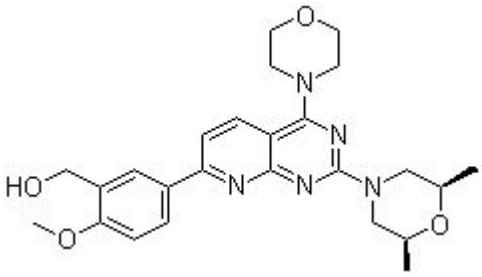
Product Introduction

KU-0063794

KU-0063794 is a potent and highly specific dual-mTOR inhibitor of **mTORC1** and **mTORC2** with **IC50** of ~10 nM; no effect on PI3Ks.

Technical Data:

Molecular Weight (MW):	465.54	
Formula:	$C_{25}H_{31}N_5O_4$	
Solubility (25°C) * <1 mg/ml means slightly soluble or insoluble:	DMSO 16 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃Powder	
	6 months-80℃in DMSO	
CAS No.:	938440-64-3	

Biological Activity

Compared with the mTOR inhibitor PP242, KU-0063794 exhibits higher specificity for mTOR, as being inactive against PI3Ks or 76 other kinases. In HEK-293 cells, KU-0063794 at 30 nM is sufficient to rapidly ablate S6K1 activity by blocking the phosphorylation of the hydrophobic motif (Thr^{389}) and subsequently the phosphorylation of the T-loop residue (Thr^{229}). In case of IGF1 stimulation of serum-starved HEK-293 cells, 300 nM of KU-0063794 is needed to inhibit the S6K1 activity by ~90%. KU-0063794 at 100-300 nM also completely inhibits the amino-acid-induced phosphorylation of S6K1 and S6 protein. Similar to S6K1,

KU-0063794 inhibits the phosphorylation of mTORC1 at Ser^{2448} and mTORC2 at Ser^{2481} in a dose-dependent and time-dependent manner. In the presence of serum or following IGF1 stimulation, KU-0063794 induces a dose-dependent inhibition of the activity and phosphorylation of Akt at Ser^{473} and unexpected Thr^{308} as well as the phosphorylation of the Akt substrates PRAS40 at Thr^{246}, GSK3α/GSK3β at Ser^{21}/Ser^{9} and Foxo-1/3a at Thr^{24}/Thr^{32}. KU-0063794 but not rapamycin inhibits SGK1 activity and Ser^{422} phosphorylation as well as its physiological substrate NDGR1 in a dose-dependent manner, to the same extent as S6K1 and Akt phosphorylation, whereas KU-0063794 dose not inhibit phorbol ester induced ERK or RSK phosphorylation and RSK activation. Compared with rapamycin, KU-0063794 exhibits more significant potency to induce the complete dephosphorylation of 4E-BP1 at Thr^{37}, Thr^{46} and Ser^{65}. KU-0063794 inhibits cell growth of both wild-type and mLST8-deficient MEFs and induces a G1 cell cycle arrest, more significantly than rapamycin. [1]

References

[1] García-Martínez JM, et al. Biochem J, 2009, 421(1), 29

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