产品名称：IC-87114
产品别名：IC-87114

生物活性：

Description	IC-87114 is a potent and selective PI3Kδ inhibitor with IC_{50} of 0.5 μM.		
IC_{50} & Target	PI3Kδ	PI3Kγ	PI3Kβ
	0.5 μM (IC_{50})	29 μM (IC_{50})	75 μM (IC_{50})
In Vitro	IC-87114 (IC87114), an analog of the original inhibitor, is synthesized and tested for PI3Kδ selectivity relative to the other class I PI3Ks. The IC50 of IC87114 for PI3Kδ inhibition is 0.5 μM whereas the IC50 values for PI3Kα, PI3Kβ, and PI3Kγ are >100, 75, and 29 μM, respectively. Thus IC87114 is 58-fold more selective for PI3Kδ relative to PI3Kγ, and over 100-fold selective relative to PI3Kα and PI3Kβ. IC87114 selectively antagonizes PI3Kδ over at least a concentration range of 0.3-10 μM[1]. IC-87114 (10 μM) is also used to selectively inhibit PI3Kδ catalytic activity to address this question. IC87114 (10 μM) effectively inactivates Akt in macrophages after treatment for 1 hour (n=6; P<0.001 versus control). The effect of IC-87114 (IC87114) is next detected ton AP-1 DNA-binding activity. The electrophoretic mobility shift assay assay demonstrates that DNA-binding activity of AP-1 is significantly increased after the treatment with TNF-α (10 ng/mL; P<0.001) and TNF-α (20 ng/mL; P<0.001). IC87114 alone induces AP-1 DNA-binding activity after treatment for 1 hour. Furthermore, there is stronger AP-1 DNA-binding activity after costimulation of IC87114 (10 μM) and TNF-α (0-20 ng/mL) than only treatment with TNF-α (0-20 ng/mL; n=5; P<0.01). IC87114 (10 μM) also effectively inhibits p110δ catalytic activities (Akt phosphorylation) in macrophages with or without TNF-α treatment for 24 hours (n=6; P<0.001)[2].		
In Vivo	Treatment with PD 89059 (10 mg/kg), IC-87114 (0.3 mg/kg) and BAY 11-7085 (10 mg/kg), significantly (P<0.05) reduces the OVA- induced inflammatory cell influx into the airways and the histopathological airway remodeling. However, these treatments does not significantly improve OVA induced-AHR (P>0.05). Of note, the observed reduction in the histopathological airway remodeling induced by PD 89059, IC-87114 and BAY 11-7085 are less effective as compared to the reduction seen with AG 1478 and SU6656[3].		

Solvent&Solubility

In Vitro:

DMSO : 10 mg/mL (25.16 mM; Need ultrasonic)

Preparing Stock Solutions (Solvent / Mass / Concentration)	1 mg	5 mg	10 mg
1 mM	2.5162 mL	12.5808 mL	25.1617 mL
5 mM	0.5032 mL	2.5162 mL	5.0323 mL
10 mM	0.2516 mL	1.2581 mL	2.5162 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: ≥ 1 mg/mL (2.52 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (2.52 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 10.0 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: ≥ 1 mg/mL (2.52 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (2.52 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 10.0 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: ≥ 1 mg/mL (2.52 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (2.52 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 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Sadhu C, et al. Essential role of phosphoinositide 3-kinase delta in neutrophil directional movement. J Immunol. 2003 Mar 1;170(5):2647-54. [2]. Zheng L, et al. Inactivation of PI3Kδ induces vascular injury and promotes aneurysm development by upregulating the AP-1/MMP-12 pathway in macrophages. Arterioscler Thromb Vasc Biol. 2015 Feb;35(2):368-77. [3]. El-Hashim AZ, et al. Src-dependent EGFR transactivation regulates lung inflammation via downstream signaling involving ERK1/2, PI3Kδ/Akt and NFκB induction in a murine asthma model. Sci Rep. 2017 Aug 30;7(1):9919.

实验参考：

Cell Assay	The murine macrophage cell line RAW264.7 and peritoneal macrophages from both types of mice are maintained in Dulbecco's modified Eagle's medium (DMEM) with 10% fetal calf serum (FCS). Cultures are maintained at 37°C in a humidified incubator in a 95% O_2 plus 5% CO_2 atmosphere. Cells are treated with varied concentrations of TNF-α and used IC-87114 (IC87114) to inhibit PtdIns(3,4,5)P3-dependent phosphorylation of Akt before TNF-α stimulation at early time points (30 min)[2].
Animal Administration	Mice[3] BALB/c mice are immunized once by i.p. injection of 10 μg ovalbumin (OVA) in 0.2 ml of alu-Gel-S on day 0. Ten days later, mice are intranasally (i.n.) challenged with OVA (30 μg in 50 μL PBS) or PBS, once daily, over four consecutive days. To investigate if ERK1/2, PI3Kδ and NF-κB are signaling effectors downstream of EGFR transactivation, six treatment groups (A-F, 10-30 animals per group) are established. Mice in groups A and B are pretreated intranasally with 0.2 mL of the vehicle for the drugs. Groups C, D and E are pretreated with the same volume of three different drugs (PD 98059, IC-87114 and BAY 11-7085, respectively) at 10 mg/kg, 10 mg/kg and 0.3 mg/kg respectively, and group F with Dexamethasone (1 mg/kg), 1 h before each i.n. challenge with OVA. These doses are chosen from previous studies where they are shown to be effective.
	[1]. Sadhu C, et al. Essential role of phosphoinositide 3-kinase delta in neutrophil directional

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