BI-D1870

Cat. No.: HY-10510

CAS No.: 501437-28-1

Molecular Formula: $C_{19}H_{23}F_2N_5O_2$

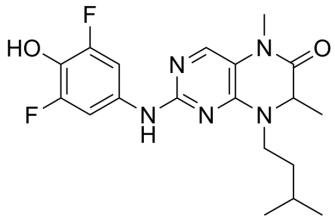
Molecular Weight: 391.42

Target: Ribosomal S6 Kinase (RSK); Autophagy

Pathway: MAPK/ERK Pathway; Autophagy

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 : 5 mg/mL (12.77 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5548 mL	12.7740 mL	25.5480 mL
5 mM	0.5110 mL	2.5548 mL	5.1096 mL
10 mM	0.2555 mL	1.2774 mL	2.5548 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: ≥ 2.5 mg/mL (6.39 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.39 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

BI-D1870 is an ATP-competitive, cell permeable and brain penetrated inhibitor of RSK isoforms, with IC_{50}s of 31 nM/24 nM/18 nM/15 nM for RSK1/RSK2/RSK3/RSK4, respectively[1][2][3][4][5].

IC_{50} & Target	RSK1	RSK2	RSK3	RSK4

In Vitro

BI-D1870 inhibits a mutant of RSK2 lacking the C-terminal kinase catalytic domain ($RSK2^{1-389:S381E}$) with an IC_{50} of approx. 30 nM. BI-D1870 inhibits RSK1 and RSK2 with IC_{50} values of 10 nM and 20 nM respectively, when the kinase assays are

	performed with 100 μM ATP. When the assays are performed at a 10-fold lower ATP concentration, the IC_{50} of BI-D1870 is reduced to 5 nM for RSK1 and 10 nM for RSK2[1]. ?BI-D1870 inhibits PLK1 with an IC_{50} of 100 nM, whilst the IC_{50} values for Aurora B, DYRK1a, CDK2-A, Lck, CK1 and GSK3β are 10- to 100-fold higher than that of the RSK isoforms. BI-D1870 (10 μM) inhibits the PMA-induced phosphorylation of GSK3α and GSK3β in HEK-293 cells. In HEK-293 cells, BI-D1870 inhibits the EGF-induced phosphorylation of LKB1 at Ser431 with an IC_{50} of approx. 1 μM[1]. ? ?BI-D1870 does not affect the activation of ERK1/ERK2 and MSK1, nor does it inhibit the phosphorylation of CREB[1]. ?BI-D1870 is a potent RSK family kinase inhibitor (K_ds: 10-100 nM), and also interact with BRD4(1) and PLK family, with K_ds of 3.5 μM and appr 10 nM[2]. ?BI-D1870 (10 μM) strongly induces p70S6K activation in serum-starved LN-229 cells, and alao stimulates the phosphorylation of rpS6 and p70S6K in LN-18 cells. BI-D1870 (1 μM) potently inhibits rpS6 phosphorylation, and inhibits PMA-induced rpS6 phosphorylation at concentrations higher than 1 μM[4]. ?BI-D1870 (1-5 μM) induces a dose- and time-dependent inhibition of cell proliferation in all cell types. BI-D1870 (1-3 μM) induces apoptosis in SCC4 cells and HSC-3 cells. BI-D1870 (0-5) modulates cell survival signaling pathways including Akt and p38 MAPK dose-dependently[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	BI-D1870 (0.5 mg/kg)-injected experimental autoimmune encephalomyelitis (EAE) mice exhibits a delayed neural deficit without obvious weight loss. Histopathological analyses shows inflammatory cell infiltration and demyelination in the spinal cord in control mice, but not in BI-D1870-treated mice. BI-D1870 protects against the infiltration of TH1 or TH17 cells into the CNS[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Purified His6-RSK1, His6-RSK2 or GST-RSK2$^{1\text{-}389:S381E}$ (1-2 units/mL) are assayed for 10 min at 30°C in a 50 μL assay mixture in Buffer A containing 30 μM substrate peptide (KEAKEKRQEQIAKRRRLSSLRASTSKSGGSQK), 10 mM magnesium acetate and 100 μM of [γ-^{32}P]ATP. Reactions are terminated and analysed. The amount of enzyme that catalysed the phosphorylation of 1 nmol of substrate peptide in 1 min is termed one unit. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [5]	Measurement of cell growth is assessed using the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide] assay in six replicates. The cells (5×10^3/200 μL) are seeded in 96-well, flat-bottom plates for 24 h and then exposed to various concentrations of test agents for the indicated time intervals. After removing the culture medium, 200 μL of the medium containing MTT at a concentration of 0.5 mg/mL is added, and the cells are incubated at 37°C for 2 h. The medium is removed, and the reduced MTT dye in each well is dissolved in 200 μL DMSO. Absorbance is determined with a multimode microplate reader Synergy HT at 570 nm. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Myelin oligodendrocyte glycoprotein (MOG) peptide 35-55 MEVGWYRSPFSRVVHLYRNGK) (BEX) is used to induce EAE in C57/BL6J mice. Mice are injecteds.c. with 200 g of MOG peptide in 100 μL of PBS emulsified in 100 μL complete Freund's adjuvant (CFA) that is further supplemented with five mg/mL Mycobacterium tuberculosis. In addition, 500 ng pertussis toxin is injected i.p. on days zero and two. The RSK inhibitor (BI-D1870; 0.5 mg/kg) is injected i.p. into mice two days after immunization with MOG peptide, and injection is repeated every other day for 11 days. Mice that receive only dimethyl sulfoxide (DMSO) solution are used as controls. Paralysis is evaluated according to the following scale: zero, no disease; one, tail limpness; two, hind limb weakness; three, hind limb paralysis; four, fore limb weakness; five, quadriplegia; six, death. For histological analysis, CNS samples are fixed with 4% paraformaldehyde and sliced at 4 μm, and then hematoxylin & eosin (H & E) staining is performed. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Adv Sci (Weinh). 2022 Oct;9(30):e2200717.
- Theranostics. 2020 May 25;10(15):6915-6927.
- Theranostics. 2019 Sep 21;9(24):7108-7121.
- Gut Microbes. 2023 Jan-Dec;15(1):2180315.
- PLoS Biol. 2022 Jun 1;20(6):e3001653.

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REFERENCES

[1]. Sapkota GP, et al. BI-D1870 is a specific inhibitor of the p90 RSK (ribosomal S6 kinase) isoforms in vitro and in vivo. Biochem J. 2007 Jan 1;401(1):29-38.

[2]. Ciceri P, et al. Dual kinase-bromodomain inhibitors for rationally designed polypharmacology. Nat Chem Biol. 2014 Mar 2.

[3]. Takada I, et al. The ribosomal S6 kinase inhibitor BI-D1870 ameliorated experimental autoimmune encephalomyelitis in mice. Immunobiology. 2016 Feb;221(2):188-92.

[4]. Roffe M, et al. Two widely used RSK inhibitors, BI-D1870 and SL0101, alter mTORC1 signaling in a RSK-independent manner. Cell Signal. 2015 Aug;27(8):1630-42.

[5]. Chiu CF, et al. Antitumor effects of BI-D1870 on human oral squamous cell carcinoma. Cancer Chemother Pharmacol. 2014 Feb;73(2):237-47.

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