# 6-[1-(2-[$^{18}$F]Fluoro-3-pyridyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]quinoline

## [$^{18}$F]FPTQ

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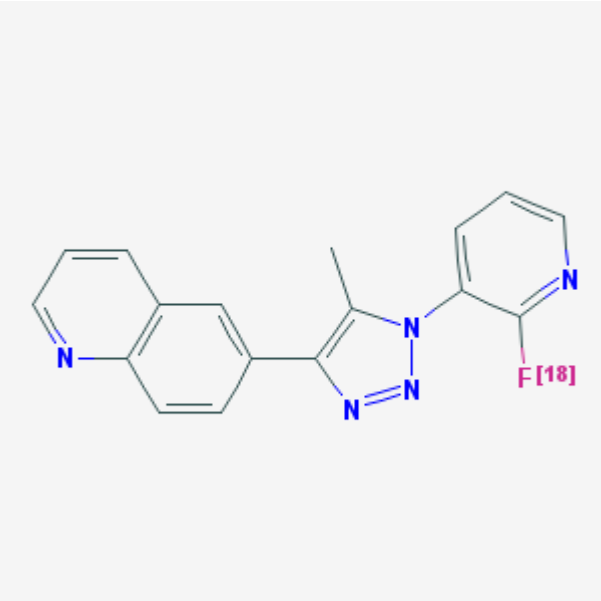
| **Chemical name:** | 6-[1-(2-[$^{18}$F]Fluoro-3-pyridyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]quinoline |
| **Abbreviated name:** | [$^{18}$F]FPTQ, [$^{18}$F]7a |
| **Synonym:** | |
| **Agent category:** | Compound |
| **Target:** | Metabotropic glutamate receptor subtype 1 (mGluR1) |
| **Target category:** | Receptor |
| **Method of detection:** | Positron emission tomography (PET) |
| **Source of signal:** | $^{18}$F |
| **Activation:** | No |
| **Studies:** | • *In vitro*<br>• Rodents |

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## Background

[PubMed]

Glutamate is a major excitatory neurotransmitter at neuronal synapses in the central nervous system (CNS) (1, 2). Glutamate produces its excitatory effects by acting on cell-surface ionotropic glutamate or metabotropic glutamate receptors (mGluRs). The mGluRs are GTP-binding protein (G-protein)–coupled receptors that play important roles in regulating the activity of many synapses in the CNS, and many neuronal projection pathways contain mGluRs. There are eight mGluR subtypes, which are further subdivided into groups I, II, and III. The group I receptors include mGluR1 and mGluR5, and they are found predominantly in postsynaptic locations. The mGluR1 is found in moderate to high density in the cerebellum, caudate, putamen, thalamus, cingulate cortex, and hippocampus, with low density in the pons. The mGluR5 is usually found in moderate to high density in the frontal cortex, caudate, putamen, nucleus accumbens, olfactory tubercle, and hippocampus, whereas the density in the cerebellum is low. The mGluR1 and mGluR5 are positively coupled to phospholipase C in the regulation of neuronal excitability (3). Dysfunction of mGluR1 and mGluR5 is implicated in a variety of diseases in the CNS, including anxiety, depression, schizophrenia, Parkinson's disease, and drug addiction or withdrawal (2, 4).

Positron emission tomography (PET) and single-photon emission tomography of radioligands targeting mGluR1 can visualize and analyze mGluR1 expression in normal physiological and pathological conditions. Several radioligands have been studied for *in vivo* imaging of mGluR1 in the brain (5). 6-[1-(2-(Fluoro-3-pyridyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]quinoline (FPTQ) was shown to be a selective mGluR1 with nanomolar affinity (3.6 nM), with little inhibition to mGluR5 (6). Fujinaga et al. (7) prepared and evaluated 6-[1-(2-[$^{18}$F] fluoro-3-pyridyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]quinoline ([$^{18}$F]FPTQ) for use with *in vivo* PET imaging of mGluR1 distribution in rats. The investigators concluded that [$^{18}$F]FPTQ is not suitable for PET imaging of GluR1 in the brain because of its rapid dissociation and the presence of radiolabeled metabolite in the brain.

