[^{18}F]Fluorobenzoyl-((VHPKQHRGGSY)$_2$K)$_2$KK

[^{18}F]4V

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Created: June 29, 2010; Updated: September 30, 2010.

Chemical name:	[^{18}F]Fluorobenzoyl-((VHPKQHRGGSY)$_2$K)$_2$KK	
Abbreviated name:	[^{18}F]4V	
Synonym:		
Agent category:	Peptide	
Target:	Vascular cell adhesion molecule-1 (VCAM-1)	
Target category:	Receptor	
Method of detection:	Positron emission tomography (PET)	
Source of signal:	^{18}F	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about VCAM-1.

Background

[PubMed]

Endothelial cells are important cells in inflammatory responses (1-2). Bacterial lipopolysaccharide, virus, inflammation, and tissue injury increase secretion of tumor necrosis factor α (TNFα), interleukin-1 (IL-1), and other cytokines and chemokines. Emigration of leukocytes from blood is dependent on their ability to 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

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NLM Citation: Leung K. [^{18}F]Fluorobenzoyl-((VHPKQHRGGSY)$_2$K)$_2$KK. 2010 Jun 29 [Updated 2010 Sep 30]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.

orchestrated through various interactions with different adhesion molecules on endothelial cells (3).

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 (4-8). VCAM-1 binds to the 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 is also induced by oxidized low-density lipoproteins under atherogenic conditions (9). Overexpression of VCAM-1 by atherosclerotic lesions plays an important role in their progression to vulnerable plaques, which may erode and rupture. Cross-linked iron oxide nanoparticles targeted with anti-VCAM-1 antibody are being developed as a noninvasive agent for VCAM-1 expression in vascular endothelial cells during different stages of inflammation in atherosclerosis (10). A tetrameric linear peptide, $((VHPKQHRGGSY)_2K)_2KK$ (TLP), was identified with phage screening against VCAM-1 and radiolabeled with 4-[^{18}F]fluorobenzaldehyde ([^{18}F]FBA) to form [^{18}F]fluorobenzoyl-TLP ([^{18}F]4V) as a potential positron emission tomography (PET) imaging agent to target atherosclerotic plaques and myocardial ischemic lesions (11).

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (VCAM-1).
- Articles in OMIM
- Clinical trials (VCAM-1)
- Drug information in FDA

Synthesis

[PubMed]

Nahrendorf et al. (11) reported the synthesis of [^{18}F]4V. The tetrameric linear peptide, TLP, was synthesized using standard Fmoc chemistry on an amide resin with a peptide synthesizer. TLP was then reacted with [^{18}F]FBA to form [^{18}F]4V using an automated synthesizer. [^{18}F]4V was purified with high-performance liquid chromatography. The specific activity, radiochemical purity, radiolabeling yield, and total time of synthesis of [^{18}F]4V were not reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Nahrendorf et al. (11) measured the binding affinity of TLP to human VCAM-1 with a 50% inhibition concentration (IC_{50}) value of 87 nM (349-fold better than the linear monomer) using ^{99m}Tc-DOTA-TLP as a ligand tracer. The accumulation of [^{18}F]4V (100 ng) in murine heart endothelial cells in culture was inhibited by >95% with 1 μg murine

soluble VCAM-1. Incubation of [^{18}F]4V with excised aortas from wild-type mice, apoE$^{-/-}$ mice, and apoE$^{-/-}$ mice treated with atorvastatin showed that aortas from apoE$^{-/-}$ mice exhibited >2-fold higher radioactivity than the aortas from wild-type mice and apoE$^{-/-}$ mice treated with atorvastatin.

Animal Studies

Rodents

[PubMed]

Nahrendorf et al. (11) performed *ex vivo* biodistribution studies in wild-type mice (n = 6) at 4 hr after injection. Each mouse received 5.55 MBq (0.15 mCi) [^{18}F]4V. The organ/tissue with the highest accumulation (percent injected dose per gram (% ID/g)) was the kidney (13.2 ± 2.8), followed by the liver (3.7 ± 1.1), lymph node (3.7 ± 0.3), lung (2.2 ± 0.8), spleen (2.1 ± 0.6), small intestine (1.9 ± 0.4), skin (1.7 ± 0.6), stomach (1.7 ± 1.1), blood (1.5 ± 0.4), large intestine (1.4 ± 0.5), aorta (1.3 ± 0.4), bone (1.3 ± 0.4), skeletal muscle (0.7 ± 0.3), heart (0.6 ± 0.2), and feces (0.2 ± 0.1). Dynamic PET/CT imaging of apoE$^{-/-}$ mice (n = 8) was conducted with intravenous injection of 13 MBq (0.35 mCi) [^{18}F]4V for 7 h. Strong focal signal in the aortic root was identified at 1–2 h with an aorta/blood ratio of 2. Atorvastatin treatment blocked the signal increase to near the signal expression of the wild-type aortas ($P < 0.05$). [^{18}F]4V radioactivity correlated with VCAM-1 mRNA levels (R = 0.79, P = 0.03) in the excised aortas.

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.

NIH Support

R01 HL078641, R24 CA092782, U01 HL080731

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