产品名称：IKK-16 (IKK Inhibitor VII)
产品别名：IKK-16

生物活性：

Description	IKK 16 is a selective IκB kinase (IKK) inhibitor for IKK2, IKK complex and IKK1 with IC_{50}s of 40 nM, 70 nM and 200 nM, respectively. IKK16 also inhibits leucine-rich repeat kinase-2 (LRRK2) with an IC_{50} of 50 nM.			
IC_{50} & Target	IKK2	IKK1	IKK	LRRK2
	40 nM (IC_{50})	200 nM (IC_{50})	70 nM (IC_{50})	50 nM (IC_{50})
In Vitro	IKK 16 is a potent inhibitor of IKK2 with IC_{50} value of 40 nM[1]. IKK 16, a leucine-rich repeat kinase-2 (LRRK2) kinase inhibitor, exhibits in vitro IC_{50}s of 50 nM. IKK 16 exhibits sub-micromolar IC_{50} concentrations for LRRK2 in vitro, which is lower than what observed for cellular inhibition of Ser935 phosphorylation. IKK 16 (20 μM) can inhibit LRRK2 Ser935 phosphorylation in HEK293 GFP-LRRK2 G2019S cells (GS) or A2016T/G2019S (IRM) cells in vitro.			
In Vivo	IKK 16 also demonstrates significant in vivo activity in an acute model of cytokine release. Both routes of administration of IKK 16 (30 mg/kg, sc) or orally (30 mg/kg, p.o) at the indicated dose results in a significant inhibition of 86% (sc) and 75% (p.o.). IKK 16(10 mg/kg, sc) is also active in the thioglycollate-induced peritonitis model in the mouse. The maximal inhibition of neutrophil extravasation in this model is about 50%[1]. Treatment of septic mice with IKK 16 (1 mg/kg body weight i.v.) results in a significantly increased degree of phosphorylation (P<0.05) of serine residues on Akt and eNOS in the liver[3].			

Solvent&Solubility

In Vitro:

DMSO : ≥ 27 mg/mL (55.83 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.0677 mL	10.3385 mL	20.6770 mL
	5 mM	0.4135 mL	2.0677 mL	4.1354 mL
	10 mM	0.2068 mL	1.0338 mL	2.0677 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 (5.17 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.17 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% (20% SBE-β-CD in saline) Solubility: ≥ 2.5 mg/mL (5.17 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.17 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 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: ≥ 2.5 mg/mL (5.17 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.17 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]. Waelchli R, et al. Design and preparation of 2-benzamido-pyrimidines as inhibitors of IKK. Bioorg Med Chem Lett. Bioorg Med Chem Lett. 2006 Jan 1;16(1):108-12. [2]. Hermanson SB, et al. Screening for novel LRRK2 inhibitors using a high-throughput TR-FRET cellular assay for LRRK2 Ser935 phosphorylation. PLoS One. 2012;7(8):e43580. [3]. Coldewey SM, et al. Inhibition of IκB kinase reduces the multiple organ dysfunction caused by sepsis in the mouse. Dis Model Mech. 2013 Jul;6(4):1031-42.

实验参考：

Cell Assay	SH-SY5Y cells are transduced with 25% (v/v) BacMam LRRK2-GFP G2019S and plated (20 μL/well, 20,000 cells/well) onto eight 384-well assay plates. Then 25% BacMam LRRK2-GFP G2019S transduced SH-SY5Y cells are incubated with indicated concentrations of indicated compounds (e.g., IKK 16, 0.01, 0.1, 1, 10 and 100 μM) for 90 min prior to the TR-FRET detection with Tb-anti-LRRK2 pSer935 antibody. The % inhibition is calculated[2].
Animal Administration	Rats and Mice[1] IKK 16 is tested in two animal models. First, its efficacy to inhibit TNFα release into plasma upon LPS-challenge in the rat is determined. IKK 16 is dosed sc (30 mg/kg) or orally (30 mg/kg) 1 h prior to the LPS-challenge. Four hours after the challenge, plasma is collected and the systemic TNFα levels are analyzed using a commercially available ELISA kit. Both routes of administration of IKK 16 at the indicated dose results in a significant inhibition of 86% (sc) and 75% (p.o.). In a second experiment, IKK 16 is also active in the thioglycollate-induced peritonitis model in the mouse. The maximal inhibition of neutrophil extravasation in this model is about 50% at a dose of 10 mg/kg sc. Mice[3] Two-month-old male C57BL/6 mice receive LPS (9 mg/kg body weight) and PepG (3 mg/kg body weight) in 0.9% saline (5 mL/kg body weight) intraperitoneally. Sham mice are not subjected to LPS/PepG, but are otherwise treated the same way. At 1 hour after LPS/PepG co-administration, mice are treated either with IKK 16 (1 mg/kg body weight i.v.) or vehicle (5 mL/kg body weight 10% DMSO i.v.). At 24 hours the experiment is terminated and organ and blood samples are collected for quantification of organ dysfunction and/or injury. Mice are randomly allocated into four different groups: (1) sham+vehicle (n=10); (2) sham+IKK 16 (n=3); (3) LPS/PepG+vehicle (n=9); (4) LPS/PepG+IKK 16 (n=10).
	[1]. Waelchli R, et al. Design and preparation of 2-benzamido-pyrimidines as inhibitors of IKK. Bioorg Med Chem Lett. Bioorg Med Chem Lett. 2006 Jan 1;16(1):108-12.

References	[2]. Hermanson SB, et al. Screening for novel LRRK2 inhibitors using a high-throughput TR-FRET cellular assay for LRRK2 Ser935 phosphorylation. PLoS One. 2012;7(8):e43580. [3]. Coldewey SM, et al. Inhibition of IκB kinase reduces the multiple organ dysfunction caused by sepsis in the mouse. Dis Model Mech. 2013 Jul;6(4):1031-42.

源叶生物