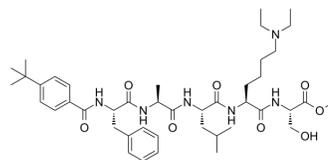


UNC3866

Cat. No.:	HY-100832		
CAS No.:	1872382-47-2		
Molecular Formula:	C ₄₃ H ₆₆ N ₆ O 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.

	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
Preparing Stock Solutions	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

- 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
- 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
- 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 (IC₅₀=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.

IC₅₀ & 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 μ L reaction mixture containing ³H-SAM at substrate concentrations close to the K_m values for each enzyme. Three concentrations (1 μ M, 10 μ M, and 50 μ M) of UNC3866 are used in all selectivity assays. To stop the enzymatic reactions, 7.5 M Guanidine hydrochloride is added, followed by 180 μ L 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 μ M to 0.4 μ M 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 μ g/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.

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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.

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