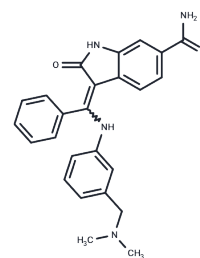


(E/Z)-BIX02188

Chemical Properties

CAS No. : 1094614-84-2
 Formula: C₂₅H₂₄N₄O₂
 Molecular Weight: 412.48
 Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
 Actual storage temperature shall be subject to the COA.



Biological Description

Description	BIX02188 is a specific MEK5 inhibitor (IC ₅₀ : 4.3 nM), also inhibits ERK5 catalytic activity (IC ₅₀ : 810 nM), and does not inhibit closely related kinases MEK1/2, JNK2, and ERK2.
Targets(IC ₅₀)	ERK,Others,MEK,TGF-beta/Smad
In vitro	BIX02188 significantly blocks MEK5 catalytic activity with IC ₅₀ of 4.3 nM and inhibits ERK5 catalytic activity with IC ₅₀ of 0.83 μM. It shows no activity against closely related kinases MEK1, MEK2, ERK1, p38α, JNK2, TGFβR1, EGFR, and STK16 with IC ₅₀ values of 1.8 μM for TGFβR1, 3.9 μM for p38α, and >6.3 μM for other kinases. Pretreatment with BIX02188 inhibits sorbitol-induced phosphorylation of ERK5 in HeLa cells in a dose dependent manner and displays no inhibitory activity against the phosphorylation of ERK1/2, p38, and JNK1/2 MAPKs. BIX02188 treatment alone for 24 hours in HeLa or HEK293 cells does not show any cytotoxic effect. BIX02188 inhibits transcriptional activation of MEF2C through the MEK5/ERK5 signaling cascade in active MEK5/ERK5/MEF2C-driven luciferase expression system in HeLa and HEK293 cells with IC ₅₀ values of 1.15 μM and 0.82 μM, respectively. [1] BIX02188 also inhibits phosphorylation of BMK1 in bovine lung microvascular endothelial cells (BLMECs) which are stimulated with 300 μM Water ₂ , in a dose-dependent manner, with IC ₅₀ of 0.8 μM, specifically by blocking the MEK5 signal pathway. BIX02188 completely reverses the inhibitory effect on TNF-mediation; JNK activation had a similar effect on BMK1 inhibition, suggesting that it inhibits TNF signaling through activation of the MEK5-BMK1
Kinase Assay	Catalytic assay: MEK5 protein isolated from a baculovirus expression system is used to measure kinase activity utilizing PKLight ATP Detection Reagent. The assay is performed using 15 nM GST-MEK5 and 0.75 μM ATP in assay buffer consisting of 25 mM Hepes, pH 7.5, 10 mM MgCl ₂ , 50 mM KCl, 0.2% BSA, 0.01% CHAPS, 100 μM Na ₃ VO ₄ , 0.5 mM DTT and 1% DMSO in the presence of varying concentrations of BIX02188. The kinase reaction mixture is incubated for 90 minutes at room temperature followed by addition of 10 μL of an ATP detection reagent for 15 minutes. The relative light unit (RLU) signal is measured and the RLU signals are converted to percent of control (POC) values for the determination of IC ₅₀ value.
Cell Research	The cells are serum starved for 20 hours prior to stimulation with sorbitol at a final concentration of 0.4 M for 20 minutes at 37 °C. BIX02188 is added 1.5 hours prior to the addition of sorbitol. The cells are harvested and lysed in 50 μL RIPA buffer containing Halt protease and phosphate inhibitors at 4 °C for 5-10 minutes. The lysates are

A DRUG SCREENING EXPERT

Cell Research	centrifuged for 10 minutes at 14,000 rpm and 50 μ L lysate is added to 50 μ L 2 \times sample buffer and boiled for 4 minutes at 95 $^{\circ}$ C. A 20 μ L sample is run on SDS-PAGE 10% Tris-glycine gels and transferred to nitrocellulose. Western blotting is done with appropriate antibodies.(Only for Reference)
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Solubility Information

Solubility	Ethanol: 3 mg/mL (7.27 mM),Sonication is recommended. H ₂ O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 40 mg/mL (96.97 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
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Preparing Stock Solutions

	1mg	5mg	10mg
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
50 mM	0.0485 mL	0.2424 mL	0.4849 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Tatake RJ, et al. Biochem Biophys Res Commun, 2008, 377(1), 120-125.

Li L, et al. Biochem Biophys Res Commun, 2008, 370(1), 159-163.

Inhibitor · Natural Compounds · Compound Libraries · Recombinant Proteins

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