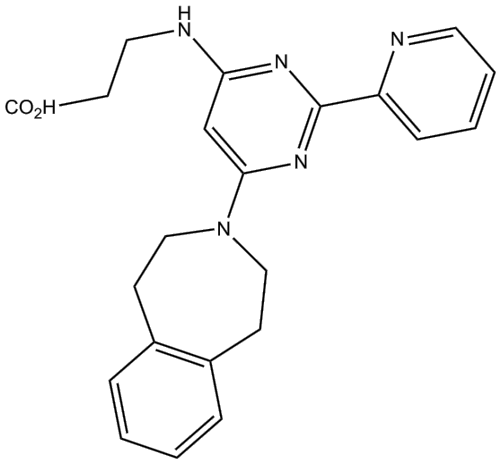
Product Data Sheet

Product Name: GSK J1
Cat. No.: GC10617

Chemical Properties

Cas. No.	1373422-53-7		
Chemical Name	3-[[2-pyridin-2-yl-6-(1,2,4,5-tetrahydro-3-benzazepin-3-yl)pyrimidin-4-yl]amino]propanoic acid		
SMILES	C1CN(CCC2=CC=CC=C21)C3=CC(=NC(=N3)C4=CC=CC=N4)NCCC(=O)O		
Formula	$C_{22}H_{23}N_5O_2$	M.Wt	389.45
Solubility	≥ 38.9 mg/mL in DMSO, ≥ 51.2 mg/mL in EtOH with ultrasonic	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

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Kinase experiment: Purified JmjD3 (1 μM) and UTX (3 μM) is incubated with 10 μM peptide [BiotinKAPRKQLATKAARK(me3)SAPATGG] in 50 mM HEPES pH 7.5, 150 mM KCl, 50 μM (NH4)2SO4·FeSO4·H2O, 1 mM 2-oxoglutarate, and 2 mM ascorbate (JmjD3, 3 minutes at 25°C; UTX, 20 minutes at 25°C) with various concentration of the inhibitor (0, 0.005, 0.01, 0.02, 0.05, 0.1 μM). 10 mM EDTA is added to stop the reaction. The reaction is desalted by zip tip and spotted on a MALDI plate with α-cyano-4-hydroxycinnamic acid MALDI matrix. Samples are analysed on a MALDI-TOF R system.

References:

[1]. Kruidenier L, et al. A selective jumonji H3K27 demethylase inhibitor modulates the proinflammatory macrophage response. Nature. 2012 Aug 16;488(7411):404-8.
[2]. Heinemann B, et al. Inhibition of demethylases by GSK-J1/J4. Nature. 2014 Oct 2;514(7520):E1-2.
[3]. Horton JR, et al. Characterization of a Linked Jumonji Domain of the KDM5/JARID1 Family of Histone H3 Lysine 4 Demethylases. J Biol Chem. 2016 Feb 5;291(6):2631-46.

Background

GSK J1 is a potent and selective inhibitor of the histone H3 lysine 27 (H3K27) demethylase JMJD3, a Fe2+- and α-ketoglutarate-dependent oxygenase involved in a variety of physiological functions including the inflammatory response, with the half maximal inhibition concentration IC50 value of 60 nM [1].

However, GSK J1 has restricted cellular permeability due to its highly polar carboxylate group, which plays a critical role in the binding of GSK J1 to JMJD3. In order to improve the cellular permeability, GSK J1 is esterified to mask the polarity generating an ethyl ester derivative that can be rapidly hydrolyzed to GSK J1 [1].

Reference

References:

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[1] Kruidenier L, Chung CW, Cheng Z, Liddle J, Che K, Joberty G, Bantscheff M, Bountra C, Bridges A, Diallo H, Eberhard D, Hutchinson S, Jones E, Katso R, Leveridge M, Mander PK, Mosley J, Ramirez-Molina C, Rowland P, Schofield CJ, Sheppard RJ, Smith JE, Swales C, Tanner R, Thomas P, Tumber A, Drewes G, Oppermann U, Patel DJ, Lee K, Wilson DM. A selective jumonji H3K27 demethylase inhibitor modulates the proinflammatory macrophage response. Nature. 2012 Aug 16;488(7411):404-8. doi: 10.1038/nature11262.

Caution: Product has not been fully validated for medical applications. For research use only.
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