

产品名称: 5-[[5-(4-氟-2-羟基苯基)-2-呋喃基]亚甲基]-2,4-噻唑烷二酮  
 产品别名: AS-252424

生物活性:				
Description		AS-252424 is a potent and selective <b>PI3K<math>\gamma</math></b> inhibitor with an <b>IC<sub>50</sub></b> of 30±10 nM.		
IC <sub>50</sub> & Target	PI3K $\alpha$	PI3K $\gamma$	PI3K $\delta$	PI3K $\beta$
	935 nM (IC <sub>50</sub> )	30 nM (IC <sub>50</sub> )	20 $\mu$ M (IC <sub>50</sub> )	20 $\mu$ M (IC <sub>50</sub> )
In Vitro	AS-252424 also inhibits PI3K $\alpha$ , PI3K $\beta$ and PI3K $\delta$ with IC <sub>50</sub> s of 935±150 nM, 20 $\mu$ M and 20 $\mu$ M, respectively. AS-252424 inhibits MCP-1-mediated chemotaxis in wild-type primary monocytes in a concentration-dependent manner with an IC <sub>50</sub> value of 52 $\mu$ M, as well as in the monocytic cell line THP-1 with an IC <sub>50</sub> value of 53 $\mu$ M. In the human monocytic cell line THP-1, MCP-1 binding to the GPCR chemokine receptor CCR2, strongly induces phosphorylation of PKB/Akt, which is effectively inhibited by AS-252424 at IC <sub>50</sub> values as low as 0.4 $\mu$ M. In contrast, induction of PKB/Akt phosphorylation by colony stimulating factor (CSF-1), binding to the growth factor receptor c-fms, is only blocked by AS-252424 at IC <sub>50</sub> values as high as 4.7 $\mu$ M[1].			
In Vivo	Oral administration of AS-252424 in a mouse model of acute peritonitis leads to a significant reduction of leukocyte recruitment. To evaluate the efficacy of AS-252424 to block leukocyte migration in vivo, it is tested in a mouse model of thioglycollate-induced peritonitis. Oral administration of AS-252424 at 10 mg/kg results in moderate reduction of neutrophil recruitment (35%±14%), almost matching the result observed in PI3K $\gamma$ -deficient mice. Given the short oral half-life of AS-252424 (t <sub>1/2</sub> =1 h) and relative high clearance (2.25 L/kg per h), investigations at later time points (24-48 h) to assess macrophage and monocyte recruitment are not undertaken. The modest pharmacokinetic properties do not appear to be caused by rapid oxidative metabolism (microsomal metabolism after 1 h: 16% (rat), 10% (human)) [1].			
Solvent&Solubility	<b>In Vitro:</b>  <b>DMSO : ≥ 57 mg/mL (186.71 mM)</b>  * "≥" means soluble, but saturation unknown.			
		<div>Solvent Mass Concentration</div>	1 mg	5 mg
	Preparing	1 mM	3.2757 mL	16.3784 mL
	Stock Solutions	5 mM	0.6551 mL	3.2757 mL
		10 mM	0.3276 mL	1.6378 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℃，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。				
References	[1]. Pomel V, et al. Furan-2-ylmethylene thiazolidinediones as novel, potent, and selective inhibitors of phosphoinositide 3-kinase gamma. J Med Chem. 2006 Jun 29;49(13):3857-71.			
实验参考:				
Cell Assay	After 3 h of starvation in serum-free medium, Raw-264 macrophages are pretreated with inhibitors (e.g., AS-252424, 1 nM, 10 nM, 100 nM, 1 $\mu$ M, 10 $\mu$ M and 100 $\mu$ M) or DMSO for 30 min and stimulated for 5 min with 50 nM C5a. PKB/Akt phosphorylation is monitored using phospho-Ser-473 Akt specific antibody and standard ELISA protocols[1]			

<b>Animal Administration</b>	<p>Mice[1]</p> <p>PI3K<math>\gamma</math> knockout (KO) mice are used. Oral administration of AS-252424 at 10 mg/kg is performed in PI3K<math>\gamma</math>-deficient mice.</p>
<b>Kinase Assay</b>	<p>A PI3K<math>\gamma</math> lipid kinase assay, based on the neomycin-coated scintillation proximity assay (SPA) bead technology, is performed in 384-well plates using ATP/[<math>\gamma</math><sup>33</sup>P]ATP and PtdIns. Kinase assays for IC<sub>50</sub> value determinations with PI3K<math>\alpha</math>, PI3K<math>\beta</math>, and PI3K<math>\delta</math> are carried out[1]</p>
<b>References</b>	<p>[1]. <u>Pomel V, et al. Furan-2-ylmethylene thiazolidinediones as novel, potent, and selective inhibitors of phosphoinositide 3-kinase gamma. J Med Chem. 2006 Jun 29;49(13):3857-71.</u></p>



源叶生物