A-395

Cat. No.: HY-101512

CAS No.: 2089148-72-9

Molecular Formula: $C_{26}H_{35}FN_4O_2S$

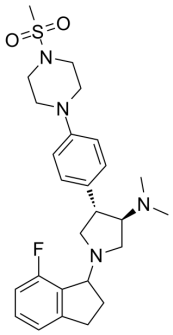
Molecular Weight: 486.65

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 : 100 mg/mL (205.49 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.0549 mL	10.2743 mL	20.5486 mL
5 mM	0.4110 mL	2.0549 mL	4.1097 mL
10 mM	0.2055 mL	1.0274 mL	2.0549 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 (1.71 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.83 mg/mL (1.71 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.83 mg/mL (1.71 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A-395 is an antagonist of polycomb repressive complex 2 (PRC2) protein-protein interactions that potently inhibits the trimeric PRC2 complex (EZH2-EED-SUZ12) with an IC_{50} of 18 nM[1].

IC_{50} & Target

IC50: 18 nM (Trimeric PRC2 complex)[1]

In Vitro

The embryonic ectoderm development (EED) protein is an essential subunit of Polycomb repressive complex 2 (PRC2). A-395 antagonizes of the H3K27me3 binding functions of EED. A-395 binds to EED in the H3K27me3-binding pocket, thereby

	preventing allosteric activation of the catalytic activity of PRC2. A-395 is capable of competing for H3K27me3 peptide binding to EED, with an IC_{50} of 7 nM. A-395, but not the close chemical analog A-395N, modulates activity of PRC2 in cells by potently reducing the H3K27 methyl mark in a highly selective manner. A-395 treatment inhibits both H3K27me2 and H3K27me3, with IC_{50} values of 390 nM and 90 nM, respectively. Furthermore, A-395 treatment results in growth inhibition of human tumor cell lines sensitive to SAM-competitive EZH2 inhibitors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The embryonic ectoderm development (EED) protein is an essential subunit of Polycomb repressive complex 2 (PRC2). A-395 antagonizes of the H3K27me3 binding functions of EED. A-395 binds to EED in the H3K27me3-binding pocket, thereby preventing allosteric activation of the catalytic activity of PRC2. A-395 is capable of competing for H3K27me3 peptide binding to EED, with an IC_{50} of 7 nM. A-395, but not the close chemical analog A-395N, modulates activity of PRC2 in cells by potently reducing the H3K27 methyl mark in a highly selective manner. A-395 treatment inhibits both H3K27me2 and H3K27me3, with IC_{50} values of 390 nM and 90 nM, respectively. Furthermore, A-395 treatment results in growth inhibition of human tumor cell lines sensitive to SAM-competitive EZH2 inhibitors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay	The embryonic ectoderm development (EED) protein is an essential subunit of Polycomb repressive complex 2 (PRC2). A-395 antagonizes of the H3K27me3 binding functions of EED. A-395 binds to EED in the H3K27me3-binding pocket, thereby preventing allosteric activation of the catalytic activity of PRC2. A-395 is capable of competing for H3K27me3 peptide binding to EED, with an IC_{50} of 7 nM. A-395, but not the close chemical analog A-395N, modulates activity of PRC2 in cells by potently reducing the H3K27 methyl mark in a highly selective manner. A-395 treatment inhibits both H3K27me2 and H3K27me3, with IC_{50} values of 390 nM and 90 nM, respectively. Furthermore, A-395 treatment results in growth inhibition of human tumor cell lines sensitive to SAM-competitive EZH2 inhibitors[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	1,000 multiple myeloma cells are seeded in each well of 96-well cell culture plates and treated with A-395 (0.001-100 μM) or DMSO control for 10 d before the cell proliferation assay. Cell proliferation assays are conducted with the CellTiter-Glo Luminescent Cell Viability Assay[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] SCID mice are inoculated with the human Pfeiffer cell line and these xenografts are grown to size match at -200 mm^3. Mice are subsequently treated with vehicle control, A-395 and A-395N at 300 mg/kg s.c. two times per week for 5 weeks or GSK126 at 50 mg/kg i.p. once per day for 36 d. Tumor volume is measured at different intervals and is represented by the average ± s.d. (eight mice per group)[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. He Y, et al. The EED protein-protein interaction inhibitor A-395 inactivates the PRC2 complex. Nat Chem Biol. 2017 Apr;13(4):389-395.

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