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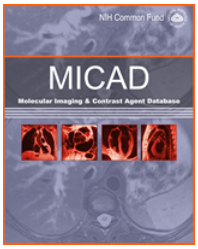

^{111}In-Diethylenetriamine pentaacetic acid-anti-epithelial glycoprotein-1 hRS7 humanized monoclonal antibody

^{111}In-DTPA-hRS7

Kam Leung, PhD[1]

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Chemical name:	^{111}In-Diethylenetriamine pentaacetic acid-anti-epithelial glycoprotein-1 hRS7 humanized monoclonal antibody	
Abbreviated name:	^{111}In-DTPA-hRS7	
Synonym:		
Agent category:	Antibody	
Target:	Epithelial glycoprotein-1 (EGP-1, also known as TROP2)	
Target category:	Receptor	
Method of detection:	Single-photon emission computed tomography (SPECT), gamma planar imaging	
Source of signal/ contrast:	^{111}In	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about EGP-1

Background

[PubMed]

Epithelial glycoprotein-1 (EGP-1, also known as TROP2) is a transmembrane glycoprotein (46 kDa) identified with murine IgG_1 monoclonal antibody (mAb) RS7 raised against human non-small cell lung carcinoma (1). EGP-1 is also present in human carcinomas of the stomach, bladder, breast, ovary, uterus, and prostate, but it is not expressed in most normal tissues. EGP-1 is expressed at low levels in glandular cells in the bronchus, breast, prostate, skin, and pancreas. EGP-1 activates intracellular calcium mobilization (2) and protein kinase C (3) after binding with RS7. EGP-1 is a cell-surface receptor with unknown physiological ligand and cellular functions. However, EGP-1 has been implicated in the activation of the ERK/MAPK pathway, leading to downstream alterations in cellular proliferation, migration, invasion, and survival of cancer cells (4). EGP-1 overexpression

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

Corresponding author.

has been associated with increased tumor invasiveness and decreased overall survival rates in multiple types of human carcinomas (5, 6). van Rij et al. (7) evaluated ^{111}In-diethylenetriamine pentaacetic acid-hRS7 (^{111}In-DTPA-hRS7) as a ^{111}In-based single-photon emission computed tomography (SPECT) agent in human prostate PC-3 tumors in nude mice.

Related Resource Links:

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

Synthesis

[PubMed]

DTPA-hRS7 was prepared by conjugation of *p*-isothiocyanatobenzyl-DTPA to hRS7 at a molar ratio of 50:1 (pH 9.5) for 60 min at 25°C (7). DTPA-hRS7 was purified with dialysis. There were two DTPA moieties per mAb. DTPA-hRS7 was incubated with $^{111}InCl_3$ in 0.25 M NH_4Ac buffer (pH 5.4) for 60 min at 25°C. ^{111}In-DTPA-hRS7 was purified with column chromatography. The specific activity was estimated to be 606 MBq/nmol (16.4 mCi/nmol). No radiochemical yield or radiochemical purity was reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Immunostaining of PC-3 tumor sections with hRS7 showed the expression of EGP-1 in the membranes and cytosol of PC-3 tumor cells (7). Immunochemical analysis of three human primary prostate tumor sections showed high homogeneous and consistent expression of EGP-1 in all three tumors and metastases in a lymph node and in the liver. The immunoreactivity of ^{111}In-DTPA-hRS7 was >80%.

Animal Studies

Rodents

[PubMed]

van Rij et al. (7) injected 0.4 MBq (0.011 mCi, 0.66 pmol) ^{111}In-DTPA-hRS7 into male nude mice (n = 5/group) bearing the EGP-1–positive PC-3 human prostate tumors for *ex vivo* biodistribution studies. *Ex vivo* tumor accumulation was 61 ± 15% injected dose/gram (ID/g) at 3 d after injection. The tumor/blood ratio was 7.2. The radioactivity levels in the other organs were <10% ID/g. Co-injection of excess hRS7 (0.66 nmol) inhibited the accumulation in the tumors to 22 ± 7% ID/g and the tumor/blood ratio to 3.0 at 3 d after injection. Little inhibition was observed in the other organs.

van Rij et al. (7) performed *ex vivo* biodistribution and SPECT imaging studies in male nude mice (n = 5/group) bearing orthotopic PC-3 xenografts (17 d after tumor inoculation) at 3 d after injection of 37 MBq (1 mCi, 0.066 nmol)) ^{111}In-DTPA-hRS7. Prostate tumor accumulation was 32 ± 13% ID/g. The radioactivity levels in the other organs were <7% ID/g, with <4% ID/g in the normal prostate. Co-injection of excess hRS7 (3.3 nmol) inhibited accumulation in the tumors to 6.1 ± 1.7% ID/g. Little inhibition was observed in the other organs. SPECT imaging showed that the tumors were clearly visualized in the prostate of all mice. The tumor/liver ratio was 7.3.

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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