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产品名称：BIX02188
产品别名：BIX02188

生物活性：

Description	BIX02188 is a potent MEK5-selective inhibitor with an IC_{50} of 4.3 nM. BIX02188 inhibits ERK5 catalytic activity, with an IC_{50} of 810 nM.			
IC_{50} & Target	MEK5	ERK5	CSF1R (FMS)	LCK
	4.3 nM (IC_{50})	810 nM (IC_{50})	280 nM (IC_{50})	390 nM (IC_{50})
	KIT	TGFβR1	ABL1	RPS6KA6 (RSK4)
	550 nM (IC_{50})	1.8 μM (IC_{50})	2.1 μM (IC_{50})	3.2 μM (IC_{50})
	RPS6KA3 (RSK2)	MAPK14 (p38 alpha)	JAK3	SRC
	4.1 μM (IC_{50})	3.9 μM (IC_{50})	7.8 μM (IC_{50})	8.9 μM (IC_{50})
In Vitro	BIX02188 is a potent inhibitor of catalytic function of purified, active MEK5 enzyme. In activated HeLa cells, BIX02188 blocks phosphorylation of ERK5, without affecting phosphorylation of ERK1/2, JNK and p38 MAP kinases. To characterize the effects of BIX02188 in cultured endothelial cells (EC), H_2O_2 is used to activate BMK1. Bovine lung microvascular endothelial cells (BLMECs) are pretreated with 0.1-10 μM BIX02188 for 30 min, and then stimulated with 300 μM H_2O_2. BMK1 is dramatically activated by H_2O_2, with peak at 20 min. Phosphorylated BMK1 is inhibited by BIX02188 in a dose-dependent manner, with an IC_{50}=0.8±1.0 μM, and maximal inhibition at concentrations >3 μM. To examine the specificity of BIX02188, The effect of 0.1-10 μM BIX02188 is measured on the activity of ERK1/2 and JNK. There is no significant inhibition of ERK1/2 and JNK at these concentrations. These observations confirm the selectivity of BIX02188 for MEK5-induced BMK1 phosphorylation[1]. BIX02188 inhibits MEK5 and ERK5 activity, with IC_{50}s of 4.3 nM and 810 nM, respectively. BIX02188 does not inhibit closely related kinases MEK1, MEK2, ERK2, and JNK2. BIX02188 inhibits ERK5 phosphorylation in a dose dependent manner[2]. To assess the proliferation of podocytes in response to the pro-fibrotic stimulus of TGFβ1, podocytes are pre-incubated in the presence and absence of BIX02188 (10 μM) for 60 min after which cells are co-treated with TGFβ1 (2.5 ng/mL) for 48 h to provide adequate time for proliferation to occur and a colorimetric cell proliferation assay is employed where metabolic activity is directly proportional to cell number. Inhibition of Erk5 activation with BIX02188 incubation reduces podocyte cell number. TGFβ1 stimulation increases podocyte cell number which is prevented following BIX02188 co-treatment[3].			

In Vitro:

DMSO : ≥ 45 mg/mL (109.10 mM)

* "≥" means soluble, but saturation unknown.

	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
Preparing Stock Solutions	1 mM	2.4244 mL	12.1218 mL	24.2436 mL
	5 mM	0.4849 mL	2.4244 mL	4.8487 mL
	10 mM	0.2424 mL	1.2122 mL	2.4244 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。

Solvent&Solubility	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 (4.05 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (4.05 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% corn oil Solubility: ≥ 1.67 mg/mL (4.05 mM); Clear solution 此方案可获得 ≥ 1.67 mg/mL (4.05 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]. Li L, et al. Fluid shear stress inhibits TNF-mediated JNK activation via MEK5-BMK1 in endothelial cells. Biochem Biophys Res Commun. 2008 May 23;370(1):159-63. [2]. Badshah II, et al. Erk5 is a mediator to TGFβ1-induced loss of phenotype and function in human podocytes. Front Pharmacol. 2014 Apr 21;5:71. [3]. Tatake RJ, et al. Identification of pharmacological inhibitors of the MEK5/ERK5 pathway. Biochem Biophys Res Commun. 2008 Dec 5;377(1):120-5.
实验参考：	
Cell Assay	Human podocyte cell lines are treated at 37°C with the growth factor TGFβ1 (2.5 ng/mL in serum-free media containing BSA (0.1% w/v)). Inhibitors are applied at 37°C in serum-free media. To diminish Erk5 activation the upstream activator Mek5 is chemically inhibited by BIX02188 (10 μM) with an additional 60 min pre-incubation. TGFβ1-mediated signaling is stopped with SB431542 (10 μM), targeting the type I TGFβ receptor Alk5, with a further 30 min pre-incubation. Transmembrane receptor-induced Ras function is prevented with an additional 30 min pre-incubation using farnesylthiosalicylic acid (FTS; 10 μM). Controls (vehicles) are treated with serum-free media containing DMSO (0.1% v/v) and BSA (0.1% w/v)[3].
References	[1]. Li L, et al. Fluid shear stress inhibits TNF-mediated JNK activation via MEK5-BMK1 in endothelial cells. Biochem Biophys Res Commun. 2008 May 23;370(1):159-63. [2]. Badshah II, et al. Erk5 is a mediator to TGFβ1-induced loss of phenotype and function in human podocytes. Front Pharmacol. 2014 Apr 21;5:71. [3]. Tatake RJ, et al. Identification of pharmacological inhibitors of the MEK5/ERK5 pathway. Biochem Biophys Res Commun. 2008 Dec 5;377(1):120-5.