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产品名称: **SR9011**
产品别名: **SR9011**

生物活性:					
Description		SR9011 is a REV-ERB α / β agonist with IC ₅₀ s of 790 nM and 560 nM for REV-ERB α and REV-ERB β , respectively.			
IC ₅₀ & Target		IC50: 790 nM (Rev-ErbB α), 560 nM (Rev-ErbB β) ^[1]			
In Vitro		SR9011 dose-dependently increases the REV-ERB-dependent repressor activity assessed in HEK293 cells expressing a chimeric Gal4 DNA Binding Domain (DBD) - REV-ERB ligand binding domain (LBD) α or β and a Gal4-responsive luciferase reporter (REV-ERB α IC ₅₀ =790 nM, REV-ERB β IC ₅₀ =560 nM). SR9011 potently and efficaciously suppresses transcription in a cotransfection assay using full-length REV-ERB α along with a luciferase reporter driven by the <i>Bmal1</i> promoter (SR9011 IC ₅₀ =620 nM). SR9011 suppresses the expression of BMAL1 mRNA in HepG2 cells in a REV-ERB α / β -dependent manner ^[1] SR9011 suppresses proliferation of the breast cancer cell lines regardless of their ER or HER2 status. SR9011 appears to pause the cell cycle of the breast cancer cells prior to M phase. Cyclin A (<i>CCNA2</i>) is identified as a direct target gene of REV-ERB suggesting that suppression of expression of this cyclin by SR9011 may mediate the cell cycle arrest. Treatment with SR9011 results in an increase in cells in the G ₀ /G ₁ phase and a decrease of cells in S and G ₂ /M phase suggesting that activation of REV-ERB may be resulting in decreased transition from G ₁ to S phase and/or from S to G ₂ /M phase ^[2] .			
In Vivo		SR9011 displays reasonable plasma exposure, thus, the expression of REV-ERB responsive genes is examined in the liver of mice treated with various doses of SR9011 for 6-days. The <i>plasminogen activator inhibitor type 1</i> gene (<i>Serpine1</i>) is a REV-ERB target gene and displays dose-dependent suppression of expression in response to SR9011. The <i>cholesterol 7α-hydroxylase</i> (<i>Cyp7a1</i>) and <i>sterol response element binding protein</i> (<i>Srebp1</i>) genes have also been shown to be responsive to REV-ERB and are dose-dependently suppressed with increasing amounts of SR9011. After 12 days in D:D conditions mice are injected with a single dose of SR9011 or vehicle at CT6 (peak expression of <i>Rev-erba</i>). Vehicle injection causes no disruption in circadian locomotor activity. However, administration of a single dose of SR9011 results in loss of locomotor activity during the subject dark phase. Normal activity returns the next circadian cycle, consistent with clearance of the drugs in less than 24h. The SR9011-dependent decrease in wheel running behavior in the mice under constant darkness conditions is dose-dependent and that the potency (ED ₅₀ =56 mg/kg) is similar to the potency of SR9011-mediated suppression of a REV-ERB responsive gene, <i>Srebf1</i> , in vivo (ED ₅₀ =67mg/kg) ^[1] .			
		In Vitro: DMSO : \geq 43 mg/mL (89.76 mM) * " \geq " means soluble, but saturation unknown.			
		<div><div>Solvent</div><div>Mass</div><div>Concentration</div></div>	1 mg	5 mg	10 mg
Preparing Stock Solutions		1 mM	2.0875 mL	10.4375 mL	20.8751 mL
		5 mM	0.4175 mL	2.0875 mL	4.1750 mL
		10 mM	0.2088 mL	1.0438 mL	2.0875 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					



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Solvent&Solubility	<p>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 (5.22 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.22 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% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (5.22 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.22 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]. Solt LA, et al. Regulation of circadian behaviour and metabolism by synthetic REV-ERB agonists. Nature. 2012 Mar 29;485(7396):62-8.</p> <p>[2]. Wang Y, et al. Anti-proliferative actions of a synthetic REV-ERBα/β agonist in breast cancer cells. Biochem Pharmacol. 2015 Aug 15;96(4):315-22.</p>
实验参考:	
Cell Assay	<p>MCF10A, MDA-MB-231, MCF-7, MDA-MB-361, SKBR3, BT474 cells are plated in 6-well plates one day before treatment. The MTT cell proliferation assays are performed. Briefly, 3×10^3 to 5×10^3 cells per well are plated in 96-well plates. Twenty-four hours later, cells are treated with SR9011 (0, 2, 4, 6, 8 and 10 μM) or DMSO. Seventy-two hours after treatment, the cells are labeled with 1.2 mM MTT and incubated for 4 hours. DMSO is then added and readings are taken on a plate reader at 540 nm^[2].</p>
Animal Administration	<p>Mice^[1]</p> <p>For circadian gene expression experiments male C57BL6 mice (8-10 weeks of age) are either maintained on a L:D (12h:12h) cycle or on constant darkness. At circadian time (CT) 0 animals are administered a single dose of 100 mg/kg SR9011 (i.p.) and groups of animals (n=6) are sacrificed at CT0, CT6, CT12 and CT18. Gene expression is determined by real time QPCR.</p>
References	<p>[1]. Solt LA, et al. Regulation of circadian behaviour and metabolism by synthetic REV-ERB agonists. Nature. 2012 Mar 29;485(7396):62-8.</p> <p>[2]. Wang Y, et al. Anti-proliferative actions of a synthetic REV-ERBα/β agonist in breast cancer cells. Biochem Pharmacol. 2015 Aug 15;96(4):315-22.</p>