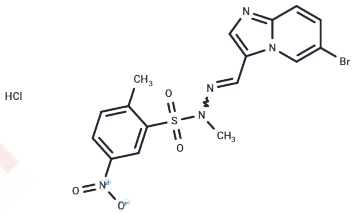
Data Sheet (Cat.No.T2287)

TargetMol

PIK-75 hydrochloride

Chemical Properties



CAS No. : 372196-77-5

Formula: C16H14BrN5O4S·HCl

Molecular Weight: 488.74

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	PIK-75 hydrochloride (PIK-75 HCl) is a p110α inhibitor with IC50 of 5.8 nM (200-fold more potently than p110β), isoform-specific mutants at Ser773, and also potently inhibits DNA-PK with IC50 of 2 nM in cell-free assays.
Targets(IC50)	Apoptosis,DNA-PK,PI3K
In vitro	In non-asthmatic airway smooth muscle cells, asthmatic ASM cells and lung fibroblasts, PIK-75 (1 μM) inhibited mitochondrial activity and induced cell death. In airway smooth muscle cells, PIK-75 (10 nM) inhibited TNF-α-induced CD38 mRNA expression and significantly reduced TNF-α-induced ADP-ribose cyclase activity. In TGFβ-stimulated ASM cells, PIK75 inhibited only asthmatic cells by decreasing mitochondrial activity.
In vivo	In non-asthmatic airway smooth muscle cells, asthmatic ASM cells and lung fibroblasts, PIK-75 (1 μM) inhibited mitochondrial activity and induced cell death. In airway smooth muscle cells, PIK-75 (10 nM) inhibited TNF-α-induced CD38 mRNA expression and significantly reduced TNF-α-induced ADP-ribose cyclase activity. In TGFβ-stimulated ASM cells, PIK75 inhibited only asthmatic cells by decreasing mitochondrial activity.
Kinase Assay	Inhibition Assays: The PI3K inhibitor PIK-75 is dissolved at 10 mM in dimethyl sulfoxide and stored at ?20°C until use. PI3K enzyme activity is determined in 50 μL of 20 mM HEPES, pH 7.5, and 5 mM MgCl2 containing 180 μM phosphatidyl inositol, with the reaction started by the addition of 100 μM ATP (containing 2.5 μCi of [γ-32P]ATP). After a 30-minute incubation at room temperature, the enzyme reaction is stopped by the addition of 50 μL of 1 M HCl. Phospholipids are then extracted with 100 μL of chloroform/methanol [1:1 (v/v)] and 250 μL of 2 M KCl followed by liquid scintillation counting. Inhibitors are diluted in 20% (v/v) dimethyl sulfoxide to generate a concentration versus inhibition of enzyme activity curve, which is then analyzed with the use of Prism version 5.00 for Windows to calculate the IC50. For kinetic analysis, a luminescent assay measuring ATP consumption is used. PI3K enzyme activity is determined in 50 μL of 20 mM HEPES, pH 7.5, and 5 mM MgCl2 with PI and ATP at various concentrations. After a 60-minute incubation at room temperature, the reaction is stopped by the addition of 50 μL of Kinase-Glo followed by a further 15-minute incubation. Luminescence is then read using a Fluostar plate reader. Results are analyzed using Prism.
Cell Research	Mitochondrial activity is assessed after stimulation with TGFβ with or without inhibitors for 48 hours using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium (MTT) assay. Harvested washed cells are resuspended in DMEM-lO% FCS and aliquoted (500 μL) into

	24-well cluster plates prior to serial dilution (1:2) in duplicates. To each well, 100 µL of an appropriate MTT concentration (dissolved in PBS and filtered through a 0.2 µm filter before use to remove any blue formazan product) is added immediately after diluting the cells, which are then incubated for 3.5 hours at 37 °C. The resulting blue formazan product is solubilized overnight (16 hours) at 37 °C by the addition of 500 µL of 10% sodium dodecyl sulfate (SDS) in 0.01 M HCl to each well. A sample (150 µL) from each duplicate well is transferred to a 96-well microplate, and the optical density determinedby automated spectrophotometry against a reagent blank (no cells). Absorbance is measured at a test wavelength of 570 nm and a reference wavelength of 690 nm. For each primary cell culture, results from three to six wells from each treatment are averaged, and data are expressed as absorbance 570 to 690 nm.(Only for Reference)

Solubility Information

Solubility	DMSO: Slightly soluble, (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0461 mL	10.2304 mL	20.4608 mL
5 mM	0.4092 mL	2.0461 mL	4.0922 mL
10 mM	0.2046 mL	1.023 mL	2.0461 mL
50 mM	0.0409 mL	0.2046 mL	0.4092 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.

Reference

Zheng Z, et al. Mol Pharmacol. 2011, 80(4), 657-664.
WO/2003/072557, 09/04/2003
Moir LM, et al. J Pharmacol Exp Ther. 2011, 337(2), 557-566.
Jude JA, et al. Am J Respir Cell Mol Biol. 2012. doi:10.1165/rcmb.2012-0025OC.
Smirnova T, et al. Oncogene. 2012, 31(6), 706-715.