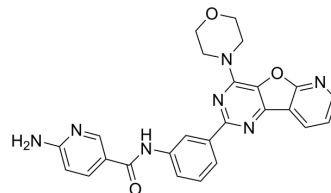


YM-201636

Cat. No.:	HY-13228		
CAS No.:	371942-69-7		
Molecular Formula:	C ₂₅ H ₂₁ N ₇ O 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	Solvent Concentration	Mass		
		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

- 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
- 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
- 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 IC₅₀ of 33 nM. YM-201636 also inhibits p110α with an IC₅₀ of 3.3 μM. YM-201636 inhibits retroviral replication.

IC₅₀ & Target

PIKfyve 33 nM (IC ₅₀)	p110α 3.3 μM (IC ₅₀)	Autophagy
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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 ($IC_{50} > 5 \mu M$). YM-201636 does not inhibit a type II γ PtdInsP kinase even at $10 \mu M$ and inhibits a mouse type I α PtdInsP kinase with an $IC_{50} > 2 \mu M$ ^[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 $100 \mu M$ 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 ($50 \mu L$ final volume) is carried out for 15 min at $37 ^\circ C$ with $15 \mu M$ ATP and [γ -³²P]ATP ($30 \mu Ci$). Lipids are extracted, spotted on TLC glass plates ($250 \mu m$), 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 ($0.4 \mu m$ pore size) with surface area of $0.33 cm^2$. Media is changed every 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)P₂ production and disrupts endomembrane transport and retroviral budding. EMBO Rep, 2008, 9(2), 164-170.

[2]. Ikononov 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]. Ikononov 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.

Caution: Product has not been fully validated for medical applications. For research use only.

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