### Related Resource Links:

- Chapters in MICAD (mGluR1, mGluR5)
- Gene information in NCBI (mGluR1, mGluR5)
- Articles in Online Mendelian Inheritance in Man (OMIM) (mGluR1, mGluR5)
- Clinical trials (mGluR1, mGluR5)

## Synthesis

[PubMed]

Fujinaga et al. (7) reported a one-step automated synthesis of [$^{18}$F]FPTQ. The bromo-precursor was subjected to nucleophilic fluorination with K[$^{18}$F]F for 10 min at 150°C,

with a radiochemical yield of 69 ± 13% and an average specific activity of 118–237 GBq/μmol (3.2–6.4 Ci/μmol, *n* = 8) at the end of synthesis. The radiochemical purity of [18F]FPTQ was >99% after purification with high-performance liquid chromatography. The total synthesis time was 75 min. [18F]FPTQ exhibited a Log D value of 2.53 ± 0.02 (*n* = 3).

## *In Vitro* Studies: Testing in Cells and Tissues

[PubMed]

*In vitro* [18F]FPTQ autoradiographic imaging studies were performed on brain sections of rats (*n* = 4) (7). [18F]FPTQ bound heterogeneously to the brain sections, with the highest accumulation of radioactivity in the mGluR1-rich cerebellum (408.8 ± 48.1 PSL/mm$^2$), followed by the thalamus (188.9 ± 44.4 PSL/mm$^2$), hippocampus (112.4 ± 29.4 PSL/mm$^2$), striatum (70.7 ± 14.2 PSL/mm$^2$), cerebral cortex (28.2 ± 4.7 PSL/mm$^2$), and pons (17.5 ± 2.7 PSL/mm$^2$). FPTQ and JNJ-16259685 (1,000 nM, mGluR1 antagonists) completely blocked radioactive signals to background levels in these brain regions. On the other hand, the mGluR5 antagonist MPEP (1,000 nM) demonstrated only marginal inhibition (~10%) of the signals.

## Animal Studies

### Rodents

[PubMed]

Fujinaga et al. (7) performed *ex vivo* biodistribution studies in rats (*n* = 3/group) at 5, 15, and 30 min after intravenous injection of 17 MBq (0.46 mCi) [18F]FPTQ (0.11 nmol). The radioactivity levels in most tissues were highest at 5 min and decreased quickly thereafter. The highest accumulation at 5 min was observed in the small intestine (3.1% injected dose/gram (ID/g)), followed by the liver (2.3% ID/g), kidney (0.76% ID/g), pancreas (0.75% ID/g), brain (0.52% ID/g), lung (0.50% ID/g), heart (0.47% ID/g), spleen (0.43% ID/g), blood (0.38% ID/g), muscle (0.28% ID/g), and bone (0.22% ID/g). [18F]FPTQ bound heterogeneously to the brain sections, with the highest accumulation of radioactivity at 5 min in the mGluR1-rich cerebellum (1.21% ID/g) and thalamus (0.73% ID/g), followed by the hippocampus (0.58% ID/g), striatum (0.54% ID/g), pons-medulla (0.47% ID/g), and cerebral cortex (0.44% ID/g). However, the accumulation levels in the cerebellum and the rest of the brain regions were 0.20% ID/g and 0.10% ID/g at 30 min, respectively.

Fujinaga et al. (7) performed dynamic PET imaging studies for 60 min in rats (*n* = 4/group) after intravenous injection of 17.5 MBq (0.5 mCi) [18F]FPTQ. Blocking studies were performed by pretreatment (0.5 min) with 1 mg/kg FPTQ, JNJ-16259685, or MPEP. Baseline tissue time-activity curves revealed a high accumulation of radioactivity at 1–3 min in the cerebellum (standard uptake value (SUV) = 2.3), followed by the thalamus (2.1), striatum (1.8), hippocampus (1.6), and cerebral cortex (1.5), whereas little

radioactivity was detected in the medulla (1.1). The radioactivity levels of all brain regions decreased faster than that of the cerebellum after the initial accumulation. The cerebellum/medulla, thalamus/medulla, striatum/medulla, hippocampus/medulla, and cerebral cortex/medulla ratios at 10–15 min were 3.73, 1.91, 1.55, 1.42, and 1.31, respectively. Pretreatment with FPTQ or JNJ-16259685 reduced the radioactivity signals to background level, whereas pretreatment with MPEP showed little inhibition.

*Ex vivo* metabolite studies were performed in mice ($n$ = 3/group) at 5–30 min after intravenous injection of [$^{18}$F]FPTQ (7). [$^{18}$F]FPTQ remained 4% intact in the plasma at 30 min with one polar metabolite. On the other hand, [$^{18}$F]FPTQ remained 67% and 34% intact at 30 min in the cerebellum and brain minus cerebellum, respectively. The investigators concluded that [$^{18}$F]FPTQ is not suitable for PET imaging of GluR1 in the brain because of the rapid dissociation and the presence of radiolabeled metabolite in the brain.

## 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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