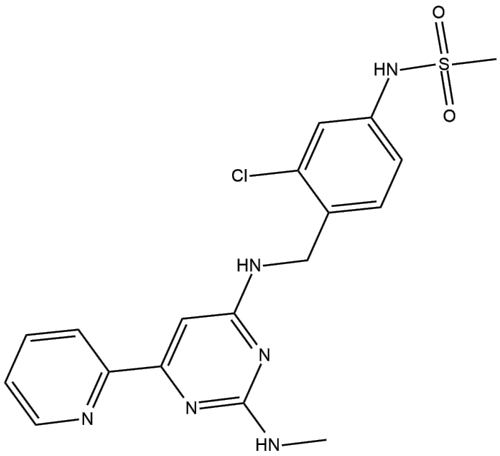
Product Data Sheet

Product Name: TC-G-1008
Cat. No.: GC19349

Chemical Properties

Cas. No.	1621175-65-2		
SMILES	CS(=O)(NC1=CC=C(CNC2=NC(NC)=NC(C3=NC=CC=C3)=C2)C(Cl)=C1)=O		
Formula	$C_{18}H_{19}ClN_6O_2S$	M.Wt	418.9
Solubility	DMSO : ≥ 100 mg/mL (238.72 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Product Data Sheet

Kinase experiment: 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% CO2. 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].

Animal experiment: Mice: Mice are given single oral doses of 10, 30, and 100 mg/kg of TC-G-1008[1].

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.

Background

TC-G-1008 (GPR39-C3) is a potent and orally available GPR39 agonist with EC50 values of 0.4 and 0.8 nM for rat and human receptors respectively.

TC-G-1008 shows selectivity over a panel of kinases (IC50s>10 uM) and does not exhibit relevant binding affinity for the related ghrelin and neurotensin-1 receptors (IC50s>30 uM)[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].

Product Data Sheet

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 uM, respectively[1].

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.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA