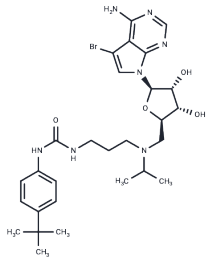
Data Sheet (Cat.No.T3082)

TargetMol

SGC0946

Chemical Properties



CAS No. : 1561178-17-3

Formula: C28H40BrN7O4

Molecular Weight: 618.57

Storage: Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	SGC0946 is a highly effective and specific DOT1L methyltransferase inhibitor (IC50: 0.3 nM); selectively kill mixed lineage leukemia cells.
Targets(IC50)	Histone Methyltransferase
In vivo	SGC 0946 significantly decreases di-methylation of H3K79 in A431 cells (IC50: 2.6 nM) and MCF10A cells (IC50: 8.8 nM), effectively and selectively killing cells with MLL translocations. Compared to its analogue EPZ004777, SGC 0946 is more potent against DOT1L, making it promising for cancer research. Moreover, SGC 0946 demonstrates over 100-fold higher selectivity for DOT1L than other histone methyltransferases (HMTs).
Kinase Assay	Determination of Inhibitor IC50 Values: EPZ004777 is serially diluted 3-fold in DMSO for a total of ten concentrations, beginning at 1 mM. A 1 µL aliquot of each inhibitor dilution is plated in a 384-well microtiter plate. The 100% inhibition control consisted of 2.5 mM ? nal concentration of the product inhibitor S-adenosyl-L-homocysteine, (SAH). Compound is incubated for 30 min with 40 ml per well of 0.25 nM DOT1L(1-416) in assay buffer (20 mM TRIS [pH 8.0] 10 mM NaCl, 0.002% Tween 20, 0.005% Bovine Skin Gelatin, 100 mM KCl, and 0.5 mM DTT). 10 ml per well of substrate mix comprising assay buffer with 200 nM 3H-SAM (American Radiolabeled Chemicals: 80 Ci/mmol), 600 nM unlabeled SAM, and 20 nM nucleosomes are added to initiate the reaction (both substrates are present in the ?nal reaction mixture at their respective KM values). Reactions are incubated for 120 min and quenched with 10 ml per well of 800 mM SAM. Incorporation of radioactivity into nucleosome substrate is measured in a ?ashplate. IC50 values for enzymes in the histone methyltransferase panel are determined under similar balanced assay conditions with both SAM and protein/peptide substrate present at concentrations equal to their respective KM values.

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 150 mg/mL (242.49 mM),Sonication is recommended. Ethanol: 93 mg/mL (150.35 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 3.3 mg/mL (5.33 mM),Sonication is recommended. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.6166 mL	8.0832 mL	16.1663 mL
5 mM	0.3233 mL	1.6166 mL	3.2333 mL
10 mM	0.1617 mL	0.8083 mL	1.6166 mL
50 mM	0.0323 mL	0.1617 mL	0.3233 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Yu W, et al. Nat Commun, 2012, 3, 1288.
Yu S, Zhou C, He J, et al. BMP4 drives primed to naïve transition through PGC-like state. Nature Communications. 2022, 13(1): 1-15
Wang W, Ren S, Lu Y, et al. Inhibition of Syk promotes chemical reprogramming of fibroblasts via metabolic rewiring and H2S production. The EMBO Journal. 2021 Jun 1;40(11):e106771. doi: 10.15252/embj.2020106771. Epub 2021 Apr 28.
Chen R, Xie W, Cai B, et al. Establishment and Identification of a CiPSC Lineage Reprogrammed from FSP-tdTomato Mouse Embryonic Fibroblasts (MEFs)[J]. Stem cells international. 2018 Dec 25;2018:5965727.
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Liu C, Li J, Xu F, et al.PARP1-DOT1L transcription axis drives acquired resistance to PARP inhibitor in ovarian cancer. Molecular Cancer.2024, 23(1): 111.