Product Data Sheet

Product Name: LYN-1604 hydrochloride
Cat. No.: GC36517

Chemical Properties

Cas. No.	2216753-86-3		
SMILES	ClC1=CC=C(C(CN2CCN(C(CN(CC(C)C)CC(C)C)=O)CC2)OCC3=CC=C(C=CC=C4)C4=C3)C(Cl)=C1.[H]Cl		
Formula	$C_{33}H_{44}Cl_3N_3O_2$	M.Wt	621.08
Solubility	DMSO: 100 mg/mL (161.01 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure	LYN-1604 hydrochloride		

Protocol

Kinase experiment:

The ULK1 kinase enzyme, substrate, ATP and compound (include LYN-1604) are diluted in kinase buffer. Then, 1 μL of compound or (5% DMSO), 2 μL of ULK1 kinase enzyme or purified wild-type and mutant ULK1 (K50A, L53A, Y89A) (10 ng), or 2 μL of MBP (0.1 μg/μL)/ATP (10 μM) mix are added to the wells of a 384 well low volume plate. After incubation at room temperature for 60 minutes, 5 μL of kinase assay reagent is added per well. The plates are incubated at room temperature for 40 minutes and then 10 μL of kinase detection reagent is added. After incubation at room temperature for 30 minutes, the luminescence is recorded. The EC50 values are calculated using nonlinear regression with normalized dose response fitting[1].

Cell experiment:

MCE-7, MDA-MB-231 and MDA-MB-468 cells are treated with LYN-1604, cell viability is measured by the MTT assay[1].

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Animal experiment:

Mice: Mice are injected subcutaneously with MDA-MB-231 cells. When the tumors reach 100 mm3 in volume, the mice are divided into four groups. Three groups are treated with different doses of LYN-1604 once a day by intragastric administration for 14 days (low dose, 25 mg/kg; median dose, 50 mg/kg; high dose, 100 mg/kg), whereas the control group is treated with vehicle control. During the treatment, the tumor volumes and body weight are measured every day until the end of the study. At the end of treatment, all mice are sacrificed. The spleen, liver, kidney and tumor tissue are harvested, weighed, and photographed, then immediately frozen in liquid nitrogen or fixed in formalin[1].

References:

[1]. Zhang L, et al. Discovery of a small molecule targeting ULK1-modulated cell death of triple negative breast cancer in vitro and in vivo. Chem Sci. 2017 Apr 1;8(4):2687-2701.

Background

LYN-1604 is an activator of unc-51-like kinase 1 (ULK1; EC_{50} = 18.94 nM).[1] It increases Beclin 1, LC3-II, and total LC3 protein levels and reduces levels of p62 in human MDA-MB-231 triple-negative breast cancer (TNBC) cells in a concentration-dependent manner, indicating an increase in autophagy. It also increases the cleavage of the pro-apoptotic protein caspase-3. LYN-1604 decreases the viability of MDA-MB-231 cells *in vitro* (IC_{50} = 1.66 μM), an effect that can be reversed by the autophagy inhibitor 3-methyladenine . LYN-1604 (25, 50, and 100 mg/kg) reduces tumor growth in an MDA-MB-231 mouse xenograft model.

1.Zhang, L., Fu, L., Zhang, S., et al.Discovery of a small molecule targeting ULK1-modulated cell death of triple negative breast cancer in vitro and in vivoChem. Sci.8(4)2687-2701(2017)

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