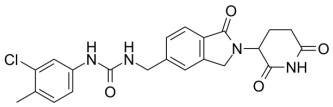
CC-885

Cat. No.:	HY-101488
CAS No.:	1010100-07-8
Molecular Formula:	$C_{22}H_{21}ClN_4O_4$
Molecular Weight:	440.88
Target:	Ligands for E3 Ligase; Molecular Glues
Pathway:	PROTAC
Storage:	Powder -20°C 3 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 66.67 mg/mL (151.22 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2682 mL	11.3410 mL	22.6819 mL
	5 mM	0.4536 mL	2.2682 mL	4.5364 mL
	10 mM	0.2268 mL	1.1341 mL	2.2682 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: 2.25 mg/mL (5.10 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.25 mg/mL (5.10 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CC-885 is a cereblon (CRBN) modulator with potent anti-tumour activity. CC-885 is also a known degrader of GSPT1, inhibiting protein translation.

IC_{50} & Target

CRBN[1].

In Vitro

Acute myeloblatlic leukemia (AML) cell lines, human liver epithelial cell line (THLE-2) and human peripheral blood mononuclear cells (PBMC) are treated with varying concentrations of CC-885, with IC_{50}s of 10^{-6}-1 μM. The effect of CC-885 on cell proliferation in AML cell lines, THLE-2 and human PBMC is more powerful than Lenalidomide and Pomalidomide with IC_{50}s>10 μM. To address whether the cereblon-dependent degradation of GSPT1 is responsible for the cytotoxic effects of CC-885, a GSPT1 mutant that retains its normal function, but loses CC-885-dependent cereblon binding, is used to distinguish the role of GSPT1 from that of other substrates. CC-885 is tested in 293T HEK cells stably expressing the CC-885-

sensitive or -resistant GSPT1 variants. Overexpression of a resistant variant GSPT1Δ(1–138)/(G575N) completely abrogate the CC-885-induced anti-proliferation, whereas overexpression of a CC-885-sensitive variant GSPT1Δ(1-138) only confer partial protection. Similar results are obtained in AML cell lines[1].

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

PROTOCOL

Cell Assay [1]

Human cancer cell lines cultured in the growth medium are seeded into black 384-well plates containing DMSO or test compounds such as CC-885 ($10\times^{-6}$-1 μM). The seeding density for each cell line is optimized to allow the cell growth in the linear range during a 3-day culture period. To test the compound effect on cell proliferation in acute myeloid leukaemia (AML) cell lines, 5,000 to 10,000 cells per well in 200 μl complete culture media are seeded into black 96-well plates containing DMSO or test compounds such as CC-885. After 48 or 72 h, cell proliferation is assessed using the CellTiter-Glo (CTG) Luminescent Cell Viability Assay[1].

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

CUSTOMER VALIDATION

- Nat Commun. 2023 Dec 19;14(1):8437.
- Nat Commun. 2022 Sep 10;13(1):5324.
- J Clin Invest. 2022 Jun 28;e153514.
- Nat Chem Biol. 2024 Mar 21.
- Cell Chem Biol. 2020 Jul 16;27(7):866-876.e8.

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REFERENCES

[1]. Jochem M, et al. Degradome analysis to identify direct protein substrates of small-molecule degraders[J]. bioRxiv, 2024: 2024.01. 28.577572.

[2]. Mary E. Matyskiela, et al. A novel cereblon modulator recruits GSPT1 to the CRL4CRBN ubiquitin ligase. Nature. 2016 Jul 14;535(7611):252-7.

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