



上海源叶生物科技有限公司
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产品名称: **CGP 57380**
产品别名: **CGP 57380**

生物活性:				
Description	CGP 57380 is a cell-permeable pyrazolo-pyrimidine compound that acts as a selective inhibitor of Mnk1 with IC ₅₀ of 2.2 μ M, but has no inhibitory activity against p38, JNK1, ERK1/2, PKC, or Src-like kinases.			
IC ₅₀ & Target	MNK1			
	2.2 μ M (IC ₅₀)			
In Vitro	CGP57380 inhibits phosphorylation of eIF4E in cellular assays with IC ₅₀ of about 3 μ M. CGP57380 causes dephosphorylation of eIF4E, and induces a further increase in the cap-dependent reporter in 293 cells[1]. CGP57380 results in dose-dependent decreases in Ang II-stimulated phosphorylation of eIF4E, protein synthesis, and VSMC hypertrophy[2]. CGP57380 sensitizes wild-type cells for serum-withdrawal induced apoptosis in mouse embryo fibroblasts (MEFs)[3]. CGP57380 prevents the serial replating function of BC progenitors[4].			
In Vivo	CGP57380 (40 mg/kg/d i.p.) potentially extinguishes the ability of BC CML cells to serially transplant-immunodeficient mice and function as LSCs[4].			
Solvent&Solubility	In Vitro: DMSO : 6 mg/mL (24.57 mM; Need ultrasonic and warming)			
	Preparing Stock Solutions	<div>Solvent / Mass / Concentration</div>	1 mg	5 mg
		1 mM	4.0945 mL	20.4725 mL
		5 mM	0.8189 mL	4.0945 mL
		10 mM	0.4095 mL	2.0473 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: \geq 2.5 mg/mL (10.24 mM); Clear solution 此方案可获得 \geq 2.5 mg/mL (10.24 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例, 取 100 μ L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 μ L PEG300 中, 混合均匀; 向上述体系中加入 50 μ L Tween-80, 混合均匀; 然后继续加入 450 μ L 生理盐水定容至 1 mL。 2.请依序添加每种溶剂: 10% DMSO→ 90% (20% SBE- β -CD in saline) Solubility: \geq 2.5 mg/mL (10.24 mM); Clear solution			



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	<p>此方案可获得 ≥ 2.5 mg/mL (10.24 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>
References	<p>[1]. Knauf U, et al. Negative regulation of protein translation by mitogen-activated protein kinase-interacting kinases 1 and 2. Mol Cell Biol. 2001 Aug;21(16):5500-11.</p> <p>[2]. Ishida M, et al. Mnk1 is required for angiotensin II-induced protein synthesis in vascular smooth muscle cells. Circ Res. 2003 Dec 12;93(12):1218-24. Epub 2003 Nov 6</p> <p>[3]. Chrestensen CA, et al. Loss of MNK function sensitizes fibroblasts to serum-withdrawal induced apoptosis. Genes Cells. 2007 Oct;12(10):1133-40.</p> <p>[4]. Lim S, et al. Targeting of the MNK-eIF4E axis in blast crisis chronic myeloid leukemia inhibits leukemia stem cell function. Proc Natl Acad Sci U S A. 2013 Jun 18;110(25):E2298-307</p>
实验参考:	
Animal Administration	<p>CD34⁺ cells (5×10^5) or GMPs (1×10^5) are resuspended in 25 μL 1% FBS/PBS solution and injected into the right femur of 8- to 10-wk-old sublethally irradiated (200 cGy) female mice (n=5 mice per group). Mice injected with 1% FBS/PBS solution serve as a sham control for each experiment.</p> <p>Beginning at 4 wk posttransplantation, mice are monitored for engraftment of human cells by flow cytometry. At 6 wk after transplantation, engrafted mice are treated with vehicle alone, dasatinib (5 mg/kg/d) by gavage, or CGP57380 (40 mg/kg/d) intraperitoneally for 3 wk (n=5 mice per group). At the end of treatment, mice are euthanized, and CD45⁺ cells are isolated from BM and spleen by using anti-human CD45-specific immunomagnetic microbeads. An aliquot of 1×10^5 human CD45⁺ cells is seeded into methylcellulose for the colony forming cell (CFC) assay, and colonies are enumerated after 2 wk. All of the remaining human cells from each primary transplant recipient are then transplanted by intrafemoral injection into secondary recipients, and human engraftment is monitored at 2-wk intervals beginning at 4 wk. At the end of 16 wk, all mice are euthanized.</p> <p>Engraftment in BM and blood is assessed by flow cytometry, and BCR-ABL1 transcripts are detected by RT-PCR.</p>
Kinase Assay	<p>Recombinant p38 isoforms are activated by Mkk6(E) under the following conditions: p38 (100 ng/mL), Mkk6(E) (30 ng/mL), ATP (100 mM) are mixed in kinase buffer (25 mM Hepes, 25 mM b-glycerophosphate, 0.1 mM sodium orthovanadate, 25 mM MgCl₂, 2.5 mM DTT, pH 7.4) and incubated for 30 min at 30°C. A typical assay reaction for Mnk1 activity contained Mnk1 (2 ng/mL), HA-eIF4E (10 ng/mL), ATP (300 mM) in kinase buffer. The reaction is started by addition of activated p38 (0.03-3 ng/mL) and stopped after 30 min at 30°C by addition of SDS loading buffer.</p> <p>Inhibitors of Mnk1 are identified under the same assay conditions, except that Mnk1 is pre-activated using active p38a before exposure to the substrate and inhibitors.</p>
References	<p>[1]. Knauf U, et al. Negative regulation of protein translation by mitogen-activated protein kinase-interacting kinases 1 and 2. Mol Cell Biol. 2001 Aug;21(16):5500-11.</p> <p>[2]. Ishida M, et al. Mnk1 is required for angiotensin II-induced protein synthesis in vascular smooth muscle cells. Circ Res. 2003 Dec 12;93(12):1218-24. Epub 2003 Nov 6</p> <p>[3]. Chrestensen CA, et al. Loss of MNK function sensitizes fibroblasts to serum-withdrawal induced</p>



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