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产品名称：IMD 0354
产品别名：IKK2 Inhibitor V

生物活性：

Description	IMD-0354 is a selective IKKβ inhibitor which inhibits NF-κB activity. IMD0354 inhibits TNF-α induced NF-κB transcription activity with an IC 50 of 1.2±0.3 uM.	
IC_{50} & Target	IKKβ	NF-κB
		1.2 μM (IC_{50})
In Vitro	IMD-0354 inhibits NF-κB activity in HMC-1 cells, resulting in complete repression of growth factor-independent proliferation of mast cells. When the DNA-binding activity of NF-κB is inhibited by treatment with IMD-0354, cell proliferation is completely suppressed. HMC-1 cells are incubated with increasing concentrations of IMD-0354 or STI571 for 24, 48, and 72 hours, and numbers and viability of cells are determined by a dye exclusion test and an MTT assay. IMD-0354 suppresses cell proliferation in a time- and dose-dependent manner. The inhibitory effect of IMD-0354 is remarkable, even at lower concentrations, when compared with that of STI571[1]. IMD0354 inhibits TNF-α induced NF-κB transcription activity with an IC 50 of 1.2±0.3 uM[2].	
In Vivo	Daily administration with 5 mg/kg IMD-0354 significantly suppresses tumor expansion in nude mice implanted with established MDA-MB-231 tumors. In mice treated with IMD-0354, tumor progression is restrained[3]. The number of infiltrating cells in aqueous humor is 53.6±9.8×10^5, 72.5±17.0×10^5, 127.25±32.0×10^5, and 132.0±25.0×10^5cells/mL in rats treated with 30, 10, 3, or 0 mg/kg of IMD-0354, respectively. The total protein concentrations of aqueous humor are 92.6±3.1 mg/mL, 101.5±6.8 mg/mL, 112.6±1.9 mg/mL, and 117.33±1.8 mg/mL in rats treated with 30, 10, 3, and 0 mg/kg of IMD-0354, respectively[4].	
Solvent&Solubility	***In Vitro:***	
	DMSO : ≥ 100 mg/mL (260.64 mM)	
	H_2O : < 0.1 mg/mL (insoluble)	
	* "≥" means soluble, but saturation unknown.	

Preparing Stock Solutions	Solvent / Mass / Concentration	**1 mg**	**5 mg**	**10 mg**
	1 mM	2.6064 mL	13.0320 mL	26.0641 mL
	5 mM	0.5213 mL	2.6064 mL	5.2128 mL
	10 mM	0.2606 mL	1.3032 mL	2.6064 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 (6.52 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.52 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 (6.52 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (6.52 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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。
References	[1]. Tanaka A, et al. A novel NF-kappaB inhibitor, IMD-0354, suppresses neoplastic proliferation of human mast cells with constitutively activated c-kit receptors. Blood. 2005 Mar 15;105(6):2324-31. [2]. Li YR, et al. Study of the inhibitory effects on TNF-α-induced NF-κB activation of IMD0354 analogs. Chem Biol Drug Des. 2017 Dec;90(6):1307-1311. [3]. Tanaka A, et al. A new IkappaB kinase beta inhibitor prevents human breast cancer progression through negative regulation of cell cycle transition. Cancer Res. 2006 Jan 1;66(1):419-26. [4]. Lennikov A, et al. Amelioration of endotoxin-induced uveitis treated with an IκB kinase β inhibitor in rats. Mol Vis. 2012;18:2586-97.

实验参考：

Cell Assay	HMC-1 cells (2×10^5 cells/mL) are incubated with various concentrations of IMD-0354 (0.1, 0.5, 1, 5 and 10 uM), STI571, or pyrrolidine dithiocarbamate (PDTC) for the indicated hours, and viable cell numbers are calculated with the use of the trypan blue dye exclusion test at each time point. Cells (2×10^5 cells/mL) are incubated in phenol red free α-MEM containing 10% FCS (for HMC-1 and IC-2 cells) or 5% FCS (for CBhCMCs), and antibiotics with or without various concentrations of IMD-0354 (0.1, 0.5, 1, 5 and 10 uM), STI571, or PDTC. IC-2^{WT} cells and CBhCMCs are incubated in the presence of 100 ng/mL recombinant rat or recombinant human SCF. One hundred microliters of cell suspension is applied to each well of 96-well culture plates and are incubated for 24, 48, and 72 hours. Before 4 hours from the end of the culture, 10 μL of 5 mg/mL MTT dissolved in PBS is added to each well. The reaction is stopped with the addition of 100 μLof 10% SDS in 0.01 N HCl. Absorbance is measured at 577 nm with ImmunoMini NJ-2300[1].
Animal Administration	Mice[3] MDA-MB-231 cells are suspended in PBS (5×10^6 cells/100 μL mouse) and s.c. injected to the back of female BALB/c nude mice at the age of 4 to 5 weeks. After growth, the tumor is removed surgically and 100 mg of each established tumor is transplanted to the back of other female nude mice at the age of 4 weeks under ether anesthesia. IMD-0354 is suspended in saline and 5 mg/kg body weight IMD-0354 (suspended in 100 μL/mouse) is given to each mouse by i.p. injection once a day for 28 days after the implantation. Saline is injected in nude mice as a control. Estimated tumor volume (mm3) and tumor weight (mg) are calculated.

	Rats[4] Eight-week-old male Lewis rats (180-220 g) are used. Endotoxin-induced uveitis (EIU) is induced with subcutaneous injection with 200 μg LPS from *Escherichia coli* that has been diluted in 200 μL PBS. At the same time, the rats are injected intraperitoneally with 30, 10, or 3 mg/kg of IMD-0354, diluted in 500 μL of 0.5% CMC. Control EIU rats are intraperitoneally administered 500 μL of CMC alone. Naïve rats are used as controls. All experiments are performed in triplicate with five animals in each group.
References	[1]. Tanaka A, et al. A novel NF-kappaB inhibitor, IMD-0354, suppresses neoplastic proliferation of human mast cells with constitutively activated c-kit receptors. Blood. 2005 Mar 15;105(6):2324-31. [2]. Li YR, et al. Study of the inhibitory effects on TNF-α-induced NF-κB activation of IMD0354 analogs. Chem Biol Drug Des. 2017 Dec;90(6):1307-1311. [3]. Tanaka A, et al. A new IkappaB kinase beta inhibitor prevents human breast cancer progression through negative regulation of cell cycle transition. Cancer Res. 2006 Jan 1;66(1):419-26. [4]. Lennikov A, et al. Amelioration of endotoxin-induced uveitis treated with an IκB kinase β inhibitor in rats. Mol Vis. 2012;18:2586-97.