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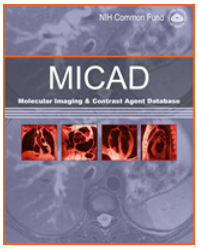

^{64}Cu-Z-E-(1,8-Diamino-3,6,10,13,16,19-hexaazabicyclo(6,6,6)eicosane)-aminohexanoyl-Asp-Gly-Glu-Ala

^{64}Cu-Z-E(diamsar)-Ahx-DGEA

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Chemical name:	^{64}Cu-Z-E-(1,8-Diamino-3,6,10,13,16,19-hexaazabicyclo(6,6,6)eicosane)-aminohexanoyl-Asp-Gly-Glu-Ala	
Abbreviated name:	^{64}Cu-Z-E(diamsar)-Ahx-DGEA	
Synonym:		
Agent category:	Peptide	
Target:	Integrin $\alpha_2\beta_1$	
Target category:	Receptor	
Method of detection:	Positron emission tomography (PET)	
Source of signal:	^{64}Cu	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about integrin α_2.

Background

[PubMed]

Integrins are a family of cell-surface heterodimeric glycoproteins that mediate diverse biological events (e.g., cell adhesion, migration, differentiation, proliferation, and apoptosis) involving cell–cell and cell–matrix interactions (1, 2). They consist of an α and a β subunit. They are important for cell adhesion and signal transduction. On the other hand, integrins affect tumor growth, tumor invasiveness, and metastasis (3, 4). The $\alpha_2\beta_1$ integrin receptor binds mainly collagen type I, laminins, E-cadherin, and matrix metalloproteinase 1 (5). The $\alpha_2\beta_1$ integrin is strongly expressed on tumor cells and has been implicated in tumor progression and metastasis (6, 7). In particular, prostate cancer cells and prostate cancer stem cells express high levels of $\alpha_2\beta_1$ integrin (8, 9). A tetrapeptide sequence consisting of Asp-Gly-Glu-Ala (DGEA) has been identified as a recognition motif used by

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the type I collagen to bind to $\alpha_2\beta_1$ integrin (10). DGEA was conjugated with Cy5.5 to study *in vivo* biodistribution of the tracer in prostate tumor-bearing mice (11). Cy5.5-DGEA has been shown to have a high accumulation in $\alpha_2\beta_1$-positive PC-3 human prostate tumor cells in nude mice. For positron emission tomography (PET) imaging of $\alpha_2\beta_1$ integrin, ^{64}Cu-Z-E-(1,8-diamino-3,6,10,13,16,19-hexaazabicyclo(6,6,6)eicosane)-aminohexanoyl-Asp-Gly-Glu-Ala (^{64}Cu-Z-E(diamsar)-Ahx-DGEA) was prepared and evaluated in nude mice bearing human PC-3 prostate tumors (12).

Related Resource Links:

- Chapters in MICAD (DGEA)
- Gene information in NCBI (α_2 integrin, β_1 integrin)
- Articles in Online Mendelian Inheritance in Man (OMIM) (α_2 integrin, β_1 integrin)

Synthesis

[PubMed]

Z-E-(diamsar)-Ahx-DGEA peptides were obtained using solid-phase synthesis (12). The diamsar group was added to carboxy group of glutamic acid of Z-E-Ahx-DGEA peptides. The measured mass of Z-E(diamsar)-Ahx-DGEA peptides confirmed the 1:1 addition. Z-E-(diamsar)-Ahx-DGEA was incubated with [^{64}Cu]acetate in ammonium acetate buffer (pH 5.5) for 30 min at 23–37°C. ^{64}Cu-Z-E-(diamsar)-Ahx-DGEA was purified with high-performance liquid chromatography. This procedure provided a radiolabeling yield of >90%, with a specific activity of 10.7 GBq/μmol (0.29 Ci/μmol) and a radiochemical purity of >98%. ^{64}Cu-Z-E-(diamsar)-Ahx-DGEA was 98% intact for 48 h at 40°C in phosphate-buffered saline.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Flow cytometry analysis showed that 99.7% of PC-3 cells, 51.4% of CWR-22 cells, and 15.6% of LNCaP cells were positive for the $\alpha_2\beta_1$ receptors using 5-Carboxyfluorescin-DGEA (FAM-DGEA) (11). Binding of 1 μM FAM-DGEA to the three cell types was analyzed with fluorescence microscopy. PC-3 cells exhibited a higher fluorescence intensity signal than CWR-22 and LNCaP cells. The binding of FAM-DGEA to PC-3 cells was completely blocked with 20 μM DGEA. Cellular accumulation of ^{64}Cu-Z-E-(diamsar)-Ahx-DGEA in PC-3 cells was low, with <0.4% incubation dose at 2 h after incubation (13). No blocking studies were carried out.

Animal Studies

Rodents

[PubMed]

Huang et al. (12) performed PET imaging in nude mice (n = 3) bearing PC-3 tumors at 30 min after injection of 11.1 MBq (0.3 mCi) ^{64}Cu-Z-E-(diamsar)-Ahx-DGEA. The tumors were clearly visualized. The tumor accumulation values were 2.08 ± 0.47% injected dose/gram (ID/g). The liver and kidney accumulation values were 1.25 ± 0.25% ID/g and 2.8 ± 0.2% ID/g, respectively. ^{64}Cu-Z-E-(diamsar)-Ahx-DGEA exhibited tumor/kidney, tumor/liver, and tumor/muscle ratios of 0.8, 1.8, and 5.8, respectively. Co-injection of DGEA (10 mg/kg) inhibited the tumor, kidney, liver, and muscle accumulation of ^{64}Cu-Z-E-(diamsar)-Ahx-DGEA by 60%, 30%, 50%, and 5%, respectively, at 30 min after injection (13).

In another PET study, Huang et al. (13) performed imaging in nude mice (n = 3/group) bearing PC-3 tumors at 30, 60, and 120 min after injection of 9.16 MBq (0.25 mCi) ^{64}Cu-Z-E-(diamsar)-Ahx-DGEA. The tumor

accumulation values were 2.28 ± 0.47% ID/g, 0.94 ± 0.53% ID/g, and 0.36 ± 0.55% ID/g at 30, 60, and 120 min after injection, respectively. There was a rapid washout from the tumors as well as from the kidney, liver, and muscle. Co-injection of DGEA (10 mg/kg) reduced the PC-3 tumor accumulation to 0.9 ± 0.31%ID/g at 30 min after injection. In the CWR-22 control tumor, the uptake was 0.3 ± 0.2%ID/g at 30 min after injection.

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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