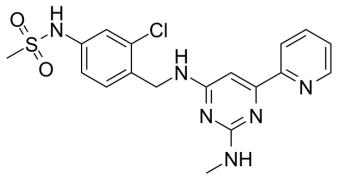
TC-G-1008

Cat. No.:	HY-103007
CAS No.:	1621175-65-2
Molecular Formula:	$C_{18}H_{19}ClN_6O_2S$
Molecular Weight:	418.9
Target:	GHSR
Pathway:	GPCR/G Protein
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.97 mM); Clear solution

BIOLOGICAL ACTIVITY

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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Mice are given single oral doses of 10, 30, and 100 mg/kg of TC-G-1008[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Transl Stroke Res. 2024 Mar 15.
- Neural Regen Res. 2024 Mar, 19(3): 687-696.

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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.

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