PIK-93

Cat. No.: HY-12046

CAS No.: 593960-11-3

Molecular Formula: $C_{14}H_{16}ClN_3O_4S_2$

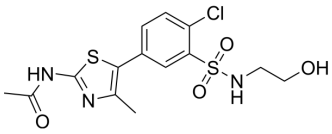
Molecular Weight: 389.88

Target: PI4K; PI3K; Virus Protease

Pathway: PI3K/Akt/mTOR; Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (256.49 mM; Need ultrasonic)

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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 4.55 mg/mL (11.67 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (6.41 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (6.41 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PIK-93 is the first potent, synthetic PI4K (PI4KIIIβ) inhibitor with IC_{50} of 19 nM, and also inhibits PI3Kγ and PI3Kα with IC_{50} of 16 nM and 39 nM, respectively.

IC_{50} & Target

PI4KIIIβ 19 nM (IC_{50})	PI4KIIIα 1.1 μM (IC_{50})	p110γ 16 nM (IC_{50})	p110α 39 nM (IC_{50})
p110δ 120 nM (IC_{50})	p110β 590 nM (IC_{50})	PI3KC2β 140 nM (IC_{50})	PI3KC2α 16 μM (IC_{50})

	hsVPS34 320 nM (IC_{50})	DNA-PK 64 nM (IC_{50})	ATM 490 nM (IC_{50})	mTORC1 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]

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.

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Cell Assay [1]

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.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Molecules. 2020 Apr 23;25(8):1980.
- Patent. US20220273624A1.
- Harvard Medical School LINCS LIBRARY

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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

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