Product Data Sheet

Product Name: PD 151746
Cat. No.: GC10561

Chemical Properties

Cas. No.	179461-52-0		
Chemical Name	(Z)-3-(5-fluoro-1H-indol-3-yl)-2-mercaptoacrylic acid		
SMILES	FC1=CC(C(/C([H])=C(S)/C(O)=O)=CN2)=C2C=C1		
Formula	$C_{11}H_8FNO_2S$	M.Wt	237.25
Solubility	≥ 11.6mg/mL in DMSO	Storage	Desiccate at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	PD 151746		

Protocol

Cell experiment [1]:

Cell lines	Cerebellar granule cells
Preparation method	The solubility of this compound in DMSO is > 11.6 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below - 20 °C for several months.

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Reacting condition	20 or 40 μM; 24 hrs
Applications	In cerebellar granule cells, pre-treatment with 20 or 40 μM PD 151746 for 24 hrs inhibited calpain and thus, protected neurons against the effect of serum/potassium (S/K) withdrawal, restoring the number of cell survival. Moreover, PD 151746 at the dose of 40 μM inhibited the increase of MEF2 phosphorylation and cdk5/p25 formation, as well as inhibited caspase-3 activity.

References:

[1]. Verdaguer E, Alvira D, Jiménez A, et al. Inhibition of the cdk5/MEF2 pathway is involved in the antiapoptotic properties of calpain inhibitors in cerebellar neurons. Br J Pharmacol, 2005, 145(8): 1103-1011.

Background

PD 151746 is a potent and selective inhibitor of calpain with Ki value of 0.26 μM for μ-Calpain.

Calpain is a calcium-dependent, non-lysosomal cysteine protease that expressed in mammals and many other organisms. Calpain plays an important role in cell mobility and cell cycle progression.

PD 151746 is a cell-permeable, potent and selective calpain inhibitor. PD151746 significantly inhibited NMDA-induced α-spectrin breakdown product (SBDP) of 145 kDa and completely inhibited the fragmentation of calmodulin-dependent protein kinase II-α

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(CaMPK-IIα) and nitric oxide synthase (nNOS), which were cleaved by calpain [1]. In cerebellar granule cells, PD151746 inhibited serum/potassium (S/K) withdrawal induced apoptosis by 29% through inhibition of calpain. Also, PD151746 inhibited the increase of MEF2 phosphorylation and cdk5/p25 formation and inhibited caspase-3 activity [2]. In human hepatoma G2 cells, PD151746 significantly reduced insulin-stimulated glycogen synthesis and increased the amount of protein tyrosine phosphatase-ε (PTPε), which suggested that calpain played an important role in regulation of insulin-stimulated glycogen synthesis [3]. In HEK-293 cells expressing human formyl peptide receptor (hFPR) or hFPR-like 1 (hFPRL1), PD151746 increased cytoplasmic free Ca2+ ([Ca2+]i) [4].

References:

[1]. Hajimohammadreza I, Raser KJ, Nath R, et al. Neuronal nitric oxide synthase and calmodulin-dependent protein kinase IIalpha undergo neurotoxin-induced proteolysis. J Neurochem, 1997, 69(3): 1006-1013.
[2]. Verdaguer E, Alvira D, Jiménez A, et al. Inhibition of the cdk5/MEF2 pathway is involved in the antiapoptotic properties of calpain inhibitors in cerebellar neurons. Br J Pharmacol, 2005, 145(8): 1103-1011.
[3]. Meier M, Klein HH, Kramer J, et al. Calpain inhibition impairs glycogen syntheses in HepG2 hepatoma cells without altering insulin signaling. J Endocrinol, 2007, 193(1): 45-51.
[4]. Fujita H, Kato T, Watanabe N, et al. Stimulation of human formyl peptide receptors by calpain inhibitors: homology modeling of receptors and ligand docking simulation. Arch Biochem Biophys, 2011, 516(2): 121-127.

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