

产品名称: **Ro3280**

产品别名: **Ro3280**

生物活性:					
Description	Ro3280 is a potent, highly selective inhibitor of PLK1 with an IC <sub>50</sub> and a K <sub>d</sub> of 3 nM and 0.09 nM, respectively, and nearly has no effect on PLK2 and PLK3.				
IC <sub>50</sub> & Target	PLK1	ALK	CAMKK1	CAMKK2	
	0.09 nM (Kd)	230 nM (Kd)	1100 nM (Kd)	87 nM (Kd)	
	DAPK1	DAPK3	FER	GAK	
	100 nM (Kd)	70 nM (Kd)	53 nM (Kd)	87 nM (Kd)	
	MYLK	PTK2	PTK2B	RPS6KA6 (KinDom.2)	
	170 nM (Kd)	84 nM (Kd)	130 nM (Kd)	560 nM (Kd)	
	TTK				
	51 nM (Kd)				
In Vitro	Ro3280 (RO3280) inhibits PLK1 activity in NB4 and K562 cells, with an IC <sub>50</sub> s of 13.45 nM and 301 nM, respectively. RO3280 shows inhibitory activities against the growth of six leukemia cells, with IC <sub>50</sub> s of 186 nM, 175 nM, 74 nM, 797 nM, 120 nM and 162 nM for U937, HL60, NB4, K562, MV4-11 and CCRF cell lines, respectively. RO3280 also suppresses the growth of primary ALL and AML cells, with IC <sub>50</sub> s of 35.49-110.76 nM, and 52.80-147.50 nM, respectively. RO3280 (50 or 100 nM) induces apoptosis and cell cycle disorder in acute leukemia cells <sup>[1]</sup> . Ro3280 shows potent activity in H82, H69, A549 lung cancer cell lines with EC <sub>50</sub> s of 6 nM, 7 nM and 82 nM. Ro3280 also inhibits several other cancer cell lines, with low concentration <sup>[2]</sup> . RO3280 is cytotoxic to 5637 and T24 human bladder cancer cells, with IC <sub>50</sub> s of appr 100 nM.				
In Vivo	Ro3280 (RO3280, 40 mg/kg, i.v.) inhibits 72% tumor growth in a mouse xenograft model implanted with HT-29 colorectal cancer cells, and when dosed more frequently, RO3280 completely suppresses the tumor growth <sup>[2]</sup> . RO3280 (30 mg/kg, once every 5 days, i.p.) shows significant anti-bladder cancer activities in a nude mouse model <sup>[3]</sup> .				
	<b><i>In Vitro:</i></b> <b>DMSO : 100 mg/mL (183.96 mM; Need ultrasonic)</b> <b>H<sub>2</sub>O : &lt; 0.1 mg/mL (insoluble)</b>				
	<div>Preparing Stock Solutions</div>	<div>SolventMassConcentration</div>	1 mg	5 mg	10 mg
		1 mM	1.8396 mL	9.1978 mL	18.3955 mL
		5 mM	0.3679 mL	1.8396 mL	3.6791 mL
		10 mM	0.1840 mL	0.9198 mL	1.8396 mL
<p><b>*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。</b></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><b><i>In Vivo:</i></b></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 <b>In Vitro</b> 方式配制澄清的储备液，再依次添加助溶剂。</p>					

