Matched Pair Theranostics with ^{99m}Tc and ^{188}Re-DETA-N-Onartuzumabfor the c-Met Receptor.

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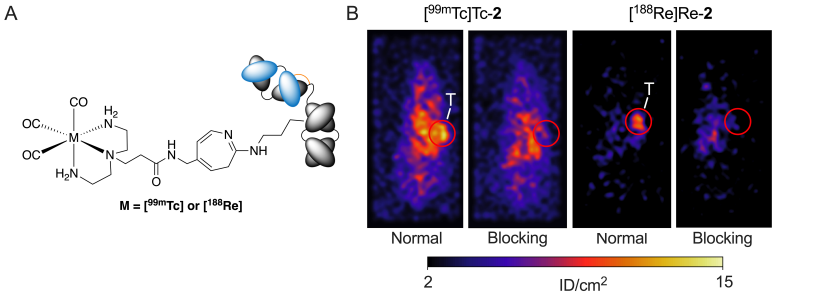
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Highly specific targeting vectors such as monoclonal antibodies (mAbs), enable a personalized radiotherapy that limits damage to the surrounding tissues.[1] The linkage between a biomolecule and the radionuclide can be made by employing rapid photoreactions.[2] The use of the matched pair ^{99m}Technetium ($t_{1/2}$ = 6 h, γ-ray = 141 keV [89%]) and ^{188}Rhenium ($t_{1/2}$ = 17 h, β_{max} = 2.12 MeV and γ-ray = 155 keV [15%]) have high potential for cancer therapy.

Herein, we report the synthesis, characterization, protein conjugation, and ^{99m}Tc/^{188}Re-radiolabeling studies on the cancer-specific mAb onartuzumab (MetMAb), with the novel photoactivatable DETA-N ligand (Figure A). Photochemical protein ligation reactions with onartuzumab were performed in water under ambient conditions in 15 min. Planar γ-ray scintigraph imaging (γ-eye, Bioemtech, Greece) was performed on female athymic nude mice bearing subcutaneous MKN-45 xenograft between 0 h and 24 h post-radiotracer injection (Figure B). Biodistribution experiments were performed after 24 h and 72 h. The tumor specificity of ^{99m}Tc/^{188}Re-onartuzumab was assessed *in vivo* by competitive inhibition (blocking) studies.

The photoradiosynthesis of [^{99m}Tc/^{188}Re][Tc/Re(CO)$_3$(DETA-N)]-onartuzumab was accomplished by irradiating the reaction mixture with 395 nm light for 15 min. Purification by size-exclusion methods yielded the radiolabeled antibody in a RCP over 99% (^{99m}Tc and ^{188}Re) and an overall RCY of 17% (^{99m}Tc) and 18% (^{188}Re). Tumor uptake reached 20.20±4.05%ID g^{-1} for ^{99m}Tc-onartuzumab and 22.13±3.11%ID g^{-1} for ^{188}Re-onartuzumab after 24 h and 20.21±1.47 %ID g^{-1} for ^{188}Re-onartuzumab after 72 h in the normal groups. Blocking experiments confirmed tumor specificity with a reduction in tumor uptake of ~70% at the time points for ^{99m}Tc and ^{188}Re.

[^{99m}Tc/^{188}Re][Tc/Re(CO)$_3$(DETA-N)]-onartuzumab is a promising candidate for further use in theranostic studies of tumors presenting high expression of the c-MET receptor.



A: Structure of [$^{99m/188}$Re][Tc/Re(CO)$_3$(DETA-N)]-onartuzumab; B: Szintigraphs of the mice (left: ^{99m}Tc, right:^{188}Re).

[1] J. Crudo, S. de Castiglia *et al.*, *J. Radioanal. Nucl. Chem.* **2004**, *261*, 337-342.
[2] D. F. Earley, J. P. Holland *et al., JACS Au* **2022**, *2*, 646–664.