产品名称：YM201636
产品别名：YM-201636

生物活性：

Description	YM-201636 is a potent and selective PIKfyve inhibitor with an IC_{50} of 33 nM. YM-201636 also inhibits p110α with IC_{50} of 3.3 μM.		
IC_{50} & Target [1]	PIKfyve	p110α	Autophagy
	33 nM (IC_{50})	3.3 μM (IC_{50})	
In Vitro	Acute treatment of cells with YM-201636 shows that the PIKfyve pathway is involved in the sorting of endosomal transport, with inhibition leading to the accumulation of a late endosomal compartment and blockade of retroviral exit. The yeast orthologue of PIKfyve, Fab1, is found to be insensitive to YM-201636 (IC50>5 μM). YM-201636 does not inhibit a type IIγ PtdInsP kinase even at 10 μM and inhibits a mouse type Iα PtdInsP kinase with an IC50>2 μM[1]. YM-201636 almost completely inhibits basal and insulin-activated 2-deoxyglucose uptake at doses as low as 160 nM, with IC50=54 nM for the net insulin response. YM-201636 also completely inhibits insulin-dependent activation of class IA PI 3-kinase[2]. At low doses (10-25 nM), YM-201636 inhibits preferentially PtdIns5P rather than PtdIns(3,5)P2 production, whereas at higher doses, the two products are similarly inhibited. YM-201636 at 160 nM inhibits PtdIns5P synthesis twice more effectively compared with PtdIns(3,5)P2 synthesis[3]. MDCK cells treated with YM-201636 accumulate the tight junction protein claudin-1 intracellularly. YM-201636 treatment blocks the continuous recycling of claudin-1/claudin-2 and delays epithelial barrier formation[4].		

Solvent&Solubility

In Vitro:

DMSO : ≥ 47 mg/mL (100.54 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1391 mL	10.6956 mL	21.3913 mL
	5 mM	0.4278 mL	2.1391 mL	4.2783 mL
	10 mM	0.2139 mL	1.0696 mL	2.1391 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 (5.35 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (5.35 mM，饱和度未知) 的澄清溶液。

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。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (5.35 mM); Suspended solution; Need ultrasonic 此方案可获得 2.5 mg/mL (5.35 mM)的均匀悬浊液，悬浊液可用于口服和腹腔注射。 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。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (5.35 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。 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。
References	[1]. Jefferies HB, et al. A selective PIKfyve inhibitor blocks PtdIns(3,5)P(2) production and disrupts endomembrane transport and retroviral budding. EMBO Rep, 2008, 9(2), 164-170. [2]. Ikonomov OC, et al. YM-201636, an inhibitor of retroviral budding and PIKfyve-catalyzed PtdIns(3,5)P2 synthesis, halts glucose entry by insulin in adipocytes. Biochem Biophys Res Commun. 2009 May 8;382(3):566-70. [3]. Sbrissa D, et al. Functional dissociation between PIKfyve-synthesized PtdIns5P and PtdIns(3,5)P2 by means of the PIKfyve inhibitor YM-201636. Am J Physiol Cell Physiol. 2012 Aug 15;303(4):C436-46. [4]. Dukes JD, et al. The PIKfyve inhibitor YM-201636 blocks the continuous recycling of the tight junction proteins claudin-1 and claudin-2 in MDCK cells. PLoS One. 2012;7(3):e28659.

实验参考：

Cell Assay	YM-201636 is dissolved in DMSO and diluted with DMEM and added to cells at a final concentration of 800 nM. Cells are treated with YM-201636 or a DMSO control for 2 h. For TER measurements cells are plated at confluency on Transwell permeable polyester filters (0.4 μm pore size) with surface area of 0.33 cm^2. Media is changed ever 2-3 days and cells are grown for 7 days prior to TER measurements[4].
Kinase Assay	Following 3T3L1 adipocyte serum-starvation and insulin stimulation, cell lysates containing protease inhibitors are clarified and then subjected to immunoprecipitation with anti-PIKfyve antibodies. Washed beads are mixed with 100 μM PtdIns and preincubated for 15 min with YM-201636 (100 nM) or vehicle in the assay buffer (50 mM Tris-HCl, pH 7.5, 1 mM EGTA and 10 mM MgCl2). The kinase assay (50 μL final volume) is carried out for 15 min at 37 °C with 15 μM ATP and [γ-^{32}P]ATP (30 μCi). Lipids are extracted, spotted on TLC glass plates (250 μm), resolved by a chloroform/methanol/water/ammonia solvent system and detected by autoradiography[2].
References	[1]. Jefferies HB, et al. A selective PIKfyve inhibitor blocks PtdIns(3,5)P(2) production and disrupts endomembrane transport and retroviral budding. EMBO Rep, 2008, 9(2), 164-170. [2]. Ikonomov OC, et al. YM-201636, an inhibitor of retroviral budding and PIKfyve-catalyzed PtdIns(3,5)P2 synthesis, halts glucose entry by insulin in adipocytes. Biochem Biophys Res Commun. 2009 May 8;382(3):566-70. [3]. Sbrissa D, et al. Functional dissociation between PIKfyve-synthesized PtdIns5P and PtdIns(3,5)P2 by means of the PIKfyve inhibitor YM-201636. Am J Physiol Cell Physiol. 2012 Aug

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