[^{18}F]α/γ-Fluorobenzylamine-folate

[^{18}F]α/γ-FBA-folate

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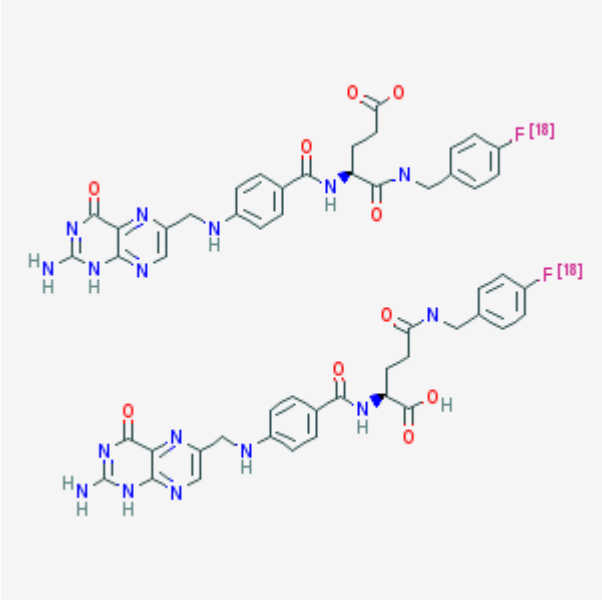
Chemical name:	[^{18}F]α/γ-Fluorobenzylamine-folate
Abbreviated name:	[^{18}F]α/γ-FBA-folate, [^{18}F]FBA-folate
Synonym:	
Agent category:	Compound
Target:	Putative folate receptor
Target category:	Receptor
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents



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Background

[PubMed]

Folic acid is a water-soluble B vitamin (1) that is essential for methylation and DNA synthesis. The primary pathway for entry of folate into cells is through the facilitated transporter, which has a low affinity for folate (Michaelis constant (K_m) = 1-5 μM). Some

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cells in the choroid plexus, kidney, lung, thyroid, spleen, placenta, and thymus also possess a higher affinity (dissociation constant (K_d) = 0.5 nM) receptor that allows folate uptake via receptor-mediated endocytosis. Some human epithelial tumor cells were found to overexpress folate-binding protein (2). More than 90% of human ovarian and endometrial cancers express the high-affinity receptor, which is absent in normal tissues. Breast, colorectal, renal, and lung carcinomas also overexpress the folate receptor but at lower frequencies (20-50%). Activated macrophages, but not resting macrophages, have been also found to have folate receptor (3).

Several folate-based conjugates (^{111}In-DTPA-folate, ^{99m}Tc-EC-folate and $^{68/67/66}$Ga-DF-folate) have been studied in tumor imaging (4-7). Bettio et al. (8) reported a synthesis of 18F-labeled folate by a reaction of [^{18}F]4-fluorobenzylamine (FBA) with the α- and γ-carboxyl groups of folic acid. [18F]α/γ-FBA-folate is being developed as a positron emission tomography (PET) agent for detection of folate receptors *in vivo*.

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (folate receptor)
- Articles in OMIM (folate receptor)
- Clinical trials (folate receptors)
- Drug information in FDA

Synthesis

[PubMed]

Bettio et al. (8) coupled folic acid with [^{18}F]FBA to yield a 4:1 mixture of [^{18}F]γ-FBA-folate and

[^{18}F]α-FBA-folate with radiochemical yields of 15-44% and specificity activity up to 24 GBq/μmol (0.65 Ci/μmol). [^{18}F]FBA was prepared by a two-step reaction by standard nucleophilic radiofluorination of 4-cyano-*N,N,*-trimethylanilinium trifluoromethane sulfonate to form 4-[^{18}F]-benzonitrile and reduction of the nitrile functional group by $LiAlH_4$ to the amino functionality with radiochemical yields of 8-13%.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The human nasopharyngeal carcinoma KB-31 cell line has putative folate receptors as determined by [^{3}H]folate binding studies in cultures (8). The mean IC_{50} values for α-FBA-folate, γ-FBA-folate and folate were 71 ± 8, 62 ± 6 and 41 nM, respectively. Therefore, the α- and γ-FBA-folate have comparable binding affinity to that of native folic acid.

Animal Studies

Rodents

[PubMed]

Bettio et al. (8) performed biodistribution studies of [^{18}F]α/γ-FBA-folate in nude mice bearing the KB-31 tumor xenografts. The organ with the highest accumulation was the kidneys (40.65%ID/g), followed by the tumor (6.65%ID/g), duodenum (5.01%ID/g), and liver (2.37%ID/g) at 125 min after [^{18}F]α/γ-FBA-folate injection. Very high radioactivity was found in bile, urine, and faces. Pretreatment with folic acid (200 μg/mouse) reduced [^{18}F]α/γ-FBA-folate accumulation by 80% in the tumor and 97% in the kidneys.

The whole body distribution of [^{18}F]α/γ-FBA-folate was also assessed by PET imaging from 75 to 120 min after injection. The highest activity concentrations were visualized in the gallbladder, urinary bladder, and parts of the intestines. Moderate accumulation was observed in the kidneys, tumors, and liver. The accumulation of [^{18}F]α/γ-FBA-folate was heterogeneous within the tumor, with higher radioactivity in the tumor rim. The accumulation of [^{18}F]α/γ-FBA-folate in the tumor and kidneys was completely blocked by folic acid pretreatment.

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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