocking experiment was performed.

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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