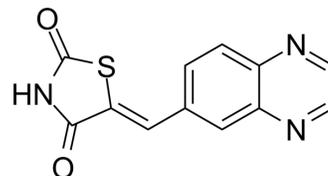


## AS-605240

<b>Cat. No.:</b>	HY-10109		
<b>CAS No.:</b>	648450-29-7		
<b>Molecular Formula:</b>	C <sub>12</sub> H <sub>7</sub> N <sub>3</sub> O <sub>2</sub> S		
<b>Molecular Weight:</b>	257.27		
<b>Target:</b>	PI3K; Autophagy		
<b>Pathway:</b>	PI3K/Akt/mTOR; Autophagy		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : 3.33 mg/mL (12.94 mM; ultrasonic and warming and heat to 80°C)  
 H<sub>2</sub>O : 2.78 mg/mL (10.81 mM; ultrasonic and warming and adjust pH to 10 with NaOH and heat to 60°C)

Preparing Stock Solutions	Solvent Concentration	Mass		
		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

Please refer to the solubility information to select the appropriate solvent.

#### In Vivo

- Add each solvent one by one: 0.5% CMC-Na >> 0.5% Tween-80  
Solubility: 6.25 mg/mL (24.29 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
Solubility: 2.5 mg/mL (9.72 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
Solubility: ≥ 2.5 mg/mL (9.72 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### 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

PI3Kγ 7.8 nM (K <sub>i</sub> )	PI3Kγ 8 nM (IC <sub>50</sub> )	PI3Kα 60 nM (IC <sub>50</sub> )	PI3Kβ 270 nM (IC <sub>50</sub> )
PI3Kδ 300 nM (IC <sub>50</sub> )	Autophagy		

<b>In Vitro</b>	<p>AS-605240 is an isoform-selective inhibitor of PI3K<math>\gamma</math> with over 30-fold selectivity for PI3K<math>\delta</math> and <math>\beta</math>, and 18- and 7.5-fold selectivity over PI3K<math>\alpha</math>, 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 <math>\mu</math>M. 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 GSK3<math>\alpha</math> and <math>\beta</math> in a concentration-dependent manner. AS605240 suppresses in a dose-dependent manner the proliferation of BDC2.5 CD4<sup>+</sup> T cells<sup>[2]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>In Vivo</b>	<p>AS-605240 (30 mg/kg BW, per os, every 12 h) markedly decreases FoxM1 expression in mouse lungs and fails to restore vascular integrity<sup>[1]</sup>. 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<sup>[2]</sup>. 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<sup>[3]</sup>. 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-<math>\alpha</math> and IL-1<math>\beta</math> in BALF to 132.7<math>\pm</math>11.2 pg/mL and 49.2<math>\pm</math>11.3 pg/mL in 25 mg/kg AS605240 + BLM group and 131.3<math>\pm</math>10.7 and 49.6<math>\pm</math>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<sup>[4]</sup>.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## PROTOCOL

<b>Kinase Assay</b> <sup>[2]</sup>	<p>Human PI3K<math>\gamma</math> (100 ng) is incubated at RT with kinase buffer (10 mM MgCl<sub>2</sub>, 1 mM <math>\beta</math>-glycerophosphate, 1 mM DTT, 0.1 mM Na<sub>3</sub>VO<sub>4</sub>, 0.1% Na Cholate and 15 M ATP/100 nCi <math>\gamma</math>[<sup>33</sup>P]ATP, 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.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Cell Assay</b> <sup>[3]</sup>	<p>A total of 5<math>\times</math>10<sup>5</sup> BDC2.5 splenocytes and 50 <math>\mu</math>g/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 <math>\mu</math>Ci of tritiated thymidine [<sup>3</sup>H] to determine cell proliferation.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
<b>Animal Administration</b> <sup>[4]</sup>	<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.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

## CUSTOMER VALIDATION

- Cell Syst. 2020 Jan 22;10(1):66-81.e11.

- Cell Syst. 2020 Jan 22;10(1):66-81.e11.
- Drug Des Devel Ther. 2023 Apr 27;17:1275-1288.
- J Neurochem. 2022 Jun;161(6):478-491.
- Molecules. 2020 Apr 23;25(8):1980.

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## REFERENCES

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- [1]. Huang X, et al. Endothelial p110 $\gamma$ PI3K Mediates Endothelial Regeneration and Vascular Repair After Inflammatory Vascular Injury. *Circulation*. 2016 Mar 15;133(11):1093-103.
- [2]. Camps M, et al. Blockade of PI3K $\gamma$  suppresses joint inflammation and damage in mouse models of rheumatoid arthritis. *Nat Med*. 2005 Sep;11(9):936-43.
- [3]. Azzi J, et al. The novel therapeutic effect of phosphoinositide 3-kinase- $\gamma$  inhibitor AS605240 in autoimmune diabetes. *Diabetes*. 2012 Jun;61(6):1509-18. Epub 2012 Mar 8.
- [4]. 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.
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**Caution: Product has not been fully validated for medical applications. For research use only.**

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