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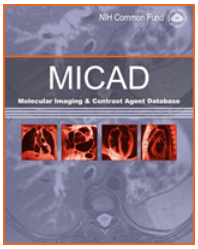

^{125}I-Labeled anti-epidermal growth factor receptor human Fab antibody fragment

^{125}I-Fab

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Chemical name:	^{125}I-Labeled anti-epidermal growth factor receptor human Fab antibody fragment	
Abbreviated name:	^{125}I-Fab	
Synonym:		
Agent category:	Antibody fragment, Fab	
Target:	Epidermal growth factor receptor (EGFR), HER1/erbB-1	
Target category:	Receptor	
Method of detection:	Single-photon emission computed tomography (SPECT)	
Source of signal:	^{125}I	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about EGFR.

Background

[PubMed]

Epidermal growth factor (EGF) is a cytokine that comprises 53 amino acids (6.2 kDa) and is secreted by ectodermic cells, monocytes, kidneys, and duodenal glands (1). EGF stimulates growth of epidermal and epithelial cells. EGF and at least seven other growth factors and their transmembrane receptor kinases play important roles in cell proliferation, survival, adhesion, migration, and differentiation. The EGF receptor (EGFR) family consists of four transmembrane receptors: EGFR (HER1/erbB-1), HER2 (erbB-2/neu), HER3 (erbB-3), and HER4 (erbB-4) (2). HER1, HER3, and HER4 comprise three major functional domains: an extracellular ligand-binding domain, a hydrophobic transmembrane domain, and a cytoplasmic tyrosine kinase domain. No ligand has been clearly identified for HER2; however, HER2 can be activated as a result of ligand binding to other HER receptors with the formation of receptor homodimers and/or heterodimers (3). HER1 and

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HER2 are overexpressed on many solid tumor cells such as breast, non-small cell lung, head and neck, and colon cancers (4-6). The high levels of HER1 and HER2 expression on cancer cells are associated with a poor prognosis (7-10).

Cetuximab is a humanized IgG_1 monoclonal antibody (mAb) against the extracellular domain of recombinant EGFR (11). Cetuximab was approved by the United States Food and Drug Administration (FDA) to treat patients with advanced colorectal cancer that has metastasized to other parts of the body. Various labeled cetuximab probes have been developed for imaging human breast cancer in small-animal tumor models (12-14). However, the pharmacokinetics of the intact radiolabeled mAb, with high liver uptake and slow blood elimination, are generally not ideal for imaging. Smaller antibody fragments, such as Fab or $F(ab')_2$, have better imaging pharmacokinetics because they are rapidly excreted by the kidneys. Wang et al. (15) generated a human Fab antibody fragment against the extracellular domain of EGFR from a human naive Fab phage library. Xu et al. (16) evaluated ^{125}I-anti-EGFR human Fab antibody fragment (^{125}I-Fab) for single-photon emission computed tomography (SPECT) imaging in nude mice bearing human EGFR-expressing tumors.

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (EGFR)
- Articles in OMIM
- Clinical trials (EGFR)
- FDA Drug information (EGFR)

Synthesis

[PubMed]

Anti-EGFR Fab (0.2 nmol) was labeled with 74 MBq (2 mCi) ^{125}I in the presence of chloramine-T (16). ^{125}I-Fab was isolated from the incubation mixture with a PD-10 column. The labeling efficiency was ~75%, and the radiochemical purity was >95%. ^{125}I-Fab exhibited an immunoreactivity of 63%. The specific activity was not reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

In vitro binding of Fab showed a binding affinity of 30 nM using noncompetitive radioimmunoassay (15). *In vitro* cell uptake assays were performed using three cell lines with different degree of EGFR expression (A431 > U118 > NIH3T3 cells) (16). The radioactivity levels were 120,000, 40,000, and 8,000 cpm in A431, U118, and NIH3T3 cells, respectively, at 1 h of incubation with 0.06 nM ^{125}I-Fab. The radioactivity levels were reduced to 40,000, 20,000, and 7,000 cpm, respectively, by co-incubation with 1.2 nM anti-EGFR Fab.

Animal Studies

Rodents

[PubMed]

Whole-body gamma imaging analysis was performed in nude mice bearing A431, U118, or M14 tumors after intravenous injection of 11.1 MBq (300 μCi) ^{125}I-Fab (16). The tumors (A431 > U118 > M14) and urinary bladder were clearly visualized at 15 h after injection. The tumor/muscle ratio was 15, 4, and 2 for A431, U118,

and M14 tumors at 24 h after injection, respectively. No blocking experiment was performed. The use of low EGFR-expression tumors provided some specificity of ^{125}I-Fab.

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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