Solvent&Solubility	<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 Solubility: ≥ 2.5 mg/mL (4.60 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.60 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 400 <math>\mu</math>L PEG300 中，混合均匀向上述体系中加入 50 <math>\mu</math>L Tween-80，混合均匀；然后继续加入 450 <math>\mu</math>L 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-<math>\beta</math>-CD in saline) Solubility: 2.5 mg/mL (4.60 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (4.60 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 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 20% 的 SBE-<math>\beta</math>-CD 生理盐水溶液中，混合均匀。</p> <p>3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (4.60 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.60 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 <math>\mu</math>L 25.0 mg/mL 的澄清 DMSO 储备液加到 900 <math>\mu</math>L 玉米油中，混合均匀。</p>
References	<p>[1]. Wang NN, et al. <u>Molecular targeting of the oncoprotein PLK1 in pediatric acute myeloid leukemia: RO3280, a novel PLK1 inhibitor, induces apoptosis in leukemia cells.</u> Int J Mol Sci. 2015 Jan 7;16(1):1266-92.</p> <p>[2]. Chen S, et al. Identification of novel, potent and selective inhibitors of Polo-like kinase 1. Bioorg Med Chem Lett. 2012 Jan 15;22(2):1247-50.</p> <p>[3]. Zhang Z, et al. Targeted inhibition of Polo-like kinase 1 by a novel small-molecule inhibitor induces mitotic catastrophe and apoptosis in human bladder cancer cells. J Cell Mol Med. 2017 Apr;21(4):758-767.</p>
实验参考：	
Cell Assay	<p>Leukemia cells or primary leukemia cells (<math>2 \times 10^4</math>) are seeded in 96-well plates overnight and incubated with DMSO, or increasing concentrations of RO3280 (0.05-120 <math>\mu</math>M) for 24 h. The same volume of DMSO added to the vehicle treated wells. Each drug concentration is replicated four times. Then, 10 <math>\mu</math>L CCK8 solution is added to each well, incubated at 37°C for 2-4 h and the optical density (OD) values are measured at 450 nm using a scanning multi-well spectrophotometer. Relative survival rate is calculated from the absorbance values compared with the control group. The proliferation of cells is calculated as a percentage of the DMSO-treated control wells with 50% inhibitory concentration (<math>IC_{50}</math>) values derived after plotting proliferation values on a logarithmic curve. The <math>IC_{50}</math> of PLK1 inhibitor is calculated by Graph Prism software<sup>[1]</sup></p>
Animal Administration	<p>Briefly, mice (female, 4-5 weeks of age) are used in the assay. Cells (<math>5 \times 10^6</math> cells in 150 <math>\mu</math>L) are suspended in RPMI 1640 and injected subcutaneously into the flank of each BALB/c nude mouse. On day 5, tumour size is measured, the animals are randomized into two groups (n = 15 per group), and RO3280 (40 mg/kg, once every 5 days) treatment is initiated by intraperitoneal injection. The control group is treated with vehicle (1.5% DMSO in PBS). The drug (or vehicle) treatment is performed for 40 days. The length and width of the resulting tumours (in millimetres) are measured</p>

	<p>every 3 days with callipers. The tumour diameter is measured, and the volume (<math>\text{length} \times \text{width}^2 \times 0.52</math>) is calculated. The mice are humanely killed on day 45, and the tumours are dissected and weighed. Western blot and immunohistochemistry assays are also performed with these sections. Then, the tumours are fixed, embedded and cut into 3 - <math>\mu\text{m}</math> - thick sections, which are subsequently stained with haematoxylin and eosin to permit the observation of the tumour margin[3]</p>
References	<p>[1]. Wang NN, et al. <u>Molecular targeting of the oncoprotein PLK1 in pediatric acute myeloid leukemia: RO3280, a novel PLK1 inhibitor, induces apoptosis in leukemia cells.</u> Int J Mol Sci. 2015 Jan 7;16(1):1266-92.</p> <p>[2]. Chen S, et al. <u>Identification of novel, potent and selective inhibitors of Polo-like kinase 1.</u> Bioorg Med Chem Lett. 2012 Jan 15;22(2):1247-50.</p> <p>[3]. Zhang Z, et al. <u>Targeted inhibition of Polo-like kinase 1 by a novel small-molecule inhibitor induces mitotic catastrophe and apoptosis in human bladder cancer cells.</u> J Cell Mol Med. 2017 Apr;21(4):758-767.</p>



源叶生物