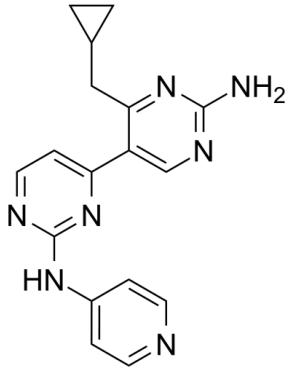
Data Sheet

Product Name:	Vps34-PIK-III
Cat. No.:	CS-6326
CAS No.:	1383716-40-2
Molecular Formula:	C17H17N7
Molecular Weight:	319.36
Target:	Autophagy; PI3K
Pathway:	Autophagy; PI3K/Akt/mTOR
Solubility:	DMSO : ≥ 31 mg/mL (97.07 mM)



BIOLOGICAL ACTIVITY:

Vps34-PIK-III is a potent and selective inhibitor of **VPS34** with an **IC_{50}** of 18 nM. IC50 & Target: IC50: 18 nM (VPS34)[1][2], 3.96 μM (PI3Kα), 1.2 μM (PI3Kδ), 3.04 μM (PI3Kγ)[2] **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 leads to an increase in the levels of LC3-I in H4 and PSN1 cells[2]. **In Vivo:** The DFX-induced NCOA4-dependent turnover of FTH1 and FTL is blocked with PIK-III suggesting an autophagy-dependent process[2].

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.

CAIndexNames:

[4,5'-Bipyrimidine]-2,2'-diamine, 4'-(cyclopropylmethyl)-N2-4-pyridinyl-

SMILES:

NC1=NC=C(C2=CC=NC(NC3=CC=NC=C3)=N2)C(CC4CC4)=N1

Tel: 732-484-9848 Fax: 888-484-5008 E-mail: sales@ChemScene.com

Address: 1 Deer Park Dr, Suite Q, Monmouth Junction, NJ 08852, USA