Anti-vascular cell adhesion molecule-1 monoclonal antibody M/K-2.7 microbubbles

MB$_{VCAM-1}$

Kam Leung, PhD[1]

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Chemical name:	Anti-vascular cell adhesion molecule-1 monoclonal antibody M/K-2.7 microbubbles	
Abbreviated name:	MB$_{VCAM-1}$	
Synonym:		
Agent category:	Antibody	
Target:	Vascular cell adhesion molecule-1 (VCAM-1)	
Target category:	Adhesion molecule	
Method of detection:	Ultrasound (US)	
Source of signal:	Microbubbles	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about VCAM-1.

Background

[PubMed]

Ultrasound is widely used imaging modality (1), and its role in noninvasive molecular imaging with ligand-carrying microbubbles (MBs) is expanding (2). MBs are spherical cavities encapsulated in a shell and filled by a gas. The shells are made of phospholipids, surfactants, denatured human serum albumin, or synthetic polymers. Ligands and antibodies can be incorporated into the MB shell surface. MBs are usually 2–8 μm in

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

Corresponding author.

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diameter. MBs of this size provide a strongly reflective interface and resonate to ultrasound waves. They are used as ultrasound contrast agents in imaging of inflammation, angiogenesis, intravascular thrombus, and tumors (2-4). They also can potentially be used for drug and gene delivery (5).

Endothelial cells are important cells in inflammatory responses (6, 7). Bacterial lipopolysaccharide (LPS), virus, inflammation, and tissue injury increase tumor necrosis factor α (TNFα), interleukin-1 (IL-1), and other cytokine and chemokine secretion. Leukocyte emigration from blood is dependent on their ability to roll along and subsequently adhere to endothelial cell surfaces. Inflammatory mediators and cytokines induce chemokine secretion from endothelial cells and other vascular cells and increase their expression of cell surface adhesion molecules, such as intracellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), integrins, and selectins. Chemokines are chemotactic toward leukocytes and toward sites of inflammation and tissue injury. The movements of leukocytes through endothelial junctions into the extravascular space are highly orchestrated through various interactions with different adhesion molecules on endothelial cells (8).

VCAM-1 is found in very low amounts on the cell surface of resting endothelial cells and other vascular cells, such as smooth muscle cells and fibroblasts (9-13). VCAM-1 binds to its counterligand very late antigen-4 (VLA-4) integrin on the cell-surface of leukocytes. IL-1 and TNFα increase expression of VCAM-1 and other cell adhesion molecules on the vascular endothelial cells, which leads to leukocyte adhesion to the activated endothelium. Furthermore, VCAM-1 expression was also induced by oxidized low-density lipoproteins under atherogenic conditions (14). Overexpression of VCAM-1 by atherosclerotic lesions plays an important role in their progression towards vulnerable plaques, which may erode and rupture. MBs targeted with antibodies against VCAM-1 are being developed as a noninvasive agent for VCAM-1 expression in vascular endothelial cells during different stages of inflammation in atherosclerosis (15).

Related Resource Links:

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

Synthesis

[PubMed]

For targeted MBs, Kaufmann et al. (15) prepared biotinylated MBs by sonication of an aqueous dispersion of decafluorobutane gas, distearoylphosphatidylcholine, polyoxyethylene-40-stearate, and distearoylphosphatidylethanolamine-polyethyleneglycol-biotin. MBs were combined with streptavidin, washed, and conjugated with biotinylated mouse monoclonal antibody M/K-2.7 against VCAM-1 (MB_{VCAM-1})

or isotype control monoclonal antibody (MB_c). The MBs were about 3-4 μm in diameter. An antibody/MB ratio was estimated to be >50,000 by flow cytometry.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Kaufmann et al. (15) reported that MB_{VCAM-1} (3×10^6/ml) perfused through the flow chamber coated with endothelial cells at a wall-shear rate of 0.5-12.0 dynes/cm^2. There was a significantly greater number of MB_{VCAM-1} attached to TNF–activated endothelial cells than to normal endothelial cells at 0.5 dynes/cm^2 ($P < 0.05$). The number of MB_{VCAM-1} adherent to activated endothelial cells decreased with increasing shear rate. No attachment of MBc to normal and activated endothelial cells was observed.

Animal Studies

Rodents

[PubMed]

Kaufmann et al. (15) studied MB_{VCAM-1} attachment to aortic plaque by microscopy of the thoracic aorta 10 min after intravenous injection in wild-type or apolipoprotein E–deficient ($apoE^{-/-}$) mice on either normal chow or hypercholesterolemic diet. Contrast-enhanced ultrasound (CEU) molecular imaging of the thoracic aorta 10 min after intravenous MB injection was performed for the same animal groups. Aortic attachment of MB_{VCAM-1} and CEU signal were very low in control wild-type mice on normal chow diet, whereas $apoE^{-/-}$ mice on hypercholesterolemic diet exhibited the highest attachment and signal. Aortic attachment of MB_{VCAM-1} and CEU signal for MB_{VCAM-1} differed between treatment groups according to the extent of VCAM-1–positive plaque formation (median CEU videointensity was 1.8, 3.7, 6.8, and 11.2 for wild-type mice on normal chow diet, wild-type mice on hypercholesterolemic diet, $apoE^{-/-}$ mice on normal chow diet, and $apoE^{-/-}$ mice on hypercholesterolemic diet, respectively; $P < 0.001$). On the other hand, MB_c exhibited minimal contrast in all groups.

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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