BX-912

Cat. No.: HY-11005

CAS No.: 702674-56-4

Molecular Formula: $C_{20}H_{23}BrN_8O$

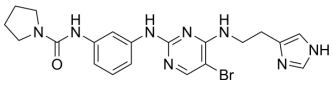
Molecular Weight: 471.35

Target: PDK-1; Apoptosis

Pathway: PI3K/Akt/mTOR; Apoptosis

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 : ≥ 100 mg/mL (212.16 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent, Mass	1 mg	5 mg	10 mg
1 mM	2.1216 mL	10.6078 mL	21.2157 mL
5 mM	0.4243 mL	2.1216 mL	4.2431 mL
10 mM	0.2122 mL	1.0608 mL	2.1216 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: ≥ 2.75 mg/mL (5.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (5.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.75 mg/mL (5.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BX-912 is a direct, selective, and ATP-competitive PDK1 inhibitor (IC_{50}=26 nM). BX-912 blocks PDK1/Akt signaling in tumor cells and inhibits the anchorage-dependent growth of a variety of tumor cell lines in culture or induces apoptosis[1].

IC_{50} & Target

IC50: 26 nM (PDK1)[1]

In Vitro

BX-912 promotes a block at the G2/M phase of the cell cycle in MDA-468 cells[1].

BX-912 binds to the ATP binding site of PDK1, and is 9-fold selective for PDK1 relative to PKA. BX-912 blocks PDK1 activity in PTEN-negative PC-3 cells. PTEN-negative PC-3 cells display constitutive activation of Akt which is reflected in high levels of the PDK1 product, phospho-Thr^{308}-Akt[1].
BX-912 is identified in a coupled assay measuring PDK1- and PtdIns-3,4-P_2-mediated Akt activation, which can detect inhibitors of PDK1, AKT2, or other steps critical for activation of AKT2[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

PDK1 is assayed in a direct kinase assay and a coupled assay format measuring PDK1 and PtdIns-3,4-P_2 mediated activation of AKT2. For the coupled assay, the final assay mixture (60 µL) contains: 15 mM MOPS, pH 7.2, 1 mg/mL bovine serum albumin, 18 mM β-glycerol phosphate, 0.7 mM dithiothreitol, 3 mM EGTA, 10 mM MgOAc, 7.5 µM ATP, 0.2 µCi of [γ-^{33}P]ATP, 7.5 µM biotinylated peptide substrate (biotin-ARRRDGGGAQPFRPRAATF), 0.5 µL of PtdIns-3,4-P_2-containing phospholipid vesicles, 60 pg of purified recombinant human PDK1, and 172 ng of purified recombinant human AKT2. After incubation for 2 h at room temperature, the biotin-labeled peptide is captured from 10 µL of the assay mixture on Streptavidin-coated SPA beads, and product formation is measured by scintillation proximity in a Wallac MicroBeta counter. The product formed is proportional to the time of incubation and to the amount of PDK1 and inactive AKT2 added. PDK1 is added at suboptimal levels so that the assay can sensitively detect inhibitors of AKT2 activation as well as direct inhibitors of PDK1 or AKT2[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Assay [1]

The cell lines MDA-468, MDA-453, HCT-116, U87-MG, U2OS, PC-3, B16F10, and MiaPaCa; LOX amelanotic human melanoma cells; and HeLa cells seeded at a low density (1,500-3,000 cells/well, 0.1 mL/well, 96-well plates) are incubated overnight. Compound treatments are made by adding 10 µL/well of BX-912 (1, 10, 100 and 1000 nM) in 1% DMSO and growth medium (final concentration of DMSO, 0.1%), followed by brief shaking. Treated cells are incubated for 72 h, and viability is measured by the addition of 10 µL of the metabolic dye WST-1. The WST-1 signal is read in a plate reader at 450 nm, and a no cell, or zero time cell, background is subtracted to calculate the net signal[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Cancer Sci. 2023 Oct 15.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Feldman RI, et al. Novel small molecule inhibitors of 3-phosphoinositide-dependent kinase-1. J Biol Chem. 2005 May 20;280(20):19867-74.

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