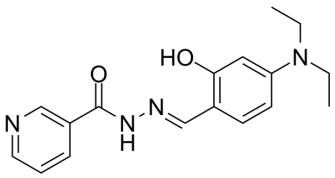
SCFSkp2-IN-2

Cat. No.:	HY-148900
CAS No.:	1375060-02-8
Molecular Formula:	$C_{17}H_{20}N_4O_2$
Molecular Weight:	312.37
Target:	E1/E2/E3 Enzyme
Pathway:	Metabolic Enzyme/Protease
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 : 125 mg/mL (400.17 mM; ultrasonic and warming and heat to 60°C)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.2013 mL	16.0067 mL	32.0133 mL
	5 mM	0.6403 mL	3.2013 mL	6.4027 mL
	10 mM	0.3201 mL	1.6007 mL	3.2013 mL

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

BIOLOGICAL ACTIVITY

Description

SCFSkp2-IN-2 (Compound AAA-237) is a Skp2 inhibitor with a K_D of 28.77 μM. AAA-237 induces apoptosis of NSCLC cells and shows antitumor activities[1].

IC_{50} & Target

KD: 28.77 μM (Skp2)[1]

In Vitro

SCFSkp2-IN-2 (Compound AAA-237) (0.3-3 μM; 24-72 h) can directly bind to Skp2, causing the degradation of Skp2 by proteasome. AAA-237 has no significant effect on the mRNA expression of Skp2 but inhibits the protein expression of Skp2 in NSCLC cells in a time-dependent manner[1].

SCFSkp2-IN-2 (0.3-3 μM; 24-72 h) inhibits the proliferation of A549 and H1299 cells in a dose- and time-dependent manner[1].

SCFSkp2-IN-2 (0.3-3 μM; 24-72 h) arrests the cell cycle at the G0/G1 checkpoint by regulating the Skp2-Cip/Kip and PI3K/Akt-FOXO1 signaling pathways[1].

SCFSkp2-IN-2 (0.3-3 μM; 24-72 h) induces apoptosis of A549 and H1299 cells in a dose- and time-dependent manner[1].

SCFSkp2-IN-2 (0.3 μM; 1-7 days) induces cellular senescence of the NSCLC cells[1].

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

Western Blot Analysis[1]

Cell Line:	A549 and H1299 cells
Concentration:	0.3, 1 and 3 μM
Incubation Time:	24, 48 and 72 h
Result:	Increased the expression levels of p21Cip1 and p27Kip1. Decreased the level of Skp2. Reduced the expression levels of CDK2, p-CDK2, cyclin E1, CDK4, p-CDK4 and cyclin D. Increased the levels of cleaved PARP, cleaved caspase 3, cleaved caspase 9 and Bax. Decreased the expression of PARP and Bcl-2.

Cell Proliferation Assay[1]

Cell Line:	A549 and H1299 cells
Concentration:	0.3, 1 and 3 μM
Incubation Time:	24, 48 and 72 h
Result:	Inhibited the proliferation of A549 and H1299 cells in a dose- and time-dependent manner. The IC_{50} for A549 was 3 μM at 24 h, 2.5 μM at 48 h and 0.7 μM at 72 h. The IC_{50} for H1299 was 3.9 μM at 24 h, 1.8 μM at 48 h and 1.1 μM at 72 h.

Cell Cycle Analysis[1]

Cell Line:	A549 and H1299 cells
Concentration:	0.3, 1 and 3 μM
Incubation Time:	24, 48 and 72 h
Result:	Arrested the cell cycle at G0/G1 in a dose- and time-dependent manner.

Apoptosis Analysis[1]

Cell Line:	A549 and H1299 cells
Concentration:	0.3, 1 and 3 μM
Incubation Time:	24, 48 and 72 h
Result:	The ratio of JC-1 monomer/JC-1 polymer was increased in A549 and H1299 cells as the concentration was increased.

In Vivo

SCFSkp2-IN-2 (Compound AAA-237) (15 or 45 mg/kg; i.p.; daily for 14 days) shows antitumor activity in lung cancer A549 xenograft mice model[1].

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

Animal Model:	A549 xenograft model[1]
Dosage:	15 or 45 mg/kg
Administration:	Intraperitoneal administration, daily for 14 days
Result:	Significantly reduced tumor volume and weight. The tumor growth inhibition of the low dose and high dose was 55% and 64%, respectively. No obvious weight loss or abnormal behavior was observed. Reduced the expression of Ki67 in tumor tissue. Reduced the

	expression of Skp2 and Bcl-2 and increased the expression of p27, the cleaving of caspase 3, caspase 9, PARP and Bax.

REFERENCES

[1]. Liu J, et al. Anti-tumor effects of Skp2 inhibitor AAA-237 on NSCLC by arresting cell cycle at G0/G1 phase and inducing senescence. Pharmacol Res. 2022 Jul;181:106259.

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