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产品名称：GI 254023X
产品别名：GI4023; SRI028594

生物活性：

Description	GI254023X is a potent MMP9 and ADAM10 inhibitor with IC50s of 2.5 and 5.3 nM, respectively.
IC_{50} & Target	IC50: 2.5 nM (MMP9), 5.3 nM (ADAM10)[1]
In Vitro	In cellular assay 25 μM and even a concentration of 1 μM GI254023X strongly reduces constitutive RAGE shedding; also PACAP-inducing shedding of RAGE is significantly reduced. At a concentration of 100 nM, a slight inhibition of RAGE shedding is still observed. In in vitro assays with recombinant proteinases, GI254023X discriminates between ADAM17 (IC50=541 nM) and ADAM10 (IC50=5.3 nM)/MMP9 (IC50=2.5 nM)[1]. CXCL16 shedding is inhibited by ADAM protease inhibitors (e.g GI254023x). A2780 cells are incubated with the ADAM-10/ADAM-17 inhibitor TAPI-2, as well as the ADAM-10-selective inhibitor GI254023x, as the level of expressed ADAM-10 is on average 9.8-fold higher on mRNA level compare with ADAM-17. In addition, GI254023x also prevents CXCL16 shedding from the cell membrane and is even more potent than TAPI-2[2]. When apply the specific ADAM10 (α-secretase) inhibitor GI254023X (5 mM) to serum/glucose-deprived slices, PI counts are significantly increased in comparison with DMSO (carrier)-treated controls[3].
Solvent&Solubility	***In Vitro:*** **DMSO： 100 mg/mL (255.43 mM;** Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.5543 mL	12.7714 mL	25.5428 mL
	5 mM	0.5109 mL	2.5543 mL	5.1086 mL
	10 mM	0.2554 mL	1.2771 mL	2.5543 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 (6.39 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (6.39 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 (6.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.39 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 (6.39 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.39 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]. Verena V. Metz, et al. Induction of RAGE Shedding by Activation of G Protein-Coupled Receptors. PLoS One. 2012. [2]. M J M Gooden, et al. Elevated serum CXCL16 is an independent predictor of poor survival in ovarian cancer and may reflect pro-metastatic ADAM protease activity. British Journal of Cancer (2014) 110, 1535–1544. [3]. N Milosch, et al. Holo-APP and G-protein-mediated signaling are required for sAPPa-induced activation of the Akt. Cell Death Dis. 2014 Aug 28;5:e1391.
实验参考：	
Cell Assay	Cell death is quantified based on plasma membrane permeabilization. When apply the ADAM10 (a-secretase) inhibitor GI254023X (5 mM), slices are cultured in serum-/glucose-free medium for 48 h containing the inhibitor or its respective carrier (DMSO) as control. Round circles of identical size (Ø 500mm) are positioned in equivalent locations within the CA1 region of each hippocampus image and all PI-stained cells are counted using software. Cell viability assays are performed with a commercial kit according to the manufacturer's instructions. The assay quantitates ATP levels, an indicator of metabolically active cells, photometrically with a fluorescence plate reader. Additionally, the live-dead cell staining kit are applied according to the manual. Cells are simultaneously stained with green fluorescent calcein-AM (4mM; ex/em: 495/515 nm) to detect intracellular esterase activity (viable cells) and red fluorescent ethidium homodimer-3 (2mM; ex/em: 530/635 nm) to indicate loss of plasma membrane integrity (dead cells)[3].
References	[1]. Verena V. Metz, et al. Induction of RAGE Shedding by Activation of G Protein-Coupled Receptors. PLoS One. 2012. [2]. M J M Gooden, et al. Elevated serum CXCL16 is an independent predictor of poor survival in ovarian cancer and may reflect pro-metastatic ADAM protease activity. British Journal of Cancer (2014) 110, 1535–1544. [3]. N Milosch, et al. Holo-APP and G-protein-mediated signaling are required for sAPPa-induced activation of the Akt. Cell Death Dis. 2014 Aug 28;5:e1391.