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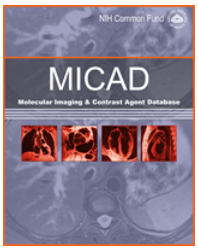

[^{123}I]Vascular endothelial growth factor

[^{123}I]VEGF$_{165}$

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Chemical name:	[^{123}I]Vascular endothelial growth factor	
Abbreviated name:	[^{123}I]VEGF$_{165}$	
Synonym:		
Agent Category:	Polypeptide	
Target:	VEGF receptors	
Target Category:	Receptor binding	
Method of detection:	SPECT, planar	
Source of signal:	^{123}I	
Activation:	No	
Studies:	• *In vitro* • Rodents • Humans	Click on protein, nucleotide (RefSeq), and gene for more information about VEGF.

Background

[PubMed]

Vascular endothelial growth factor (VEGF) consists of at least six isoforms of various number of amino acids (121, 145, 165, 183, 189 and 206) produced through alternative splicing (1). VEGF$_{121}$, VEGF$_{165}$ and VEGF$_{189}$ are the major forms secreted by most cell types. They are active as homodimers linked by disulfide bonds. VEGF$_{165}$ is the best-characterized VEGF species. VEGF is a potent angiogenic factor inducing proliferation, sprouting, migration, and tube formation of endothelial cells. There are three high affinity tyrosine kinase receptors (VEGFR-1, Flt-1; VEGFR-2, KDR/Flt-1; and VEGFR-3, Flt-4) on endothelial cells. Several types of non-endothelial cells such as hematopoietic stem cells, melanoma cells, monocytes, osteoblasts and pancreatic beta cells also express VEGF receptors (1).

VEGF receptors were found to be overexpressed in various tumor cells and tumor-associated endothelial cells (2). Inhibition of VEGF receptor function has been shown to inhibit pathological angiogenesis and tumor growth and metastasis (3, 4). [^{123}I]VEGF$_{165}$ was developed as a SPECT tracer for imaging solid tumors and angiogenesis (5).

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Synthesis

[PubMed]

$VEGF_{165}$ was labeled with sodium [^{123}I]iodide by electrophilic radioiodination using the chloramine-T method (5). This method gave a radiochemical yield of >25% and a radiochemical purity of >97% in a specific activity of 42.3 mCi/nmol (1.66 GBq/nmol).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

[^{123}I]$VEGF_{165}$ (0.001 nM) induced proliferation of human umbilical vein endothelial cells (HUVECs) and A431 mammary carcinoma cells to a similar extent as unlabeled $VEGF_{165}$ (5). Two classes of high-affinity [^{123}I]$VEGF_{165}$-binding sites (B_{max1} = 518 sites/cell, K_{d1} = 26 pM and B_{max2} = 6,100 sites/cell, K_{d2} = 2.07 nM) were found on the cell surfaces of HUVECs. In contrast, one class of binding site (B_{max} = 1,290-3,540 sites/cell and K_d = 88-167 pM) was found on various human cell lines such as HMC-1 mast cells, A431 mammary carcinoma, HEP-G2 hepatoma, HEP-1 hepatic endothelioma, and U937 monocyte cells as well as many human primary tumors (5). No specific binding sites were detected in undifferentiated adenocarcinoma cells as compared with differentiated adenocarcinoma cells (B_{max} = 15.6 fmol/10^7 cells, K_d = 143 pM) (6). Tumor cells expressed a significantly higher number of [^{123}I]$VEGF_{165}$ binding sites on their cell surfaces than normal blood cells and adjacent normal tissues (5).

Animal Studies

Rodents

[PubMed]

Cornelissen et al. (7) performed biodistribution and imaging studies of [^{123}I]$VEGF_{165}$ in normal mice. The organs with the highest accumulation were the kidneys (30.1 ± 11.2% ID at 1.5 min), liver (14.6 ± 4.9% ID at 1.5 min) and stomach (13.2 ± 3.5% ID at 3 h). Low background activity was observed in the lungs, heart, body and head (containing the thyroid, which was not dissected separately). Bladder content radioactivity was found to be high. Background levels in the lungs and intestines were low, as shown by both biodistribution and planar gamma camera images. Biodistribution in A2058 tumor-bearing nude mice showed tumor/thigh ratios of 0.40 ± 0.14, 6.12 ± 2.11, 1.16 ± 0.30 and 0.48 ± 0.12 at 1, 2, 4 and 6 h after injection, respectively. Other organs did not differ significantly from the results obtained from normal mice. Co-injection of 80 µg of $VEGF_{165}$ resulted in a significant decrease of the tumor/thigh from 6.01 ± 1.95 to 1.30±0.34 (P<.05) at 2 h after injection. Tumor/thigh ratio of the CAPAN-II-(VEGF receptor negative) bearing mice was 1.11±0.23.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

[^{123}I]VEGF$_{165}$ (184 ± 18 MBq, 5 ± 0.5 mCi; 0.13 nmol) was administered intravenously to 18 patients with gastrointestinal tumors (8). SPECT images with [^{123}I]VEGF$_{165}$ were compared with computed tomography (CT) and magnetic resonance imaging (MRI). Binding of [^{123}I]VEGF$_{165}$ to primary tumors and metastases was visible shortly after injection. In patients with pancreatic adenocarcinoma, primary tumors were visualized by imaging in 7 of 9, lymph node metastases in 3 of 4, liver metastases in 3 of 6 and lung metastases in 1 of 3. Cholangiocarcinomas were visualized by imaging in 1 of 2 patients. Hepatocellular carcinomas were visible by imaging in 2 of 4 patients. [^{123}I]VEGF$_{165}$ images were weakly positive in one patient with abdominal schwannoma and in 1 patient with peritoneal carcinosis. A ring-shaped tracer accumulation around the necrotic tumors was observed. [^{123}I]VEGF$_{165}$ SPECT provided an overall specificity of 58% and CT/MRI provided a specificity of 95%.

Human dosimetry of [^{123}I]VEGF$_{165}$ was determined from blood samples and SPECT images in 9 patients with pancreatic adenocarcinoma after intravenous injection of 189 ± 17 MBq (5.1 ± 0.5 mCi). [^{123}I]VEGF$_{165}$ disappeared rapidly from the blood to 4% in 30 min postinjection (6).High uptake in the lungs, liver, kidneys and spleen was observed in 30 min. There was a rapid uptake of the tracer by the primary pancreatic adenocarcinoma (tumor/background ratios, 1.3 to 2.7) within 30 min by SPECT scans. The images were still visible at 3 h. The overall sensitivity of [^{123}I]VEGF$_{165}$ scintigraphy for detecting primary pancreatic tumors and their metastases was 64% (14 of 22 lesions) visualizing primary pancreatic adenocarcinoma in 7 of 9 patients (sensitivity, 78%). The effective dose was estimated to be 0.017 mSv/MBq (63 mrem/mCi). The organ that received the highest dose was the thyroid (0.058 mGy/MBq or 0.21 rad/mCi), followed by the spleen (0.046 mGy/MBq or 0.17 rad/mCi), urinary bladder (0.040 mGy/MBq or 0.15 rad/mCi), lungs (0.034 mGy/MBq or 0.13 rad/mCi) kidneys (0.033 mGy/MBq or 0.12 rad/mCi), and liver (0.029 mGy/MBq or 0.11 rad/mCi).

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