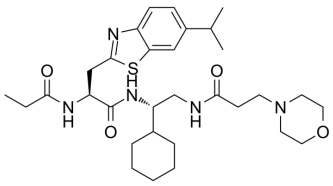
DI-591

Cat. No.:	HY-124602
CAS No.:	2245887-38-9
Molecular Formula:	$C_{31}H_{47}N_5O_4S$
Molecular Weight:	585.8
Target:	E1/E2/E3 Enzyme
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (21.34 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.7071 mL	8.5353 mL	17.0707 mL
	5 mM	0.3414 mL	1.7071 mL	3.4141 mL
	10 mM	0.1707 mL	0.8535 mL	1.7071 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (2.13 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.13 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.13 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

DI-591 is a potent, high-affinity and cell-permeable inhibitor of the DCN1-UBC12 interaction. DI-591 binds to DCN1 and DCN2 with K_i values of 12 nM and 10.4 nM, respectively and has no appreciable binding to DCN3, DCN4, and DCN5 proteins. DI-591 selectively inhibits neddylation of cullin 3 but has no or minimal effect on neddylation of other cullin family members[1].

IC_{50} & Target

DCN1-UBC12[1]

In Vitro

DI-591 (Compound 44) binds to DCN1 and DCN2 with K_i values of 12 nM and 10.4 nM, respectively and has no appreciable binding to DCN3, DCN4, and DCN5 proteins. Hence, DI-591 displays a very-high binding affinity to recombinant human DCN1

and DCN2 proteins and >1000-fold selectivity over recombinant human DCN3-5 proteins[1].
DI-591 (Compound 44; 0-10 μM; 1 hour; KYSE70 cells) binds to both cellular DCN1 and DCN2 proteins and disrupts the association of cellular DCN1 and UBC12 proteins[1].
DI-591 (Compound 44; 10 μM; 24 hours; THLE2 cells) treatment robustly increases the mRNA levels of NQO1 and HO1, leading to upregulation of HO1 protein in the cells. Significantly, DI-591 has no effect on the mRNA level of NRF2[1].
The selective inhibition of neddylation of cullin 3 by DI-591 leads to accumulation NRF2 protein and its transcriptional activation. Knockdown experiments indicate that DCN1, but not DCN2, plays a key role in regulation of neddylation of cullin 3 but not of other cullins. DI-591 is an excellent probe compound to investigate the role of the cullin 3 CRL (Cullin-RING E3 ubiquitin ligase) in biological processes and human diseases[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Western Blot Analysis[1]

Cell Line:	KYSE70 cells
Concentration:	0 μM, 1 μM, 3 Mm or 10 μM
Incubation Time:	1 hour
Result:	Potently bound to cellular DCN1 and DCN2 proteins. Enhanced the stability of DCN1 and DCN2 protein in a dose-dependent manner.

RT-PCR[1]

Cell Line:	THLE2 cells
Concentration:	10 μM
Incubation Time:	24 hours
Result:	Robustly increases the mRNA levels of NQO1 and HO1.

REFERENCES

[1]. Zhou H, et al. A potent small-molecule inhibitor of the DCN1-UBC12 interaction that selectively blocks cullin 3 neddylation. Nat Commun. 2017 Oct 27;8(1):1150.

Caution: Product has not been fully validated for medical applications. For research use only.

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