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产品名称：GGTI-298
产品别名：GGTI298

生物活性：

Description	GGTI298 is a CAAZ peptidomimetic geranylgeranyltransferase I (GGTase I) inhibitor, strongly inhibiting the processing of geranylgeranylated Rap1A with little effect on processing of farnesylated Ha-Ras, with IC_{50} values of 3 and > 20 μM in vivo, respectively.
IC_{50} & Target	IC50: 3 μM (Rap1A, in vivo), > 20 μM (Ha-Ras, in vivo)[3]
In Vitro	Both RhoA inhibitor (GGTI298) and ROCK inhibitor (H1152) significantly reduce cAMP agonist-stimulated IK(ap), whereas the latter additionally reduces colocalization of KCNN4c with the apical membrane marker wheat germ agglutinin in T84WT cells[1]. Knockdown of DR4 abolishes NF-κB activation, leading to sensitization of DR5-dependent apoptosis induced by the combination of GGTI298 and TRAIL. GGTI298/TRAIL activates NF-κB and inhibits Akt. knockdown of DR5, prevents GGTI298/TRAIL-induced IκBα and p-Akt reduction, suggesting that DR5 mediates reduction of IκBα and p-Akt induced by GGTI298/TRAIL. In contrast, DR4 knockdown further facilitates GGTI298/TRAIL-induced p-Akt reduction[2].
In Vivo	The vivo mouse ileal loop experiments show fluid accumulation is reduced in a dose-dependent manner by TRAM-34, GGTI298, or H1152 when injected together with cholera toxin into the loop[1].

Solvent&Solubility

In Vitro:

DMSO : 100 mg/mL (**208.49 mM;** Need ultrasonic)

H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0849 mL	10.4247 mL	20.8494 mL
	5 mM	0.4170 mL	2.0849 mL	4.1699 mL
	10 mM	0.2085 mL	1.0425 mL	2.0849 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 (5.21 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.21 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 (5.21 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.21 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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 (5.21 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.21 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]. Sheikh IA, et al. The Epac1 signaling pathway regulates Cl- secretion via modulation of apical KCNN4c channels in diarrhea. J Biol Chem. 2013 Jul 12;288(28):20404-15 [2]. Chen S, et al. Dissecting the roles of DR4, DR5 and c-FLIP in the regulation of geranylgeranyltransferase I inhibition-mediated augmentation of TRAIL-induced apoptosis. Mol Cancer. 2010 Jan 29;9:23. [3]. McGuire TF, et al. Platelet-derived growth factor receptor tyrosine phosphorylation requires protein geranylgeranylation but not farnesylation. J Biol Chem. 1996 Nov 1;271(44):27402-7.

实验参考：

Cell Assay	Cells are seeded in 96-well cell culture plates and treated the next day with the agents indicated. The viable cell number is determined using the sulforhodamine B assay. [2]
Animal Administration	The ileal loop experiment is performed in 6-8-week-old mice by a modified rabbit ileal loop assay. Following gut sterilization, the animals are kept fasted for 24 h prior to surgery and fed only water ad libitum. Anesthesia is induced by a mixture of ketamine (35 mg/kg of body weight) and xylazine (5 mg/kg of body weight). A laparotomy is performed, and the experimental loops of 5-cm length are constricted at the terminal ileum by tying with non-absorbable silk. The following fluids are instilled in each loop by means of a tuberculin syringe fitted with a disposable needle through the ligated end of the loop as the ligatured is tightened: pure CT (1 μg; positive control), saline (negative control), CT (1 μg) + TRAM-34 (different concentrations in μM as indicated in Fig. 7), CT (1 μg) + H1152 (1 μM), and CT (1 μg) + GGTI298 (different concentrations in μM), a specific inhibitor of Rap1A. The intestine is returned to the peritoneum, and the mice are sutured and returned to their cages. After 6 h, these animals are sacrificed by cervical dislocation, and the loops are excised. The fluid from each loop is collected, and the ratio of the amount of fluid contained in the loop with respect to the length of the loop (fluid accumulation ratio in g/cm) is calculated as a reflection of the efficacy of various inhibitors. [1]
Kinase Assay	The given cells are lysed with Reporter Lysis Buffer and subjected to luciferase activity assay using Luciferase Assay System in a luminometer. Relative luciferase activity is normalized to protein content. [2]
	[1]. Sheikh IA, et al. The Epac1 signaling pathway regulates Cl- secretion via modulation of apical KCNN4c channels in diarrhea. J Biol Chem. 2013 Jul 12;288(28):20404-15

References	[2]. Chen S, et al. Dissecting the roles of DR4, DR5 and c-FLIP in the regulation of geranylgeranyltransferase I inhibition-mediated augmentation of TRAIL-induced apoptosis. Mol Cancer. 2010 Jan 29;9:23. [3]. McGuire TF, et al. Platelet-derived growth factor receptor tyrosine phosphorylation requires protein geranylgeranylation but not farnesylation. J Biol Chem. 1996 Nov 1;271(44):27402-7.