

产品名称: (Z)-5-(quinoxalin-6-ylmethylene)thiazolidine-2,4-dione  
产品别名: AS-605240

生物活性:					
Description	AS-605240 is a specific and orally active inhibitor of the PI3Kγ, with an IC <sub>50</sub> of 8 nM, and a K <sub>i</sub> of 7.8 nM.				
IC <sub>50</sub> & Target [2]	PI3Kγ	PI3Kα	PI3Kβ	PI3Kδ	Autophagy
	8 nM (IC <sub>50</sub> )	60 nM (IC <sub>50</sub> )	270 nM (IC <sub>50</sub> )	300 nM (IC <sub>50</sub> )	
In Vitro	AS-605240 is an isoform-selective inhibitor of PI3Kγ with over 30-fold selectivity for PI3Kδ and β, and 18- and 7.5-fold selectivity over PI3Kα, respectively. AS-605240 shows an inhibitory effect on C5a-mediated PKB phosphorylation in RAW264 mouse macrophages with an IC <sub>50</sub> of 0.09 μM. AS-605240 blocks PKB phosphorylation induced by MCP-1 and has little or no effect after stimulation with CSF-1. AS-605240 inhibits MCP-1-mediated phosphorylation of PKB and its downstream substrates GSK3α and β in a concentration-dependent manner. AS605240 suppresses in a dose-dependent manner the proliferation of BDC2.5 CD4+ T cells[2].				
In Vivo	AS-605240 (30 mg/kg BW, per os, every 12 h) markedly decreases FoxM1 expression in mouse lungs and fails to restore vascular integrity[1]. AS-605240 reduces RANTES-induced peritoneal neutrophil recruitment, with ED <sub>50</sub> of 9.1 mg/kg. In the CCL5 model, AS-605240 shows an ED <sub>50</sub> value of 10 mg/kg, in correlation with the percentage of reduction of neutrophil recruitment observed in Pik3cg <sup>-/-</sup> mice. AS-605240 (50 mg/kg, p.o.) substantially reduces clinical and histological signs of joint inflammation to a similar extent to that of Pik3cg <sup>-/-</sup> mice[2]. AS605240 (30 mg/kg, i.p.) suppresses intracellular PAkt in splenocytes of NOD mice and delays diabetes onset. AS605240 also prevents autoimmune diabetes in prediabetic NOD mice, and suppresses autoreactive T cells while increasing Tregs in NOD mice. AS605240 (30 mg/kg, i.p.) reverses hyperglycemia in newly hyperglycemic NOD mice, reverses hyperglycemia in early diabetic NOD mice through Tregs and suppresses T-cell infiltration in pancreatic islets while increasing Tregs[3]. AS605240 (25, 50 mg/kg) markedly reduces total cell count and numbers of macrophages, neutrophils and lymphocytes in rats. AS605240 significantly reduces the levels of TNF-α and IL-1β in BALF to 132.7±11.2 pg/mL and 49.2±11.3 pg/mL in 25 mg/kg AS605240 + BLM group and 131.3±10.7 and 49.6±8.8 pg/mL in 50 mg/kg AS605240 + BLM group, respectively. AS605240 inhibits profibrotic cytokines production in bleomycin-induced pulmonary fibrosis. AS605240 inhibits phosphorylation of Akt of inflammatory cells in bleomycin-induced pulmonary fibrosis model[4].				
Solvent&Solubility	<b>In Vitro:</b> DMSO : 5.8 mg/mL (22.54 mM; Need warming)				
	<div>Preparing Stock Solutions</div>	<div>Solvent / Mass Concentration</div>	1 mg	5 mg	10 mg
		1 mM	3.8870 mL	19.4348 mL	38.8697 mL
		5 mM	0.7774 mL	3.8870 mL	7.7739 mL
		10 mM	0.3887 mL	1.9435 mL	3.8870 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℃, 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>					
[1]. Huang X, et al. Endothelial p110γPI3K Mediates Endothelial Regeneration and Vascular Repair After					

