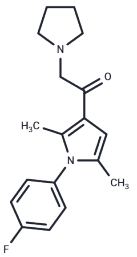
Data Sheet (Cat.No.T6107)

TargetMol

IU1

Chemical Properties



CAS No. : 314245-33-5

Formula: C18H21FN2O

Molecular Weight: 300.37

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	IU1(IC50=4.7 μ M), a reversible, specific human USP14 proteasome inhibitor, can penetrate the cell.
Targets(IC50)	Autophagy,DUB
In vitro	IU1 binds specifically to the activated form of USP14. IU1 can potentially inhibit USP14 by preventing its docking on the proteasome, exhibiting little or no activity toward 8 other DUBs, IsoT, UCH37, BAP1, UCH-L1, UCH-L3, USP15, USP2, USP7. USP14 inhibition is rapidly established upon addition of IU1 and rapidly reversed upon its removal. IU1 inhibits USP14 induced chain trimming and decreases electrophoretic mobility of Ub-CCNB species. IU1 enhances proteasomal degradation of Ub-CCNB in the presence of USP14. IU1 promots degradation of tau and depletes TDP-43, ATXN3, and glial fibrillary acidic protein (GFAP) in proteotoxic mechanisms. [1]
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).
Cell Research	MTT(Only for Reference)

Solubility Information

Solubility	DMSO: 48 mg/mL (159.8 mM),Sonication is recommended. Ethanol: 15 mg/mL (49.94 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+90% Saline: < 4.8 mg/mL (15.98 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. 10% DMSO+40% PEG300+5% Tween 80+45% Saline: 4.8 mg/mL (15.98 mM),Solution. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.3292 mL	16.6461 mL	33.2923 mL
5 mM	0.6658 mL	3.3292 mL	6.6585 mL
10 mM	0.3329 mL	1.6646 mL	3.3292 mL
50 mM	0.0666 mL	0.3329 mL	0.6658 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.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Byung-Hoon L, et al. Nature, 2010, 467(7312), 179-184.
Wu W, Xu H, Liao C, et al. Blockade of USP14 potentiates type I interferon signaling and radiation-induced antitumor immunity via preventing IRF3 deubiquitination. Cellular Oncology. 2022: 1-15
Yue X, Liu T, Wang X, et al.Pharmacological inhibition of BAP1 recruits HERC2 to competitively dissociate BRCA1-BARD1, suppresses DNA repair and sensitizes CRC to radiotherapy.Acta Pharmaceutica Sinica B.2023