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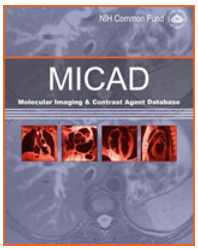

Cy5.5-Ferritin nanocages

Cy5.5-Fn nanocages

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Chemical name:	Cy5.5-Ferritin nanocages	
Abbreviated name:	Cy5.5-Fn nanocages	
Synonym:		
Agent category:	Polypeptide nanoparticle	
Target:	Non-targeted	
Target category:	Non-targeted	
Method of detection:	Optical, near-infrared (NIR) fluorescence	
Source of signal:	Cy5.5	
Activation:	No	
Studies:	• *In vitro* • Rodents	Structure is not available in PubChem.

Background

[PubMed]

Optical fluorescence imaging is increasingly used to monitor biological functions of specific targets in small animals (1-3). However, the intrinsic fluorescence of biomolecules poses a problem when fluorophores that absorb visible light (350–700 nm) are used. Near-infrared (NIR) fluorescence (700–1,000 nm) detection avoids the background fluorescence interference of natural biomolecules, providing a high contrast between target and background tissues. NIR fluorophores have a wider dynamic range and minimal background as a result of reduced scattering compared with visible fluorescence detection. They also have high sensitivity, resulting from low fluorescence background, and high extinction coefficients, which provide high quantum yields. The NIR region is also compatible with solid-state optical components, such as diode lasers and silicon detectors. NIR fluorescence (NIRF) imaging is becoming a noninvasive alternative to radionuclide imaging in small animals (4).

Endothelial cells are important cells in inflammatory responses (5, 6). Bacterial lipopolysaccharides, viruses, 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

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cells and other vascular cells and increase their expression of cell-surface adhesion molecules, such as intracellular adhesion molecule-1, vascular cell adhesion molecule-1, integrins, and selectins. Chemokines are chemotactic to inflammatory cells (leukocytes and macrophages) attracting them to sites of inflammation and tissue injury. Under atherogenic conditions, deposition of lipids on the endothelial cell surfaces of the aorta and inflammatory cells leads to the development of atherosclerotic plaques (7), which may erode and rupture.

Ferritin (Fn) is composed of 24 subunits of heavy and light chains, which self-assemble to form a cagelike nanoparticle (nanocage) at physiological pH (7.4) with internal and external diameters of 8 nm and 12 nm (8, 9), respectively. The outer surface of Fn can be chemically or genetically modified with ligands, and the cavity of Fn can capture metal ions with high affinity (10). Terashima et al. (11) chemically coupled Cy5.5 onto human heavy chain Fn (Cy5.5-Fn) nanocages. Cy5.5-Fn nanocages have been studied for NIRF imaging of vascular macrophages in atherosclerotic plaques in mice.

Related Resource Links:

- Chapters in MICAD (Ferritin)
- Gene information in NCBI (Ferritin heavy chain, ferritin light chain)
- Articles in Online Mendelian Inheritance in Man (OMIM) (Ferritin heavy chain, ferritin light chain)
- Clinical trials (Ferritin)

Synthesis

[PubMed]

Recombinant human Fn subunits were purified from transfected *Escherichia coli* cell lysates. Cy5.5-Fn was prepared by incubation of Cy5.5-NHS ester with Fn (pH 8.2) for 1 h at room temperature, followed by overnight incubation at 4°C. Cy5.5-Fn was isolated with column chromatography (11). There were four Cy5.5 molecules per Fn nanocage.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The external diameters of Cy5.5-Fn nanocages and unlabeled Fn-nanocages were determined to be ~12 nm with transmission electron microscopy at pH 7.4 (11).

Animal Studies

Rodents

[PubMed]

Terashima et al. (11) performed NIRF imaging of macrophages in atherosclerotic carotid arteries in streptozotocin (STZ)-induced diabetic mice. At day 14 after STZ injection, the left common carotid artery (LCA) was ligated in 11 mice and sham-operated in 3 mice. Cy5.5-Fn nanocages (8 nmol Cy5.5) were injected intravenously *via* retro-orbital injection. NIRF images of both LCA and right common carotid artery (RCA) were obtained at 48 h after injection. There was a clear signal localized to the macrophage-rich ligated LCA, but not to the control RCA or to either artery in sham-operated mice. Quantitative analysis showed that the NIRF signal was significantly higher in the ligated LCA compared to the contralateral RCA and sham controls ($P < 0.04$). *Ex vivo* NIRF images of the arteries confirmed the findings with *in vivo* NIRF imaging ($P < 0.002$). Immunohistochemical analysis showed macrophage infiltration in the ligated LCA but not in the non-ligated

RCA. Cy5.5-Fn was co-localized with macrophages in the LCA. However, no blocking studies were reported, but permeability differences between ligated LCA and control have been reported

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

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