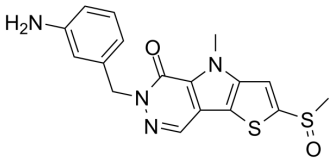
TEPP-46

Cat. No.:	HY-18657
CAS No.:	1221186-53-3
Molecular Formula:	$C_{17}H_{16}N_4O_2S_2$
Molecular Weight:	372.46
Target:	Pyruvate Kinase
Pathway:	Metabolic Enzyme/Protease
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 50 mg/mL (134.24 mM; Need ultrasonic)

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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 50% PEG300 >> 50% saline
   Solubility: 10 mg/mL (26.85 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 0.5% CMC-Na/saline water
   Solubility: 5 mg/mL (13.42 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.87 mg/mL (7.71 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (6.71 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (6.71 mM); Suspended solution; Need ultrasonic
6. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (5.58 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

TEPP-46 (ML-265) is a potent and selective pyruvate kinase M2 (PKM2) activator with an AC_{50} of 92 nM, showing little or no

	effect on PKM1, PKL and PKR[1].
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	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). MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	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, 2 mM glutamine, and hygromycin for transgene selection. Cells are harvested, resuspended in sterile PBS, and 5×10^5 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. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Kidney Int. 2023 Jan 30;S0085-2538(23)00052-2.
- Sci Transl Med. 2019 Feb 6;11(478):eaau8866.
- Nat Commun. 2022 May 16;13(1):2698.
- Neuro Oncol. 2023 Jun 5;noad103.
- Sci Adv. 2022 Sep 23;8(38):eabo0987.

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REFERENCES

[1]. Anastasiou D, et al. Pyruvate kinase M2 activators promote tetramer formation and suppress tumorigenesis. Nat Chem Biol. 2012 Oct;8(10):839-847.

[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.

Caution: Product has not been fully validated for medical applications. For research use only.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com
Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA