A Novel RGD-Containing Cyclic Peptide for use in Cancer Imaging and as a Targeted-Therapy Ligand

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ABSTRACT

Integrin plays a key role in the angiogenesis and metastasis of human tumors. αvβ3 integrin binding ligands have value in cancer diagnostic imaging and targeted therapy. The RGD motif binds to several integins, including αvβ3, αIIbβ3, αvβ5, and α5β1. It is known that amino acids lateral to RGD affect RGD binding specificity to different integrins. Researchers at the University of California Davis have discovered a novel RGD-containing peptide useful in cancer imaging and as a targeted-therapy ligand.

FULL DESCRIPTION

The compound has the ability to bind to target αvβ3 integrin on tumor cells and neovasculatures and can be used in tumor diagnostic imaging and therapy. This compound outperforms existing commonly used RGD ligands in both targeting efficacy and lower non-specific binding to normal organ tissues. The compound can be easily functionalized to conjugate imaging payload without decreasing binding strength.

- The compound bound αvβ3 integrin as evidenced by stained glioblastoma U-87 MG cells and melanoma A375M cells. The binding of the compound to said cells was blocked by anti-αvβ3 antibody.
- The compound specifically targeted tumor xenografts on nude mouse models. Six hours after injecting a biotinylated form of the compound coupled to Streptavidin-Cy5.5 into tail vein of nude mice implanted with U-87 MG xenograft, imaging displayed preferential uptake of biotinylated compound in the tumor. Experimental design was replicated for nude mice implanted with A375M xenograft, with similar results.
- Tumor uptake was higher and liver uptake was lower in mouse studies, compared to three commonly used RGD ligands.

APPLICATIONS

- Targeting reagent against αvβ3 integrin.
- Payload carrier (such as radioisotype or drug) for tumor radioimaging, radiotherapy, and targeting chemotherapy.

FEATURES/BENEFITS

- The compound shows remarkable positive binding with αvβ3; very weak cross-reaction with αIIbβ3; and no binding with α1, α2, α3, α4, α5, α6 and α9.
- In contrast to other RGD-containing peptides, the incorporation of payloads (labeling groups, etc.) at the C-terminus of this novel compound does not affect the binding affinity of the ligand to the integrin.
- Tumor uptake is higher and liver uptake is lower, compared to other existing RGD ligands.

RELATED MATERIALS

- Lam, et al. 2010. The Use of One-Bead One-Compound Combinatorial Library Technology to Discover High-Affinity avβ3 Integrin and Cancer Targeting Arginine-Glycine-Aspartic Acid Ligands with a Built-in Handle. Mol Cancer Ther. October 2010 9:2714-2723; Published Online First September 21, 2010; doi:10.1158/1535-7163.MCT-10-0308 - 09/21/2010

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,073,974	07/07/2015	2010-162

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OTHER INFORMATION

KEYWORDS

integrin, peptide, cancer, imaging, ligand, RGD, alpha v beta 3 integrin, cancer imaging, avß3

CATEGORIZED AS

- **Biotechnology**
  - Health
- **Medical**
  - Delivery Systems
  - Diagnostics
  - Disease: Cancer
  - Imaging
  - New Chemical Entities, Drug Leads

RELATED CASES

2010-162-0

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Novel Solid Tumor Chemodrug LLS2
- Affinity Peptides for Diagnosis and Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 and Zika Virus Infections
- Nanoparticles for Drug Delivery, Tissue Targeting and Imaging Analysis
- Conjugates That Combine HDAC Inhibitors and Retinoids into Disease Preventatives/Treatments
- Site-Specific Ligation and Compound Conjugation to Existing Antibodies
- Functional Illumination in Living Cells
- Multifunctional Porphyrin-Based Nanomedicine Platform
- A Two-step Drug Delivery System Based on Click Chemistry
- Transformable Smart Peptides as Cancer Therapeutics
- Engineered Biomaterial to Prevent Endothelial Inflammation
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