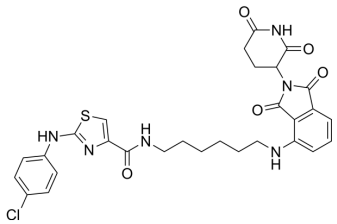
PROTAC-O4I2

Cat. No.:	HY-141881
CAS No.:	2785323-62-6
Molecular Formula:	$C_{29}H_{29}ClN_6O_5S$
Molecular Weight:	609.1
Target:	PROTACs; Apoptosis; SF3B1
Pathway:	PROTAC; Apoptosis; Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 250 mg/mL (410.44 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.6418 mL	8.2088 mL	16.4177 mL
5 mM	0.3284 mL	1.6418 mL	3.2835 mL
10 mM	0.1642 mL	0.8209 mL	1.6418 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: ≥ 2.08 mg/mL (3.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PROTAC-O4I2 is a PROTAC targets splicing factor 3B1 (SF3B1). PROTAC-O4I2 induces FLAG-SF3B1 degradation with an IC_{50} value of 0.244 μM in K562 cells. PROTAC-O4I2 also induces cellular apoptosis in K562 WT cells[1].

IC_{50} & Target

Cereblon

In Vitro

PROTAC-O4I2 introduces Thalidomide to ubiquitin E3 ligase cereblon (CRBN), which selectively degrades SF3B1 and inhibits tumor growth in cells[1].

PROTAC-O4I2 degrades and inhibits SF3B1 in K562 cells. PROTAC-O4I2 exhibits anti-proliferation effects on SF3B1 WT, SF3B1 OE, and SF3B1 K700E cells with IC_{50}s of 228, 63, and 90 nM, respectively[1].

PROTAC-O4I2 induces FLAG-SF3B1 degradation in a concentration-dependent manner with a half maximal inhibitory concentration (IC_{50}) value of 0.244 μM in K562 cells[1].

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

Cell Proliferation Assay[1]

Cell Line:	K562 control cells (WT), cells overexpressing SF3B1 (OE), and cells expressing $SF3B1^{K700E}$ (K700E)
Concentration:	1 pM, 0.1 nM, 10 nM, 1 μM, 100 μM
Incubation Time:	72 hours
Result:	In K562 WT cells, the parental compound O4I2 exhibited a marginal anti-proliferation effect (IC_{50} >10 μM). In contrast, PROTAC-O4I2 showed significantly higher toxicity with an IC_{50} of 228 nM, nearly 3-fold less potent than pladienolide B (IC_{50}, 76 nM). Cells overexpressing SF3B1 WT was slightly resistant to pladienolide B (IC_{50}, 134 nM), but more sensitive to PROTAC-O4I2 (an IC_{50} value of 63 nM).

Apoptosis Analysis[1]

Cell Line:	K562 cell
Concentration:	1 μM
Incubation Time:	48 h
Result:	Induced cellular apoptosis s in cells expressing $SF3B1^{WT}$ or $SF3B1^{K700E}$.

In Vivo

PROTAC-O4I2 (10 μM) significantly increases survival by interference with the maintenance and proliferation of tumor in a Drosophila intestinal tumor model[1].

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

Animal Model:	Drosophila melanogaster[1]
Dosage:	10 μM
Administration:	Flies were fed on a round filter paper loaded with PROTAC-O4I2 in a 5% sucrose solution, maintained at 18℃ and flipped into a freshly prepared vial every 2 days
Result:	Decreased stem cell activity, blocked the initiation and growth of tumor, and improved the survival of the Drosophila ISC tumor model.

REFERENCES

[1]. Rodrigo A Gama-Brambila, et al. A PROTAC targets splicing factor 3B1. Cell Chem Biol. 2021 Nov 18;28(11):1616-1627.e8.

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