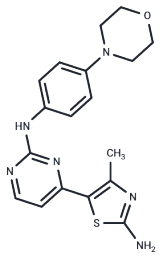
Data Sheet (Cat.No.T6458)

TargetMol

CYC-116

Chemical Properties



CAS No. : 693228-63-6

Formula: C18H20N6OS

Molecular Weight: 368.46

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	CYC116 is a potent inhibitor of Aurora A/B with Ki of 8.0 nM/9.2 nM, is less potent to VEGFR2 (Ki of 44 nM), with 50-fold greater potency than CDKs, not active against PKA, Akt/PKB, PKC, no effect on GSK-3α/β, CK2, Plk1 and SAPK2A. Phase 1.
Targets(IC50)	FLT,CDK,Aurora Kinase,S6 Kinase,VEGFR
In vitro	The most Aurora-selective CYC116 shows inhibitory effect on Aurora A and B kinases 50-fold more potently than any of the CDKs assayed. [1] CYC116 is initially screened against a panel of human leukemia and solid tumor cell lines using an MTT antiproliferative assay. The results show that CYC116 has broad-spectrum antitumor activity and shows specific cytotoxicity against the acute myelogenous leukemia cell line MV4-11 with IC50 of 34 nM. [1] In addition, anti-proliferative activity of CYC116 is found to be associated with Aurora A and B modulation such as, inhibition of Aurora autophosphorylation, reduction of histone H3 phosphorylation, polyploidy, followed by cell death, resulting from a failure in cytokinesis. [1]
In vivo	Mice bearing subcutaneous NCI-H460 xenografts are given CYC116 orally for 5 days, at dose levels of 75 and 100 mg/kg q.d. It leads to tumor growth delays of 2.3 and 5.8 days, which translated into specific growth delays of 0.32 and 0.81, respectively. [1]
Kinase Assay	Kinase Assays: Aurora A kinase assays are performed using a 25 μL reaction volume (25 mM β-glycerophosphate, 20 mM Tris/HCl, pH 7.5, 5 mM EGTA, 1 mM DTT, 1 mM Na3VO4, 10 μg of kemptide (peptide substrate)). Recombinant Aurora A kinase is diluted in 20 mM Tris/HCl, pH 8, containing 0.5 mg/mL BSA, 2.5% glycerol, and 0.006% Brij-35. Reactions are started by the addition of 5 μL Mg/ATP mix (15 mM MgCl2, 100 μM ATP, with 18.5 kBq γ-32P-ATP per well) and incubated at 30°C for 30 minutes before termination with 25 μL of 75 mM H3PO4. Aurora B kinase assays are performed like Aurora A except that prior to use, Aurora B is activated in a separate reaction at 30°C for 60 minutes with inner centromere protein.
Cell Research	Standard MTT assays are performed. In short, cells are seeded into 96-well plates according to doubling time and incubated overnight at 37°C. Test compounds are made up in DMSO, a 3-fold dilution series is prepared in 100 μL of cell medium, added to cells (in triplicates) and incubated for 72 or 96 hours at 37°C. MTT is made up as a stock of 5 mg/mL in cell medium, and the solution is filter-sterilized. Medium is removed from the cells followed by a wash with PBS. MTT solution is then added at 20 μL/well and incubated in the dark at 37°C for 4 hours. MTT solution is removed and cells are again washed with 200 μL of PBS. MTT dye is solubilized with 200 μL/well of DMSO by

agitation. Absorbance is read at 540 nm and data analyzed using curve-fitting software to determine IC50 values. (Only for Reference)

Solubility Information

Solubility	DMSO: < 1 mg/mL H2O: < 1 mg/mL (insoluble or slightly soluble), Ethanol: < 1 mg/mL (insoluble or slightly soluble), (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.714 mL	13.570 mL	27.140 mL
5 mM	0.5428 mL	2.714 mL	5.428 mL
10 mM	0.2714 mL	1.357 mL	2.714 mL
50 mM	0.0543 mL	0.2714 mL	0.5428 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Reference

Wang S, et al. J Med Chem. 2010, 53(11), 4367-4378.