<b>References</b>	<p><a href="#">Inflammatory Vascular Injury. Circulation. 2016 Mar 15;133(11):1093-103.</a></p> <p>[2]. <a href="#">Camps M, et al. Blockade of PI3Kgamma suppresses joint inflammation and damage in mouse models of rheumatoid arthritis. Nat Med. 2005 Sep;11(9):936-43.</a></p> <p>[3]. <a href="#">Azzi J, et al. The novel therapeutic effect of phosphoinositide 3-kinase-γ inhibitor AS605240 in autoimmune diabetes. Diabetes. 2012 Jun;61(6):1509-18. Epub 2012 Mar 8.</a></p> <p>[4]. <a href="#">Wei X, et al. A phosphoinositide 3-kinase-gamma inhibitor, AS605240 prevents bleomycin-induced pulmonary fibrosis in rats. Biochem Biophys Res Commun. 2010 Jun 25;397(2):311-7. Epub 2010 May 26.</a></p>
<b>实验参考:</b>	
<b>Cell Assay</b>	<p>A total of <math>5 \times 10^5</math> BDC2.5 splenocytes and 50 μg/mL BDC2.5-peptide are incubated in vitro in a 96-well round-bottom plate for 48 h. Then the cultures are pulsed with 1 μCi of tritiated thymidine [<math>^3\text{H}</math>] to determine cell proliferation. [3]</p>
<b>Animal Administration</b>	<p>In this study, rats are bred for one week to affirm body weight and then randomly divided into four experimental groups: (a) control group (rats are given vehicle only); (b) BLM group (rats are induced with BLM); (c) BLM + 25 mg/kg AS605240 group (rats are induced with BLM and then administrated with 25 mg/kg AS605240); (d) BLM + 50 mg/kg AS605240 group (the same protocol as the former group except a different dose of 50 mg/kg AS605240). In addition, five rats are given 50 mg/kg AS605240 only to detect whether AS605240 has any side effect simultaneously as the previous four groups. Rats in (c), (d) and AS605240-given-only group are administered orally 25, 50 and 50 mg/kg AS605240 by gavage while rats in control group and BLM group are given only equivalent saline at day-1 (the day rats are given BLM is marked as day-0). The same dosage is maintained once everyday for 28 days. [4]</p>
<b>Kinase Assay</b>	<p>Human PI3Kγ (100 ng) is incubated at RT with kinase buffer (10 mM <math>\text{MgCl}_2</math>, 1 mM β-glycerophosphate, 1 mM DTT, 0.1 mM <math>\text{Na}_3\text{VO}_4</math>, 0.1% Na Cholate and 15 M ATP/100 nCi <math>\gamma\text{[}^{32}\text{P]ATP}</math>, final concentrations) and lipid vesicles containing 18 M PtdIns and 250 M of PtdSer (final concentrations), in the presence of inhibitors or DMSO. Kinase reaction is stopped by adding 250 g of Neomycin-coated Scintillation Proximity Assay (SPA) bead and proceeded. [2]</p>
<b>References</b>	<p>[1]. <a href="#">Huang X, et al. Endothelial p110γPI3K Mediates Endothelial Regeneration and Vascular Repair After Inflammatory Vascular Injury. Circulation. 2016 Mar 15;133(11):1093-103.</a></p> <p>[2]. <a href="#">Camps M, et al. Blockade of PI3Kgamma suppresses joint inflammation and damage in mouse models of rheumatoid arthritis. Nat Med. 2005 Sep;11(9):936-43.</a></p> <p>[3]. <a href="#">Azzi J, et al. The novel therapeutic effect of phosphoinositide 3-kinase-γ inhibitor AS605240 in autoimmune diabetes. Diabetes. 2012 Jun;61(6):1509-18. Epub 2012 Mar 8.</a></p> <p>[4]. <a href="#">Wei X, et al. A phosphoinositide 3-kinase-gamma inhibitor, AS605240 prevents bleomycin-induced pulmonary fibrosis in rats. Biochem Biophys Res Commun. 2010 Jun 25;397(2):311-7. Epub 2010 May 26.</a></p>