

产品名称: SAR405
产品别名: SAR405

生物活性:

Description	SAR405 is a first-in-class, selective, and ATP-competitive PI3K class III (PIK3C3) isoform Vps34 inhibitor (IC ₅₀ =1.2 nM; K _d =1.5 nM). SAR405 inhibits autophagy induced either by starvation or by mTOR inhibition. Anticancer activity[1][2].				
IC ₅₀ & Target	Vps34	Vps34	Autophagy		
	1.2 nM (IC ₅₀)	1.5 nM (Kd)			
In Vitro	<p>The activity of SAR405 is next evaluated on a dedicated Vps34 cellular assay using a GFP-FYVE-transfected HeLa cell line[1].</p> <p>SAR405 prevents autophagy and synergizes with mTOR inhibition in tumor cells. SAR405 prevents autophagosome formation with an IC50 of 42 nM. Treatment of starved cells with SAR405 completely inhibits the conversion to LC3-II in a dose-dependent manner. The effect of SAR405 on autophagy is then investigated. The GFP-LC3 model is used for the HTS and confirmed its activity on starved cells (IC50=419 nM). The conversion of LC3-I into LC3-II is also analyzed by western blotting on wild-type HeLa and H1299 cells[2].</p>				
Solvent&Solubility	<p>In Vitro:</p> <p>DMSO : ≥ 27 mg/mL (60.83 mM)</p> <p>* "≥" means soluble, but saturation unknown.</p>				
	Preparing Stock Solutions	<div>SolventMassConcentration</div>	1 mg	5 mg	10 mg
		1 mM	2.2530 mL	11.2651 mL	22.5301 mL
		5 mM	0.4506 mL	2.2530 mL	4.5060 mL
		10 mM	0.2253 mL	1.1265 mL	2.2530 mL
	<p>*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。</p> <p>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。</p> <p>In Vivo:</p> <p>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：</p> <p>——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</p>				
	<p>1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline</p> <p>Solubility: ≥ 2.5 mg/mL (5.63 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.63 mM，饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例，取 100 μL 25.0 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。</p>				
	<p>2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline)</p> <p>Solubility: ≥ 2.5 mg/mL (5.63 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.63 mM，饱和度未知) 的澄清溶液。</p>				

	<p>以 1 mL 工作液为例，取 100 μL 25.0 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。</p> <p>3.请依序添加每种溶剂： 10% DMSO \rightarrow90% corn oil</p> <p>Solubility: \geq 2.5 mg/mL (5.63 mM); Clear solution</p> <p>此方案可获得 \geq 2.5 mg/mL (5.63 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。</p> <p>以 1 mL 工作液为例，取 100 μL 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</p>
References	<p>[1]. Ronan B, et al. A highly potent and selective Vps34 inhibitor alters vesicle trafficking and autophagy. <u>Nat Chem Biol.</u> 2014 Dec;10(12):1013-9.</p> <p>[2]. Pasquier B. SAR405, a PIK3C3/Vps34 inhibitor that prevents autophagy and synergizes with MTOR inhibition in tumor cells. <u>Autophagy.</u> 2015 Apr 3;11(4):725-6.</p>
实验参考：	
Kinase Assay	<p>KiNativ profiling is performed. Jurkat cell lysates are treated with 1 μM of SAR405. After 15-min incubation, the desthiobiotin-ATP-acylphosphate probe is added and incubated for 10 min. Samples are prepared for targeted MS analysis. Briefly, samples are prepared for trypsin digestion (denature and then reduce alkylate) and digested with trypsin, and desthiobiotinylated peptides are enriched on streptavidin resin. Enriched probe-labeled peptides are analyzed by LC tandem MS on a Thermo-LTQ ion trap mass spectrometer using proprietary data collection methodology. All quantification is performed by extracting characteristic fragment ion signals from targeted MS/MS spectra and comparing signals in control and treated samples[1].</p>
References	<p>[1]. Ronan B, et al. A highly potent and selective Vps34 inhibitor alters vesicle trafficking and autophagy. <u>Nat Chem Biol.</u> 2014 Dec;10(12):1013-9.</p> <p>[2]. Pasquier B. SAR405, a PIK3C3/Vps34 inhibitor that prevents autophagy and synergizes with MTOR inhibition in tumor cells. <u>Autophagy.</u> 2015 Apr 3;11(4):725-6.</p>

源叶生物