

产品名称: LY-2584702 (tosylate salt)
产品别名: LY-2584702 tosylate salt

生物活性:					
Description	LY-2584702 tosylate salt 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]. In S6K1 enzyme assay, the IC50 of LY-2584702 (LY2584702) is 2 nM. 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 : 10.25 mg/mL (16.60 mM; Need ultrasonic and warming) H₂O : < 0.1 mg/mL (insoluble)				
	Preparing Stock Solutions	Solvent Concentration Mass	1 mg	5 mg	10 mg
		1 mM	1.6191 mL	8.0956 mL	16.1912 mL
		5 mM	0.3238 mL	1.6191 mL	3.2382 mL
		10 mM	0.1619 mL	0.8096 mL	1.6191 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℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 储存时，请在 1 个月内使用。				
	In Vivo: 请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 In Vitro 方式配制澄清的储备液，再依次添加助溶剂： ——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出				

	现沉淀、析出现象，可以通过加热和/或超声的方式助溶 1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline Solubility: ≥ 1 mg/mL (1.62 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (1.62 mM, 饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 1 mg/mL (1.62 mM); Suspended solution; Need ultrasonic 此方案可获得 1 mg/mL (1.62 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 1 mg/mL (1.62 mM); Clear solution 此方案可获得 ≥ 1 mg/mL (1.62 mM, 饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 10.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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. [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.
实验参考：	
Cell Assay	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 5×10^3 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].
Animal Administration	Mice[2] 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 (0.3×10^6) 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].
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.

	<u>Cancer Res. 2015 Jan 1;75(1):40-50.</u> [3]. <u>Chen B. et al. Hyperphosphorylation of RPS6KB1, rather than overexpression, predicts worse</u> <u>prognosis in non-small cell lung cancer patients. PLoS One. 2017 Aug 9;12(8):e0182891.</u>
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源叶生物