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产品名称：IT1t (dihydrochloride)
产品别名：IT1t dihydrochloride

生物活性：

Description	IT1t dihydrochloride is a potent CXCR4 antagonist; inhibits CXCL12/CXCR4 interaction with an IC50 of 2.1 nM.		
IC_{50} & Target	CXCL12/CXCR4	HIV-1 (X4)	HIV-1 (X4)
	2.1 nM (IC_{50})	14.2 nM (IC_{50}, in MT-4 cells)	19 nM (IC_{50}, in PBMCs)
In Vitro	The CXCR4 is involved in chemotaxis and serves as a coreceptor for T-tropic HIV-1 viral entry and in cancer metastasis. IT1t is a small, drug-like, isothiourea derivative. IT1t shows very potent and dose-dependent inhibition of the CXCL12/CXCR4 interaction with an IC50 of 2.1 nM. This calcium flux is also inhibited by IT1t with an IC50 of 23.1[1]. Strong electron density is observed for IT1t in the binding cavity of both subunits of the CXCR4 homodimer. In dimers of CXCR4 bound to IT1t, the monomers interact only at the extracellular side of helices V and VI, leaving at least a 4 Å gap between the intracellular regions, which is presumably filled by lipids. The IT1t compound and CVX15 peptide have both been characterized as competitive inhibitors of CXCL12, and many of the receptor-ligand contacts in the co-crystal structures presented are important for CXCL12 binding, including the acidic Asp187, Glu2887.39 and Asp972.63. The binding site of IT1t may point to the major anchor region for this domain[2].		
In Vivo	IT1t reduces the formation of TNBC early metastases in the zebrafish xenograft model. Tumor cell invasion at the metastatic site is effectively reduced upon CXCR4 silencing (Fig. 7B), similar to the antagonist IT1t [3].		

Solvent&Solubility

In Vitro:

DMSO : ≥ 30 mg/mL (62.56 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0852 mL	10.4260 mL	20.8520 mL
	5 mM	0.4170 mL	2.0852 mL	4.1704 mL
	10 mM	0.2085 mL	1.0426 mL	2.0852 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: ≥ 1.67 mg/mL (3.48 mM); Clear solution

	此方案可获得 ≥ 1.67 mg/mL (3.48 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 16.699999 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: ≥ 1.67 mg/mL (3.48 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (3.48 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 16.699999 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: ≥ 1.67 mg/mL (3.48 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (3.48 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 16.699999 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Van Hout A, et al. Comparison of cell-based assays for the identification and evaluation of competitive CXCR4 inhibitors. PLoS One. 2017 Apr 14;12(4):e0176057. [2]. Wu B, et al. Structures of the CXCR4 chemokine GPCR with small-molecule and cyclic peptide antagonists. Science. 2010 Nov 19;330(6007):1066-71. [3]. Tulotta C, et al. Inhibition of signaling between human CXCR4 and zebrafish ligands by the small molecule IT1timpairs the formation of triple-negative breast cancer early metastases in a zebrafish xenograft model. Dis Model Mech. 2016 Feb;9(2):141-53.
实验参考：	
Cell Assay	Jurkat cells are incubated with serial dilutions (0.001, 0.01, 0.1, 1, 10, 100, 1000 μM) of IT1t at room temperature for two hours. Cytotoxicity of IT1t is also evaluated at 37°C over a longer period of time in MT-4 cells and PHA-stimulated PBMCs (ten day incubation) because these cell types are used in anti-HIV activity assays which last up to ten days. Cytotoxicity is evaluated microscopically and viability is assessed using the a kit[1].
References	[1]. Van Hout A, et al. Comparison of cell-based assays for the identification and evaluation of competitive CXCR4 inhibitors. PLoS One. 2017 Apr 14;12(4):e0176057. [2]. Wu B, et al. Structures of the CXCR4 chemokine GPCR with small-molecule and cyclic peptide antagonists. Science. 2010 Nov 19;330(6007):1066-71. [3]. Tulotta C, et al. Inhibition of signaling between human CXCR4 and zebrafish ligands by the small molecule IT1timpairs the formation of triple-negative breast cancer early metastases in a zebrafish xenograft model. Dis Model Mech. 2016 Feb;9(2):141-53.