8. Engineered PSCA antibody for Targeted Radiology

(City of Hope)

5TH KDDF GLOBAL C&D TECH FAIR

Asset Overview

Product Type	Antibody
Diseases Area	Oncology
Indication	Prostate Cancer
Current Stage	Lead Optimization
Target	anti-PSCA
MoA	Prostate Stem Cell Antigen (PSCA) / Engineered anti-PSCA antibody delivering therapeutic radionuclides to prostate cancer
Brief Description	**Intact Antibodies and Engineered Fragments** • Protein engineering offers extensive control over biological properties such as PK and organ of clearance • Critical for efficacious delivery of therapeutic radionuclides **PET imaging to evaluate tumor targeting and clearance** • MicroPET imaging in xenograft-bearing mice using ^{124}I-labeled antibodies and fragments • Requires up to a week using intact antibodies • 20-120 h for scFv-Fc • 20 h (minibody) or 4 h (diabody) for smaller fragments **ScFv-Fc fragments with tailored PK** • Serum persistence of intact antibodies is governed by interaction between Fc and FcRn receptor • Point mutations can weaken or eliminate FcRn interactions and accelerate clearance • CEA-specific scFv-Fc fragments: - Wild-type - Single mutant: H435Q, I253A, H310A - Double mutant (DM) H435Q/H310A • Serum half-lives from 8 – 80 h
Intellectual Property	WO2021236645A1
Publication	-
Inventors	Anna M. Wu, Kirstin A. Zettlitz, Robert E. Reiter

Highlights

- PSCA expression is highly restricted and low levels were observed in the normal prostate, bladder and stomach but no expression was seen in the bone, bone marrow or lymph nodes
- Ex vivo biodistribution of [124I]A11 Mb at 44 h p.i. in hPSCA KI mice confirmed higher uptake in the stomach as seen in the in vivo immuno-PET scans (2.0 ± 0.2 %ID/g compared to 0.8 ± 0.1 %ID/g in wild type C57BL/6J)
- Ex vivo biodistribution (20 h post injection) confirmed that tumor uptake was significantly higher in RM-9-hPSCA compared with RM-9 (2.96 ± 0.7 %ID/g vs 1.36 ± 0.3 %ID/g, p = 0.0049)

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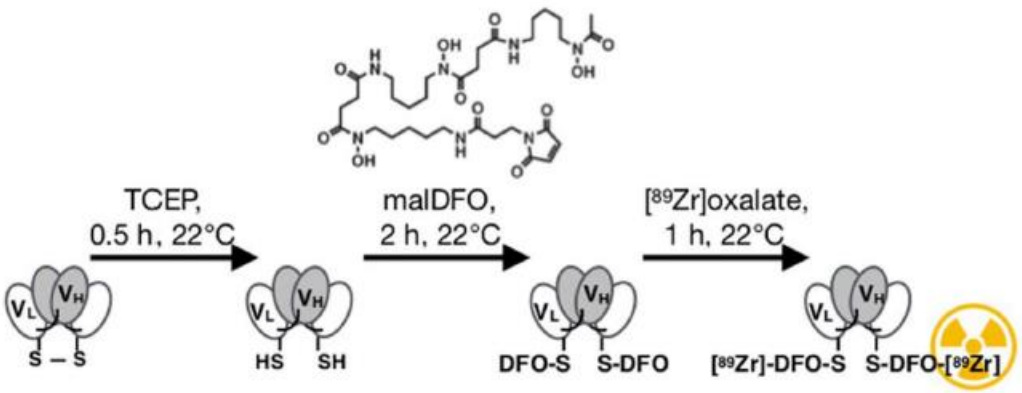
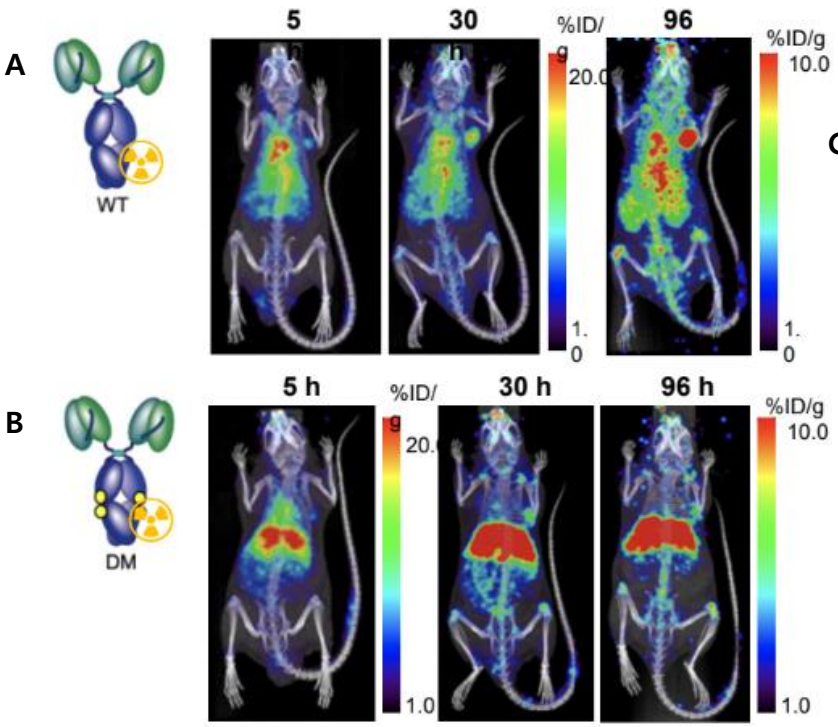
▶ Key Data

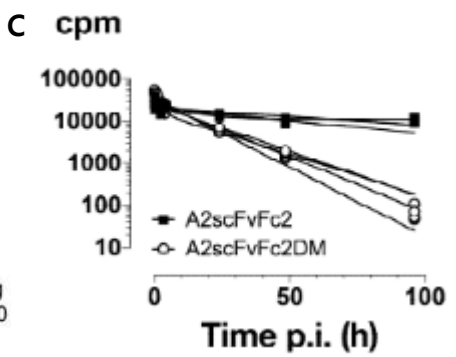
Prototype anti-PSCA cys-diabody



- The A2cDb is reduced under mild conditions and conjugated site-specifically with maleimide-DFO followed by chelation of Zr-89.

Lead candidate: Engineered anti-PSCA scFv-Fc





Half lives: 12.2 h (DM) vs 74.7 h (WT)
T:B ratio at 96 h: 32.8 (DM) vs 1.9 (WT)

A : 89Zr-labeled scFv-Fc wild type (WT)
B : candidate scFv-Fc DM