OG488-Cyclo(Cys-Asn-Gly-Arg-Cys)-Gly-Lys

OG488-cNGR

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Chemical name:	OG488-Cyclo(Cys-Asn-Gly-Arg-Cys)-Gly-Lys	
Abbreviated name:	OG488-cNGR	
Synonym:		
Agent category:	Peptide	
Target:	Aminopeptidase N (CD13)	
Target category:	Enzyme	
Method of detection:	Optical, fluorescence imaging	
Source of signal/contrast:	OG488	
Activation:	No	
Studies:	• *In vitro* • Rodents	No structure is available in PubChem.

Background

[PubMed]

Extracellular matrix (ECM) adhesion molecules consist of a complex network of fibronectins, collagens, chondroitins, laminins, glycoproteins, heparin sulfate, tenascins, and proteoglycans that surround connective tissue cells, and they are mainly secreted by fibroblasts, chondroblasts, and osteoblasts (1). Cell substrate adhesion molecules are considered essential regulators of cell migration, differentiation, and tissue integrity and remodeling. These molecules play a role in inflammation and atherogenesis, but they also participate in the process of invasion and metastasis of malignant cells in the host tissue (2). Fibrosis is the formation of excess fibrous connective tissue (mainly collagen type I) in

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an organ or tissue as a reparative or reactive process in many chronic diseases in the heart, liver, kidneys, lungs, or vasculature.

Tumor angiogenesis represents a continuous and important process in tumor development in which the tumor attempts to gain an independent blood supply (3). This process is driven by the tumor's overproduction of angiogenic factors, which bind to receptors on nearby vessel endothelial cells. Angiogenesis is essential for the growth of solid tumors and their metastases. Imaging angiogenesis may be useful for monitoring angiogenic treatments of tumors and cardiovascular diseases (4-6). Aminopeptidase N (APN, CD13) is a membrane bound glycoprotein with MMP activity that cleaves unsubstituted, N-terminal amino acids with neutral side chains from peptides (7). APN has been shown to play a role in tumor angiogenesis, invasion, and metastasis (8). In addition to endothelial cells of angiogenic vessels, most cells of myeloid origin, epithelial cells, fibroblasts and smooth muscle cells also express CD13 (9, 10). The tumor homing peptide cyclo(Cys-Asn-Gly-Arg-Cys)-Gly-Lys (cNGR) contains the Asn-Gly-Arg (NGR) motif that binds to APN (11). Buehler et al. (12) has conjugated cNGR with Oregon Green 488 (OG488) to study angiogenesis in a murine myocardial infarction model.

Synthesis

[PubMed]

Cyclic NAc-Cys-Asn-Gly-Arg-Cys-Gly-Gly-Lys(Ac)-NH_2 peptide was synthesized using solid-phase peptide synthesis and then labeled on the resin with Oregon Green 488 (OG488) *via* the ε-amino group of the lysine (12). OG488-cNGR was purified with high-pressure liquid chromatography with >95% purity. The molar ratio of Cy5.5 to cNGR was estimated to be ~1.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Histoimmunostaining of CD13 was performed on HT-1080 and MCF-7 cancer cell lines (13). The APN enzyme was expressed in HT-1080 tumor cells, whereas expression in MCF-7 tumor cells was near background level. The APN activity in HT-1080 cells could be blocked with anti-CD13 antibodies and the cNGR peptide.

Animal Studies

Rodents

[PubMed]

Buehler et al. (12) studied OG488-cNGR homing in the murine myocardial infarction model in male Swiss mice (n = 7) by ligation of the left coronary artery. At day 7 after ligation, OG488-cNGR (0.75 mg/kg) or OG488 (0.31 mg/kg) was injected intravenously.

The fluorescent intensity (Fl) was measured in the border zone and infarct area with fluorescence microscopy. FI peaked at 15 min after injection and decreased to 17.8% of the peak FI value at 12 h (residence half-life ($t_{1/2}$), 9.1 h), and then to background level (2%) at 24 h. Administration of 20-fold excess cNGR 15 min after OG488-cNGR injection rapidly decreased FI in the infarct heart with the residence $t_{1/2}$ of 1.3 h. No accumulation in normal myocardium was detected. OG488-cNGR and OG488 were rapidly cleared from the plasma by the kidney with the plasma $t_{1/2}$ of 15 min and 7.7 min, respectively. No accumulation of OG488-cNGR was observed in the sham-operated heart (n = 3). OG488 alone exhibited little accumulation in the infarct heart (n = 3). Two-photon laser scanning microscopy experiments confirmed co-localization of OG488-cNGR with CD13/APN and the endothelial marker CD31 on the vessels in the border zone and infarct area of the infarct heart. CD13 mRNA expression was significantly up-regulated in the border zone and infarct area, but not in other areas of the infarcted heart and the sham operated hearts. CD13 mRNA expression in the border zone and infarct area peaked at 7 days after myocardial infarction with a significant increase of 10-20 folds, confirming that CD13 is induced in the murine myocardial infarction model.

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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