For Research Use Only

BI-D1870

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Catalog Number: CM06360

产品信息

Catalog Number:
CM06360

CAS号:
501437-28-1

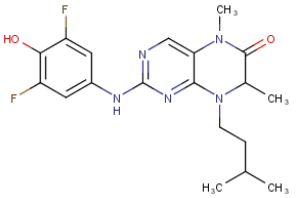
分子式:
$C_{19}H_{23}F_2N_5O_2$

主要靶点:
Autophagy|S6 Kinase

主要通路:
MAPK信号通路|PI3K/Akt/mTOR信号通路|自噬

分子量:
391.42

溶解度:
DMSO:72 mg/mL (183.9 mM),H2O:<1 mg/mL,Ethanol:<1 mg/mL



靶点活性

RSK3:18 nM (cell free)|RSK4:15 nM (cell free)|RSK1:31 nM (cell free)|RSK2:24 nM (cell free)

体外活性

BI-D1870 is cell permeant and prevents the RSK-mediated phorbol ester- and EGF (epidermal growth factor)-induced phosphorylation of GSK-3β and LKB1 in HEK 293 cells and Rat-2 cells. In contrast, BI-D1870 does not affect the agonist-triggered phosphorylation of substrates for six other AGC kinases. Moreover, BI-D1870 does not suppress the phorbol ester- or EGF-induced phosphorylation of CREB (cAMP-response-element-binding protein) [1]. In LN-229 cells, 1 μM BI-D1870 did not affect the phosphorylation of p70S6K, and rpS6 was scarcely reduced. However, 10 μM BI-D1870 strongly induced p70S6K activation after 90 min of incubation. In LN-18 cells, BI-D1870 at 10 μM stimulated the phosphorylation of rpS6 and p70S6K, displaying a peak at 90 min [2]. BI-D1870 exhibited a dose-responsive antiproliferative effect on OSCC cells with relative sparing of normal human oral keratinocytes. The compound inhibited the downstream RSK target YB-1 and caused apoptosis. In addition, BI-D1870 also induced G2/M arrest by modulating the expression of p21 and other cell cycle regulators. Other newly discovered anticancer attributes of BI-D1870 included the generation of reactive oxygen species and increases in endoplasmic reticulum stress and autophagy [3].

体内活性

BI-D1870 (0.5 mg/kg) administration protected mice from experimental autoimmune encephalomyelitis (EAE) by reducing the infiltration of TH1 and TH17 cells into the CNS and decreasing mRNA levels of Ccr6 in TH17 cells [4].

动物实验

Myelin oligodendrocyte glycoprotein (MOG) peptide 35–55. (MEVGWYRSPFSRVVHLYRNGK) (BEX) was used to induce EAE in C57/BL6J mice. Mice were injecteds.c. with 200 g of MOG peptide in100 L of PBS emulsified in 100 L complete Freund's adjuvant (CFA) that was further supplemented with five mg mL?1 Mycobacterium tuberculosis (H37Ra). In addition, 500 ng pertussis toxin was injected i.p. on days zero and two. The RSK inhibitor (BI-D1870; 0.5 mg kg?1) was injected i.p. into mice two days after immunization with MOG peptide, and injection was repeated every other day for 11 days. Mice that received only dimethyl sulfoxide (DMSO) solution were used as controls. Paralysis was evaluated according to the following scale: zero, no disease; one, tail limpness; two, hind limb weakness; three, hind limb paralysis; four, forelimb weakness; five, quadriplegia; six, death. For histological analysis, CNS samples were fixed with 4% paraformaldehyde and sliced at 4 m, and then hematoxylin & eosin (H & E) staining was performed [4].

细胞实验

The rat embryo fibroblast cell line, Rat-2 cells were cultured on 10 cm-diameter dishes in Dulbecco's Modified Eagle's medium supplemented with 10% (v/v) FBS. HEK-293 cells were cultured on 10 cm-diameter dishes in Dulbecco's Modified Eagle's medium supplemented with 10% FBS and 1×antimycotic/antibiotic solution. Prior to stimulation, cells were cultured in the absence of serum for 16 h. Inhibitors were dissolved in DMSO at a 1000-fold higher concentration than they were used at. These inhibitors, or the equivalent volume of DMSO as a control, were added to the tissue culture medium 30 min prior to stimulation unless indicated otherwise. The final concentration of DMSO in the culture medium was 0.1% and had no effect on agonist-induced activation or phosphorylation of any of the substrates examined. The cells were stimulated with the indicated agonists and lysed in 1 ml of ice-cold Lysis Buffer and centrifuged at 16000 g at 4 °C for 5 min. The supernatants were frozen in liquid nitrogen and stored at ?80 °C until use. Protein concentrations were determined using the Bradford method with BSA as the standard [1].

描述

BI-D1870 is a cell-permeable, ATP-competitive inhibitor of ribosomal S6 kinases (RSKs; IC50s: 31/24/18/15 nM for RSK1/2/3/4).

储存

Powder: -20°C for 3 years | In solvent: -80°C for 2 years