



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

产品名称: **TEPP-46**
产品别名: **ML-265**

生物活性:

Description	TEPP-46 is a potent and selective pyruvate kinase M2 (PKM2) activator with an AC50 of 92 nM, showing little or no effect on PKM1, PKL and PKR.				
IC ₅₀ & Target	AC50: 92 nM (PKM2)				
In Vitro	TEPP-46 and DASA-58 activate PKM2 by a mechanism similar to that of the endogenous activator FBP. Pre-treatment of cells with TEPP-46 or DASA-58 prevents pervanadate-induced inhibition of PKM2 activity. TEPP-46 also induces a decrease in the intracellular levels of acetyl-coA, lactate, ribose phosphate and serine[1]. TEPP-46 inhibits LPS-induced Hif-1α and IL-1β, as well as the expression of a range of other Hif-1α-dependent genes. TEPP-46 treatment significantly downregulates the expression of the M1 markers Il12p40 and Cxcl-10. Activation of PKM2 using TEPP-46 significantly inhibits FSL-1 and CpG-induced Il1b mRNA expression. TEPP-46 inhibits Mtb-induced Il1b mRNA levels, boosts Mtb-induced levels of Il10 mRNA, and has no effect on levels of Tnf[2].				
In Vivo	TEPP-46 exhibits good oral bioavailability with relatively low clearance, long half-life, and good volume of distribution-parameters that predict for drug exposure in tumor tissues. TEPP-46 at 150 mg/kg readily achieves maximal PKM2 activation measured in A549 xenograft tumors[1].				
Solvent&Solubility	In Vitro: DMSO : 50 mg/mL (134.24 mM; Need ultrasonic) H ₂ O : < 0.1 mg/mL (insoluble)				
	Preparing Stock Solutions	Solvent Mass Concentration	1 mg	5 mg	10 mg
		1 mM	2.6849 mL	13.4243 mL	26.8485 mL
		5 mM	0.5370 mL	2.6849 mL	5.3697 mL
		10 mM	0.2685 mL	1.3424 mL	2.6849 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℃, 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。				
	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 (6.71 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.71 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。				



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

	<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 (6.71 mM); Suspended solution; Need ultrasonic</p> <p>此方案可获得 2.5 mg/mL (6.71 mM)的均匀悬浊液, 悬浊液可用于口服和腹腔注射。</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 (6.71 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (6.71 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]. Anastasiou D, et al. Pyruvate kinase M2 activators promote tetramer formation and suppress tumorigenesis. Nat Chem Biol. 2012 Oct;8(10):839-847.</p> <p>[2]. Palsson-McDermott EM, et al. Pyruvate kinase M2 regulates Hif-1α activity and IL-1β induction and is a critical determinant of the warburg effect in LPS-activated macrophages. Cell Metab. 2015 Jan 6;21(1):65-80.</p>
实验参考:	
Cell Assay	<p>2,000 cells are seeded in 96-well plates 24 h prior to treatment start. CellTiter96® AQueous is used to assess cell viability following oxidant and PKM2 activator combination treatments. MTS: (3-(4,5-dimethylthiazol-2-yl)-5- (3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium). [1]</p>
Animal Administration	<p>H1299 parental and H1299 cells with constitutive expression of a mouse PKM1 cDNA (H1299-PKM1 cells) are propagated in RPMI supplemented with 10% fetal bovine serum, penicillin/streptomycin, 2 mM glutamine, and hygromycin for transgene selection. Cells are harvested, resuspended in sterile PBS, and 5×10⁵ cells are injected subcutaneously into nu/nu mice. Tumor growth is monitored by caliper measurement, the mice are sacrificed and tumors harvested after the time indicated. Tumors are weighed, divided and either flash-frozen in liquid nitrogen or fixed in formalin for later analysis. [1]</p>
Kinase Assay	<p>Pyruvate kinase activity is measured by monitoring pyruvate-dependent conversion of NADH to NAD⁺ by lactate dehydrogenase (LDH) as described previously. Briefly, for cell line experiments, the medium is replaced with fresh medium 1 hour prior to the start of treatment with DMSO or activator. Also, where indicates, 100 μM pervanadate is added 10 minutes prior to cell lysis. Cells are lysed on ice with NP-40 buffer containing 2 mM DTT and protease inhibitors and clarified by centrifugation at 21,000 x g. 5 μL of the supernatant is used to assess pyruvate kinase activity. Pyruvate kinase activity is subsequently normalized for total protein content. [1]</p>
References	<p>[1]. Anastasiou D, et al. Pyruvate kinase M2 activators promote tetramer formation and suppress tumorigenesis. Nat Chem Biol. 2012 Oct;8(10):839-847.</p> <p>[2]. Palsson-McDermott EM, et al. Pyruvate kinase M2 regulates Hif-1α activity and IL-1β induction and is a critical determinant of the warburg effect in LPS-activated macrophages. Cell Metab. 2015 Jan 6;21(1):65-80.</p>