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产品名称: **I-CBP 112**
产品别名: **I-CBP112**

生物活性:				
Description	I-CBP112 is a specific and potent acetyl-lysine competitive protein-protein interaction inhibitor, that inhibits the CBP/p300 bromodomains, enhances acetylation by p300.			
IC ₅₀ & Target	IC ₅₀ : 5.5±1.1 μM (CBP/p300, Leukemia cell); 9.1±1.2 μM (CBP/p300, Prostate cancer cell) ^[1]			
In Vitro	I-CBP112 significantly enhances acetylation by p300 at the histone H3K18 and H3K23 sites. I-CBP112 stimulated H3K18ac by ~3-fold, I-CBP112 induced enhances acetylation of these same sites by CBP as well as at H4K5. The EC ₅₀ 's of activation of I-CBP112 on p300- and CBP-mediated H3K18 acetylation are ~2 μM ^[1] . Exposure of human and mouse leukemic cell lines to I-CBP112 results in substantially impaired colony formation and induces cellular differentiation without significant cytotoxicity. Exposure of the BioMAP primary cell panel to I-CBP112 results in a unique response on cytokine and marker protein expression ^[2] .			
In Vivo	I-CBP112 significantly reduces the leukemia-initiating potential of mLL-AF9+ Aml cells in a dose-dependent manner in vitro and in vivo. The synergistic effects of I-CBP112 and current standard therapy (doxorubicin) as well as emerging treatment strategies (BET inhibition) provide new opportunities for combinatorial treatment of leukemia and potentially other cancers ^[2] .			
Solvent&Solubility	In Vitro: DMSO : ≥ 32 mg/mL (68.29 mM) * "≥" means soluble, but saturation unknown.			
	Preparing Stock Solutions	Solvent	Mass	
		Concentration	1 mg	5 mg
		1 mM	2.1341 mL	10.6703 mL
		5 mM	0.4268 mL	2.1341 mL
		10 mM	0.2134 mL	1.0670 mL
	*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。 储备液的保存方式和期限: -80°C, 6 months; -20°C, 1 month。 -80°C 储存时, 请在 6 个月内使用, -20°C 储存时, 请在 1 个月内使用。 In Vivo: 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 In Vitro 方式配制澄清的储备液, 再依次添加助溶剂: ——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 1.请依序添加每种溶剂: 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 2.5 mg/mL (5.34 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.34 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中, 混合均匀向上述体系中加入 50 μL Tween-80, 混合均匀; 然后继续加入 450 μL 生理盐水定容至 1 mL。			



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	<p>2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (5.34 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.34 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水溶液中, 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 (5.34 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.34 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 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中, 混合均匀。</p>
References	<p>[1]. Zucconi BE, et al. Modulation of p300/CBP Acetylation of Nucleosomes by Bromodomain LigandI-CBP112. Biochemistry. 2016 Jul 12;55(27):3727-34.</p> <p>[2]. Picaud S, et al. Generation of a Selective Small Molecule Inhibitor of the CBP/p300 Bromodomain for Leukemia Therapy. Cancer Res. 2015 Dec 1;75(23):5106-19.</p>
实验参考:	
Cell Assay	<p>I-CBP112 is dissolved in DMSO and diluted with appropriate medium before use. Cells (6000 KG1a and 13000 LNCaP cells/well) are plated in 96-well flat-bottom plates approximately 24 h prior to drug treatment. After 24 h, 10–20% fetal bovine serum-containing medium is replaced with 2.5% serum medium, and cells are treated with I-CBP112 in 0.18% DMSO; 0.18% DMSO is shown to have negligible cell growth effects under the conditions used in our experiments. After being exposed to I-CBP112 for 66 h, cells are subjected to a final concentration of 0.476% [3H]thymidine per well and allowed to proliferate for an additional 6 h (exposure to I-CBP112 for a total of 72 h). Cells are harvested, and the counts of 3H in each well are taken relative to those treated with vehicle alone to quantify the effect of the ligand on proliferation[1].</p>
Animal Administration	<p>Mice: Leukemic blasts expressing MLL-AF9 are treated in liquid culture with 5 μM of I-CBP112 for 3 days. Control cells are exposed to the corresponding concentration of the DMSO vehicle. Treated cells are then transplanted into sublethally irradiated syngeneic mice via tail vein injection. Upon the development of signs of disease the mice are sacrificed and analysed[2].</p>
References	<p>[1]. Zucconi BE, et al. Modulation of p300/CBP Acetylation of Nucleosomes by Bromodomain LigandI-CBP112. Biochemistry. 2016 Jul 12;55(27):3727-34.</p> <p>[2]. Picaud S, et al. Generation of a Selective Small Molecule Inhibitor of the CBP/p300 Bromodomain for Leukemia Therapy. Cancer Res. 2015 Dec 1;75(23):5106-19.</p>