



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

产品名称: 5-PyriMidinecarboxaMide,
2-[[2-(3-chloro-4-hydroxyphenyl)ethyl]aMino]-4-[(phenylMethyl)aMino]-
产品别名: AS1517499

生物活性:				
Description	AS1517499 is a potent STAT6 inhibitor with an IC ₅₀ of 21 nM.			
IC ₅₀ & Target	STAT6			
	21 nM (IC ₅₀)			
In Vitro	AS1517499 shows potent STAT6 inhibition with an IC ₅₀ value of 21 nM, and also inhibits IL-4-induced Th2 differentiation of mouse spleen T cells with an IC ₅₀ value of 2.3 nM and without influencing T-helper cell 1 (Th1) differentiation induced by IL-12. AS1517499 selectively inhibits Th2 differentiation without affecting Th1 differentiation[1]. In cultured human BSM cells, IL-13 (100 ng/mL) causes a phosphorylation of STAT6 and an up-regulation of RhoA, a monomeric GTPase responsible for Ca ²⁺ sensitization of smooth muscle contraction: both events are inhibited by co-incubation with AS1517499 (100 nM)[2].			
In Vivo	In BALB/c mice that are actively sensitized and repeatedly challenged with ovalbumin antigen, an increased IL-13 level in bronchoalveolar lavage fluids and a phosphorylation of STAT6 in bronchial tissues are observed after the last antigen challenge. These mice have an augmented BSM contractility to acetylcholine together with an up-regulation of RhoA in bronchial tissues. Intraperitoneal injections of AS1517499 (10 mg/kg) 1 hour before each ovalbumin exposure inhibits both the antigen-induced up-regulation of RhoA and BSM hyperresponsiveness, almost completely[2].			
Solvent&Solubility	In Vitro: DMSO : ≥ 35 mg/mL (87.97 mM) * "≥" means soluble, but saturation unknown.			
	Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg
		1 mM	2.5134 mL	12.5672 mL
		5 mM	0.5027 mL	2.5134 mL
		10 mM	0.2513 mL	1.2567 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。 In Vivo: 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 Solubility: ≥ 2.5 mg/mL (6.28 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (6.28 mM, 饱和度未知) 的澄清溶液。			



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

	<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 \rightarrow 90% corn oil</p> <p>Solubility: \geq 2.5 mg/mL (6.28 mM); Clear solution</p> <p>此方案可获得 \geq 2.5 mg/mL (6.28 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]. Nagashima S, et al. Synthesis and evaluation of 2-[[2-(4-hydroxyphenyl)-ethyl]amino]pyrimidine-5-carboxamide derivatives as novel STAT6 inhibitors. Bioorg Med Chem. 2007 Jan 15;15(2):1044-55.</p> <p>[2]. Chiba Y, et al. A novel STAT6 inhibitor AS1517499 ameliorates antigen-induced bronchial hypercontractility in mice. Am J Respir Cell Mol Biol. 2009 Nov;41(5):516-24.</p>
实验参考:	
Cell Assay	<p>Normal human BSM cells (hBSMCs) are maintained in SmBM medium supplemented with 5% fetal bovine serum, 0.5 ng/mL human epidermal growth factor (hEGF), 5 μg/mL insulin, 2 ng/mL human fibroblast growth factor-basic (hFGF-b), 50 μg/mL gentamicin, and 50 ng/mL amphotericin B. Cells are maintained at 37°C in a humidified atmosphere (5% CO₂), fed every 48 to 72 hours, and passaged when cells reached 90 to 95% confluence. Then the hBSMCs (passages 7-9) are seeded in 6-well plates and 8-well chamber slides at a density of 3,500 cells/cm² and, when 80 to 85% confluence observed, cells are cultured without serum for 24 hours before addition of recombinant human IL-13. AS1517499 (100 nM) or its vehicle (0.3% DMSO) is treated 30 minutes before the addition of IL-13 (100 ng/mL). In some experiments, AS1517499 is treated 0 (co-incubation), 3, or 12 hours after the addition of IL-13. In another series of experiments, a selective Rho-kinase inhibitor Y-27632 (1 μM) or its vehicle (0.3% DMSO) is also applied 15 minutes before the IL-13 application. At the indicated time after the IL-13 treatment, cells are washed with PBS, immediately collected, and disrupted with 1\times SDS sample buffer (250 μL/well), and used for Western blot analyses[2].</p>
Animal Administration	<p>Mice[2]</p> <p>Male BALB/c mice are used. Preparation of a murine model of allergic bronchial asthma, which has an in vivo AHR, is performed. In brief, BALB/c mice (8 wk of age) are actively sensitized by intraperitoneal injections of 8 μg ovalbumin (OVA) with 2 mg Imject Alum on Day 0 and Day 5. The sensitized mice are challenged with aerosolized OVA-saline solution (5 mg/mL) for 30 minutes on Days 12, 16, and 20. A control group of mice received the same immunization procedure but inhaled saline aerosol instead of OVA challenge. The aerosol is generated with an ultrasonic nebulizer and introduced to a Plexiglas chamber box (130\times200 mm, 100 mm height) in which the mice are placed. Animals also received intraperitoneal injection with AS1517499 (1 or 10 mg/kg/d; dissolved in 20% DMSO in saline) or its vehicle 1 hour before each antigen inhalation (Days 12, 16, and 20). Twenty-four hours after the last OVA challenge, mice are killed by exsanguination from abdominal aorta under urethane (1.6 g/kg, intraperitoneally) anesthesia.</p>



上海源叶生物科技有限公司
Shanghai yuanye Bio-Technology Co., Ltd
电话: 021-61312973 传真: 021-55068248
网址: www.shyuanye.com
邮箱: shyysw@sina.com

References	<p>[1]. Nagashima S, et al. Synthesis and evaluation of 2-[[2-(4-hydroxyphenyl)-ethyl]amino]pyrimidine-5-carboxamide derivatives as novel STAT6 inhibitors. Bioorg Med Chem. 2007 Jan 15;15(2):1044-55.</p> <p>[2]. Chiba Y, et al. A novel STAT6 inhibitor AS1517499 ameliorates antigen-induced bronchial hypercontractility in mice. Am J Respir Cell Mol Biol. 2009 Nov;41(5):516-24.</p>
-------------------	---