^{125}I-Anti-malondialdehyde-modified low-density lipoprotein monoclonal antibody

^{125}I-MDA2

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Chemical name:	^{125}I-Anti-malondialdehyde-modified low-density lipoprotein monoclonal antibody	
Abbreviated name:	^{125}I-MDA2	
Synonym:		
Agent category:	Antibody	
Target:	Malondialdehyde-modified low-density lipoprotein (MDA-LDL)	
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 • Other non-primate mammals	Click on protein, nucleotide (RefSeq), and gene for more information about apolipoprotein B.

Background

[PubMed]

Apolipoprotein E (apoE) is essential for the normal catabolism of triglyceride-rich lipoprotein chylomicrons (lipoprotein particles) (1). Oxidation of low-density lipoprotein (LDL) generates a number of highly reactive short chain-length aldehydic fragments of

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oxidized fatty acids capable of conjugating with lysine residues of apoliprotein B and other proteins. Oxidized LDL is present in atherosclerotic lesions and is essential for formation of foam cells in atherosclerotic plaques. During atherogenic conditions, depositions of lipids and extracellular matrix proteins on the endothelial cell surfaces of the aorta and cells lead to the development of atherosclerotic plaques (2), which may erode and rupture. MDA2 is a murine monoclonal antibody (mAb) to malondialdehyde-lysine epitopes of MDA-LDL and other oxidatively modified proteins but not to normal LDL (3). Tsimikas and colleagues (4-6) have studied ^{125}I-MDA2 for imaging atherosclerotic plaques in small animals.

Synthesis

[PubMed]

MDA2 was labeled with ^{125}I *via* the lactoperoxidase/glucose oxidase method (5). ^{125}I-MDA2 had a specific activity of 555 MBq/μmol (15 mCi/μmol).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

^{125}I-MDA2 has been shown to bind specifically to human MDA-LDL but not to normal human LDL, high-density lipoprotein, very low-density lipoprotein, or bovine serum albumin (5).

Animal Studies

Rodents

[PubMed]

Tsimikas et al. (6) measured accumulation of ^{125}I-MDA2 in the aorta of 6-month-old LDLR$^{-/-}$ knockout mice that were fed a high-fat, high-cholesterol diet (n = 9 mice), a normal chow diet (n = 8 mice), or a normal chow diet supplemented with vitamin E+C (n = 9 mice) for 6 months. The aortic weight was 35, 18, and 15 mg, respectively. The percent of injected dose was 0.14 ± 0.03, 0.03 ± 0.01, and 0.03 ± 0.01, respectivelyat 24 h after injection. There was a high amount of oxidized LDL in the aorta of mice fed the high-fat diet.

Other Non-Primate Mammals

[PubMed]

Tsimikas et al. (5) performed *ex vivo* assessment of ^{125}I-MDA2 for atherosclerotic lesions in LDL receptor–deficient Watanabe heritable hyperlipidemic rabbits (WHHL, n = 7) and normal New Zealand white rabbits (NZW, n = 2) at 24 h after injection. ^{125}I-Halb, an isotype-matched irrelevant mAb that binds to human albumin, was used as a control. The

blood half-life was 12 h for ^{125}I-MDA2 and 9 h for ^{125}I-Halb in both WHHL and NZW rabbits. Aortic autoradiography was performed, and the mean uptake of mAbs was measured as the percent of injected dose per gram (% ID/g) of aortic tissueat 24 h after injection. Mean uptake of ^{125}I-MDA2 in the entire aorta (0.09% ID/g) was 17.4-fold higher in WHHL than in NZW aortas ($P < 0.001$) and 2.8-fold higher than mean uptake of ^{125}I-Halb in the WHHL aortas ($P < 0.01$). ^{125}I-MDA2 also had higher specificity for lesioned areas than did ^{125}I-Halb (plaque/normal ratio, 6.3 *versus* 2.9, $P < 0.001$). Autoradiographic analysis of aortasat 24 h after injection from NZW rabbits injected with ^{125}I-MDA2 did not yield any visible signal. Injection of 10 mg MDA-LDL 24 h after injection of ^{125}I-MDA2 in WHHL rabbits reduced the residual blood radioactivity from 31% to 7.5% ($P < 0.001$). There was no significant difference in the aortic accumulation in the two groups; however, there was an improvement in the plaque/blood ratio from 0.6 to 1.4. Autoradiographs of aortas of ^{125}I-MDA2-injected WHHL rabbits revealed uptake in lipid-stained lesions with an absence of signal in adjacent normal arterial tissue. Immunostaining of WHHL lesions revealed that uptake was highest in areas with abundant foam cells and in lipid-rich necrotic core areas.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

NIH Support

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