

产品名称: **GGTI 298 (Trifluoroacetate Salt)**

产品别名: **GGTI298 Trifluoroacetate**

|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                      |             |              |
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| 生物活性:                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                      |             |              |
| Description               | GGTI298 Trifluoroacetate is a CAAZ peptidomimetic geranylgeranyltransferase I (GGTase I) inhibitor, which can inhibit Rap1A with IC <sub>50</sub> of 3 μM; little effect on Ha-Ras with IC <sub>50</sub> of >20 μM.                                                                                                                                                                                                                                                                                                                                                                                                      |                      |             |              |
| IC <sub>50</sub> & Target | IC50: 3 μM (Rap1A, in vivo), > 20 μM (Ha-Ras, in vivo)[3]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                      |             |              |
| In Vitro                  | RhoA inhibitor (GGTI298 Trifluoroacetate) significantly reduces cAMP agonist-stimulated apical K <sup>+</sup> conductance[1]. Knockdown of DR4 abolishes NF-κB activation, leading to sensitization of DR5-dependent apoptosis induced by the combination of GGTI298 Trifluoroacetate and TRAIL. GGTI298 Trifluoroacetate/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 Trifluoroacetate, or H1152 when inject together with cholera toxin into the loop[1].                                                                                                                                                                                                                                                                                                                                                                                                             |                      |             |              |
| Solvent&Solubility        | <b>In Vitro:</b><br><b>DMSO : 150 mg/mL (252.67 mM; Need ultrasonic and warming)</b><br><b>H<sub>2</sub>O : &lt; 0.1 mg/mL (insoluble)</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                      |             |              |
|                           | <b>Preparing Stock Solutions</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <b>Solvent</b>       | <b>Mass</b> |              |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | <b>Concentration</b> |             |              |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                      | <b>1 mg</b> | <b>5 mg</b>  |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                      |             | <b>10 mg</b> |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 1 mM                 | 1.6845 mL   | 8.4223 mL    |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 5 mM                 | 0.3369 mL   | 1.6845 mL    |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 10 mM                | 0.1684 mL   | 0.8422 mL    |
|                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                      |             | 1.6845 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。<br>储备液的保存方式和期限：-80℃，6 months；-20℃，1 month。-80℃ 储存时，请在 6 个月内使用，-20℃ 储存时，请在 1 个月内使用。                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                      |             |              |
|                           | <b>In Vivo:</b><br>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 <b>In Vitro</b> 方式配制澄清的储备液，再依次添加助溶剂：<br>——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                                                                                                                                                                                                                                                                                                                                                                                                  |                      |             |              |

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|                       | <p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO <math>\rightarrow</math>90% corn oil</p> <p>Solubility: <math>\geq</math> 2.5 mg/mL (4.21 mM); Clear solution</p> <p>此方案可获得 <math>\geq</math> 2.5 mg/mL (4.21 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。</p> <p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中，混合均匀。</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| References            | <p>[1]. Sheikh IA, et al. <u>The Epac1 signaling pathway regulates Cl- secretion via modulation of apical KCNN4c channels in diarrhea</u>. J Biol Chem. 2013 Jul 12;288(28):20404-15.</p> <p>[2]. Chen S, et al. <u>Dissecting the roles of DR4, DR5 and c-FLIP in the regulation of geranylgeranyltransferase I inhibition-mediated augmentation of TRAIL-induced apoptosis</u>. Mol Cancer. 2010 Jan 29;9:23.</p> <p>[3]. McGuire TF, et al. <u>Platelet-derived growth factor receptor tyrosine phosphorylation requires protein geranylgeranylation but not farnesylation</u>. J Biol Chem. 1996 Nov 1;271(44):27402-7.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| 实验参考：                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Cell Assay            | Cells are seeded in 96-well cell culture plates and treated the next day with the agents (including GGTI298 Trifluoroacetate). 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 modifying 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 fitting with a disposable needle through the ligated end of the loop: pure CT (1 $\mu$ g; positive control), saline (negative control), CT (1 $\mu$ g)+TRAM-34 (different concentrations in $\mu$ M), CT (1 $\mu$ g)+ H1152 (1 $\mu$ M), and CT (1 $\mu$ g)+GGTI298 Trifluoroacetate (different concentrations in $\mu$ M), 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[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].                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| References            | <p>[1]. Sheikh IA, et al. <u>The Epac1 signaling pathway regulates Cl- secretion via modulation of apical KCNN4c channels in diarrhea</u>. J Biol Chem. 2013 Jul 12;288(28):20404-15.</p> <p>[2]. Chen S, et al. <u>Dissecting the roles of DR4, DR5 and c-FLIP in the regulation of geranylgeranyltransferase I inhibition-mediated augmentation of TRAIL-induced apoptosis</u>. Mol Cancer. 2010 Jan 29;9:23.</p> <p>[3]. McGuire TF, et al. <u>Platelet-derived growth factor receptor tyrosine phosphorylation requires protein geranylgeranylation but not farnesylation</u>. J Biol Chem. 1996 Nov 1;271(44):27402-7.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |