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产品名称：FITM
产品别名：FITM

生物活性：

Description	FITM is a negative allosteric modulator of mGlu1 receptor with a Ki of 2.5 nM.
IC_{50} & Target	Ki: 2.5 nM (mGlu1)[1]
In Vitro	FITM fits tightly into the long and narrow pocket. Most of the ligand-receptor interactions are hydrophobic with the exception of the contacts of the pyrimidine-amine group with the T815 $^{7.38}$ side chain. The mGlu1 binding pocket for FITM largely corresponds to mutagenic data for the common allosteric site in mGlus and likely extends to other class C GPCRs. FITM which shows high affinity and selectivity for mGlu1 over mGlu5[1]. FITM has the high hydrogen bonds occupancy with Thr815 and Tyr805 in dimer A and B of mGlu1 during molecular dynamics simulations. The nitrogen and hydrogen atoms of FITM form the dynamical hydrogen bonds with the hydrogen atom of Tyr805 and oxygen atom of Thr815, respectively. It indicates that there is a strong attraction interaction between FITM and allosteric sites[2].
In Vivo	The pretreatment of rats with unlabeled FITM (1 mg/kg) occupies an mGluR1 binding site of 18F-FITM by more than 99% and does not affect the input function. The K_d (nM) and B_{max} (pmol/mL) obtained by the Scatchard analyses with the multidose ligand assays are 2.1 and 36.3, respectively, for the thalamus; 2.1 and 27.5, respectively, for the hippocampus; 1.5 and 22.2, respectively, for the striatum; and 1.5 and 20.5, respectively, for the cingulate cortex with a high confidence[3]. ^{18}F-FITM shows excellent pharmacokinetics, namely the dense and specific accumulation in mGlu1-positive melanomas versus mGlu1-negative hepatoma and normal tissues. Furthermore, the accumulation levels of radioactivity corresponded to the extent of tumor and to levels of mGlu1 protein expression in melanomas and melanoma metastasis[4].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 150 mg/mL (403.84 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.6923 mL	13.4615 mL	26.9230 mL
5 mM	0.5385 mL	2.6923 mL	5.3846 mL
10 mM	0.2692 mL	1.3461 mL	2.6923 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

	1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (6.73 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.73 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (6.73 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.73 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Wu H, et al. Structure of a class C GPCR metabotropic glutamate receptor 1 bound to an allosteric modulator. Science. 2014 Apr 4;344(6179):58-64. [2]. Bai Q, et al. Investigation of allosteric modulation mechanism of metabotropic glutamate receptor 1 by molecular dynamics simulations, free energy and weak interaction analysis. Sci Rep. 2016 Feb 18;6:21763. [3]. Yamasaki T, et al. In vivo measurement of the affinity and density of metabotropic glutamate receptor subtype 1 in rat brain using 18F-FITM in small-animal PET. J Nucl Med. 2012 Oct;53(10):1601-7. [4]. Xie L, et al. Molecular imaging of ectopic metabotropic glutamate 1 receptor in melanoma with a positron emission tomography radioprobe (18) F-FITM. Int J Cancer. 2014 Oct 15;135(8):1852-9.

实验参考：

Animal Administration	Rats: Sprague–Dawley rats are treated with different doses of unlabeled FITM (0, 1, 5, or 30 μg/kg or 1 mg/kg) just before a bolus injection of ^{18}F-FITM (17–18 MBq, 30–40 pmol, 0.1 mL). Estimations of equilibrium state and BPND were acquired[3].
References	[1]. Wu H, et al. Structure of a class C GPCR metabotropic glutamate receptor 1 bound to an allosteric modulator. Science. 2014 Apr 4;344(6179):58-64. [2]. Bai Q, et al. Investigation of allosteric modulation mechanism of metabotropic glutamate receptor 1 by molecular dynamics simulations, free energy and weak interaction analysis. Sci Rep. 2016 Feb 18;6:21763. [3]. Yamasaki T, et al. In vivo measurement of the affinity and density of metabotropic glutamate receptor subtype 1 in rat brain using 18F-FITM in small-animal PET. J Nucl Med. 2012 Oct;53(10):1601-7. [4]. Xie L, et al. Molecular imaging of ectopic metabotropic glutamate 1 receptor in melanoma with a positron emission tomography radioprobe (18) F-FITM. Int J Cancer. 2014 Oct 15;135(8):1852-9.