产品名称：**TPCA-1**
产品别名：**TPCA-1**

生物活性：		
Description	TPCA-1 is a potent and selective inhibitor of IKK-2 with IC_{50} of 17.9 nM. TPCA-1 is an effective inhibitor of STAT3phosphorylation, DNA binding, and transactivation.	
IC_{50} & Target	IKK-2	STAT3
	17.9 nM (IC_{50})	
In Vitro	TPCA-1 inhibits lipopolysaccharide-induced human monocyte production of TNF-α, IL-6, and IL-8 with an IC50 of 170 to 320 nM[1][2]. TPCA-1 (0-2 μM) inhibits STAT3 phosphorylation and transactivation induced by cytokines and nonreceptor tyrosine kinase in dose- and time-dependent manner. TPCA-1 completely inhibits STAT3 phosphorylation without changing total STAT3 levels[3]. TPCA-1 increased sensitivity to ZD1839 in both TKI sensitive cells and insensitive cells[3].	
	Cell Viability Assay[2]	
	Cell Line:	human peripheral blood monocytes stimulated with LPS.
	Concentration:	0-10 μM.
	Incubation Time:	~24 hours.
	Result:	TPCA-1 Inhibits LPS-Induced TNF-α, IL-6, and IL-8 production by human monocytes.
	Cell Viability Assay[3]	
	Cell Line:	HCC827 and H1975 cells.
	Concentration:	0-10 μM.
	Incubation Time:	0.5-2 hours.
	Result:	Suppressed proliferation of HCC827 and H1975 cells. Led to a G_2-M cell-cycle arrest in HCC827 but not A549.
	Western Blot Analysis[3]	
	Cell Line:	HEK-293T cell lines.
	Concentration:	0-2 μM (before IL-2 or IFN-α treatment).
	Incubation Time:	0.5-2 hours.
	Result:	Inhibited STAT3 phosphorylation and transactivation induced by cytokines and nonreceptor tyrosine kinase in dose- and time-dependent manner.
In Vivo	TPCA-1 (3, 10, or 20 mg/kg, i.p.) results in a dose-dependent reduction in the severity of murine collagen-induced arthritis (CIA)[2]. TPCA-1(10 mg/kg, i.p. daily) inhibits growth of NSCLC with EGFR mutation and potentiates antitumor effect of ZD1839 in xenograft models[3].	
	Animal Model:	10-12 weeks old male DBA/1 OlaHsd mice[2].
	Dosage:	3, 10, or 20 mg/kg.
	Administration:	I.P., b.i.d, from days 1 to 47.
	Result:	Reduced the severity and delays the onset of CIA. Attenuated ex vivo antigen-induced T cell proliferation in CIA.

	Animal Model:	Six-week-old BALB/c female nude mice injected subcutaneously with HCC827 cells (5×106)[3].
	Dosage:	10 mg/kg.
	Administration:	Intraperitoneally daily.
	Result:	The tumor weight inhibition rate of TPCA-1, ZD1839, and their combination are 0.419(E_{TPCA-1}), 0.680(E_{ZD1839}), and 0.837($E_{observed}$), respectively.

Solvent&Solubility

In Vitro:

DMSO : ≥ 100 mg/mL (358.05 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.5805 mL	17.9025 mL	35.8051 mL
	5 mM	0.7161 mL	3.5805 mL	7.1610 mL
	10 mM	0.3581 mL	1.7903 mL	3.5805 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: ≥ 7.5 mg/mL (26.85 mM); Clear solution

此方案可获得 ≥ 7.5 mg/mL (26.85 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 75.0 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% (20% SBE-β-CD in saline)

Solubility: ≥ 7.5 mg/mL (26.85 mM); Clear solution

此方案可获得 ≥ 7.5 mg/mL (26.85 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 75.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。

3.请依序添加每种溶剂： 10% DMSO →90% corn oil

Solubility: ≥ 7.5 mg/mL (26.85 mM); Clear solution

此方案可获得 ≥ 7.5 mg/mL (26.85 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 75.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。

[1]. Sachse F, et al. IKK-2 inhibitor TPCA-1 represses nasal epithelial inflammation in vitro.Rhinology. 2011 Jun;49(2):168-73.

References	[2]. Podolin PL, et al. Attenuation of murine collagen-induced arthritis by a novel, potent, selective small molecule inhibitor of IkappaB Kinase 2, TPCA-1 (2-[(aminocarbonyl)amino]-5-(4-fluorophenyl)-3-thiophenecarboxamide), occurs via reduction of proinflamm [3]. Nan J, et al. TPCA-1 is a direct dual inhibitor of STAT3 and NF-κB and regresses mutant EGFR-associated human non-small cell lung cancers. Mol Cancer Ther. 2014 Mar;13(3):617-29.

源叶生物