



上海源叶生物科技有限公司
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产品名称: **BIX02189**
产品别名: **BIX02189**

生物活性:

Description	BIX02189 is a potent and selective MEK5 inhibitor with an IC ₅₀ of 1.5 nM. BIX02189 also inhibits ERK5 catalytic activity with an IC ₅₀ of 59 nM.				
IC ₅₀ & Target	MEK5	ERK5	CSF1R (FMS)	LCK	
	1.5 nM (IC ₅₀)	59 nM (IC ₅₀)	46 nM (IC ₅₀)	250 nM (IC ₅₀)	
	JAK3	TGFβR1	RPS6KA6 (RSK4)	RPS6KA3 (RSK2)	
	440 nM (IC ₅₀)	580 nM (IC ₅₀)	990 nM (IC ₅₀)	2.1 μM (IC ₅₀)	
	FGFR1	KIT	ABL1	MAPK14 (p38 alpha)	
	1 μM (IC ₅₀)	1.1 μM (IC ₅₀)	2.4 μM (IC ₅₀)	3.7 μM (IC ₅₀)	
	SRC				
	7.6 μM (IC ₅₀)				
In Vitro	BIX02189 blocks phosphorylation of ERK5, without affecting phosphorylation of ERK1/2 in sorbitol-stimulated HeLa cells. BIX02189 inhibits ERK5 phosphorylation in a dose dependent manner ^[1] . Fluvastatin reduces advanced glycation endproduct (AGE)-induced vascular smooth muscle cells (VSMCs) proliferation. To confirm this effect, VSMCs are treated with AGEs in the presence or absence of Fluvastatin and then subject to MTT assay. AGEs are found to dose-dependently induce cell proliferation, and this is significantly suppressed by Fluvastatin. In addition to MTT assay, the similar results are got with cell counting. This suppressive effect of Fluvastatin is prevented when VSMCs are pretreated with BIX02189. Whether ERK5 activation can reduce proliferation is also examined by using Ad-CA-MEK5α encoding a constitutively active mutant form of MEK5α (an upstream kinase of ERK5). AGE-induced proliferation determined by both MTT assay and cell counting is significantly diminished in the presence of Ad-CA-MEK5α, and Nrf2 depletion using siRNA restored AGE-induced proliferation ^[2] .				
In Vivo	Mice are treated with either 10 mg/kg of BIX02189 (in 25% DMSO) or vehicle control (same volume of 25% DMSO) by intraperitoneal injection. The nuclear localization of Nrf2 is inhibited in aortic endothelial cells from mice treated with BIX02189[3].				
	In Vitro: DMSO : ≥ 49.4 mg/mL (112.14 mM) * "≥" means soluble, but saturation unknown.				
		<div>Solvent Concentration</div> <div>Mass</div>	1 mg	5 mg	10 mg
Preparing Stock Solutions		1 mM	2.2699 mL	11.3497 mL	22.6994 mL
		5 mM	0.4540 mL	2.2699 mL	4.5399 mL
		10 mM	0.2270 mL	1.1350 mL	2.2699 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℃, 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。				



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Solvent&Solubility	<p>In Vivo:</p> <p>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:</p> <p>——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</p> <p>1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.67 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p> <p>2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.67 mM, 饱和度未知) 的澄清溶液。</p> <p>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。</p> <p>3.请依序添加每种溶剂: 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (5.67 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.67 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 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀</p>
References	<p>[1]. Tatake RJ, et al. Identification of pharmacological inhibitors of the MEK5/ERK5 pathway. Biochem Biophys Res Commun. 2008 Dec 5;377(1):120-5.</p> <p>[2]. Hwang AR, et al. Fluvastatin inhibits AGE-induced cell proliferation and migration via an ERK5-dependent Nrf2 pathway in vascular smooth muscle cells. PLoS One. 2017 May 22;12(5):e0178278.</p> <p>[3]. Kim M, et al. Laminar flow activation of ERK5 protein in vascular endothelium leads to atheroprotective effect via NF-E2-related factor 2 (Nrf2) activation. J Biol Chem. 2012 Nov 23;287(48):40722-31.</p>
实验参考:	
Cell Assay	AGE-induced proliferation is quantified using the MTT assay. Briefly, VSMCs are cultured on 24-well plates and when ~80% confluent, medium is replaced with serum free DMEM. Cells are then pretreated with BIX02189 (2 μ M) and stimulated with Fluvastatin (5 μ M) for 24 h. MTT reagents are added for 4 h at 37°C the removed by washing with PBS, and eluted with DMSO. Proliferation is measured using a microplate reader at 570 nm[2].
	<p>Mice[3]</p> <p>C57BL/6-specific pathogen-free mice are used. To determine the role of ERK5 on laminar flow-dependent Nrf2 nuclear translocation in vivo, 6-week-old male C57BL/6 mice are intraperitoneally treated with BIX02189 (10 mg/kg of body weight in 25% DMSO) or vehicle control. Following euthanization, vascular perfusion is performed with saline for 5 min followed by fixation</p>



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Animal Administration	with 4% paraformaldehyde for 5 min. Isolated aorta is incubated with 0.1% PBS with Tween, and then fat is removed. 5% goat serum is used for blocking and antibody diluents. Aortic endothelial cells are stained with anti-vascular endothelial-cadherin antibody and Topro3 for endothelial cell junction and nuclear, respectively. Cellular localization of Nrf2 is determined by immunofluorescence staining with anti-Nrf2 antibody under the Confocal microscope[3].
References	<p>[1]. Tatake RJ, et al. Identification of pharmacological inhibitors of the MEK5/ERK5 pathway. Biochem Biophys Res Commun. 2008 Dec 5;377(1):120-5.</p> <p>[2]. Hwang AR, et al. Fluvastatin inhibits AGE-induced cell proliferation and migration via an ERK5-dependent Nrf2 pathway in vascular smooth muscle cells. PLoS One. 2017 May 22;12(5):e0178278.</p> <p>[3]. Kim M, et al. Laminar flow activation of ERK5 protein in vascular endothelium leads to atheroprotective effect via NF-E2-related factor 2 (Nrf2) activation. J Biol Chem. 2012 Nov 23;287(48):40722-31.</p>

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