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产品名称：CC-930
产品别名：Tanzisertib

生物活性：

Description	Tanzisertib (CC-930) is a potent JNK1/2/3 inhibitor with IC50s of 61/7/6 nM, respectively.

IC_{50} & Target	JNK3	JNK2	JNK1	
	6 nM (IC_{50})	7 nM (IC_{50})	61 nM (IC_{50})	

In Vitro	Tanzisertib (CC-930) inhibits the formation of phospho-cJun in human PBMC stimulated by phorbol-12-myristate-13-acetate and phytohemeagglutinin (IC50=1 μM)[1]. Tanzisertib (CC-930) (1-2 μM) substantially reduces hepatocyte apoptosis and necrosis, abrogates apoptosis and necrosis in FC-loaded WT hepatocytes[2]. Tanzisertib (CC-930) blocks the JNK pathway that is activated by pro-fibrotic cytokines in systemic sclerosis[3].
In Vivo	Tanzisertib (CC-930) (10 and 30 mg/kg, p.o.) inhibits the production of TNFa by 23% and 77% in the acute rat LPS-induced TNFa production PK-PD model[1]. Tanzisertib (CC-930) (150 mg/kg) prevents the development of fibrosis in different models, but can also induce the regression of pre-existing fibrosis[3].

Solvent&Solubility

In Vitro:

DMSO : ≥ 33 mg/mL (73.59 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2300 mL	11.1498 mL	22.2995 mL
	5 mM	0.4460 mL	2.2300 mL	4.4599 mL
	10 mM	0.2230 mL	1.1150 mL	2.2300 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 (5.57 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.57 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 (5.57 mM); Clear solution

	此方案可获得 ≥ 2.5 mg/mL (5.57 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 (5.57 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.57 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]. Plantevin Krenitsky V, et al. Discovery of CC-930, an orally active anti-fibrotic JNK inhibitor. Bioorg Med Chem Lett. 2012 Feb 1;22(3):1433-8. [2]. Gan LT, et al. Hepatocyte free cholesterol lipotoxicity results from JNK1-mediated mitochondrial injury and is HMGB1 and TLR4-dependent. J Hepatol. 2014 Dec;61(6):1376-84. [3]. Reich N, et al. Jun N-terminal kinase as a potential molecular target for prevention and treatment of dermal fibrosis. Ann Rheum Dis. 2012 May;71(5):737-45. [4]. Tavernier SJ, et al. Regulated IRE1-dependent mRNA decay sets the threshold for dendritic cell survival. Nat Cell Biol. 2017 Jun;19(6):698-710.

实验参考：

Cell Assay	Systemic sclerosis (SSc) fibroblasts are incubated with 1 μM Tanzisertib (CC-930) in 96-well plates for 20 h. Then MTT is added at a final concentration of 1 mg/mL, and the cells are further incubated at 37°C for 4 h. Mock-treated fibroblasts are used as controls, and all other results are normalised to untreated cells. [3]
Animal Administration	To evaluate the regression of fibrosis on inhibition of JNK, a modified model of bleomycin-induced dermal fibrosis is used. In this model, treatment is initiated 3 weeks after the beginning of the challenge with bleomycin, when significant dermal fibrosis is already established. The outcome of six different groups with a total number of 40 mice is analysed. The first group of mice receive subcutaneous injections of NaCl for 6 weeks. The second group is injected for 3 weeks with bleomycin followed by injections of NaCl for another 3 weeks to analyse the degree of fibrosis before treatment, and to control the spontaneous regression of fibrosis. The third group of mice is killed after 6 weeks of injections with bleomycin. The fourth and the fifth group are treated with Tanzisertib (CC-930) at doses of 50 mg/kg and 150 mg/kg for the last 3 weeks of continuous challenge with bleomycin for 6 weeks. The sixth group is a positive control group consisting of mice challenged with bleomycin for 6 weeks and treated in parallel with imatinib at doses of 50 mg/kg for the last 3 weeks. [3]
References	[1]. Plantevin Krenitsky V, et al. Discovery of CC-930, an orally active anti-fibrotic JNK inhibitor. Bioorg Med Chem Lett. 2012 Feb 1;22(3):1433-8. [2]. Gan LT, et al. Hepatocyte free cholesterol lipotoxicity results from JNK1-mediated mitochondrial injury and is HMGB1 and TLR4-dependent. J Hepatol. 2014 Dec;61(6):1376-84. [3]. Reich N, et al. Jun N-terminal kinase as a potential molecular target for prevention and treatment

	of dermal fibrosis. Ann Rheum Dis. 2012 May;71(5):737-45. [4]. Tavernier SJ, et al. Regulated IRE1-dependent mRNA decay sets the threshold for dendritic cell survival. Nat Cell Biol. 2017 Jun;19(6):698-710.