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产品名称: **Motolimod**
 产品别名: **VTX-2337; VTX-378**

生物活性:					
Description	Motolimod (VTX-2337;VTX-378) is a selective Toll-like receptor 8 (TLR8) agonist, with an EC ₅₀ of approximately 100 nM.				
IC₅₀ & Target	EC ₅₀ : 100 nM (TLR8)[1]				
In Vitro	Among the TLRs tested (TLR2, 3, 4, 5, 7, 8, and 9), Motolimod (VTX-2337) selectively activates TLR8. Motolimod stimulates the production of both TNFα (EC ₅₀ =140±30 nM based on 10 donors) and IL-12 (EC ₅₀ =120±30 nM based on 10 donors) in PBMCs. The EC ₅₀ value for MIP-1β induction is 60 nM for Motolimod[1].				
In Vivo	Monkeys receive a subcutaneous injection of Motolimod (1 or 10 mg/kg), and plasma is collected predose, 6, 12, 24, and 96 h post-injection. For the 10 mg/kg dose, mean plasma levels of IL-1β increase from baseline levels of 0.5 pg/mL, up to 9.12±2.7 ng/mL (p<0.05, t-test) at 6 h post-administration of Motolimod (10 mg/kg). Circulating levels of IL-18 also increase from a baseline of ~ 1 pg/mL to 68.7±4.4 pg/mL (p<0.05, t-test) at 6 h in response to the Motolimod (VTX-2337) treatment (10 mg/kg). Levels of IL-6 are monitored, as this mediator is induced in response to TLR8 activation, but the release is independent of NLRP3 inflammasome activation. In addition, plasma levels of IFNγ are assessed as a measure of NK cell activation in response to Motolimod treatment[2].				
Solvent&Solubility	In Vitro: DMSO : 50 mg/mL (109.03 mM; Need ultrasonic)				
		Solvent Mass Concentration	1 mg	5 mg	10 mg
	Preparing	1 mM	2.1805 mL	10.9027 mL	21.8055 mL
	Stock Solutions	5 mM	0.4361 mL	2.1805 mL	4.3611 mL
		10 mM	0.2181 mL	1.0903 mL	2.1805 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°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。</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 (5.45 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.45 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 (5.45 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.45 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 →90% corn oil</p> <p>Solubility: ≥ 2.5 mg/mL (5.45 mM); Clear solution</p> <p>此方案可获得 ≥ 2.5 mg/mL (5.45 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>
<p>References</p>	<p>[1]. Lu H, et al. VTX-2337 is a novel TLR8 agonist that activates NK cells and augments ADCC. Clin Cancer Res. 2012 Jan 15;18(2):499-509.</p> <p>[2]. Dietsch GN, et al. Coordinated Activation of Toll-Like Receptor8 (TLR8) and NLRP3 by the TLR8 Agonist, VTX-2337, Ignites Tumoricidal Natural Killer Cell Activity. PLoS One. 2016 Feb 29;11(2):e0148764.</p>
<p>实验参考:</p>	
<p>Cell Assay</p>	<p>PBMCs or purified NK cells are prepared, and the purity of NK cells is approximately 99%. NK cell-mediated cytotoxicity is assessed by Calcein AM release from labeled target cells. In brief, PBMCs or purified NK cells are cultured for 48 hours in RPMI medium in the presence of Motolimod (167 or 500 nM) before incubation with target cells[1].</p>
<p>Animal Administration</p>	<p>Monkeys[2]</p> <p>The male monkeys (2.9-4.9 kg) are housed individually (cage dimensions of 0.76 m wide×0.74 m deep×0.81 m in height), but commingled periodically as part of the environmental enrichment program. The animals are also given fruit, vegetable, or additional supplements as a form of environmental enrichment, as well as given various cage enrichment devices. Animals are given Certified Primate Diet, two times daily and water ad libitum. Motolimod is administered as a bolus subcutaneous (SC) injection in the intrascapular area at doses of 1 and 10 mg/kg. Blood samples are collected at baseline (pre-dose), and 6, 12, 24, and 96 h post injection to monitor levels of IL-1β and IL-18 in the plasma using the human MAP v.1.6 inflammation panel.</p>
<p>Kinase Assay</p>	<p>Human embryonic kidney cells (HEK293) expressing TLR2, 3, 4, 5, 7, 8, or 9 are cultured in Dulbecco's Modified Eagle's Media containing 4.5 g/L L-glucose and 10% FBS. The activity of specific TLR agonists is assessed using the secretory embryonic alkaline phosphatase (SEAP) reporter gene that is linked to NF-κB activation in response to TLR stimulation. Measurement of SEAP activity using the Quanti-blue substrate after TLR agonist treatment is carried out similarly[1].</p>
<p>References</p>	<p>[1]. Lu H, et al. VTX-2337 is a novel TLR8 agonist that activates NK cells and augments ADCC. Clin Cancer Res. 2012 Jan 15;18(2):499-509.</p> <p>[2]. Dietsch GN, et al. Coordinated Activation of Toll-Like Receptor8 (TLR8) and NLRP3 by the TLR8 Agonist, VTX-2337, Ignites Tumoricidal Natural Killer Cell Activity. PLoS One. 2016 Feb 29;11(2):e0148764.</p>