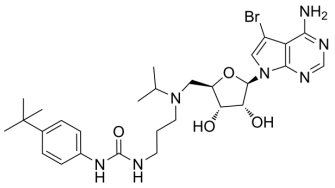
SGC0946

Cat. No.:	HY-15650
CAS No.:	1561178-17-3
Molecular Formula:	$C_{28}H_{40}BrN_7O_4$
Molecular Weight:	618.57
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (80.83 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6166 mL	8.0832 mL	16.1663 mL
	5 mM	0.3233 mL	1.6166 mL	3.2333 mL
	10 mM	0.1617 mL	0.8083 mL	1.6166 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 (3.36 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (3.36 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (3.36 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

SGC0946 is a selective DOT1LH3K79 methyltransferase) inhibitor, with an IC_{50} of 0.3 nM. SGC0946 results in G1 arrest, inhibits potential of cell self-renewal and metastatic, also induces cell differentiation. SGC0946 can be used in studies of leukemia and solid tumors and also serve as a probe to further investigate the cellular mechanism of DOT1L in both normal and diseased cells[1][2][3].

IC_{50} & Target

DOT1L
.3 nM (IC_{50})

In Vitro

SGC0946 (0-100 μM; 4 days) inhibits DOT1L with IC_{50} of 2.65 nM in A431 cells[1].

?SGC0946 (1, 5 μM; 14 days) displays selective reduction of cell viability in an experimental leukaemia model derived from human cord blood cells (transformed with the MLL-AF9 fusion oncogene)[1].

?SGC0946 (1 μM; 3-7 days) shows time- and dose-dependent reductions in the H3K79me2 mark in the Molm13 MLL cell line that has the MLL/AF9 translocation[1].

?SGC0946 (1 μM, 7 days) effectively inhibits MLL target genes, HOXA9 and Meis1[1].

?SGC0946 (0.2, 2, or 20 μM; 12 days) reduces proliferation and survival of ovarian cancer cells by inhibiting DOT1L enzymatic activity[2].

?SGC0946 (10 μM; 12 days) induces G1 phase arrest by blocking DOT1L in SK-OV-3 and TOV21G cells[2].

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

Cell Viability Assay[1]

Cell Line:	A431 cells
Concentration:	0-100 μM
Incubation Time:	4 days
Result:	Showed potent inhibitory activity against DOT1L with IC_{50} of 2.65 nM in A431 cells.

Cell Viability Assay[1]

Cell Line:	Human cord blood cells (transformed with the MLL-AF9 fusion oncogene).
Concentration:	1, 5 μM
Incubation Time:	14 days
Result:	Killed human cord blood cells transformed with an MLL-AF9 fusion oncogene.

Western Blot Analysis[1]

Cell Line:	Molm13 MLL cells
Concentration:	1 μM
Incubation Time:	3-7 days
Result:	Reduced H3K79me2 in Molm13 MLL cells in a time- and dose-dependent manner, and a complete inhibition exhibited at day 7.

Cell Proliferation Assay[2]

Cell Line:	SK-OV-3 and TOV21G cells
Concentration:	0.2, 2, or 20 μM
Incubation Time:	12 days
Result:	Inhibited the growth of both SK-OV-3 and TOV21G cells in a dose- and time-dependent manner. Reduced the colony of both SK-OV-3 and TOV21G cells.

Cell Cycle Analysis[2]

Cell Line:	SK-OV-3 and TOV21G cells
Concentration:	10 μM

Incubation Time:	12 days
Result:	Induced increased G1 population and decreased S phase and G2/M phase cells in asynchronized SK-OV-3 and TOV21G cells.

In Vivo

SGC0946 (10 mg/kg; i.p.; twice a week for 6 weeks) significantly suppresses tumor progression in a mouse orthotopic xenograft ovarian cancer model and also inhibits DOT1L enzymatic activity and levels of H3K79me2,CDK6, and cyclin D3 in the tumors[2].

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

Animal Model:	Female NOD-SCID mice (4-week-old; mouse orthotopic xenograft ovarian cancer model)[2] .
Dosage:	10 mg/kg
Administration:	Intraperitoneal injection; twice a week for 6 weeks.
Result:	Significantly suppressed growth of tumor (size and weight of tumor masses smaller than the untreated group). Inhibited DOT1L enzymatic activity and decreased H3K79me2,CDK6, and cyclin D3 levels in the tumors.

CUSTOMER VALIDATION

- Mol Cell. 2021 Oct 7;81(19):4076-4090.e8.
- Sci Adv. 2023 Jun 2;9(22):eadc9273.
- Elife. 2020 Oct 1;9:e57858.
- Oncogenesis. 2021 Jul 12;10(7):48.
- Mol Carcinog. 2023 May 5.

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REFERENCES

[1]. Yu W, et al. Catalytic site remodelling of the DOT1L methyltransferase by selective inhibitors. Nat Commun. 2012;3:1288.

[2]. Zhang X, et al. Prognostic and therapeutic value of disruptor of telomeric silencing-1-like (DOT1L) expression in patients with ovarian cancer. J Hematol Oncol. 2017 Jan 23;10(1):29.

[3]. Zhang L, et al. Inhibition of histone H3K79 methylation selectively inhibits proliferation, self-renewal and metastatic potential of breast cancer. Oncotarget. 2014 Nov 15;5(21):10665-77.

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