A-366

Cat. No.: HY-12583

CAS No.: 1527503-11-2

Molecular Formula: $C_{19}H_{27}N_3O_2$

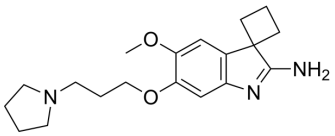
Molecular Weight: 329.44

Target: Histone Methyltransferase; Epigenetic Reader Domain

Pathway: Epigenetics

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 : 50 mg/mL (151.77 mM; Need ultrasonic)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.0355 mL	15.1773 mL	30.3545 mL
5 mM	0.6071 mL	3.0355 mL	6.0709 mL
10 mM	0.3035 mL	1.5177 mL	3.0355 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: ≥ 2.5 mg/mL (7.59 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.59 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

A-366 is a potent, highly selective, peptide-competitive histone methyltransferase G9a inhibitor with IC_{50}s of 3.3 and 38 nM for G9a and GLP (EHMT1), respectively. A-366 shows >1000-fold selectivity over 21 other methyltransferases. A-366 is also a potent, nanomolar inhibitor of the Spindlin1-H3K4me3-interaction (IC_{50}=182.6 nM). A-366 displays high affinity at human histamine H3 receptor (K_i=17 nM) and shows subtype selectivity among subsets of the histaminergic and dopaminergic receptor families[1][2][3][4].

IC_{50} & Target	EHMT2/G9a/KMT1C	EHMT1/GLP/KMT1D

In Vitro

A-366 (0.01-10 μM; 14 days) induces differentiation and affects viability in MV4;11 cells[4].
?A-366 (0.3-3 μM; 72 hours) reduces the total levels of H3K9me2 in a time and concentration dependent manner with a

cellular EC50 of ~300 nM in PC-3 prostate adenocarcinoma cells. A-366 (0.01-10 μM; 4 days; HL-60 cells) results in a dose-dependent differentiation and a corresponding decrease in proliferation. DNA content analysis of A-366-treated HL-60 cells showed an accumulation of cells in G1 consistent with cytostasis[4].

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

Cell Viability Assay[4]

Cell Line:	MV4;11 cells
Concentration:	0.01-10 μM
Incubation Time:	14 days
Result:	Resulted in inhibited proliferation and a decrease in viability corresponding to the dose response observed for CD11b staining.

In Vivo

A-366 (30 mg/kg; osmotic mini-pump; daily for 14 days) treatment of MV4;11 xenografts elicits growth inhibition[4].

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

Animal Model:	6-8 week old SCID-beige female mice (MV4;11 xenografts)[4]
Dosage:	30 mg/kg
Administration:	By osmotic mini-pump; daily for 14 days
Result:	A modest 45% tumor growth inhibition resulting from A-366 treatment in this model.

CUSTOMER VALIDATION

- Theranostics. 2018 Apr 15;8(10):2884-2895.
- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Reiner D, et al. Epigenetics meets GPCR: inhibition of histone H3 methyltransferase (G9a) and histamine H3 receptor for Prader-Willi Syndrome. Sci Rep. 2020;10(1):13558. Published 2020 Aug 11.

[2]. Wagner T, et al. Identification of a small-molecule ligand of the epigenetic reader protein Spindlin1 via a versatile screening platform. Nucleic Acids Res. 2016;44(9):e88.

[3]. Sweis RF, et al. Discovery and development of potent and selective inhibitors of histone methyltransferase g9a. ACS Med Chem Lett. 2014;5(2):205-209. Published 2014 Jan 2.

[4]. Pappano WN, et al. The Histone Methyltransferase Inhibitor A-366 Uncovers a Role for G9a/GLP in the Epigenetics of Leukemia. PLoS One. 2015;10(7):e0131716. Published 2015 Jul 6.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA