^{124}I-Anti-CD44v6 chimeric monoclonal antibody U36

^{124}I-cMAb U36

Kam Leung, PhD[1]

Created: October 5, 2007; Updated: November 19, 2007.

Chemical name:	^{124}I-Anti-CD44v6 chimeric monoclonal antibody U36	
Abbreviated name:	^{124}I-cMAb U36, ^{124}I-U36	
Synonym:		
Agent Category:	Antibody	
Target:	CD44v6	
Target Category:	Antibody-antigen binding	
Method of detection:	PET	
Source of signal:	^{124}I	
Activation:	No	
Studies:	• *In Vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about CD44.

Background

[PubMed]

Extracellular matrix (ECM) adhesion molecules consist of a complex network of fibronectins, collagens, chondroitins, laminins, glycoproteins, heparin sulfate, tenascins, and proteoglycans that surround connective tissue cells, and they are mainly secreted by fibroblasts, chondroblasts, and osteoblasts (1). Cell substrate adhesion molecules are considered essential regulators of cell migration, differentiation, and tissue integrity and remodeling. These molecules play a role in inflammation, but they also participate in the process of invasion and metastasis of malignant cells in the host tissue (2). Invasive tumor

[1] National Center for Biotechnology Information, NLM, NIH, Bethesda, MD; Email: micad@ncbi.nlm.nih.gov.

NLM Citation: Leung K. ^{124}I-Anti-CD44v6 chimeric monoclonal antibody U36. 2007 Oct 5 [Updated 2007 Nov 19]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.

cells adhere to the ECM, which provides a matrix environment for permeation of tumor cells through the basal lamina and underlying interstitial stroma of the connective tissue. Overexpression of matrix metalloproteinases by tumor cells allows intravasation of tumor cells into the circulatory system after degrading the basement membrane and ECM (3).

The splice variant v6 of the cell membrane glycoprotein CD44 (CD44v6) is expressed in only a few normal epithelial tissues (e.g., thyroid and prostate gland). CD44 binds to ECM and is associated with cell adhesion, lymphocyte activation, and tumor cell metastasis (4, 5). Elevated levels of CD44v6 have been found in epithelial tumors associated with a poor prognosis for cancer patients (5). U36, an anti-CD44v6 chimeric (mouse/human) monoclonal antibody (cMAb), was found not bind to follicles or C cells from normal human thyroid (6). CD44v6 is generally highly expressed in thyroid carcinoma (7). ^{124}I-cMAb U36 was developed for imaging of CD44v6 expression in thyroid carcinomas and other epithelial tumors (8, 9).

Synthesis

[PubMed]

cMAb U36 was labeled with sodium [^{124}I]iodide by electrophilic radioiodination *via* the chloramine-T (8) or Iodogen method (9). ^{124}I-cMAb U36 was purified by gel filtration. Both methods provided labeling yields of >70%. The radiochemical purity was >97%. No specific activity values were reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Fortin et al. (8) reported that high-affinity ^{125}I-cMAb U36 binding sites (B_{max} = 570,000 ± 30,000 sites/cell, K_d = 11 ± 2 nM) were found on the cell surfaces of KAT-4 human anaplastic thyroid carcinoma cells lacking the sodium iodide symporter. Furthermore, 20% of ^{125}I-cMAb U36 accumulated in the cells after 24 h at 37°C. The accumulation was reduced to 1% by excess cMAb U36. The labeled cells retained 29% of radioactivity after incubation in tracer-free medium alone for another 24 h at 37°C. No free ^{125}I could be detected in the incubation medium. Verel et al. (9) reported that the immunoreactivity of ^{124}I-cMAb U36 was 91.1 ± 3.9%.

