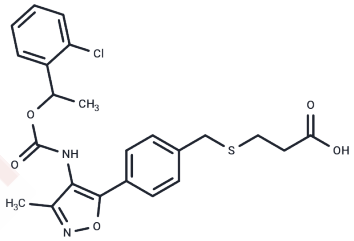
Data Sheet (Cat.No.T6108)

TargetMol

Ki16425

Chemical Properties



CAS No. : 355025-24-0

Formula: C23H23ClN2O5S

Molecular Weight: 474.96

Appearance: no data available

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

Biological Description

Description	Ki16425 (Debio 0719) is a competitive, potent, and reversible antagonist to LPA1, LPA2, and LPA3, with Ki values of 0.34 μM, 6.5 μM, and 0.93 μM, respectively.
Targets(IC50)	LPA Receptor,LPL Receptor
In vitro	Kil6425 preferentially inhibits LPA1- and LPA3-mediated responses but has only a moderate effect on LPA2. Ki16425 inhibits the LPA-induced Ca(2+) response in THP-1 cells, 3T3 fibroblasts, and A431 cells, but had only a marginal effect in PC-12 cells and HL-60 cells, which means that Ki16425 seems to be a useful tool for evaluating the involvement of specific LPA receptors in the short-term response to LPA. Ki16425 inhibits long-term DNA synthesis and cell migration as induced by LPA in Swiss 3T3 fibroblasts. [1] Ki16425 reduces the LPA-induced activation of p42/p44 mitogen activated protein kinase (MAPK), while acting as a weak stimulator of p42/p44 MAPK on its own, properties typical of a protean agonist. Ki16425 also significantly reduces the NGF-induced stimulation of p42/p44 MAPK and inhibited NGF-stimulated neurite outgrowth in PC-12 cells. [2] Ki16425 markedly inhibits the expressions of COX-2 protein induced by synovial fluids. The enhancement of the IL-1 action by LPA on COX-2 expression is also inhibited by Ki16425. [3]
In vivo	Ki-16425 (30 mg/kg, i.p.) completely blocks LPA-induced neuropathic pain-like behaviors, when administered 30 min but not 90 min before lysophosphatidic acid injection, suggesting that Ki-16425 is a short-lived inhibitor. Ki-16425 also inhibits nerve injury-induced up-regulation of Caα2δ-1 in the dorsal root ganglion and reduction of SP immunoreactivity in the spinal dorsal horn. [4]
Kinase Assay	High-throughput screening: Screening is conducted at the ICCB-Longwood screening facility. 10 μL of recombinant USP14 protein are dispensed into each well of a 384-well low volume plate in duplicate, using a Wellmate plate dispenser. 33.3?nL of compound from the library are pin-transferred into the wells using a Seiko pin transfer robotic system, followed by pre-incubation for about 30?min. The last two columns of each plate are used for positive and negative controls for the assay. To initiate the enzyme reaction, 10?μL of VS-proteasome plus Ub-AMC mixture are added to each well, using a Wellmate dispenser. Samples are then incubated for another 45?min. Ub-AMC hydrolysis is measured at Ex355/Em460 using an Envision plate reader. The final concentrations of USP14, VS-proteasome and Ub-AMC are 15?nM, 1?nM and 0.8 μM, respectively. The final concentration of test compound is approximately 17?μM. Enzymes and substrates are prepared in Ub-AMC assay buffer (50?mM Tris-HCl (pH?7.5), 1?mM EDTA, 1?mM ATP, 5

mM MgCl2, 1?mM DTT, and 1 mg/Ml ovalbumin).

Solubility Information

Solubility	DMSO: 94 mg/mL (197.91 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: 84 mg/mL (176.86 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.1054 mL	10.5272 mL	21.0544 mL
5 mM	0.4211 mL	2.1054 mL	4.2109 mL
10 mM	0.2105 mL	1.0527 mL	2.1054 mL
50 mM	0.0421 mL	0.2105 mL	0.4211 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

Ohta H, et al, Mol Pharmacol, 2003, 64(4), 1994-12005.
Moughal NA, et al. J Neurochem, 2006, 98(6), 1920-1929.
Nochi H, et al. J Immunol, 2008, 181(7), 5111-5119.
Ma L, et al. J Neurochem, 2009, 109(2), 603-610.