产品名称：**PIK-90**
产品别名：**PIK-90**

生物活性：

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	p110γ	p110δ	p110β	hsVPS34	PI3KC2β
11 nM (IC_{50})	18 nM (IC_{50})	58 nM (IC_{50})	350 nM (IC_{50})	830 nM (IC_{50})	64 nM (IC_{50})
PI3KC2α	DNA-PK	ATM	PI4KIIIα	PI4KIIIβ	mTORC1
47 nM (IC_{50})	13 nM (IC_{50})	610 nM (IC_{50})	830 nM (IC_{50})	3.1 μM (IC_{50})	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].

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].

Solvent&Solubility

In Vitro:

DMSO : 1.75 mg/mL (4.98 mM; Need ultrasonic and warming)

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	---	---	---
	10 mM	---	---	---

*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。

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.

实验参考：

Cell Assay	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 (DiOC6) and 10 μg/mL Propidium iodide (PI). Within 30 minutes, the cells are then analyzed by flow cytometry. Viable cells show high DiOC6 and low PI fluorescence, whereas apoptotic cells have low DiOC6 and PI fluorescence; necrotic cells are characterized by low DiOC6 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 DiOC6 and PI[2].
Animal Administration	Mice[3] Human primary GBM43 cells (106) 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 mm3), mice are randomly allocated to daily i.p. treatment with 40 mg/kg PIK-90 (DMSO:H2O), 50 mg/kg Roscovitine (DMSO:PBS), 40 mg/kg PIK-90 plus 50 mg/kg Roscovitine, and DMSO:H2O:PBS (control). Tumor diameters are measured with calipers at 3-d intervals, and volumes are calculated.
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.

源叶生物