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产品名称：Reparixin
产品别名：Repertaxin; DF 1681Y

生物活性：

Description	Reparixin is a non-competitive allosteric inhibitor of the chemokine receptors CXCR1 and CXCR2 activation with IC50s of 1 and 100 nM, respectively.			
IC_{50} & Target	$CXCR1^{wt}$	$CXCR1^{Ile43Val}$	CXCR1	CXCR2
	5.6 nM (IC_{50}, in L1.2 cells)	80 nM (IC_{50}, in L1.2 cells)	1 nM (IC_{50}, in cells)	~100 nM (IC_{50}, in cells)
In Vitro	Reparixin is a potent functional inhibitor of CXCL8-induced biological activities on human PMNs with a marked selectivity (around 400-fold) for CXCR1, as shown in specific experiments on CXCR1/L1.2 and CXCR2/L1.2 transfected cells and on human PMNs. The efficacy of Reparixin is significantly lower in L1.2 cells expressing Ile43Val CXCR1 mutant (IC50 values of 5.6 nM and 80 nM for CXCR1 wt and CXCR1 Ile43Val, respectively)[1]. Reparixin is a non-competitive allosteric inhibitor of IL-8 receptors with a 400-fold higher efficacy in inhibiting CXCR1 activity than CXCR2[2].			
In Vivo	Reparixin is an inhibitor of CXCL8 receptor CXCR1 and CXCR2 activation, has been shown to attenuate inflammatory responses in various injury models. Spontaneously hypertensive rats (SHR) are administered a subcutaneous injection of Reparixin (5 mg/kg) daily for 3 weeks. Reparixin effectively decreases systolic blood pressure and increased the blood flow[3]. Reparixin reduces the levels of IL-1β in the brain after middle cerebral artery occlusion/reperfusion (MCAo) in mice. Bars represent levels of IL-1β (pg/100 mg) measured by ELISA in the brain tissues of mice subjected or not (SHAM) to MCAo and pretreated with vehicle or Reparixin (30 mg/kg, s.c.)[4].			

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (352.87 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.5287 mL	17.6435 mL	35.2871 mL
	5 mM	0.7057 mL	3.5287 mL	7.0574 mL
	10 mM	0.3529 mL	1.7644 mL	3.5287 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 (8.82 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.82 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 (8.82 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.82 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 (8.82 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.82 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]. Moriconi A, et al. Design of noncompetitive interleukin-8 inhibitors acting on CXCR1 and CXCR2. J Med Chem. 2007 Aug 23;50(17):3984-4002. [2]. Bertini R, et al. Receptor binding mode and pharmacological characterization of a potent and selective dual CXCR1/CXCR2non-competitive allosteric inhibitor. Br J Pharmacol. 2012 Jan;165(2):436-54. [3]. Kim HY, et al. Reparixin, an inhibitor of CXCR1 and CXCR2 receptor activation, attenuates blood pressure and hypertension-related mediators expression in spontaneously hypertensive rats. Biol Pharm Bull. 2011;34(1):120-7. [4]. Sousa LF, et al. Blockade of CXCR1/2 chemokine receptors protects against brain damage in ischemic stroke in mice. Clinics (Sao Paulo). 2013;68(3):391-4. [5]. Bertini R, et al. Noncompetitive allosteric inhibitors of the inflammatory chemokine receptors CXCR1 and CXCR2: prevention of reperfusion injury. Proc Natl Acad Sci U S A. 2004 Aug 10;101(32):11791-6. [6]. Krishnamurthy A, et al. Identification of a novel chemokine-dependent molecular mechanism underlying rheumatoid arthritis-associated autoantibody-mediated bone loss. Ann Rheum Dis. 2016 Apr;75(4):721-9. [7]. Crespo J, et al. Human Naive T Cells Express Functional CXCL8 and Promote Tumorigenesis. J Immunol. 2018 Jul 15;201(2):814-820.

实验参考：

Cell Assay	L1.2 Cell suspension (1.5-3×10^6 cells/mL) is incubated at 37°C for 15 min in the presence of vehicle or of Reparixin (1 nM-1μM) and next seeded in triplicates in the upper compartment of the chemotactic chamber. Different agonists are seeded in the lower compartment of the chamber at the following concentrations: 1 nM CXCL8, 0.03 nM fMLP, 10 nM CXCL1, 2.5 nM CCL2, 30 nM C5a. The chemotactic chamber is incubated at 37°C in air with 5% CO_2 for 45 min (human PMNs) or 2 h (monocytes). At the end of incubation, the filter is removed, fixed, and stained and five oil immersion fields at high magnification (100×) are counted for each migration well after sample coding. L1.2

	migration is evaluated using 5 μm pore size Transwell filters[1].
Animal Administration	Rats[3] The Reparixin-treated group contained 5 SHR (SHR-R), where equal numbers of normal saline-treated SHR (SHR-N) and WKY (WKY-N) served as controls. Eighteen-week-old SHR received a subcutaneous injection of Reparixin (5 mg/kg) once per day for 3 weeks. Reparixin effects on blood flow, blood pressure and body weight are measured before treatment and then weekly until 1 week after the final injection. The effect of Reparixin on the expression of hypertension-related mediators in thoracic aortas, as well as nitric oxide (NO) plasma levels, is examined 1 week after the final injection. Mice[4] C57BL/6J mice (8-10 weeks old/20-25 g) are used. The subcutaneous administration of Reparixin (30 mg/kg) is performed 60 minutes before cerebral ischemia induction. The animals are divided into the following three experimental groups: Sham (i.e., the group in which the arteries are visualized, but there is no occlusion of the middle cerebral artery), Vehicle (i.e., the group pre-treated with the vehicle, phosphate buffer solution, 60 minutes before MCAo) and Reparixin (i.e., the group pre-treated with the drug 60 minutes before MCAo). To evaluate neurological signs secondary to MCAo, the animals are assessed with the SHIRPA battery 24 h after reperfusion.
References	[1]. Moriconi A, et al. Design of noncompetitive interleukin-8 inhibitors acting on CXCR1 and CXCR2. J Med Chem. 2007 Aug 23;50(17):3984-4002. [2]. Bertini R, et al. Receptor binding mode and pharmacological characterization of a potent and selective dual CXCR1/CXCR2non-competitive allosteric inhibitor. Br J Pharmacol. 2012 Jan;165(2):436-54. [3]. Kim HY, et al. Reparixin, an inhibitor of CXCR1 and CXCR2 receptor activation, attenuates blood pressure and hypertension-related mediators expression in spontaneously hypertensive rats. Biol Pharm Bull. 2011;34(1):120-7. [4]. Sousa LF, et al. Blockade of CXCR1/2 chemokine receptors protects against brain damage in ischemic stroke in mice. Clinics (Sao Paulo). 2013;68(3):391-4. [5]. Bertini R, et al. Noncompetitive allosteric inhibitors of the inflammatory chemokine receptors CXCR1 and CXCR2: prevention of reperfusion injury. Proc Natl Acad Sci U S A. 2004 Aug 10;101(32):11791-6. [6]. Krishnamurthy A, et al. Identification of a novel chemokine-dependent molecular mechanism underlying rheumatoid arthritis-associated autoantibody-mediated bone loss. Ann Rheum Dis. 2016 Apr;75(4):721-9. [7]. Crespo J, et al. Human Naive T Cells Express Functional CXCL8 and Promote Tumorigenesis. J Immunol. 2018 Jul 15;201(2):814-820.