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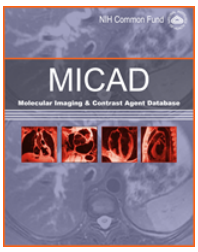

^{89}Zr-*N*-Succinyldesferal-chimeric monoclonal antibody G250

^{89}Zr-Df-cG250

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Chemical name:	^{89}Zr-*N*-Succinyldesferalchimeric monoclonal antibody G250	
Abbreviated name:	^{89}Zr-Df-cG250	
Synonym:		
Agent category:	Antibody	
Target:	Carbonic anhydrase IX	
Target category:	Enzyme	
Method of detection:	Positron emission tomography (PET)	
Source of signal:	^{89}Zr	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about human carbonic anhydrase IX.

Background

[PubMed]

In a variety of solid tumors, hypoxia was found to lead to tumor progression and the resistance of tumors to chemotherapy and radiotherapy (1-3). Tumor oxygenation is heterogeneously distributed within human tumors (4). Hypoxia in malignant tumors is thought to be a major factor limiting the efficacy of chemotherapy and radiotherapy. It would be beneficial to assess tumor oxygenation before and after therapy to provide an evaluation of tumor response to treatment and an insight into new therapeutic treatments (5). Tumor oxygenation is measured invasively using computerized polarographic oxygen-sensitive electrodes, which is regarded as the gold standard (6). Functional and non-invasive imaging of intratumoral hypoxia has been demonstrated to be feasible for the measurement of tumor oxygenation (7).

Chapman proposed the use of 2-nitroimidazoles for hypoxia imaging (8). 2-Nitroimidazole compounds are postulated to undergo reduction in hypoxic condition, forming highly reactive oxygen radicals that subsequently bind covalently to macromolecules inside the cells (9). [^{18}F]Fluoromisonidazole ([^{18}F]FMISO) is the most

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widely used positron emission tomography (PET) tracer for imaging tumor hypoxia (7). Carbonic anhydrase (CA) IX is one of the most overexpressed genes in cells under hypoxic conditions (10). It is a transmembrane glycoprotein with CA activity in the extracellular domain, and it is found to be overexpressed in renal cell, cervical, lung, and colorectal tumors. Murine monoclonal antibody G250 against CA IX has been developed for *in vitro* and *in vivo* localization of CA IX in cells (11-13). G250 is found to bind to >94% of human clear-cell renal carcinoma. A murine-human chimeric G250 (cG250) has been generated to be less immunogenic in humans. ^{124}I-cG250 has been evaluated as a PET imaging agent for renal cell carcinoma in mice (14) and patients (15). Brouwers et al. (16) explored the use of a ^{89}Zr positron emitter (half-life, 3.27 days) to radiolabel cG250. ^{89}Zr was conjugated to a bifunctional derivative of desferrioxamine B (Df) to cG250 for PET imaging of CA IX expression in tumors. ^{89}Zr-Df-cG250 has been evaluated as a PET imaging agent for renal cell carcinoma in rats.

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (Carbonic anhydrase IX)
- Articles in OMIM
- Clinical trials (G250)

Synthesis

[PubMed]

cG250 was coupled with *N*-SucDf *via* an amide linkage and labeled with ^{89}Zr (16). Df-cG250 (2.4 nmol) was incubated with 165 MBq (4.5 mCi) ^{89}Zr for 30 min at room temperature. ^{89}Zr-Df-cG250 was purified by gel filtration. The radiochemical purity was >97% with >95% immunoreactivity. Maximum specific activity was 60 MBq/nmol (1.6 mCi/nmol). There was one *N*-SucDf group per cG250 molecule. ^{89}Zr-Df-cG250 showed <10% loss of ^{89}Zr in human serum for 4 d at 37°C.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Lawrentschuk et al. (17) performed binding experiments with ^{124}I-cG250 in SK-RC-52 human renal carcinoma cells. The dissociation constant (K_d) was found to be 2.2 nM with 400,000 antibody molecules per cell.

Animal Studies

Rodents

[PubMed]

Brouwers et al. (16) studied *ex vivo* biodistribution of ^{89}Zr-Df-cG250 in nude rats (n = 8) bearing SK-RC-52 tumors at 72 h after injection. The tracer accumulation in the tumors was 5.0 ± 2.4% injected dose per gram (ID/g). The liver, spleen, lung, intestines, muscle, blood, and kidneys had lower radioactivity levels than the tumors. The radioactivity in the blood was ~1.6% ID/g, and the tumor/blood ratio was 3.1. ^{111}In-DTPA-cG250 exhibited a similar biodistribution pattern with a tumor/blood ratio of 2.9. No blocking experiment was performed. PET imaging with the ^{89}Zr-Df-cG250 showed localization of radioactivity to the tumors and the abdomen area in the rats at 48 h and 72 h 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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