产品名称：Compound 401
产品别名：Compound 401

生物活性：

Description	Compound 401 is a synthetic inhibitor of DNA-PK (IC_{50} = 0.28 μM) that also targets mTOR but not PI3K in vitro.	
IC_{50} & Target	DNA-PK	mTOR
	0.28 μM (IC_{50})	5.3 μM (IC_{50})
In Vitro	Compound 401 is a potent inhibitor of DNA-PK (IC50=0.28 μM). Compound 401 is reported to be a poor inhibitor of PI3K, ATM, and ATR in vitro, but it is active against mTOR. Compound 401 shows activity against mTOR (IC50=5.3 μM) but not p110α/p85α PI3K (IC50>100 μM). Treatment of cells with Compound 401 blocks the phosphorylation of sites modified by mTOR-Raptor and mTOR-Rictor complexes (ribosomal protein S6 kinase 1 Thr389 and Akt Ser473, respectively). By contrast, there is no direct inhibition of Akt Thr308 phosphorylation, which is dependent on PI3K. Similar effects are also observed in cells that lack DNA-PK. Compound 401 inhibits immunoprecipitated epitope-tagged mTOR or endogenous mTOR in Raptor immunoprecipitates. In both cases, inhibition of 67% or 78% is obtained at 5 μM or 10 μM Compound 401, respectively. By contrast, dose response curves show that the p110α/p85α or p110β/p85α PI3K complexes are poorly inhibited by Compound 401 at these concentrations. The proliferation of TSC1-/- fibroblasts is inhibited in the presence of Compound 401, but TSC1+/+ cells are resistant[1].	
Solvent&Solubility	***In Vitro:*** **DMSO : 6 mg/mL (21.33 mM; Need ultrasonic and warming)**	

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	3.5548 mL	17.7740 mL	35.5480 mL
	5 mM	0.7110 mL	3.5548 mL	7.1096 mL
	10 mM	0.3555 mL	1.7774 mL	3.5548 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References	[1]. Ballou LM, et al. Inhibition of mammalian target of rapamycin signaling by 2-(morpholin-1-yl)pyrimido[2,1-alpha]isoquinolin-4-one. J Biol Chem. 2007 Aug 17;282(33):24463-70.

实验参考：

Kinase Assay	FreeStyle 293-F cells are transfected with cDNA for AU1-mTOR using 293fectin. Two days later, the cells are lysed and mTOR immunoprecipitates are prepared using AU1 antibody. Alternatively, the mTORC1 complex is immunoprecipitated from untransfected cells using Raptor antibody. Kinase activity in the immunoprecipitates is assayed in the presence of vehicle (DMSO) or Compound 401 (1, 5 and 10 μM) using bacterially expressed glutathione S-transferase (GST)-4E-BP1 as a substrate. Kinase reactions are stopped by boiling in SDS sample buffer and the samples are subjected to SDS-PAGE. Phosphorylated 4E-BP1 is detected by autoradiography. Radioactivity in the bands is quantified by scintillation counting[1].
	[1]. Ballou LM, et al. Inhibition of mammalian target of rapamycin signaling by

References	2-(morpholin-1-yl)pyrimido[2,1-alpha]isoquinolin-4-one. J Biol Chem. 2007 Aug 17;282(33):24463-70.