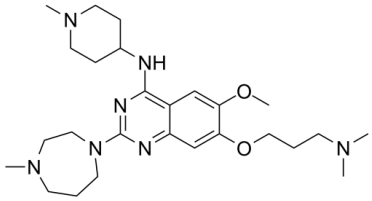
Data Sheet

Product Name:	UNC0224
Cat. No.:	CS-2210
CAS No.:	1197196-48-7
Molecular Formula:	C26H43N7O2
Molecular Weight:	485.67
Target:	Histone Methyltransferase
Pathway:	Epigenetics
Solubility:	DMSO : 16.67 mg/mL (34.32 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

UNC0224 is a potent and selective G9a inhibitor with IC50 of 15 nM in the G9a Thioglo assay. IC50 value: 15 nM [1] Target: G9a UNC0224 (Compound 8) also potently inhibited GLP with an IC50 of 20 nM and 58 nM in the Thioglo assay and and AlphaScreen, respectively. 8 was more than 1000-fold selective for G9a over SET7/9 (a H3K4 HMT) and SET8/PreSET7 (a H4K20 HMT) in Thioglo-based biochemical assays [1] [2].

PROTOCOL (Extracted from published papers and Only for reference)

Enzyme assay [1] Histone methyltransferase assay was performed using a coupled assay (Collazo et al. 2005). In this assay SAHH (S-adenosylhomocysteine hydrolase) and adenosine deaminase convert the methyltransferase reaction product (S-adenosylhomocysteine) to homocysteine and inosine. Homocysteine can be quantified using Thioglo (Calbiochem). Substrate peptide used in this assay was the first 25 residues of histone 3 [H3 (1-25)]. SAHH clone was provided by Dr. Trievel, University of Michigan. For IC50 determination, assay mixtures were prepared with 5 μM SAHH, about 0.3 U/mL of adenosine deaminase from Sigma, 16 μM SAM, 25 nM G9a and 15 μM Thioglo. UNC0224 was added at concentrations ranging from 6 nM to 25 μM. After 5 min incubation, reactions were initiated by the addition of 5 μM H3 (1-25) peptide. The methylation reaction was followed by monitoring the increase in fluorescence using BioTek Synergy2 plate reader with 360/40 nm excitation filter and 528/20 nm emission filter for 20 min in 384 well-plate format. Homocysteine generated in the assay was quantitated using standard curves. Activity values were corrected by subtracting background caused by the peptide and the protein. IC50 values were calculated using four parameter logistic equation by Sigmaplot software. Standard deviations were calculated from two independent xperiments.

References:

[1]. Liu F, et al. Discovery of a 2,4-diamino-7-aminoalkoxyquinazoline as a potent and selective inhibitor of histone lysine methyltransferase G9a. J Med Chem. 2009 Dec 24;52(24):7950-3.

[2]. Liu F, et al. Protein lysine methyltransferase G9a inhibitors: design, synthesis, and structure activity relationships of 2,4-diamino-7-aminoalkoxy-quinazolines. J Med Chem. 2010 Aug 12;53(15):5844-57.

CAIndexNames:

4-Quinazolinamine, 7-[3-(dimethylamino)propoxy]-2-(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)-6-methoxy-N-(1-methyl-4-piperidinyl)-

SMILES:

CN1CCC(NC2=C3C=C(OC)C(OCCCN(C)C)=CC3=NC(N4CCN(C)CCC4)=N2)CC1

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