UNC0638

Cat. No.: HY-15273

CAS No.: 1255580-76-7

Molecular Formula: $C_{30}H_{47}N_5O_2$

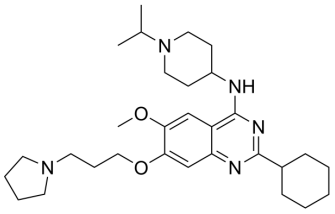
Molecular Weight: 509.73

Target: Histone Methyltransferase; Autophagy; Influenza Virus; VSV

Pathway: Epigenetics; Autophagy; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

1M HCl : 100 mg/mL (196.18 mM; ultrasonic and adjust pH to 1 with HCl)

DMSO : ≥ 30 mg/mL (58.85 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.9618 mL	9.8091 mL	19.6182 mL
5 mM	0.3924 mL	1.9618 mL	3.9236 mL
10 mM	0.1962 mL	0.9809 mL	1.9618 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 (4.90 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.90 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.90 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UNC0638 selectively inhibits G9a and GLP histone methyltransferase activity with IC_{50}s of less than 15 nM and 19 nM, respectively. UNC0638 has anti-FMDV (foot-and-mouth disease virus) and anti-VSV (vesicular stomatitis virus) activities.

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

In Vitro	UNC0638, an inhibitor of G9a and GLP with excellent potency and selectivity over a wide range of epigenetic and non-epigenetic targets.The K_i of UNC0638 is determined to be 3.0±0.05 nM (n=2). Consistent with this, the Morrison K_i for UNC0638 is 3.7±0.2 nM (n=3). The selectivity of UNC0638 over a wide range of epigenetic targets is evaluated. Notably, UNC0638 is inactive against other H3K9 (SUV39H1 and SUV39H2), H3K27 (EZH2), H3K4 (SETD7, MLL and SMYD3), H3K79 (DOT1L) and H4K20 (SETD8) methyltransferases, as well as PRDM1, PRDM10 and PRDM12. In addition, UNC0638 is inactive against protein arginine methyltransferases PRMT1 and PRMT3, and HTATIP, a histone acetyltransferase. Of note, UNC0638 has weak but measurable activity against JMJD2E (IC_{50}=4,500±1,100 nM), a Jumonji protein demethylase and DNA methyltransferase DNMT1 (IC_{50}=107,000±6,000 nM). Nevertheless, the selectivity of UNC0638 for G9a and GLP over JMJD2E is >200-fold, and selectivity for G9a and GLP over DNMT1 is >5,000-fold[1]. UNC0638 is a type of small molecule that can specifically inhibit the enzyme activity of histone methyltransferase EHMT and reduce the H3K9 dimethylation (H3K9me2) levels in cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The enzymatic reactions are conducted in duplicate at room temperature for 1 hour in a 50 µL mixture containing PKMT assay buffer, substrate coated plate, 10 M SAM, a HMT enzyme (EZH2 (800 ng/reaction), MLL (300 ng/reaction), PRMT1 (0.5 ng/reaction), SUV39H1 (75 ng/reaction) and UNC0638 (0-1.25 µM). After enzymatic reactions, 100 µL of first antibody is added to each well and the plate is incubated at room temperature for an additional 1 h. 100 µL of secondary antibody is added to each well and the plate is incubated at room temperature for an additional 30 min. 100 µL of developer reagents are added to wells and luminescence is measured using a BioTek SynergyTM 2 microplate reader. Enzyme activity assays are performed in duplicates at each concentration. The luminescence data are analyzed using the computer software, Graphpad Prism[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	MDA-MB-231, PC3, HCT116 cells are cultured in RPMI with 10% FBS, 22RV1 cells in alphaMEM and 10% FBS, MCF7 and IMR90 cells in DMEM with 10% FBS. Cells are grown in the presence or absence of UNC0638 (10 nM, 100 nM, 1 µM, 10 µM, and 100 µM) for stated amount of time. The media is removed and replaced with DMEM 10% FBS without phenol red supplemented with 1mg/mL of MTT and incubated for 1-2 h. Live cells reduce yellow MTT to purple formazan. The resulting formazan is solubilized in acidified isopropanol and 1% Triton and absorbance measured at 570 nm, corrected for 650 nm background[1] . MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] Standard DMPK studies in male Swiss albino mice (3 animals per data point) are conducted, following intravenous (IV, 1 mg/kg), oral (PO, 3 mg/kg), and intraperitoneal (IP, 2.5 mg/kg) administration of UNC0638. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Proc Natl Acad Sci U S A. 2019 Feb 19;116(8):2961-2966.
- Cell Death Dis. 2018 Jan 26;9(2):129.
- Cell Chem Biol. 2022 Jun 18;S2451-9456(22)00198-2.
- Acta Pharmacol Sin. 2021 Apr 13.
- Cell Biosci. 2023 Jan 12;13(1):7.

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REFERENCES

[1]. Vedadi M, et al. A chemical probe selectively inhibits G9a and GLP methyltransferase activity in cells. Nat Chem Biol. 2011 Jul 10;7(8):566-74.

[2]. Fu L, et al. Effects of the Histone Methyltransferase Inhibitor UNC0638 on Histone H3K9 Dimethylation of Cultured Ovine Somatic Cells and Development of Resulting Early Cloned Embryos. Reprod Domest Anim. 2014 Apr;49(2):e21-5.

[3]. Singh N, et al. Inhibition of EHMT2 Induces a Robust Antiviral Response Against Foot-and-Mouth Disease and Vesicular Stomatitis Virus Infections in Bovine Cells. J Interferon Cytokine Res. 2016 Jan;36(1):37-47.

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