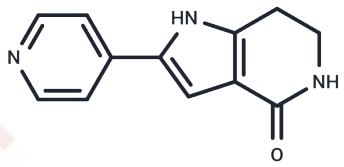
Data Sheet (Cat.No.T6206)

TargetMol

PHA-767491

Chemical Properties



CAS No. : 845714-00-3

Formula: C12H11N3O

Molecular Weight: 213.24

Appearance: no data available

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

Biological Description

Description	PHA-767491 (CAY10572) is a potent ATP-competitive dual Cdc7/CDK9 inhibitor with IC50 of 10 nM and 34 nM, respectively.
Targets(IC50)	CDK,Cholecystokinin Receptor,GSK-3
In vitro	PHA-767491 reduces Chk1 phosphorylation and increases in situ apoptosis in tumor tissues from nude mouse HCC xenograft slices.
In vivo	PHA-767491 inhibits cell proliferation in two cell lines, achieving IC50 values of 0.64 μM in HCC1954 cells and 1.3 μM in Colo-205 cells. Additionally, PHA-767491 (2 μM) completely abolishes Mcm2 phosphorylation in HCC1954 cells within 24 hours. In combination with 5-FU, PHA-767491 exhibits enhanced cytotoxic effects in HCC cells, inducing significant apoptosis characterized by increased activation of caspase-3 and poly (ADP-ribose) polymerase fragmentation. It directly counteracts 5-FU-induced phosphorylation of Chk1 and reduces the expression of the anti-apoptotic protein, myeloid cell leukemia sequence 1 (Mcl-1). Furthermore, PHA-767491 (0-10 μM) reduces the viability of glioblastoma cells in a time- and dose-dependent manner, with IC50 values around 2.5 μM in U87-MG and U251-MG cells.
Kinase Assay	20 ng of purified human DDK, together with increasing concentrations of each DDK inhibitor is pre-incubated for 5 min. Then 10 μCi (γ)-32P ATP and 1.5 μM cold ATP are added in a buffer containing 50 mM Tris-HCl (pH 7.5), 10 mM MgCl2, and 1 mM DTT and incubated for 30 min at 30°C. The proteins are denatured in 1X Laemmli buffer at 100°C followed by SDS-PAGE and autoradiography on HyBlot CL film. DDK kinase activity is indicated by Auto-phosphorylation of DDK. 32P-labeled bands are quantified using ImageJ and the IC50 values are calculated using GraphPad.
Cell Research	For assays in 96 well plates 2500 cells are plated per well. After 24 hours, cells are treated with small molecule inhibitors and incubated for 72 hours at 37°C. Subsequently the cells are lysed and the ATP content is measured as an indicator of metabolically active cells using the CellTiter-Glo assay. IC50 values are calculated using the GraphPad software. For assays in six well plates, 100,000 cells are plated per well. After 24 hours, cells are treated with small molecule inhibitors and incubated for varying time points. Cells are trypsinized and a suspension is made in 5 mL of phosphate buffered saline. 30 μL of this suspension is mixed with 30 μL of CellTiter-Glo reagent followed by a 10-minute incubation at room temperature. Luminescence is measured using EnVision 2104 Multilabel Reader and BioTek Synergy Neo Microplate Reader.

Solubility Information

Solubility	H2O: < 1 mg/mL (insoluble or slightly soluble), DMSO: 40 mg/mL (187.58 mM),Sonication is recommended. 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	4.6896 mL	23.4478 mL	46.8955 mL
5 mM	0.9379 mL	4.6896 mL	9.3791 mL
10 mM	0.469 mL	2.3448 mL	4.6896 mL
50 mM	0.0938 mL	0.469 mL	0.9379 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

Montagnoli A, et al. Nat Chem Biol, 2008, 4(6), 357-365.
Yu Z, Deng P, Chen Y, et al. Inhibition of the PLK1-Coupled Cell Cycle Machinery Overcomes Resistance to Oxaliplatin in Colorectal Cancer. Advanced Science. 2021: 2100759.
Yecies D, et al. Blood, 2010, 115(16), 3304-3313.
Shan X, Jiang R, Gou D, et al.Identification of a diketopiperazine-based O-GlcNAc transferase inhibitor sensitizing hepatocellular carcinoma to CDK9 inhibition.The FEBS Journal.2023
Liu S, Deng P, Yu Z, et al.CDC7 Inhibition Potentiates Antitumor Efficacy of PARP Inhibitor in Advanced Ovarian Cancer.Advanced Science.2024: 2403782.
Natoni A, et al. Mol Cancer Ther, 2011, 10(9), 1624-1634.