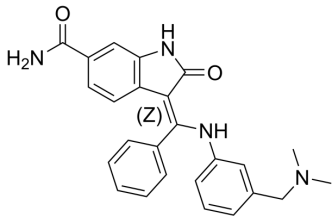
BIX02188

Cat. No.:	HY-12055
CAS No.:	334949-59-6
Molecular Formula:	$C_{25}H_{24}N_4O_2$
Molecular Weight:	412.48
Target:	MEK; ERK
Pathway:	MAPK/ERK Pathway; Stem Cell/Wnt
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 45 mg/mL (109.10 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (4.05 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (4.05 mM); Clear solution

BIOLOGICAL ACTIVITY

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 4.3 nM (IC_{50})	ERK5 810 nM (IC_{50})	CSF1R (FMS) 280 nM (IC_{50})	LCK 390 nM (IC_{50})
KIT 550 nM (IC_{50})	TGFβR1 1.8 μM (IC_{50})	ABL1 2.1 μM (IC_{50})	RPS6KA6 (RSK4) 3.2 μM (IC_{50})

	RPS6KA3 (RSK2) 4.1 μM (IC_{50})	MAPK14 (p38 alpha) 3.9 μM (IC_{50})	JAK3 7.8 μM (IC_{50})	SRC 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [3]

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].

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CUSTOMER VALIDATION

- Cell Signal. 2016 Feb;28(2):81-93.
- Research Square Preprint. 2021 Dec.
- Harvard Medical School LINCS LIBRARY

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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]. Tatake RJ, et al. Identification of pharmacological inhibitors of the MEK5/ERK5 pathway. Biochem Biophys Res Commun. 2008 Dec 5;377(1):120-5.

[3]. 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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