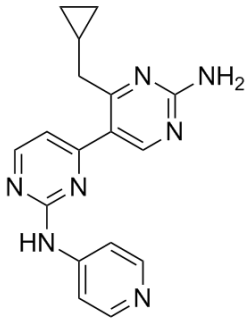
Vps34-PIK-III



Cat. No.:	HY-12794
CAS No.:	1383716-40-2
Molecular Formula:	$C_{17}H_{17}N_7$
Molecular Weight:	319.36
Target:	PI3K; Autophagy
Pathway:	PI3K/Akt/mTOR; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 6 months -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 31 mg/mL (97.07 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	3.1313 mL	15.6563 mL	31.3126 mL
5 mM	0.6263 mL	3.1313 mL	6.2625 mL
10 mM	0.3131 mL	1.5656 mL	3.1313 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 (7.83 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (7.83 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (7.83 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Vps34-PIK-III is a potent and selective inhibitor of VPS34 with an IC_{50} of 18 nM.

IC_{50} & Target

Vps34	PI(3)Kδ	PI(3)Kγ	PI(3)Kα
18 nM (IC_{50})	1.2 μM (IC_{50})	3.04 μM (IC_{50})	3.96 μM (IC_{50})

Autophagy

In Vitro	PIK-III is a selective inhibitor of VPS34 that binds a unique hydrophobic pocket not present in related kinases such as PI3Kα. PIK-III is at least 100-fold-selective for VPS34 over related lipid kinases such as PI3K and the protein kinase mTOR. PIK-III acutely inhibits autophagy and de novo lipidation of LC3, and leads to the stabilization of autophagy substrates. In H4 cells expressing the mCherry-GFP-LC3 reporter PIK-III inhibits the formation of mCherry-positive autolysosomes and increases the cytosolic signal of LC3 under basal conditions and when autophagy is induced with the mTOR inhibitor AZD8055. PIK-III prevents the turnover of GFP-tagged p62 under basal conditions and when autophagy is activated. PIK-III treatment leadsto an increase in the levels of LC3-I in H4 and PSN1 cells[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The DFX-induced NCOA4-dependent turnover of FTH1 and FTL is blocked with PIK-III suggesting an autophagy-dependent process[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Honda A, et al. Potent, Selective, and Orally Bioavailable Inhibitors of VPS34 Provide Chemical Tools to Modulate Autophagy in Vivo. ACS Med Chem Lett. 2015 Nov 13;7(1):72-6.

[2]. Dowdle WE, et al. Selective VPS34 inhibitor blocks autophagy and uncovers a role for NCOA4 in ferritin degradation and iron homeostasis in vivo. Nat Cell Biol. 2014 Nov;16(11):1069-79.

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