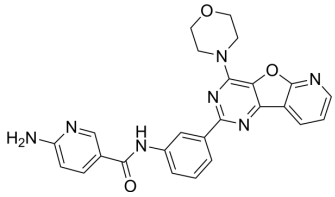
YM-201636

Cat. No.:	HY-13228
CAS No.:	371942-69-7
Molecular Formula:	$C_{25}H_{21}N_7O_3$
Molecular Weight:	467.48
Target:	PIKfyve; PI3K; Autophagy; Influenza Virus
Pathway:	PI3K/Akt/mTOR; Autophagy; Anti-infection
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 47 mg/mL (100.54 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / 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

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.5 mg/mL (5.35 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.35 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

YM-201636 is a potent and selective PIKfyve inhibitor with an IC_{50} of 33 nM. YM-201636 also inhibits p110α with an IC_{50} of 3.3 μM. YM-201636 inhibits retroviral replication.

IC_{50} & Target	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 (IC_{50}>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 IC_{50}>2 μM[1]. YM-201636 almost completely inhibits basal and insulin-activated 2-deoxyglucose uptake at doses as low as 160 nM, with IC_{50}=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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [2]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [4]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Commun. 2023 Jan 14;14(1):226.
- Nat Commun. 2020 Mar 27;11(1):1620.
- J Med Virol. 2023 Jan 25.
- J Thromb Haemost. 2020 Jul;18(7):1756-1772.
- Ecotoxicol Environ Saf. 25 December 2021, 112993.

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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.

[5]. Ikonomov OC, et al. YM201636, 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.

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