U7D-1

Cat. No.: HY-148369

Molecular Formula: $C_{53}H_{65}N_9O_7$

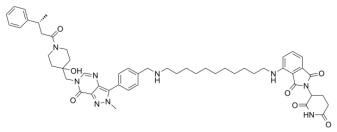
Molecular Weight: 940.14

Target: PROTACs; Deubiquitinase; Apoptosis; MDM-2/p53

Pathway: PROTAC; Cell Cycle/DNA Damage; Apoptosis

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 : 100 mg/mL (106.37 mM; Need ultrasonic)

Preparing Stock Solutions

Concentration \ Solvent \ Mass	1 mg	5 mg	10 mg
1 mM	1.0637 mL	5.3184 mL	10.6367 mL
5 mM	0.2127 mL	1.0637 mL	2.1273 mL
10 mM	0.1064 mL	0.5318 mL	1.0637 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: ≥ 2.5 mg/mL (2.66 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (2.66 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

U7D-1 is a first-in-class potent and selective USP7 (ubiquitin-specific protease 7) PROTAC degrader, with a DC_{50} of 33 nM in RS4;11 cells. U7D-1 shows anticancer activity. U7D-1 induces apoptosis in Jeko-1 cells[1].

IC_{50} & Target

DC_{50}: 33 nM (USP7 in RS4;11 cells)[1]

In Vitro

U7D-1 (0-1 μM, 0-24 h) induced USP7 degradation in RS4;11 cell, reducing the USP7 protein level by 83.2% at 1 μM[1].
U7D-1 (0-20 μM, 3 days) shows anti-proliferative activity in p53 wild-type cell lines, and maintains potent cell growth inhibition in p53 mutant cancer cells[1].
U7D-1 (1 μM, 0-24 h) upregulates the level of p53 and p21 proteins in a time-dependent manner, and induces cleavage of caspase-3 in the Jeko-1 cell line in a time dependent manner[1].
U7D-1 (1 μM, 24 h) up-regulates the expression of apoptotic related genes and down-regulates the expression of E2F related

genes in Jeko-1 cells[1].

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

Western Blot Analysis[1]

Cell Line:	RS4;11 cells
Concentration:	0, 5, 20, 50, 100, and 500 nM
Incubation Time:	24 h
Result:	Induced USP7 degradation in RS4;11 cell in a dose dependent manner, with a DC_{50} (half-maximal degradation) value of 33 nM.

Cell Proliferation Assay[1]

Cell Line:	p53 wild-type cell lines (RS4;11, OCI-ly10, MV4;11, Reh and MOLT4 cell lines); p53 mutant cell lines (Jeko-1 cells, Mino, RPMI-8226, Jurkat, SU-DHL-6, CCRF-CEM)
Concentration:	0-20 μM
Incubation Time:	3 days
Result:	Showed antiproliferative activity in p53 wild-type cell lines (RS4;11, OCI-ly10, MV4;11, Reh and MOLT4 cell lines), and p53 mutant cell lines (Jeko-1 cells, Mino, RPMI-8226, Jurkat, SU-DHL-6, CCRF-CEM), with IC_{50} values for 3 days of 79.4, 227.0, 830.3, 1367.2, 4948.0, 1034.9, 1175.3, 1860.6, 6077.6, 9078.0, and 10675.0, respectively. Had an antiproliferative activity with an IC_{50} value of 53.5 nM in Jeko-1 cells for 7 days but exhibited a 13-fold loss in antiproliferative activity with an IC_{50} value of 727 nM in Jeko-1 CRBN KO cells.

Western Blot Analysis[1]

Cell Line:	RS4;11 cells, Jeko-1 and Mino cell
Concentration:	1 μM
Incubation Time:	0, 2, 4, 6, 8, 10, 12, 20, 24, 36, 48, 60, and 72 h
Result:	USP7 degradation in RS4;11 cells induced by U7D-1 started after 4 h of exposure and more effective degradation was observed after 8 h of exposure. Up-regulated the level of p53 and p21 proteins in RS4;11 cells in a time-dependent manner. Had no effect onthe level of p53 protein in p53-mutant cell lines. Induced cleavage of caspase-3 inthe Jeko-1 cell line in a time dependent manner.

REFERENCES

[1]. Pei Y, et al. Discovery of a Potent and Selective Degrader for USP7. Angew Chem Int Ed Engl. 2022 Aug 15;61(33):e202204395.

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