产品名称：**PIK-93**
产品别名：**PIK-93**

生物活性：

Description

PIK-93 is the first potent, synthetic PI4K (PI4KIIIβ) inhibitor with IC_{50} of 19 nM, and also inhibits PI3Kγ and PI3Kαwith IC_{50} of 16 nM and 39 nM, respectively.

IC_{50} & Target

p110α	p110β	p110δ	p110γ	PI3KC2α	PI3KC2β
39 nM (IC_{50})	590 nM (IC_{50})	120 nM (IC_{50})	16 nM (IC_{50})	16 μM (IC_{50})	140 nM (IC_{50})
PI4KIIIβ	PI4KIIIα	hsVPS34	DNA-PK	ATM	mTORC1
19 nM (IC_{50})	1.1 μM (IC_{50})	320 nM (IC_{50})	64 nM (IC_{50})	490 nM (IC_{50})	1.38 μM (IC_{50})
ATR					
17 μM (IC_{50})					

In Vitro

PIK-93 inhibits PI3Kγ and PI4KIIIβ, with IC_{50} values of 16 nM and 19 nM, respectively. PIK-93 also inhibits other members of PI3Ks, including PI3Kα, β, and δ, with IC_{50} values of 39 nM, 0.59 μM, and 0.12 μM, respectively. PIK-93 shows no obvious inhibitory effect against a panel of other kinases, even at a concentration of 10 μM[1]. In differentiated HL60 (dHL60) cells, PIK-93 (0.5 μM-1 μM) impairs consolidation and stability of the leading edge formed after treatment with uniform f-Met-Leu-Phe (fMLP). PIK-93 alters the localization, but not the amount, of the fMLP-dependent accumulation of total F-actin. In fMLP gradients, PIK-93 reduces the chemotactic index and triples the cells' turning frequency[2]. In COS-7 cells, PIK-93 (250 nM) effectively abrogates the accumulation of CERT-PH domain and FL-Cer in Golgi. PIK-93 of the same concentration also significantly inhibits the conversion of [^{3}H]serine-labeled endogenous ceramide to sphingomyelin. These facts indicate a key role of PI4KIIIβ in ceramide transport between the ER and Golgi, as well as in the regulation of spingomyelin synthesis[3]. In T6.11 cells, PIK-93 (300 nM) reduces carbachol-induced translocation of TRPC6 to the plasma membrane and net Ca^{2+} entry[4]. A recent report shows that PIK-93 has anti-enterovirus effects, as revealed by its inhibition of both poliovirus (PV) and hepatitis C virus (HCV) replication, with EC_{50} values of 0.14 μM and 1.9 μM, respectively[5].

Solvent&Solubility

In Vitro:

DMSO : ≥ 150 mg/mL (384.73 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.5649 mL	12.8245 mL	25.6489 mL
5 mM	0.5130 mL	2.5649 mL	5.1298 mL
10 mM	0.2565 mL	1.2824 mL	2.5649 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: ≥ 4.55 mg/mL (11.67 mM); Clear solution 此方案可获得 ≥ 4.55 mg/mL (11.67 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 45.5 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 (6.41 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.41 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 (6.41 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.41 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]. Knight ZA, et al. A pharmacological map of the PI3-K family defines a role for p110alpha in insulin signaling. Cell. 2006 May 19;125(4):733-47 [2]. Van Keymeulen A, et al. To stabilize neutrophil polarity, PIP3 and Cdc42 augment RhoA activity at the back as well as signals at the front. J Cell Biol. 2006 Jul 31;174(3):437-45 [3]. Toth B, et al. Phosphatidylinositol 4-kinase IIIbeta regulates the transport of ceramide between the endoplasmic reticulum and Golgi. J Biol Chem. 2006 Nov 24;281(47):36369-77 [4]. Monet M, et al. Involvement of phosphoinositide 3-kinase and PTEN protein in mechanism of activation of TRPC6 protein in vascular smooth muscle cells. J Biol Chem. 2012 May 18;287(21):17672-81 [5]. Arita M, et al. Phosphatidylinositol 4-kinase III beta is a target of enviroxime-like compounds for antipoliovirus activity. J Virol. 2011 Mar;85(5):2364-72
实验参考：	
Cell Assay	For actin staining, dHL60 cells are preincubated in suspension with PIK-93 or vehicle for 40 min, centrifuged for 5 min at 2000 rpm at room temperature in a J6-B centrifuge, resuspended in mHBSS containing the respective agent at the same concentration, allowed to stick to fibronectin-covered coverslips, and subjected to stimulation with a uniform concentration of 100 nM f-Met-Leu-Phe (fMLP) for 3 min. Cells are fixed in 3.7% PFA and stained with 10 units/mL rhodamine-phalloidin for 15 min. [1]
Kinase Assay	IC_{50} values are measured using a standard TLC assay for lipid kinase activity. Kinase reactions are performed by preparing areaction mixture containing kinase, PIK-93 (2% DMSO final concentration), buffer (25 mM HEPES, pH 7.4, 10 mM $MgCl_2$), and freshly sonicated phosphatidylinositol (100 μg/mL). Reactions are initiated by the addition of ATP containing 10 μCi of γ-^{32}P-ATP to a final concentration 10 or 100 μM, and allowed to proceed for 20 min at room temperature. For TLC analysis, reactions are then terminated by the addition of 105 μL 1N HCl followed by 160 μL $CHCl_3$:MeOH (1:1). The biphasic mixture is vortexed, briefly centrifuged, and the organic phase

	transferred to a new tube using a gel loading pipette tip precoated with $CHCl_3$. This extract is spotted on TLC plates and developed for 3 hours-4 hours in a 65:35 solution of n-propanol:1M acetic acid. The TLC plates are then dried, exposed to a phosphorimager screen, and quantitated. Kinase activity is typically measured at 10-12 concentrations of PIK-93 representing two-fold dilutions from the highest concentration of 100 μM. [1]
References	[1]. Knight ZA, et al. A pharmacological map of the PI3-K family defines a role for p110alpha in insulin signaling. Cell. 2006 May 19;125(4):733-47 [2]. Van Keymeulen A, et al. To stabilize neutrophil polarity, PIP3 and Cdc42 augment RhoA activity at the back as well as signals at the front. J Cell Biol. 2006 Jul 31;174(3):437-45 [3]. Toth B, et al. Phosphatidylinositol 4-kinase IIIbeta regulates the transport of ceramide between the endoplasmic reticulum and Golgi. J Biol Chem. 2006 Nov 24;281(47):36369-77 [4]. Monet M, et al. Involvement of phosphoinositide 3-kinase and PTEN protein in mechanism of activation of TRPC6 protein in vascular smooth muscle cells. J Biol Chem. 2012 May 18;287(21):17672-81 [5]. Arita M, et al. Phosphatidylinositol 4-kinase III beta is a target of enviroxime-like compounds for antipoliovirus activity. J Virol. 2011 Mar;85(5):2364-72