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产品名称：MBX-2982
产品别名：MBX-2982

生物活性：

Description	MBX-2982 is a selective, orally-available G protein-coupled receptor 119 (GPR119) agonist.
IC_{50} & Target	GPR119[1]
In Vitro	In cells pre-treated with MBX-2982 (1 μM) in "chronic incubation/washout" experiments, cAMP accumulation captured by IBMX inclusion is significantly increased compared to control cells (P<0.01; ANOVA; n=3-6) despite extensive washing to remove excess agonist. AR-231,453 produces sustained responses in a similar concentration range to those observed with acute stimulation (a small 1.82 fold shift), with pEC50s of 8.67±0.11 and 8.93±0.17, respectively. Likewise, a large but less severe shift in concentration responses (57.54 fold) is observed for MBX-2982 with respective sustained and acute pEC50s of 7.03±0.13 and 8.79±0.12[1].
In Vivo	To examine whether the observations in GLUTag and the primary intestinal cells has physiological relevance, C57BL/6 mice are treated with the GPR119 agonist MBX-2982 at a dose of 10 mg/kg. Note that in order to examine a direct GPR119 effect, no DPP-IV inhibitor is co-administered in this experiment, but a DPP-IV inhibitor is used to preserve active GLP-1 in the blood samples. The plasma GLP-1 levels from the mice dosed with MBX-2982 are increased without a glucose load, indicating that GPR119-mediated GLP-1 secretion is not dependent on glucose[2].

Solvent&Solubility

In Vitro:

DMSO : 50 mg/mL (111.47 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.2295 mL	11.1473 mL	22.2946 mL
5 mM	0.4459 mL	2.2295 mL	4.4589 mL
10 mM	0.2229 mL	1.1147 mL	2.2295 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 →90% corn oil

Solubility: ≥ 2.75 mg/mL (6.13 mM); Clear solution

此方案可获得 ≥ 2.75 mg/mL (6.13 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 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Hothersall JD, et al. Sustained wash-resistant receptor activation responses of GPR119 agonists. Eur J Pharmacol. 2015 Sep 5;762:430-42. [2]. Lan H, et al. Agonists at GPR119 mediate secretion of GLP-1 from mouse enteroendocrine cells through glucose-independent pathways. Br J Pharmacol. 2012 Apr;165(8):2799-807. [3]. Yang JW, et al. GPR119: a promising target for nonalcoholic fatty liver disease. FASEB J. 2016 Jan;30(1):324-35.

实验参考：

Cell Assay	HEK-GPR119 cells are grown to confluency in flasks, and cell suspensions are made by dislodging cells using PBS wash and accutase treatment followed by resuspension in culture media. Cells are then washed twice by pelleting through centrifugation (227g, 7 min, 20°C) and resuspension in warm assay buffer (Hank's Balanced Salt Solution supplemented with 20 mM HEPES and 0.01% fatty acid free BSA, pH 7.4), with a 5 min incubation at 37°C after the second wash. Cells are then counted and diluted to 200,000 cells/mL in warm assay buffer[1].
Animal Administration	Mice[2] C57BL/6 male mice are used. Overnight fasted, 10 week-old male mice (n=20 per group) are given either vehicle (15% polyethylene glycol 400+85% of 23.5% hydroxypropyl-β-cyclodextrin) or MBX-2982 at 10 mg/kg via oral gavage. Half of the animals (n=10 per group) are killed by CO2 asphyxiation 30 min after compound dosing, and blood is collected by cardiac puncture. To preserve active GLP-1, a DPP-IV inhibitor (10 μL per 1 mL of blood) is pre-added to the blood collection tubes and, before the cardiac puncture, the walls of the syringes are rinsed with the DPP-IV inhibitor. The other half of the animals (n=10 per group) received a bolus of oral glucose (3 g/kg) 30 min after compound dosing, and are killed for blood collection 10 min after the glucose load. GLP-1 levels in the plasma samples are measured using the active GLP-1 (ver 2) kit.
Kinase Assay	HEK-GPR119 cells are transfected with GloSensor 22F plasmid and used for dynamic cAMP measurements 24-30 h later. Cell suspensions are made by dislodging the cells using PBS wash and Accutase treatment followed by resuspension in culture media. Cells are then washed twice by pelleting through centrifugation (300g, 5 min) and resuspension in assay buffer (Hank's Balanced Salt Solution supplemented with 20 mM HEPES and 0.01% fatty acid free BSA, pH 7.4). Cells are then counted and diluted to 600,000 cells/mL in buffer, before GloSensor cAMP reagent is added (2% v/v) and equilibrated with the cells for 2 h at 20°C with periodic mixing. 50 μl/well of cells are added to white-bottomed 384 well plates (30,000 cells/well) in triplicate and baseline luminescence is measuring using an Envision plate-reader. 5 μL of MBX-2982 (serially diluted in DMSO and then diluted 1:100 in assay buffer to obtain ×10 concentrated solution) is manually added to the assay wells to achieve the stated final concentration. Plates are incubated at 20°C with luminescence read at regular intervals to detect dynamic cAMP changes over time within the same wells. cAMP responses at each time-point are expressed as fold over control (vehicle-treated cells)[1].
	[1]. Hothersall JD, et al. Sustained wash-resistant receptor activation responses of GPR119

References	agonists. Eur J Pharmacol. 2015 Sep 5;762:430-42. [2]. Lan H, et al. Agonists at GPR119 mediate secretion of GLP-1 from mouse enteroendocrine cells through glucose-independent pathways. Br J Pharmacol. 2012 Apr;165(8):2799-807. [3]. Yang JW, et al. GPR119: a promising target for nonalcoholic fatty liver disease. FASEB J. 2016 Jan;30(1):324-35.