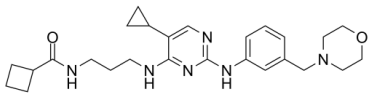
Data Sheet

Product Name:	MRT67307
Cat. No.:	CS-0249
CAS No.:	1190378-57-4
Molecular Formula:	$C_{26}H_{36}N_6O_2$
Molecular Weight:	464.60
Target:	Autophagy; IKK; ULK
Pathway:	Autophagy; NF-κB
Solubility:	DMSO : ≥ 100 mg/mL (215.24 mM)



BIOLOGICAL ACTIVITY:

MRT67307 is a dual inhibitor of the **IKKε** and **TBK-1** with **IC_{50}**s of 160 and 19 nM, respectively[1]. MRT67307 also inhibits **ULK1** and **ULK2** with **IC_{50}**s of 45 and 38 nM, respectively. MRT67307 also blocks **autophagy** in cells[2]. IC50 & Target: IC50: 160 nM (IKKε, ATP), 19 nM (TBK-1, ATP), 45 nM (ULK1), 38 nM (ULK2) **In Vitro:** MRT67307 inhibits IKKε and TBK1 with IC_{50} values of 160 and 19 nM when assayed at 0.1 mM ATP in vitro, but did not inhibit IKKα or IKKβ even at 10 μM[1].

MRT67307 (2 μM) prevents the phosphorylation of IRF3 in bone-marrow-derived macrophages (BMDMs). MRT67307 (2 μM) dose not suppresse the activation of JNK or p38 MAPK by poly(I:C)[1].

MRT67307 (1 nM-10 μM) prevents the production of IFNβ in macrophages[1].

MRT67307 (10 μM) is sufficient to reduce phospho-ATG13 to control levels[2].

MRT67307 (10 μM) blocks autophagy in mouse embryonic fibroblasts (MEFs)[2].

MRT67307 (5 μM; 4 h) abrogates TBK1/IKKε-induced CYLD phosphorylation in 293T cells[3].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: [3]Cells are rinsed in ice-cold PBS and extracted in lysis buffer (50 mM Tris·HCl at pH 7.4, 1 mM EDTA, 1 mM EGTA, 50 mM NaF, 5 mM sodium pyrophosphate, 10 mM sodium β-glycerol 1-phosphate, 1 mM DTT, 1 mM sodium orthovanadate, 0.27mol/Lsucrose, 1% (vol/vol) Triton X-100, 1 μg/mL aprotinin, 1 μg/ mL leupeptin, and 1 mM phenylmethylsulphonyl fluoride). Cell extracts are clarified by centrifugation at 14,000 × g for 10 min at 4°C, and protein concentrations are determined by using the Bradford assay. FLAG-CRTC3 is purified on anti-FLAG M2 agarose, whereas endogenous CRTC3 is immunoprecipitated from cell extracts by using anti-CRTC3 raised against the peptide CWKEEKHPGFR (S277D bleed 2) and coupled to Protein GSepharose. To detect proteins in cell lysates, 20 μg of protein extract is separated by SDS/PAGE. After transfer to PVDF membranes, proteins are detected by immunoblotting and visualized by treating the blots with ECL followed by autoradiography. The following antibodies are used for immunoblotting: pSer133 CREB, pSer171 CRTC2, total CRTC2, GAPDH, total STAT3, pTyr705 STAT3, FLAG (M2 clone), CRTC3, HA (3F10), and 14-3-3; and antibodies against pSer329 (S256D bleed 2) and pSer370 (S253D bleed 2) of CRTC3 are raised against the phosphopeptides GLQSSRpSNPSIQ and RLFSLpSNPSLST.

References:

[1]. Clark K, et al. Novel cross-talk within the IKK family controls innate immunity. Biochem J. 2011 Feb 15;434(1):93-104.

[2]. Petherick KJ, et al. Pharmacological inhibition of ULK1 kinase blocks mammalian target of rapamycin (mTOR)-dependent autophagy. J Biol Chem. 2015 May 1;290(18):11376-83.

[3]. Zhu Z, et al. Inhibition of KRAS-driven tumorigenicity by interruption of an autocrine cytokine circuit. 26.37Cancer Discov. 2014 Apr;4(4):452-65.

CAIndexNames:

Cyclobutanecarboxamide, N-[3-[[5-cyclopropyl-2-[[3-(4-morpholinylmethyl)phenyl]amino]-4-pyrimidinyl]amino]propyl]-

SMILES:

O=C(NCCCNC1=NC(NC2=CC=CC(CN3CCOCC3)=C2)=NC=C1C4CC4)C5CCC5

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