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产品名称：TC-G-1008
产品别名：GPR39-C3

生物活性：

Description	TC-G-1008 (GPR39-C3) is a potent and orally available GPR39 agonist with EC_{50} values of 0.4 and 0.8 nM for rat and human receptors respectively.
IC_{50} & Target	IC50: 0.4 nM (GPR39), 0.8 nM (GPR39)[1]
In Vitro	TC-G-1008 shows selectivity over a panel of kinases (IC_{50}s>10 μM) and does not exhibit relevant binding affinity for the related ghrelin and neurotensin-1 receptors (IC_{50}s>30 μM)[1]. In HEK293-GPR39 cells, GPR39-C3, which is a positive allosteric modulator, activates cAMP production (downstream of Gs), IP1 accumulation (downstream of Gq), SRF-RE-dependent transcription (downstream of G12/13), and β-arrestin recruitment. GPR39-C3 induces dose- and time-dependent loss of response in cAMP production by second challenge of the compound[2].
In Vivo	Rat and mouse plasma protein binding for TC-G-1008 is measured as 99.3% and 99.1%, respectively. TC-G-1008 is orally bioavailable in mice and robustly induces acute GLP-1 levels. Upon single oral doses of 10, 30, and 100 mg/kg of aqueous suspensions in 0.5% methylcellulose/0.1% Tween 80, TC-G-1008 achieves, between 1 and 1.5 h, maximal exposures of 1.4, 6.1, and 25.3 μM, respectively[1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 100 mg/mL (238.72 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.3872 mL	11.9360 mL	23.8720 mL
	5 mM	0.4774 mL	2.3872 mL	4.7744 mL
	10 mM	0.2387 mL	1.1936 mL	2.3872 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 (5.97 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.97 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% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.97 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 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.97 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]. Peukert S, et al. Discovery of 2-Pyridylpyrimidines as the First Orally Bioavailable GPR39 Agonists. ACS Med Chem Lett. 2014 Aug 4;5(10):1114-8. [2]. Shimizu Y, et al. Rho kinase-dependent desensitization of GPR39; a unique mechanism of GPCR downregulation. Biochem Pharmacol. 2017 Sep 15;140:105-114.

实验参考：

Animal Administration	Mice: Mice are given single oral doses of 10, 30, and 100 mg/kg of TC-G-1008[1].
Kinase Assay	HEK293-GPR39 cells are plated and cultured in poly-d-lysine-coated, white, 384-well plates (4000 cells/well) in the growth medium overnight at 37°C in the presence of 5% CO_2. For pretreatment of the cells with GPR39 ligands (TC-G-1008) or vehicle control (DMSO), the culture medium is removed and the cells are stimulated with GPR39 ligands in assay buffer for the indicated time at 37°C. Then, the compound solution is removed and washed twice with PBS containing 0.1% BSA. For measurement of intracellular cAMP, the cells are stimulated with drugs in stimulation buffer for 30 min at 37°C. The intracellular cAMP level is determined by using HTRF cAMP dynamic 2 kit[2].
References	[1]. Peukert S, et al. Discovery of 2-Pyridylpyrimidines as the First Orally Bioavailable GPR39 Agonists. ACS Med Chem Lett. 2014 Aug 4;5(10):1114-8. [2]. Shimizu Y, et al. Rho kinase-dependent desensitization of GPR39; a unique mechanism of GPCR downregulation. Biochem Pharmacol. 2017 Sep 15;140:105-114.