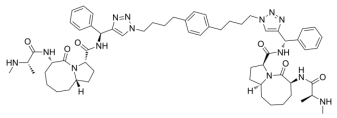
SM-164

Cat. No.:	HY-15989
CAS No.:	957135-43-2
Molecular Formula:	$C_{62}H_{84}N_{14}O_6$
Molecular Weight:	1121.42
Target:	IAP; Apoptosis
Pathway:	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 : 25 mg/mL (22.29 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	0.8917 mL	4.4586 mL	8.9173 mL
5 mM	0.1783 mL	0.8917 mL	1.7835 mL
10 mM	0.0892 mL	0.4459 mL	0.8917 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: 0.83 mg/mL (0.74 mM); Clear solution; Need ultrasonic

BIOLOGICAL ACTIVITY

Description

SM-164 is a cell-permeable Smac mimetic compound. SM-164 binds to XIAP protein containing both the BIR2 and BIR3 domains with an IC_{50} value of 1.39 nM and functions as an extremely potent antagonist of XIAP.

IC_{50} & Target

cIAP-1	cIAP-2	cIAP
0.31 nM (Ki)	1.1 nM (Ki)	

In Vitro

SM-164 is a non-peptide, cell-permeable, bivalent small-molecule, which mimics Smac protein for targeting XIAP. SM-164 binds to XIAP containing both BIR domains with an IC_{50} value of 1.39 nM, being 300 and 7000-times more potent than its monovalent counterparts and the natural Smac AVPI peptide, respectively. SM-164 concurrently interacts with both BIR domains in XIAP and functions as an ultra-potent antagonist of XIAP in both cell-free functional and cell-based assays. SM-164 targets cellular XIAP and effectively induces apoptosis at concentrations as low as 1 nM in leukemia cancer cells, while having a minimal toxicity to normal human primary cells at 10,000 nM[1]. The binding affinities of SM-164 to XIAP, cIAP-1, and

	cIAP-2 proteins are determined using fluorescence-polarization based assays. SM-164 has a K_i value of 0.56 nM to XIAP protein containing both BIR2 and BIR3 domains. SM-164 has a K_i value of 0.31 nM to cIAP-1 protein containing both BIR2 and BIR3 domains. SM-164 binds to cIAP-2 BIR3 protein with K_i values of 1.1 nM. Addition of exogenous TNFα can significantly enhance the activity of these Smac mimetics, especially for SM-164, in resistant cancer cell lines such as HCT116 and MDA-MB-453[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	SM-164 is evaluated for its ability to inhibit tumor growth. SM-164 is highly effective in inhibition of tumor growth and capable of achieving tumor regression in the MDA-MB-231 xenograft model. Treatment with SM-164 at 1 mg/kg completely inhibits tumor growth during the treatment. Treatment with SM-164 at 5 mg/kg reduces the tumor volume from 147±54 mm ^{3} at the beginning of the treatment (day 25) to 54±32 mm^3 at the end of the treatment (day 36), a reduction of 65%. The strong antitumor activity by SM-164 is long lasting and not transient. SM-164 at 5 mg/kg is statistically more effective than Taxotere at the end of the treatment (P<0.01) or when the tumor size in the control group reached 750 mm^3 (P<0.02)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	A set of sensitive and quantitative fluorescence polarization (FP)-based assays are developed to determine the binding affinities of our designed Smac mimetics to XIAP BIR3, XIAP containing both BIR2 and BIR3 domains, cIAP-1 BIR3, cIAP-1 containing both BIR2 and BIR3 domains, and cIAP-2 protein. The FP-based assay for XIAP BIR3 protein is measured. Briefly, 5-carboxyfluorescein is coupled to the lysine side chain of a mutated Smac peptide with the sequence (AbuRPFK-Fam) and this fluorescently tagged peptide (named SM5F) is used as the fluorescent tracer in FP-based binding assay to XIAP BIR3. The K_d value of this fluorescent tracer is determined to be 17.9 nM to XIAP BIR3. In competitive binding experiments, a tested compound is incubated with 30 nM of XIAP BIR3 protein and 5 nM of SM5F in the assay buffer (100 mM potassium phosphate, pH 7.5; 100μg/mL bovine gamma globulin; 0.02 % sodium azide)[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [2]	HCT116 colon cancer cells are treated with SM-164 (1, 10, and 100 nM) alone, TNFα alone, or the combination for 48 h. Cell growth inhibition is determined by a WST assay[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [2]	Mice[2] SCID mice (8-10 per group) bearing MDA-MB-231 xenograft tumors are treated i.v. with 1 and 5 mg/kg of SM-164 or 7.5 mg/kg of Taxotere or vehicle control daily, 5 d/wk for 2 wk. Tumor sizes and animal weights are measured thrice a week[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Signal Transduct Target Ther. 2020 Oct 9;5(1):235.
- Proc Natl Acad Sci U S A. 2022 Sep 6;119(36):e2117396119.
- Cell Death Dis. 2018 Nov 15;9(12):1140.
- J Med Chem. 2023 Mar 12.
- J Med Chem. 2023 Feb 23;66(4):3073-3087.

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REFERENCES

[1]. Sun H, et al. Design, synthesis, and characterization of a potent, nonpeptide, cell-permeable, bivalent Smac mimetic that concurrently targets both the BIR2 and BIR3 domains in XIAP. J Am Chem Soc. 2007 Dec 12;129(49):15279-94.

[2]. Lu J, et al. SM-164: a novel, bivalent Smac mimetic that induces apoptosis and tumor regression by concurrent removal of the blockade of cIAP-1/2 and XIAP. Cancer Res. 2008 Nov 15;68(22):9384-93.

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