产品名称：Z-IETD-FMK
产品别名：Z-IETD-FMK

生物活性：

Description	Z-IETD-FMK is a selective caspase-8 inhibitor[1]. Z-IETD-FMK is a granzyme B inhibitor.
IC_{50} & Target	Caspase-8 [1]
In Vitro	Z-IETD-FMK causes full inhibition only of the proapoptotic effect of TNFα with an IC50 of 0.46 μM[1]. Z-IETD-FMK and Z-VAD-FMK at non-toxic doses are found to be immunosuppressive and inhibit human T cell proliferation induced by mitogens and IL-2. They are shown to block NF-κB in activated primary T cells, but have little inhibitory effect on the secretion of IL-2 and IFN-γ during T cell activation[2]. Z-IETD-FMK inhibits the cleavage of caspase-8 and only partially inhibits the cleavage of caspase-3 and PARP. Z-IETD-FMK can prevent the execution of apoptosis in retinal cells exposed to different apoptotic stimuli[3].
In Vivo	Pharmacological inhibition of caspase-8 by z-IETD-FMK robustly reduces tumour outgrowth and this is closely associated with a reduction in the release of pro-inflammatory cytokines, IL-6, TNF-α, IL-18, IL-1α, IL-33, but not IL-1β. Furthermore, inhibition of caspase-8 reduces the recruitment of innate suppressive cells, such as myeloid-derived suppressor cells, but not of regulatory T cells to lungs of tumour-bearing mice[4].
Solvent&Solubility	***In Vitro:*** **DMSO : 125 mg/mL** (**190.93 mM**; Need ultrasonic) **H_2O : < 0.1 mg/mL** (insoluble)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.5275 mL	7.6373 mL	15.2746 mL
	5 mM	0.3055 mL	1.5275 mL	3.0549 mL
	10 mM	0.1527 mL	0.7637 mL	1.5275 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: ≥ 2.08 mg/mL (3.18 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (3.18 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (3.18 mM); Clear solution

	此方案可获得 ≥ 2.08 mg/mL (3.18 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (3.18 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (3.18 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Cowburn AS, et al. z-VAD-fmk augmentation of TNF alpha-stimulated neutrophil apoptosis is compound specific and does not involve the generation of reactive oxygen species. [2]. Lawrence CP, et al. Suppression of human T cell proliferation by the caspase inhibitors, z-VAD-FMK and z-IETD-FMK is independent of their caspase inhibition properties. Toxicol Appl Pharmacol. 2012 Nov 15;265(1):103-12. [3]. Tezel G, et al. Inhibition of caspase activity in retinal cell apoptosis induced by various stimuli in vitro. Invest Ophthalmol Vis Sci. 1999 Oct;40(11):2660-7. [4]. Terlizzi M, et al. Pharmacological inhibition of caspase-8 limits lung tumour outgrowth. Br J Pharmacol. 2015 Aug;172(15):3917-28.

实验参考：

Cell Assay	T cell proliferation following mitogen stimulation is determined using [^{3}H]-thymidine incorporation. In brief, PBMCs or purified T cells are seeded at 1×10^6 cells/mL in 96 well plates and stimulated with either PHA (5 μg/mL or co-stimulated with anti-CD3 mAb (5 μg/mL) and anti-CD28 mAb (2.5 μg/mL) in the presence or absence of caspase inhibitor Z-IETD-FMK. The cells are cultured for 72 h with the last 16 h pulsed with [^{3}H]-labelled methyl-thymidine (0.037 MBq) prior to harvest onto glass fibre filter mats using a Tomtec automated multi-well harvester[2].
Animal Administration	Mice: Mice are divided into three groups: (1) naive, non-treated, mice; (2) CTR (control), i.t. instilled with NMU; and (3) lung cancer-bearing mice treated with Z-IETD-FMK (0.5 μg per mouse). The involvement of caspase-8 in lung cancer development is the determined at different time points (3, 7 and 28 days)[4].
References	[1]. Cowburn AS, et al. z-VAD-fmk augmentation of TNF alpha-stimulated neutrophil apoptosis is compound specific and does not involve the generation of reactive oxygen species. [2]. Lawrence CP, et al. Suppression of human T cell proliferation by the caspase inhibitors, z-VAD-FMK and z-IETD-FMK is independent of their caspase inhibition properties. Toxicol Appl Pharmacol. 2012 Nov 15;265(1):103-12. [3]. Tezel G, et al. Inhibition of caspase activity in retinal cell apoptosis induced by various stimuli in vitro. Invest Ophthalmol Vis Sci. 1999 Oct;40(11):2660-7. [4]. Terlizzi M, et al. Pharmacological inhibition of caspase-8 limits lung tumour outgrowth. Br J Pharmacol. 2015 Aug;172(15):3917-28.