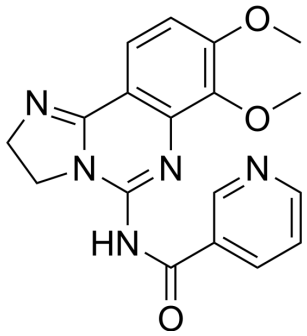
PIK-90

Cat. No.:	HY-12030
CAS No.:	677338-12-4
Molecular Formula:	$C_{18}H_{17}N_5O_3$
Molecular Weight:	351.36
Target:	PI3K; DNA-PK
Pathway:	PI3K/Akt/mTOR; Cell Cycle/DNA Damage
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 : 6.67 mg/mL (18.98 mM; ultrasonic and adjust pH to 2 with HCl)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8461 mL	14.2304 mL	28.4608 mL
	5 mM	0.5692 mL	2.8461 mL	5.6922 mL
	10 mM	0.2846 mL	1.4230 mL	2.8461 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: ≥ 0.67 mg/mL (1.91 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 0.67 mg/mL (1.91 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 0.67 mg/mL (1.91 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

PIK-90 is a DNA-PK and PI3K inhibitor, which inhibits p110α, p110γ and DNA-PK with IC_{50}s of 11, 18 and 13 nM, respectively.

IC_{50} & Target

p110α 11 nM (IC_{50})	p110γ 18 nM (IC_{50})	p110δ 58 nM (IC_{50})	p110β 350 nM (IC_{50})
hsVPS34 830 nM (IC_{50})	PI3KC2β 64 nM (IC_{50})	PI3KC2α 47 nM (IC_{50})	DNA-PK 13 nM (IC_{50})

	ATM 610 nM (IC_{50})	PI4KIIIα 830 nM (IC_{50})	PI4KIIIβ 3.1 μM (IC_{50})	mTORC1 1.05 μM (IC_{50})
	ATR 15 μM (IC_{50})			
In Vitro	PIK-90 also inhibits p110β, p110δ, PI3KC2α, PI3KC2β, hsVPS34, PI4KIIIα, PI4KIIIβ, ATR, ATM and mTORC1 with IC_{50}s of 350 nM, 58 nM, 47 nM, 64 nM, 830 nM, 830 nM, 3.1 μM, 15 μM, 610 nM and 1.05 μM, respectively[1]. To determine the effects of PIK-90 on chronic lymphocytic leukemia (CLL) cell viability, CLL cells from different patients are incubated with various concentrations of PIK-90 (1 μM and 10 μM) for 24, 48, and 72 hours. PIK-90 reveals the strong apoptosis-inducing effects at both concentrations and at all different time points. Using a concentration of 10 μM, PIK-90 reduces the viability of CLL cells to 51.1% plus or minus 6.6% at 24 hours, whereas 1 μM PIK-90 reduces the viability to 77.8% plus or minus 6.4%[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			
In Vivo	To test the efficacy of Roscovitine and PIK-90 in vivo, GBM43 cells are implanted s.c. into nude mice. Mice with established tumors are randomized into four treatment groups: vehicle (PBS:H_2O), Roscovitine, PIK-90, or PIK-90 plus Roscovitine. After 12 d of treatment, both Roscovitine and PIK-90 show clear single-agent efficacy, with tumor size in mice treated with Roscovitine and PIK-90 in combination significantly smaller than either vehicle or monotherapy-treated controls. Roscovitine is less effective than PIK-90 in blocking proliferation (levels of Ki-67), whereas combination therapy shows essentially additive antiproliferative effects[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.			

PROTOCOL

Cell Assay [2]	To determine the viability of CLL B cells, 200 μL cells are removed from the wells of a 24-well plate at the indicated time points and incubated for 15 minutes in fluorescence-activated cell sorter buffer (RPMI+0.5% BSA) containing 40 nM 3,3′-dihexyloxacarbocyanine iodide ($DiOC_6$) and 10 μg/mL Propidium iodide (PI). Within 30 minutes, the cells are then analyzed by flow cytometry. Viable cells show high $DiOC_6$ and low PI fluorescence, whereas apoptotic cells have low $DiOC_6$ and PI fluorescence; necrotic cells are characterized by low $DiOC_6$ and high PI fluorescence. The normal PBMCs are also cultured under the same conditions, with or without the various PI3K inhibitors (e.g., PIK-90, 1 μM and 10 μM), Fludarabine, and with or without stromal cell support, and their viability is also determined by staining with $DiOC_6$ and PI[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Mice[3] Human primary GBM43 cells (10^6) are injected s.c. just caudal to the left forelimb in 4- to 6-wk-old female ***BALB/c nu/nu*** mice . After tumors are established (50-100 mm^3), mice are randomly allocated to daily i.p. treatment with 40 mg/kg PIK-90 (DMSO:H_2O), 50 mg/kg Roscovitine (DMSO:PBS), 40 mg/kg PIK-90 plus 50 mg/kg Roscovitine, and DMSO:H_2O:PBS (control). Tumor diameters are measured with calipers at 3-d intervals, and volumes are calculated. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Molecules. 2020 Apr 23;25(8):1980.
- bioRxiv. 2024 Feb 10.

See more customer validations on www.MedChemExpress.com

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]. Niedermeier M, et al. Isoform-selective phosphoinositide 3'-kinase inhibitors inhibit CXCR4 signaling and overcome stromal cell-mediated drug resistance in chronic lymphocytic leukemia: a novel therapeutic approach. Blood. 2009 May 28;113(22):5549-57.

[3]. Cheng CK, et al. Dual blockade of lipid and cyclin-dependent kinases induces synthetic lethality in malignant glioma. Proc Natl Acad Sci U S A. 2012 Jul 31;109(31):12722-7.

Tel: 609-228-6898 Fax: 609-228-5909 E-mail: tech@MedChemExpress.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA