

产品名称: **Trametinib(GSK1120212)**
 产品别名: **Trametinib; 曲美替尼; JTP-74057**

生物活性:					
Description	Trametinib (GSK1120212;JTP-74057) is a potent MEK inhibitor that inhibits MEK1 and MEK2 with IC ₅₀ s of about 2 nM.				
IC ₅₀ & Target	MEK1	MEK2			
	2 nM (IC ₅₀)	2 nM (IC ₅₀)			
In Vitro	Trametinib (GSK1120212;JTP-74057) (0.1-100 nM) blocks tumor necrosis factor-α and interleukin-6 production from peripheral blood mononuclear cells (PBMCs). Trametinib (JTP-74057) inhibits the growth of 9 out of 10 human colorectal cancer cell lines, and they shows cell-cycle arrest at the G1 phase after drug tratment[1]. The combination of GSK2118436 and Trametinib (GSK1120212) effectively inhibits cell growth, decreases ERK phosphorylation, decreases cyclin D1 protein, and increases p27(kip1) protein in the resistant clones[2].				
In Vivo	Adjuvant-induced arthritis (AIA) and type II collageninduced arthritis (CIA) development are suppressed almost completely by 0.1 mg/kg of Trametinib (GSK1120212;JTP-74057) or 10 mg/kg of Leflunomide[1]. Trametinib (0.3 mg/kg, 1 mg/kg, p.o.) is effective in inhibiting the HT-29 xenograft growth in a nude mouse xenograft model[2].				
Solvent&Solubility	In Vitro: DMSO : 33.33 mg/mL (54.16 mM; Need ultrasonic)				
	<div>Preparing Stock Solutions</div>	<div><div>Solvent</div><div>Mass</div><div>Concentration</div></div>	1 mg	5 mg	10 mg
		1 mM	1.6250 mL	8.1249 mL	16.2499 mL
		5 mM	0.3250 mL	1.6250 mL	3.2500 mL
		10 mM	0.1625 mL	0.8125 mL	1.6250 mL
	<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>In Vivo:</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 In Vitro 方式配制澄清的储备液，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>				
	1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline				
	Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution				
	此方案可获得 ≥ 2.5 mg/mL (4.06 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。				
2.请依序添加每种溶剂： 10% DMSO →90% corn oil					
Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution					

	<p>此方案可获得 ≥ 2.5 mg/mL (4.06 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]. Yamaguchi T, et al. <u>Suppressive effect of an orally active MEK1/2 inhibitor in two different animal models for rheumatoid arthritis: a comparison with leflunomide</u>. Inflamm Res, 2012, 61(5), 445-454.</p> <p>[2]. Yamaguchi T, et al. <u>Antitumor activities of JTP-74057 (GSK1120212), a novel MEK1/2 inhibitor, on colorectal cancer cell lines in vitro and in vivo</u>. Int J Oncol, 2011, 39(1), 23-31.</p> <p>[3]. Abe H, et al. <u>Discovery of a Highly Potent and Selective MEK Inhibitor: GSK1120212 (JTP-74057 DMSO Solvate)</u>. ACS Med Chem Lett. 2011 Feb 28;2(4):320-4.</p> <p>[4]. Liu H, et al. <u>Identifying and Targeting Sporadic Oncogenic Genetic Aberrations in Mouse Models of Triple Negative Breast Cancer</u>. Cancer Discov. 2018 Mar;8(3):354-369.</p> <p>[5]. Lai J, et al. <u>Elimination of melanoma by sortase A-generated TCR-like antibody-drug conjugates (TL-ADCs) targeting intracellular melanoma antigen MART-1</u>. Biomaterials. 2018 Sep;178:158-169.</p>
实验参考:	
Cell Assay	<p>Cells are treated with various concentrations of Trametinib (JTP-74057) in 100 mm dishes for 3 or 4 days. Both floating and adherent cells are collected and fixed with 70% ethanol. After washing with PBS, the cells are suspended in 100 μL/mL RNase and 25 μL/mL Propidium iodide (PI) and incubated at 37°C for 30 min in the dark. The DNA content of each single cell is determined using the flow cytometer Cytomics FC500 or Guava EasyCyte plus[2]</p>
Animal Administration	<p>Mice[2]</p> <p>Female BALB/c-nu/nu mice are used. On day 0, HT-29 cells or COLO205 cells suspended in ice-cold HBSS (-) are inoculated subcutaneously into the right flank of the mice at 5×10^6 cells/100 μL/site or 1×10^6 cells/100 μL/site, respectively. The acetic acid-solvated form of Trametinib (JTP-74057, 0.3 mg/kg, 1 mg/kg) is dissolved in 10% Cremophor EL-10% PEG400 and is administered orally once daily for 14 days from the day when the mean tumor volume reached 100 mm³. The tumor length [L(mm)] and width [W(mm)] are measured using a microgauge twice a week after commencement of dosing, and the tumor volume is calculated using the following formula: tumor volume (mm³)=L×W×W/2.</p>
Kinase Assay	<p>The nonphosphorylated myelin basic protein (MBP) is coated onto an ELISA plate, and the active form of B-Raf/c-Raf is mixed with unphosphorylated MEK1/MEK2 and ERK2 in 10 μM ATP and 12.5 mM MgCl₂ containing MOPS buffer in the presence of various concentrations of Trametinib (JTP-74057). The phosphorylation of MBP is detected by the anti-phosphoMBP antibody. Kinase inhibitory activities against a total of 99 kinases are tested at 10 μM ATP[2]</p>
References	<p>[1]. Yamaguchi T, et al. <u>Suppressive effect of an orally active MEK1/2 inhibitor in two different animal models for rheumatoid arthritis: a comparison with leflunomide</u>. Inflamm Res, 2012, 61(5), 445-454.</p> <p>[2]. Yamaguchi T, et al. <u>Antitumor activities of JTP-74057 (GSK1120212), a novel MEK1/2 inhibitor, on colorectal cancer cell lines in vitro and in vivo</u>. Int J Oncol, 2011, 39(1), 23-31.</p> <p>[3]. Abe H, et al. <u>Discovery of a Highly Potent and Selective MEK Inhibitor: GSK1120212 (JTP-74057 DMSO Solvate)</u>. ACS Med Chem Lett. 2011 Feb 28;2(4):320-4.</p> <p>[4]. Liu H, et al. <u>Identifying and Targeting Sporadic Oncogenic Genetic Aberrations in Mouse Models of Triple Negative Breast Cancer</u>. Cancer Discov. 2018 Mar;8(3):354-369.</p>

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源叶生物