Animal Studies

Rodents

[PubMed]

Fortin et al. (8) performed biodistribution and scintigraphic studies of ^{124}I-cMAb U36 in nude mice bearing KAT-4 tumors in the left flank and the right front leg. The organs with the highest accumulation of ^{124}I-cMAb U36 (in percent injected dose per gram (% ID/g))

were the urinary bladder (13.1 ± 4.0), lung (7.0 ± 1.3), heart (5.2 ± 1.3), spleen (4.5 ± 1.4), liver (3.9 ± 0.5), and kidneys (3.8 ± 1.0) at 24 h after injection. ^{124}I-cMAb U36 uptake in the flank tumors was 8.2 ± 3.6% ID/g, 13.7 ± 0.7% ID/g, 21.8 ± 2.8% ID/g, and 12.8 ± 5.2% ID/g at 4, 24, 48, and 72 h, respectively. The uptake values in the leg tumors were similar to those of the flank tumors. The radioactivity in the thyroid was <1% ID/g at all time points studied. ^{124}I-cMAb U36 exhibited a high blood radioactivity (21.8% ID/g) at 4 h, which gradually decreased to 9.5% ID/g at 72 h. On the other hand, ^{124}I-cMAb U36 exhibited a low accumulation in the stomach with 5.1% ID/g at 4 h and 1.0% ID/g at 72 h. Scintigraphic images were obtained in the tumor-bearing mice at 24, 48, and 72 h after ^{124}I-cMAb U36 injection. The tumors were clearly visible at all time points with the highest uptakes at 48 h. No blocking experiment was performed.

Verel et al. (9) performed biodistribution and scintigraphic studies in nude mice bearing tumors from the HNX-OE human head and neck tumor cell line. Co-injection of ^{124}I-cMAb U36 and ^{131}I-cMAb U36 with a similar iodine/MAb molar ratio provided similar tissue uptake values. Selective tumor uptake was confirmed with positron emission tomography imaging at 24, 48, and 72 h, which detected 15 out of 15 tumors.

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.

References

1. Bosman F.T., Stamenkovic I. Functional structure and composition of the extracellular matrix. J Pathol. 2003;**200**(4):423–8. PubMed PMID: 12845610.
2. Jiang W.G., Puntis M.C., Hallett M.B. Molecular and cellular basis of cancer invasion and metastasis: implications for treatment. Br J Surg. 1994;**81**(11):1576–90. PubMed PMID: 7827878.
3. Albelda S.M. Role of integrins and other cell adhesion molecules in tumor progression and metastasis. Lab Invest. 1993;**68**(1):4–17. PubMed PMID: 8423675.
4. Van Hal N.L., Van Dongen G.A., Rood-Knippels E.M., Van Der Valk P., Snow G.B., Brakenhoff R.H. Monoclonal antibody U36, a suitable candidate for clinical

immunotherapy of squamous-cell carcinoma, recognizes a CD44 isoform. Int J Cancer. 1996;**68**(4):520–7. PubMed PMID: 8945625.

5. Heider K.H., Kuthan H., Stehle G., Munzert G. CD44v6: a target for antibody-based cancer therapy. Cancer Immunol Immunother. 2004;**53**(7):567–79. PubMed PMID: 14762695.
6. Schrijvers A.H., Quak J.J., Uyterlinde A.M., van Walsum M., Meijer C.J., Snow G.B., van Dongen G.A. MAb U36, a novel monoclonal antibody successful in immunotargeting of squamous cell carcinoma of the head and neck. Cancer Res. 1993;**53**(18):4383–90. PubMed PMID: 8364934.
7. Aogi K., Kitahara K., Urquidi V., Tarin D., Goodison S. Comparison of telomerase and CD44 expression as diagnostic tumor markers in lesions of the thyroid. Clin Cancer Res. 1999;**5**(10):2790–7. PubMed PMID: 10537343.
8. Fortin M.A., Salnikov A.V., Nestor M., Heldin N.E., Rubin K., Lundqvist H. Immuno-PET of undifferentiated thyroid carcinoma with radioiodine-labelled antibody cMAb U36: application to antibody tumour uptake studies. Eur J Nucl Med Mol Imaging. 2007;**34**(9):1376–87. PubMed PMID: 17277931.
9. Verel I., Visser G.W., Vosjan M.J., Finn R., Boellaard R., van Dongen G.A. High-quality 124I-labelled monoclonal antibodies for use as PET scouting agents prior to 131I-radioimmunotherapy. Eur J Nucl Med Mol Imaging. 2004;**31**(12):1645–52. PubMed PMID: 15290121.