

产品名称: LY-2584702 (free base)

产品别名: LY-2584702 free base

生物活性:

Description	LY-2584702 free base is a selective ATP competitive inhibitor of p70S6K with an IC ₅₀ of 4 nM. In S6K1 enzyme assay, the IC ₅₀ of LY-2584702 is 2 nM.					
IC ₅₀ & Target	S6K1	p70S6K				
	2 nM (IC ₅₀)	4 nM (IC ₅₀)				
In Vitro	LY-2584702 (LY2584702) inhibits phosphorylation of the S6 ribosomal protein (pS6) in HCT116 colon cancer cells with an IC50 of 0.1-0.24 μM[1]. For pS6 inhibition in cells, the IC50=100 nM. LY-2584702 has some activity against the S6K-related kinases MSK2 and RSK at high concentrations (enzyme assay IC50=58-176 nM). LY-2584702 inhibits S6K activity in EOMA cells, as determined by the phosphorylation of its downstream effector S6, in a dose-dependent manner[2]. Proliferation of A549 is significantly inhibited by LY-2584702 (LY2584702) treating over 24 h at 0.1 μM (P<0.05); and the trend of decline is more conspicuous with longer treatment and/or with the increased drug concentration (all P<0.05). Similar results are also observed in SK-MES-1, although the obvious inhibition is led by LY-2584702 at 0.6 μM (P<0.05), much higher than that of A549[3].					
In Vivo	LY-2584702 demonstrates significant single-agent efficacy in both U87MG glioblastoma and HCT116 colon carcinoma xenograft models at two dose levels of 2.5 mg/kg twice daily (BID) and 12.5 mg/kg BID. LY-2584702 demonstrates statistically significant tumour growth reduction at TMED50 (threshold minimum effective dose 50%) (2.3 mg/kg) and TMED90 (10 mg/kg) in the HCT116 colon carcinoma xenograft model[1]. To examine the role of S6K in vivo, EOMA cells expressing shAkt3 are implanted in nu/nu mice, then treated for 14 days with LY-2584702 or Rapamycin. Analysis of tumors removed after 14 days shows that LY-2584702 inhibits S6 phosphorylation almost as effectively as Rapamycin. Loss of Akt3 increases tumor growth as compared with pLKO. LY-2584702 treatment alone does not significantly affect the growth of pLKO tumors. However, LY-2584702 significantly reduces the growth of tumors with shAkt3[2].					
Solvent&Solubility	In Vitro: DMSO : ≥ 4.5 mg/mL (10.10 mM) * "≥" means soluble, but saturation unknown.					
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg
		1 mM	2.2451 mL	11.2254 mL	22.4507 mL	
		5 mM	0.4490 mL	2.2451 mL	4.4901 mL	
		10 mM	0.2245 mL	1.1225 mL	2.2451 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。						
References	[1]. Tolcher A, et al. A phase I trial of LY2584702 tosylate, a p70 S6 kinase inhibitor, in patients with advanced solid tumors. Eur J Cancer. 2014 Mar;50(5):867-75. [2]. Phung TL, et al. Akt1 and akt3 exert opposing roles in the regulation of vascular tumor growth. Cancer Res. 2015 Jan 1;75(1):40-50.					

	<p>[3]. Chen B, et al. Hyperphosphorylation of RPS6KB1, rather than overexpression, predicts worse prognosis in non-small cell lung cancer patients. PLoS One. 2017 Aug 9;12(8):e0182891.</p>
实验参考:	
Cell Assay	<p>LY-2584702 is fully dissolved in 20 mL 10% DMSO and reserved at -80°C. When conducted the experiments in vitro, LY-2584702 is further diluted in 0.5% Tween 80, 5% propylene glycol and 30% PEG400 to reach different DMSO concentrations of 0.1 μM, 0.2 μM, 0.6 μM, and 1.0 μM. Cell Counting Kit-8 (CCK-8) is used to measure the cells proliferation in vitro. Cell lines A549 and SK-MES-1 treated by LY-2584702 for 24 h with different concentrations are seeded in 96-well plates at a density of 5×10³ per well, with six repeats. DMSO treated, or in other words, the concentration of LY-2584702 of 0 is used as negative control. Cells absorbance at 450 nm is detected every 24 h after seeding to measure the proliferative activities[3].</p>
Animal Administration	<p>Mice[2]</p> <p>LY-2584702 is prepared in 0.25% Tween-80 and 0.05% antifoam, and administered orally to mice (12.5 mg/kg twice daily). EOMA cells (0.3×10⁶) are injected subcutaneously in 6- to 8-week-old nu/nu female mice (2 sites/mouse, 4-5 mice/group). Tumor size is measured daily. For drug treatment, when tumors reach 0.01 cm³ in size, the animals are treated with vehicle control or LY-2584702 (12.5 mg/kg twice daily, oral dosing). Tumor size is measured every 3 to 4 days[2]</p>
References	<p>[1]. Tolcher A, et al. A phase I trial of LY2584702 tosylate, a p70 S6 kinase inhibitor, in patients with advanced solid tumors. Eur J Cancer. 2014 Mar;50(5):867-75.</p> <p>[2]. Phung TL, et al. Akt1 and akt3 exert opposing roles in the regulation of vascular tumor growth. Cancer Res. 2015 Jan 1;75(1):40-50.</p> <p>[3]. Chen B, et al. Hyperphosphorylation of RPS6KB1, rather than overexpression, predicts worse prognosis in non-small cell lung cancer patients. PLoS One. 2017 Aug 9;12(8):e0182891.</p>

源叶生物