

产品名称: **ZSTK474**

产品别名: **ZSTK474**

生物活性:					
Description	ZSTK474 is an ATP-competitive pan-class I PI3K inhibitor with IC ₅₀ s of 16 nM, 44 nM, 4.6 nM and 49 nM for PI3K α , PI3K β , PI3K δ and PI3K γ , respectively.				
IC₅₀ & Target	PI3K α	PI3K β	PI3K δ	PI3K γ	Autophagy
	16 nM (IC ₅₀)	44 nM (IC ₅₀)	4.6 nM (IC ₅₀)	49 nM (IC ₅₀)	
In Vitro	Lineweaver-Burk plot analysis revealed that ZSTK474 inhibits all four PI3K isoforms in an ATP-competitive manner. The K _i values determined for the four PI3K isoforms showed that ZSTK474 inhibited the PI3K δ isoform most effectively with a K _i of 1.8 nM, whereas the other isoforms are inhibited with 4-10-fold higher K _i values. Therefore, ZSTK474 should be regarded as a pan-PI3K inhibitor. We also determined the IC ₅₀ values for inhibiting the four PI3K isoforms with ZSTK474 and LY294002. The IC ₅₀ values of ZSTK474 (16, 44, 4.6 and 49 nM for PI3K α , PI3K β , PI3K δ and PI3K γ , respectively) are shown to be consistent with the K _i values (6.7, 10.4, 1.8 and 11.7 nM for PI3K α , PI3K β , PI3K δ and PI3K γ , respectively), which further supported the idea that ZSTK474 inhibits PI3K δ most potently. Even at a concentration of 100 μ M, ZSTK474 inhibits mTOR activity rather weakly[1].				
In Vivo	In mice subjected to MCAO, treatment with ZSTK474 is tested at dosages of 50, 100, 200, and 300 mg/kg. Since the 200 mg/kg dose produces significant improvement and no obvious toxic effects (P<0.01), mice are treated with ZSTK474 at a dose of 200 mg/kg/day daily for three post-MCAO days during the remaining experiments of this study. Neurological function is examined in mice suffered from MCAO followed by 24, 48, and 72 h of reperfusion. In the ZSTK474 group, neurological function scores are significantly better than the control group except the corner test[2].				
Solvent&Solubility	In Vitro: DMSO : 2 mg/mL (4.79 mM; Need ultrasonic)				
	Preparing Stock Solutions	Solvent \ Mass \ Concentration	1 mg	5 mg	10 mg
		1 mM	2.3957 mL	11.9786 mL	23.9573 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。 In Vivo: 1. ZSTK474 is suspended in 5% hydroxypropyl cellulose[3].					
References	[1]. Kong D, et al. ZSTK474 is an ATP-competitive inhibitor of class I phosphatidylinositol 3 kinase isoforms. <i>Cancer Sci</i> , 2007, 98(10), 1638-1642. [2]. Liu F, et al. Prolonged inhibition of class I PI3K promotes liver cancer stem cell expansion by augmenting SGK3/GSK-3 β / β -catenin signalling. <i>J Exp Clin Cancer Res</i> . 2018 Jun 25;37(1):122. [3]. Wang P, et al. Class I PI3K inhibitor ZSTK474 mediates a shift in microglial/macrophage phenotype and inhibits inflammatory response in mice with cerebral ischemia/reperfusion injury. <i>J Neuroinflammation</i> .				

实验参考:

Animal Administration	<p>Mice[2]</p> <p>Mice are randomly assigned to receive different doses of ZSTK474 (50, 100, 200, and 300 mg/kg) to determine the optimum dose; in our experiment, the optimum dose is 200 mg/kg. Then mice are randomly assigned to one of three groups: a sham-operated group (phosphate-buffered saline, PBS); a control group (MCAO+PBS); a ZSTK474-treated group (MCAO+ZSTK474). In the ZSTK474-treated group, the mice are given the optimum dose of 200 mg/kg ZSTK474. In the sham-operated group and control group, mice are given an equivalent volume of PBS. All mice receive that same dose daily via oral gavage beginning at 6 h after the onset of focal ischemia and continuing for two more days, i.e., for a total of 3 days.</p>
Kinase Assay	<p>The linear phase of each kinetic reaction is defined at the respective enzyme amount (0.05, 0.1, 0.12 and 1 $\mu\text{g/mL}$ for PI3Kα, PI3Kβ, PI3Kδ and PI3Kγ, respectively) and reaction time (20 min). PI3K activity is assayed at various concentrations of ATP (5, 10, 25, 50, 100 μM) in the presence of increasing concentrations of ZSTK474. A Lineweaver-Burk plot is developed by plotting $1/v$ (the inverse of v, where v is obtained by subtracting the HTRF signal of the kinase test sample from the HTRF signal of the minus-enzyme control) versus $1/[\text{ATP}]$ (the inverse of the ATP concentration). For the minus-enzyme control, PIP2 is incubated with ATP in the absence of kinase. To determine the K_i value (inhibition constant) of ZSTK474 for each PI3K isoform, the slope of the respective Lineweaver-Burk plot is replotted against the ZSTK474 concentration. The K_i values are calculated by analysis using GraphPad Prism 4[1].</p>
References	<p>[1]. Kong D, et al. ZSTK474 is an ATP-competitive inhibitor of class I phosphatidylinositol 3 kinase isoforms. <i>Cancer Sci.</i> 2007, 98(10), 1638-1642.</p> <p>[2]. Liu F, et al. Prolonged inhibition of class I PI3K promotes liver cancer stem cell expansion by augmenting SGK3/GSK-3β/β-catenin signalling. <i>J Exp Clin Cancer Res.</i> 2018 Jun 25;37(1):122.</p> <p>[3]. Wang P, et al. Class I PI3K inhibitor ZSTK474 mediates a shift in microglial/macrophage phenotype and inhibits inflammatory response in mice with cerebral ischemia/reperfusion injury. <i>J Neuroinflammation.</i> 2016 Aug 22;13(1):192.</p>

源叶生物