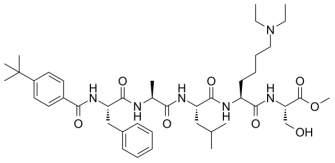
UNC3866

Cat. No.:	HY-100832
CAS No.:	1872382-47-2
Molecular Formula:	$C_{43}H_{66}N_6O_8$
Molecular Weight:	795.02
Target:	Histone Methyltransferase
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 : ≥ 27 mg/mL (33.96 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.2578 mL	6.2891 mL	12.5783 mL
	5 mM	0.2516 mL	1.2578 mL	2.5157 mL
	10 mM	0.1258 mL	0.6289 mL	1.2578 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 (3.14 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (3.14 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (3.14 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

UNC3866 is a potent antagonist of the CBX7-H3 interaction as determined by AlphaScreen (IC_{50}=66±1.2 nM) and is more than 100-fold selective for CBX7 over the other nine members of this methyl-lysine (Kme) reader panel.

IC_{50} & Target

IC50: 66±1.2 nM (CBX7)[1]

In Vitro

UNC3866, a potent antagonist of the methyl-lysine (Kme) reading function of the Polycomb CBX and CDY families of

chromodomains. UNC3866 binds the chromodomains of CBX4 and CBX7 most potently with a K_d of 100 nM for each, and is 6- to 18-fold selective versus seven other CBX and CDY chromodomains while being highly selective versus >250 other protein targets. UNC3866 inhibits PC3 cell proliferation, a known CBX7 phenotype, while UNC4219, a methylated negative control compound, has negligible effects. UNC3866 is a potent and cellularly active antagonist of PRC1 chromodomains. UNC3866 is the most potent ligand reported for CBX7 with a K_d of 97±2.4 nM. UNC3866 is equipotent for CBX4, which is most similar to CBX7, while it is 18-, 6- and 12-fold selective for CBX4/7 over CBX2, -6 and -8, respectively. Additionally, UNC3866 is 65-fold selective for CBX4/7 over CDY1 and 9-fold selective for CBX4/7 over CDYL1b and CDYL2[1].

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

PROTOCOL

Kinase Assay [1]

The effect of UNC3866 on the methyltransferase activity of G9a, EHMT1, SUV39H1, SUV39H2, SETDB1, SETD8, SUV420H1, SUV420H2, SETD7, MLL1 trimeric complex, MLL3 tetrameric complex, EZH2 trimeric complex, PRMT1, PRMT3, PRMT5-MEP50 complex, PRMT6, PRMT7, PRMT8, PRDM9, SETD2, SMYD2, SMYD3, BCDIN3D and DNMT1 is assessed by monitoring the incorporation of tritium-labeled methyl group to lysine or arginine residues of peptide substrates using Scintillation Proximity Assay (SPA). Assays are performed in a 20 µL reaction mixture containing ^{3}H-SAM at substrate concentrations close to the K_m values for each enzyme. Three concentrations (1 µM, 10 µM, and 50 µM) of UNC3866 are used in all selectivity assays. To stop the enzymatic reactions, 7.5 M Guanidine hydrochloride is added, followed by 180 µL of buffer (20 mM Tris, pH 8.0). The reactions are mixed and then transferred to a 96-well FlashPlate. The reaction mixtures in Flash plates are incubated for 1 hour and the CPM are measured using a TopCount plate reader. The CPM counts in the absence of compound for each data set are defined as 100% activity. In the absence of the enzyme, the CPM counts in each data set are defined as background (0%)[1].

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

Cell Assay [1]

PC3 cells are seeded at 200 cells/well into 24-well plates. Cells are allowed to adhere overnight. The media (DMEM supplemented with 10 % FBS) is then exchanged with fresh media containing DMSO, UNC3866 or UNC4219. On day three, the media are exchanged with fresh media containing DMSO, UNC3866 or UNC4219. For dose-response studies, the EC_{50} is derived from a six-point titration ranging from 100 µM to 0.4 µM of UNC3866 or UNC4219. At day 0, 3 or 6, cells are fixed with ice-cold methanol for 30 sec. and rehydrated with PBS. Nuclei of the cells are stained with DAPI (0.05 µg/mL) and numerated using High Content Microscopy. For dose-response studies, the cell count of UNC3866- or UNC4219-treated cells is normalized to the average cell count of DMSO-treated cells. The EC_{50} is calculated using the “log[inhibitor] vs. the normalized response-Variable slope” equation in GraphPad Prism 5[1].

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

CUSTOMER VALIDATION

- Acta Pharmacol Sin. 2021 Apr 13.
- bioRxiv. 2021 May 26.

See more customer validations on www.MedChemExpress.com

REFERENCES

[1]. Stuckey JI, et al. A cellular chemical probe targeting the chromodomains of Polycomb repressive complex 1. Nat Chem Biol. 2016 Mar;12(3):180-7.

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