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产品名称: **SR-3029**  
产品别名: **SR-3029**

生物活性:				
Description	SR-3029 is a potent and ATP competitive CK1δ and CK1ε inhibitor, with IC <sub>50</sub> s of 44 nM and 260 nM, respectively, and K <sub>s</sub> of 97 nM for both kinases.			
IC <sub>50</sub> & Target	CK1δ	CK1ε	CDK6/cyclin D3	CDK6/cyclin D1
	44 nM (IC <sub>50</sub> )	260 nM (IC <sub>50</sub> )	427 nM (IC <sub>50</sub> )	428 nM (IC <sub>50</sub> )
	CDK4/cyclin D3	CDK4/cyclin D1	FLT3	
	368 nM (IC <sub>50</sub> )	576 nM (IC <sub>50</sub> )	3000 nM (IC <sub>50</sub> )	
In Vitro	SR-3029 is a potent CK1δ/CK1ε inhibitor, with IC <sub>50</sub> s of 44 nM and 260 nM, respectively. SR-3029 is ATP competitive, with K <sub>s</sub> of 97 nM for CK1δ/CK1ε. SR-3029 also blocks CDK6/cyclin D3, CDK6/cyclin D1, CDK4/cyclin D3, CDK4/cyclin D1 and FLT3, with IC <sub>50</sub> s of 427, 428, 368, 576, and 3000 nM, respectively. SR-3029 shows inhibitory effects on A375 cells, with an EC <sub>50</sub> of 86 nM <sup>[1]</sup> . CK1δ is a necessary and sufficient driver of Wnt/β-catenin signaling in human breast cancer. SR-3029 shows less potent activities against MCF7 and T47D breast cancer cells and the MCF10A cell line, which express low amounts of CK1δ <sup>[2]</sup> .			
In Vivo	SR-3029 (20 mg/kg daily i.p.) exhibits anti-tumor effects in rthotopic MDA-MB-231, MDA-MB-468 (TNBC), SKBR3 and BT474 (HER2+) tumor xenografts with no overt toxicity in mice. SR-3029 (20 mg/kg daily i.p.) also effectively inhibits the growth of tumor in primary patient-derived xenograft (PDX) models. In addition, SR-3029 (20 mg/kg, i.p.) strongly reduces the expression of nuclear β-catenin in tumors of mice <sup>[2]</sup> .			
Solvent&Solubility	<b>In Vitro:</b> DMSO : ≥ 30 mg/mL (62.44 mM) H <sub>2</sub> O : < 0.1 mg/mL (insoluble) * "≥" means soluble, but saturation unknown.			
	Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg
		1 mM	2.0814 mL	10.4069 mL
		5 mM	0.4163 mL	2.0814 mL
		10 mM	0.2081 mL	1.0407 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。 <b>In Vivo:</b> 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			



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	<p>Solubility: <math>\geq 2.08</math> mg/mL (4.33 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.08</math> mg/mL (4.33 mM, 饱和度未知) 的澄清溶液。</p> <p>以 1 mL 工作液为例, 取 100 <math>\mu</math>L 20.8 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 <math>\rightarrow</math> 90% corn oil</p> <p>Solubility: <math>\geq 2.08</math> mg/mL (4.33 mM); Clear solution</p> <p>此方案可获得 <math>\geq 2.08</math> mg/mL (4.33 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 <math>\mu</math>L 20.8 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]. Bibian M, et al. Development of highly selective casein kinase 1<math>\delta</math>/1<math>\epsilon</math> (CK1<math>\delta</math>/1<math>\epsilon</math>) inhibitors with potent antiproliferative properties. Bioorg Med Chem Lett. 2013 Aug 1;23(15):4374-80.</p> <p>[2]. Rosenberg LH, et al. Therapeutic targeting of casein kinase 1<math>\delta</math> in breast cancer. Sci Transl Med. 2015 Dec 16;7(318):318ra202.</p>
实验参考:	
Cell Assay	<p>Human A375 melanoma cells are cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum, 1% penicillin/streptomycin and 1<math>\times</math> MEM Non-Essential Amino Acids at 37°C, 5% CO<sub>2</sub>. To evaluate the anti-proliferative activity of newly synthesized CK1<math>\delta</math>/1<math>\epsilon</math> inhibitors, each compound (SR-3029) is subjected to MTT assays against A375 melanoma cells and their EC<sub>50</sub> values are determined. Briefly, A375 melanoma cells are plated into a 96-well plate and treated with a series of concentrations of each new inhibitor, vehicle (DMSO) or with SR-3029 or SR-1277 (positive controls). MTT assays are performed four days after treatment and data are analyzed using the GraphPad Prism5<sup>[1]</sup>.</p>
Animal Administration	<p>Stable pools of MDA-MB-231-Luc, MDA-MB-231, MDA-MB-468, SKBR3, or BT474 cells are established by injection of <math>2 \times 10^6</math> cancer cells into the mammary fat pads of 6-week-old female athymic nude mice. Establishment of BCM-4013 patient-derived xenografts is performed. Briefly, fresh xenograft tumor fragments (<math>\sim 1</math> mm<sup>3</sup>) are transplanted into the cleared mammary fat pad of recipient SCID/Bg mice. Mice are treated with SR-3029 or vehicle (10:10:80, DMSO:Tween-80:Water) at 20 mg/kg daily by i.p. injection. Tumor volumes are measured as the indicated intervals using calipers or by luminescence imaging with the IVIS 100 imager after subcutaneous injection of luciferin (15 mg/mL). Average radiance (p/s/cm<sup>2</sup>/sr) is determined from tumor region-of-interest (ROI) using Living-Image analysis software<sup>[2]</sup>.</p>
Kinase Assay	<p>Briefly, final assay concentrations for CK1<math>\delta</math>, Ulight peptide substrate (Ulight-Topo-IIa(Thr1342) peptide) and ATP are 2 nM, 200 nM and 20 <math>\mu</math>M respectively. The reaction is performed at room temperature in a 10 <math>\mu</math>L final volume (384-well low volume plate) containing the following: 50 mM Hepes, pH 7.5, 5 mM MgCl<sub>2</sub>, 0.1 mg/mL bovine serum albumin, 1 mM dl-dithiothreitol, 0.01% Triton X-100 and 1% DMSO. After 10 min, the reaction is terminated by addition of 10 <math>\mu</math>L of 4 nM Eu-anti-p-Topo-IIa in Lance Detection Buffer. The fluorescent signal is detected using a plate reader. 10 point dose-response curves with 3-fold dilutions starting from 10 <math>\mu</math>M for each compound (SR-3029) is generated in duplicate and data fit to a four parameter logistic<sup>[1]</sup>.</p>



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