MS67

Cat. No.: HY-141796

CAS No.: 2407452-77-9

Molecular Formula: $C_{52}H_{59}F_4N_9O_7S$

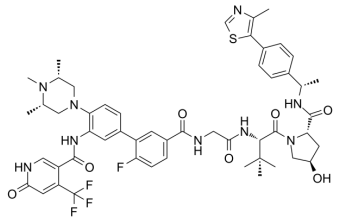
Molecular Weight: 1030.14

Target: Histone Methyltransferase; PROTACs

Pathway: Epigenetics; PROTAC

Storage: -20°C, sealed storage, away from moisture

* In solvent : -80°C, 6 months; -20°C, 1 month (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (97.07 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	0.9707 mL	4.8537 mL	9.7074 mL
	5 mM	0.1941 mL	0.9707 mL	1.9415 mL
	10 mM	0.0971 mL	0.4854 mL	0.9707 mL

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

BIOLOGICAL ACTIVITY

Description

MS67 is a potent and selective WD40 repeat domain protein 5 (WDR5) degrader with a K_d of 63 nM. MS67 is inactive against other protein methyltransferases, kinases, GPCRs, ion channels, and transporters. MS67 shows potent acticancer effects[1].

IC_{50} & Target		
	VHL	WDR5 63 nM (Kd)

In Vitro

MS67 (0.001-1 μM) induces WDR5 degradation at a concentration as low as 1 nM. MS67 induces WDR5 depletion much more effectively in all six mixed lineage leukemia (MLL)-r acute myeloid leukemia (AML) and four pancreatic ductal adenocarcinoma (PDAC) cell lines without a hook effect and in a concentration-dependent manner in PDAC cells[1].

MS67 decreases H3K4me2/3 in both MV4;11 and MIA PaCa-2 cells, whereas other examined histone methylation marks such as H3K9me3, H3K27me3, and H3K36me3 are not affected . MS67 is effective in suppressing both WDR5-related gene expression programs and WDR5/MLL-induced H3K4 methylations on chromatin[1].

The GI_{50} values of MS67 in the two most sensitive AML lines, MV4;11 and EOL-1, are 15 nM and 38 nM, respectively. MLL-r acute leukemia cell lines including MV4;11, EOL-1, MOLM13, KOPN8, RS4;11, and THP-1 are sensitive to MS67, whereas leukemia cell lines that did not harbor MLL-r (including K562, HL60, and a murine AML line transformed by Hoxa9 plus Meis1) are insensitive to MS67[1].

.MS67 binds to VCB (VHL-Elongin C-Elongin B ternary complex), with a K_d of 140 nM[1].

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

Western Blot Analysis[1]

Cell Line:	MV4;11 cells
Concentration:	0.001 μM, 0.005 μM, 0.01 μM, 0.05 μM, 0.1 μM, 0.5 μM, 1 μM
Incubation Time:	18 hours
Result:	Induced WDR5 degradation at a concentration as low as 1 nM with DC_{50} of 3.7 nM.

In Vivo

MS67 (75 mg/kg; i.p.; twice daily; 5 days a week; for 20 days) significantly inhibits tumor growth in vivo and prolongs survival of the treated mice[1].

After a single intraperitoneal (i.p.) injection of MS67 at a dose of 75 mg/kg, the Cmax reached at about 4.2 μM, and the concentration of MS67 retained above 0.5 μM over 12 hours[1].

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

Animal Model:	MV4;11 MLL-r AML xenograft mouse[1]
Dosage:	75 mg/kg
Administration:	i.p.; twice daily; 5 days a week; for 20 days
Result:	Inhibited tumor growth in vivo.

REFERENCES

[1]. Xufen Yu, et al. A selective WDR5 degrader inhibits acute myeloid leukemia in patient-derived mouse models. Sci Transl Med. 2021 Sep 29;13(613):eabj1578.

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