

产品名称: **GSK-J4**

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生物活性:																					
Description		GSK-J4 is a potent dual inhibitor of H3K27me3/me2-demethylases JMJD3/KDM6B and UTX/KDM6A with IC50s of 8.6 and 6.6 μM, respectively. GSK-J4 inhibits LPS-induced TNF-α production in human primary macrophages with an IC50 of 9 μM. GSK J4 is a cell permeable prodrug of GSK-J1[1][2][3].																			
IC50 & Target		IC50: 8.6 μM (JMJD3/KDM6B), 6.6 μM (UTX/KDM6A)[6]																			
In Vitro		<p>GSK-J4 has cellular activity in Flag-JMJD3-transfected HeLa cells, in which GSK-J4 prevents the JMJD3-induced loss of nuclear H3K27me3 immunostaining. Administration of GSK-J4 increases total nuclear H3K27me3 levels in untransfected cells. GSK-J4 significantly reduces the expression of 16 of 34 LPS-driven cytokines, including tumour-necrosis factor-α (TNF-α)[1].</p> <p>GSK-J4 (5 μM; 48 hours) causes a more than 3-fold increase in mouse podocyte H3K27me3 content. H3K27me3 levels in cultured podocytes, GSK-J4 reduces Jagged-1 mRNA and Jagged-1 protein levels. Correspondingly, when exposed podocytes to the inducer of dedifferentiation TGF-β1, pretreatment with GSK-J4 prevents both the increase in intracellular N1-ICD levels and the increase in α-SMA and the decrease in podocin mRNA levels[2].</p> <p>GSK-J4 (10, 25 nM) acts upon DCs promoting the differentiation of Treg cells, improving Treg stability and suppressive capacities, without affecting the differentiation of Th1 and Th17 cells[3].</p> <p>GSK-J4 inhibits JMJD3 expression that is induced by TGF-β1[4].</p> <p>GSK-J4 inhibits H3K4 demethylation at Xist, Nodal, and HoxC13 in female embryonic stem cells[5].</p>																			
In Vivo		<p>GSK-J4 Hydrochloride (10 mg/kg; i.p.; thrice-weekly for 10 weeks) attenuates the development of kidney disease in diabetic mice[2].</p> <p>GSK-J4 (0.5 mg/kg, i.p.) significantly reduces the severity and delays the onset of the disease of the mouse model of experimental autoimmune encephalomyelitis[3].</p> <table><tr><td>Animal Model:</td><td colspan="3">Eight-week-old male db/m and db/db mice[2]</td></tr><tr><td>Dosage:</td><td colspan="3">10 mg/kg</td></tr><tr><td>Administration:</td><td colspan="3">i.p.; thrice-weekly for 10 weeks</td></tr><tr><td>Result:</td><td colspan="3">Attenuated the development of kidney disease in diabetic mice.</td></tr></table>			Animal Model:	Eight-week-old male db/m and db/db mice[2]			Dosage:	10 mg/kg			Administration:	i.p.; thrice-weekly for 10 weeks			Result:	Attenuated the development of kidney disease in diabetic mice.			
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		<p><b>In Vitro:</b></p> <p>DMSO : ≥ 36 mg/mL (86.23 mM)</p> <p>* "≥" means soluble, but saturation unknown.</p> <table><tr><th rowspan="4">Preparing Stock Solutions</th><th>Solvent / Mass Concentration</th><th>1 mg</th><th>5 mg</th><th>10 mg</th></tr><tr><th>1 mM</th><td>2.3952 mL</td><td>11.9760 mL</td><td>23.9521 mL</td></tr><tr><th>5 mM</th><td>0.4790 mL</td><td>2.3952 mL</td><td>4.7904 mL</td></tr><tr><th>10 mM</th><td>0.2395 mL</td><td>1.1976 mL</td><td>2.3952 mL</td></tr></table> <p>*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液。一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。</p> <p>储备液的保存方式和期限 -80℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 储存时，请在 1 个月内使用。</p> <p><b>In Vivo:</b></p> <p>请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 <b>In Vitro</b> 方式配制澄清的储</p>			Preparing Stock Solutions	Solvent / Mass Concentration	1 mg	5 mg	10 mg	1 mM	2.3952 mL	11.9760 mL	23.9521 mL	5 mM	0.4790 mL	2.3952 mL	4.7904 mL	10 mM	0.2395 mL	1.1976 mL	2.3952 mL
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<b>Solvent&amp;Solubility</b>	<p>备液，再依次添加助溶剂：</p> <p>——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶</p> <p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (5.99 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.99 mM，饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中，混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80，混合均匀；然后继续加入 450 <math>\mu</math>L 生理盐水定容至 1 mL。</p> <p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-<math>\beta</math>-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (5.99 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.99 mM，饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (5.99 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.99 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。</p> <p>以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中，混合均匀。</p>
<b>References</b>	<p>[1]. Kruidenier L, et al. <u>A selective jumonji H3K27 demethylase inhibitor modulates the proinflammatory macrophage response</u>. Nature. 2012 Aug 16;488(7411):404-8.</p> <p>[2]. Majumder S, et al. <u>Shifts in podocyte histone H3K27me3 regulate mouse and human glomerular disease</u>. J Clin Invest. 2018 Jan 2;128(1):483-499.</p> <p>[3]. Donas C, et al. <u>The histone demethylase inhibitor GSK-J4 limits inflammation through the induction of a tolerogenic phenotype on DCs</u>. J Autoimmun. 2016 Dec;75:105-117.</p> <p>[4]. Yapp C, et al. <u>H3K27me3 demethylases regulate in vitro chondrogenesis and chondrocyte activity in osteoarthritis</u>. Arthritis Res Ther. 2016 Jul 7;18(1):158</p> <p>[5]. Kamikawa YF, et al. <u>Histone demethylation maintains Prdm14 and Tsix expression and represses xist in embryonic stem cells</u>. PLoS One. 2015 May 20;10(5):e0125626</p> <p>[6]. Heinemann B, et al. <u>Inhibition of demethylases by GSK-J1/J4</u>. Nature. 2014 Oct 2;514(7520):E1-2</p>