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产品名称：UK-5099
产品别名：PF-1005023

生物活性：

Description	UK-5099 (PF-1005023) is a potent inhibitor of the mitochondrial pyruvate carrier (MPC). UK-5099 (PF-1005023) inhibits pyruvate-dependent O_2 consumption with an IC_{50} of 50 nM.
IC_{50} & Target	IC50: 50 nM (MPC)[1]
In Vitro	The trypanosomal pyruvate carrier is found to be rather insensitive to inhibition by alpha-cyano-4-hydroxycinnamate (K_i=17 mM) but can be completely blocked by UK-5099 (K_i=49 microM)[2]. UK-5099 also inhibits the monocarboxylate transporter (MCT) [3]. UK5099 significantly inhibits the glucose-stimulated rise in oxygen consumption in a dose-dependent manner and at 150 μM reduced oxygen consumption below basal levels. UK5099 reduces ATP levels and increases ADP and AMP levels in 832/13 cells[4]. The UK5099 treated cells show significantly higher proportion of side population fraction and express higher levels of stemness markers Oct3/4 and Nanog. UK5099 application may be an ideal model for Warburg effect studies[5].
In Vivo	The MPC inhibitor UK5099 increases the glucose excursion seen during an intraperitoneal glucose tolerance test in C57BLK mice[4].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 50 mg/mL (173.43 mM)** **H_2O : < 0.1 mg/mL** (insoluble) * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.4686 mL	17.3430 mL	34.6861 mL
	5 mM	0.6937 mL	3.4686 mL	6.9372 mL
	10 mM	0.3469 mL	1.7343 mL	3.4686 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 (8.67 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (8.67 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 (8.67 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (8.67 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。 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。
References	[1]. Halestrap AP. The mitochondrial pyruvate carrier. Kinetics and specificity for substrates and inhibitors. Biochem J. 1975 April; 148(1): 85-96. [2]. Wiemer EA, et al. The inhibition of pyruvate transport across the plasma membrane of the bloodstream form of Trypanosoma brucei and its metabolic implications. Biochem J. 1995 Dec 1;312 (Pt 2):479-84. [3]. Hinoi E, et al. A molecular mechanism of pyruvate protection against cytotoxicity of reactive oxygen species in osteoblasts. Mol Pharmacol. 2006 Sep;70(3):925-35. Epub 2006 Jun 9. [4]. Patterson JN, et al. Mitochondrial metabolism of pyruvate is essential for regulating glucose-stimulated secretion. J Biol Chem. 2014 May 9;289(19):13335-46. [5]. Zhong Y, et al. Application of mitochondrial pyruvate carrier blocker UK5099 creates metabolic reprogram and greater stem-like properties in LnCap prostate cancer cells in vitro. Oncotarget. 2015 Nov 10;6(35):37758-69.

实验参考：

Cell Assay	The 832/13 cell line is used for experiments. Cell viability is measured using CellTiter Blue. The assay is based on cellular reduction of resazurin to resorufin. Appearance of resorufin is monitored by fluorescence emission at 585 nm using a Spectramax M5 microplate reader with excitation at 555 nm. For UK5099-treated cells, cells are allowed to recover for 1 h before measuring cell viability. Data are expressed as -fold relative to no treatment or siCtrl[4].
Animal Administration	C57BLK mice are fasted for 16 h prior to glucose challenge. UK5099 (32 μmol/kg of body weight) or DMSO in PBS is injected into the intraperitoneal cavity 30 min before injecting glucose (1.5 mg of glucose/g of body weight). Blood glucose levels are measured at 0, 10, 20, 30, 60, and 120 min after glucose injection[4].
References	[1]. Halestrap AP. The mitochondrial pyruvate carrier. Kinetics and specificity for substrates and inhibitors. Biochem J. 1975 April; 148(1): 85-96. [2]. Wiemer EA, et al. The inhibition of pyruvate transport across the plasma membrane of the bloodstream form of Trypanosoma brucei and its metabolic implications. Biochem J. 1995 Dec 1;312 (Pt 2):479-84. [3]. Hinoi E, et al. A molecular mechanism of pyruvate protection against cytotoxicity of reactive oxygen species in osteoblasts. Mol Pharmacol. 2006 Sep;70(3):925-35. Epub 2006 Jun 9. [4]. Patterson JN, et al. Mitochondrial metabolism of pyruvate is essential for regulating glucose-stimulated secretion. J Biol Chem. 2014 May 9;289(19):13335-46. [5]. Zhong Y, et al. Application of mitochondrial pyruvate carrier blocker UK5099 creates metabolic reprogram and greater stem-like properties in LnCap prostate cancer cells in vitro. Oncotarget. 2015 Nov 10;6(35):37758-69.