UNC0642

Cat. No.: HY-13980

CAS No.: 1481677-78-4

Molecular Formula: $C_{29}H_{44}F_2N_6O_2$

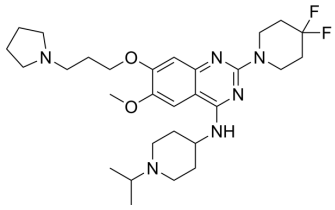
Molecular Weight: 546.7

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 (91.46 mM; Need ultrasonic)

H_2O : < 0.1 mg/mL (ultrasonic;warming;heat to 60°C) (insoluble)

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.8292 mL	9.1458 mL	18.2916 mL
5 mM	0.3658 mL	1.8292 mL	3.6583 mL
10 mM	0.1829 mL	0.9146 mL	1.8292 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 (4.57 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.57 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.57 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UNC0642 is a potent and selective lysine methyltransferases G9a and GLP inhibitor, with an IC_{50} of <2.5 nM for G9a.

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

In Vitro

UNC0642 displays high in vitro and cellular potency, low cell toxicity, and excellent selectivity. UNC0642 is competitive with the peptide substrate and non-competitive with the cofactor SAM. The K_i of UNC0642 is determined to be 3.7±1 nM.

	UNC0642 displays high in vitro potency for GLP (IC_{50}< 2.5 nM), similar to G9a. UNC0642 is more than 300-fold selective for G9a and GLP over a broad range of kinases, GPCRs, transporters, and ion channels. UNC0642 exhibits high potency at reducing the H3K9me2 mark, low cell toxicity, and good separation of functional potency and cell toxicity in a number of cell lines. It reduces clonogenicity in PANC-1 cells, a pancreatic carcinoma cell line[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	A single intraperitoneal (IP) injection (5 mg/kg) of UNC0642 results in a plasma C_{max} (maximum concentration) of 947 ng/mL and an AUC (area under the curve) of 1265 hr*ng/mL[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	MDA-MB-231, PC3, and U2OS cells are treated with inhibitors (UNC0642) for 48 h. Cell viability assays are performed by incubating cells with 0.1 mg/mL of resazurin for 3 – 4 h. Resazurin reduction is monitored with 544 nm excitation, measuring fluorescence at 590 nm. In-cell western assay is performed as described previously[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice: Standard PK studies are performed using male Swiss albino mice. Plasma and brain concentrations are measured at 0.08, 0.25, 0.5, 1, 2, 4, 8, and 24 h following a single IP injection of UNC0642 at 5 mg/kg. The compound concentration at each time point in plasma or brain is the average value from 3 test animals[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Cell Biol. 2023 Jul;25(7):1017-1032.
- 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.
- Cell Prolif. 2021 May 24;e13072.

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REFERENCES

[1]. Liu F, et al. Discovery of an in vivo chemical probe of the lysine methyltransferases G9a and GLP. J Med Chem. 2013 Nov 14;56(21):8931-8942.

[2]. Wang L, et al. Targeting EHMT2 reverses EGFR-TKI resistance in NSCLC by epigenetically regulating the PTEN/AKT signaling pathway. Cell Death Dis. 2018 Jan 26;9(2):129

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