YM201636

PIKfyve Inhibitor

Catalog code: inh-ym20

https://www.invivogen.com/ym201636

For research use only

Version 19K28-MM

PRODUCT INFORMATION

Contents

- 5 mg YM201636

Storage and stability

- YM201636 is provided as a solid and shipped at room temperature. Upon receipt, store at -20°C. Solid product is stable for 1 year at -20°C.
- Upon resuspension, prepare aliquots of YM201636 and store at -20°C. Avoid repeated freeze-thaw cycles. Resuspended product is stable for 3 months at -20°C when properly stored.

Quality control

- Purity: >97% (UHPLC)
- The inhibitory activity has been validated using cellular assays.
- The absence of bacterial contamination (e.g. lipoproteins and endotoxins) has been confirmed using HEK-Blue™ TLR2 and HEK-Blue™ TLR4 cells.

DESCRIPTION

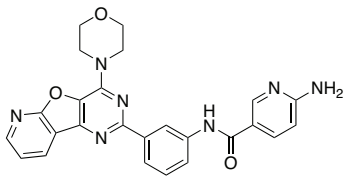
YM201636 is a potent inhibitor of mammalian phosphatidylinositol phosphate kinase PIP5KIII (PIKfyve)[1]. PIKfyve is the sole enzyme for PtdIns(3,5)P2 biosynthesis that regulates a number of intracellular membrane trafficking pathways[1]. Inhibition of PIKfyve with YM201636 disrupts endomembrane transport and inhibits retroviral release from infected cells[1,2]. YM201636 can also disrupt glucose homeostasis by halting glucose entry by insulin and inhibiting activation of PI3-kinase[2]. In neurons, YM201636 promotes cell death via a caspase-independent mechanism, and is associated with alterations in autophagy[3].

YM201636 blocks TLR9-signaling by preventing endosomal translocation of CpG-containing oligodeoxynucleotides (CpG ODNs), thus preventing co-localization of agonist and receptor[4]. Further studies reveal that YM201636 also inhibits TLR3-, TLR4- and CDS (cytosolic DNA sensor)-signaling. YM201636 blocks TBK-1/IRF3-mediated type I interferon (IFN) production without affecting NF-κB dependent cytokine production[5].

1. Jefferies H. *et al.*, 2008. A selective PIKfyve inhibitor blocks PtdIns(3,5)P(2) production and disrupts endomembrane transport and retroviral budding. EMBO Rep. 2008 Feb;9(2):164-70. **2. Ikonomov O. *et al.*, 2009.** YM201636, an inhibitor of retroviral budding and PIKfyve-catalyzed PtdIns(3,5)P2 synthesis, halts glucose entry by insulin in adipocytes. BBRC. 382(3):566-70. **3. Martin S. et al., 2013.** Inhibition of PIKfyve by YM-201636 dysregulates autophagy and leads to apoptosis-independent neuronal cell death. PLoS One. 8(3):e60152. **4. Hazeki K. et al., 2013.** PIKfyve regulates the endosomal localization of CpG oligodeoxynucleotides to elicit TLR9-dependent cellular responses. PLoS One. 8(9):e73894. **5. Kawasaki T. *et al.*, 2013.** The second messenger phosphatidylinositol-5-phosphate facilitates antiviral innate immune signaling. Cell Host Microbe. 14(2):148-58.

CHEMICAL PROPERTIES

Working concentration: 0.5 - 5 µM
CAS number: 371942-69-7
Synonym: 6-amino-N-[3-[4-(4-morpholinyl)pyrido[3',2':4,5]furo[3,2-d]pyrimidin-2-yl]phenyl]-3-pyridinecarboxamide
Formula: $C_{25}H_{21}N_7O_3$
Molecular weight: 467.5 g/mol
Solubility: 20 mg/ml in DMSO
Structure:



METHODS

Preparation of 10 mM (4.7 mg/ml) stock solution

1. Add 1.07 ml DMSO to 5 mg YM201636.
2. Vortex until completely dissolved.
3. Prepare aliquots and store at -20°C.
4. Further dilutions can be prepared with aqueous buffers.

In vitro inhibition of TLR9 activity:

The activity of YM201636 on TLR9 can be tested using HEK-Blue™ mTLR9 cells. These cells express the mouse TLR9 gene and an NF-κB-inducible secreted embryonic alkaline phosphatase (SEAP) reporter gene. For more information, visit: https://www.invivogen.com/hek-blue-mtlr9.

1. Pre-incubate HEK-Blue™ mTLR9 cells (4 x10^5 cells/well) with YM201636 (0.5 - 5 µM) in a 96-well plate for 1 hour at 37°C.
2. Stimulate cells with a TLR9 agonist, such as ODN1826 (10-100 ng/ml) in the presence or absence of YM201636 (0.5 - 5 µM).
3. Incubate from 6 hours to overnight at 37°C.
4. Determine the inhibition of TLR9 activity by SEAP expression using QUANTI-Blue™ Solution, a SEAP detection medium.

RELATED PRODUCTS

Product	Description	Cat. Code
HEK-Blue™ mTLR9 Cells	TLR9 reporter cells	hkb-mtlr9
QUANTI-Blue™ Solution	SEAP detection medium	rep-qbs
ODN1826	Murine TLR9 agonist	tlrl-1826

TECHNICAL SUPPORT
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