^{125}I-Labeled monoclonal antibody, mAb RM2, targeting the RM2 antigen

[^{125}I]-mAb RM2

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Chemical name:	^{125}I-Labeled monoclonal antibody, mAb RM2, targeting the RM2 antigen	
Abbreviated name:	[^{125}I]-mAb RM2	
Synonym:		
Agent Category:	Antibody	
Target:	RM2 antigen	
Target Category:	Antigen	
Method of detection:	Single-photon emission computed tomography (SPECT); gamma planar imaging	
Source of signal / contrast:	^{125}I	
Activation:	No	
Studies:	• *In vitro* • Rodents	Structure not available in PubChem.

Background

[PubMed]

A prostate-specific antigen (PSA) level of >4 ng/mL in the serum is considered to indicate the development of prostate cancer in men; however, PSA levels may be elevated in an individual due to benign prostatic hyperplasia or prostatitis (1). In addition, PSA is an organ-specific biomarker, not a cancer-specific biomarker, which means that the serum PSA level cannot be used to determine the stage of the cancer (2). Therefore, the occurrence of prostate cancer in men with high PSA levels has to be confirmed with an

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invasive and painful biopsy (2). In an effort to develop a more reliable diagnostic test for prostate cancer, a monoclonal antibody (mAb) that recognizes a disialoganglioside (β1,4-GalNAc-disialyl-Lc4; designated as the RM2 antigen (mAb RM2)) was developed. mAb RM2 was shown to have a high reactivity toward malignant prostate cancer cells, but it exhibited little or no binding to cells obtained from the benign glands (1). It was also shown that the RM2 antigen was overexpressed on prostate cancer cells, and the increased level of the antigen detected in the serum of prostate cancer patients correlated with the Gleason grading of the neoplasm. From this study, the investigators concluded that the RM2 antigen may be suitable for the detection of prostate cancer.

Early detection and treatment of cancer is often beneficial for the patient, but prostate cancer is not easily diagnosed during the early stages because imaging techniques that are used to detect this cancer, such as ultrasound, magnetic resonance imaging, and computed tomography, do not yield reliable results (3). Therefore, mAb RM2 was radioiodinated ([^{125}I]-mAb RM2) in an attempt to produce a tracer that could be used to detect prostate cancer (3). In a preliminary study, the biodistribution of [^{125}I]-mAb RM2 was investigated in athymic *nu/nu* mice bearing PC-3 cell tumors (a human prostate adenocarcinoma cell line that overexpresses the RM2 antigen).

Synthesis

[PubMed]

mAb RM2 was produced as described elsewhere (1). The mAb was labeled with ^{125}I using the chloramine-T method, and the specific activity of [^{125}I]-mAb RM2 was reported to be 376 MBq/6.66 nmol (13.9 mCi/6.66 nmol). The radiochemical yield, radiochemical purity, and stability of the labeled mAb were not reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The uptake of [^{125}I]-mAb RM2 by PC-3 cells (an androgen-dependent cell line), LNCaP cells (a human prostate carcinoma cell line that overexpresses the RM2 antigen; an androgen-independent cell line), and MCF-7 cells (a human mammary gland adenocarcinoma cell line that does not express the RM2 antigen) was investigated (3). The cells were incubated with 3.7 kBq (0.1 μCi) [^{125}I]-mAb RM2 without or after a 48-h exposure to nonradiolabeled mAb RM2 (concentration not reported) for various time points ranging from 1 h to 6 h. Radioactivity taken up by the different cells was reported as percent uptake of added dose (% AD). The amount of radioactivity taken up by the PC-3 cells increased from 0.045 ± 0.011% AD at 1 h to 0.061 ± 0.005% AD at 6 h ($P < 0.05$); for the LNCaP cells, the accumulation increased from 0.029 ± 0.005% AD at 1 h to 0.040 ± 0.006% AD at 6 h ($P < 0.05$). When the PC-3 cells and the LNCaP cells were pre-exposed to nonradioactive mAb RM2, no increase in uptake of the probe was observed. The MCF-7 cells showed no increase in the incorporation of radioactivity from 1 h to 6 h with or without exposure to nonradioactive mAb RM2. This study indicated that mAb

RM2 had a binding specificity for the transformed prostate cell lines that overexpress the RM2 antigen.

Animal Studies

Rodents

[PubMed]

The biodistribution of [^{125}I]-mAb RM2 was studied in athymic nu/nu male mice bearing PC-3 cell tumors (3). The animals (n = 5 mice/time point) were injected with ~0.3 MBq (10 μCi) [^{125}I]-mAb RM2 through the tail vein and euthanized at 24, 48, and 72 h postinjection (p.i.) to harvest the organs of interest and to determine the amount of radioactivity taken up by the various tissues. Data obtained from this study were expressed as percent of radioactivity of injected dose per gram tissue (% ID/g).

Table 1: Uptake of radioactivity from [^{125}I]-mAb RM2 by various organs of mice (3)**.**

Tissue	Time points (h) postinjection		
	24	48	72
	Accumulated radioactivity (% ID/g)*		
Blood	2.88 ± 0.63	0.93 ± 0.16	0.50 ± 0.08
Liver	4.32 ± 0.90	3.00 ± 0.49	2.23 ± 0.28
Muscle	0.21 ± 0.07	0.08 ± 0.02	0.05 ± 0.01
Prostate	0.48 ± 0.21	0.19 ± 0.10	0.15 ± 0.02
Tumor	0.40 ± 0.03	0.27 ± 0.10	0.17 ± 0.02
Tumor/muscle ratio#	2.12 ± 0.88	3.13 ± 0.67	3.47 ± 0.78

*** For complete data, see Hasegawa et al.** (3)**; #: *P* < 0.05 for 24 h *versus* 72 h.**

The uptake of radioactivity from [^{125}I]-mAb RM2 by select organs, including tumors, is presented in Table 1. At 24 h p.i., maximum uptake of label was in the liver followed by blood. Although both tissues showed loss of radioactivity from 24 h p.i. to 72 h p.i., the decrease in the blood was faster than that in the liver, suggesting that the probe was excreted from the body through the hepatobiliary system. The tumor/muscle (T/M) ratio was reported to significantly increase ($P < 0.05$) from 24 h p.i. (2.12 ± 0.88) to 72 h p.i. (3.47 ± 0.78). The insignificant difference in the uptake of radioactivity between the normal prostate tissue and the PC-3 cell tumors in the mice was attributed to the differences between the human and mouse species (the PC-3 cells used to generate tumors in the rodents were of human origin) (3).

From these preclinical studies, the investigators concluded that the radiolabeled mAb RM2 could probably be used in conjunction with the PSA test to diagnose prostate cancer

(3). They also suggested that mAb RM2 may be used by itself to distinguish between malignant and benign tumors in the prostate gland.

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.

Supplemental Information

[Disclaimers]

No information is currently available.

References

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