Product Data Sheet

Product Name: XL413
Cat. No.: GC18117

Chemical Properties

Cas. No.	1169558-38-6		
Chemical Name	8-chloro-2-[(2S)-pyrrolidin-2-yl]-1H-[1]benzofuro[3,2-d]pyrimidin-4-one		
SMILES	C1CC(NC1)C2=NC(=O)C3=C(N2)C4=C(O3)C=CC(=C4)Cl		
Formula	$C_{14}H_{12}ClN_3O_2$	M.Wt	289.72
Solubility	Soluble in DMSO	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	XL413		

Protocol

Kinase experiment:

20 ng of purified human DDK is pre-incubated with increasing concentrations of each DDK inhibitor 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. Auto-phosphorylation of DDK is used as an indicator of its kinase activity. 32P-labeled bands are quantified using ImageJ and the IC50 values are calculated using GraphPad.

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Cell experiment:

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.

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References:

[1]. Koltun ES, et al. Discovery of XL413, a potent and selective CDC7 inhibitor. Bioorg Med Chem Lett. 2012 Jun 1;22(11):3727-31.
[2]. Sasi NK, et al. The potent Cdc7-Dbf4 (DDK) kinase inhibitor XL413 has limited activity in many cancer cell lines and discovery of potential new DDK inhibitor scaffolds. PLoS One. 2014 Nov 20;9(11):e113300.

Background

XL413 is a potent, selective and ATP competitive inhibitor of Cdc7, with an IC50 of 3.4 nM, and also shows potent effect with IC50s of 215, 42 nM on CK2, PIM1, respectively, and an EC50 of 118 nM on pMCM.

XL413 inhibits the cell proliferation (IC50 = 2685 nM), decreases cell viability (IC50 = 2142 nM) and elicits the caspase 3/7 activity (EC50 = 2288 nM) in Colo-205 cells. XL413 also significantly inhibits the anchorage-independent growth of colo-205 in soft agar (IC50 = 715 nM)[1]. XL413 shows cytotoxic effects on tumors, with IC50 of 22.9 μM in

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HCC1954 cells and 1.1 μM in Colo-205 cells. XL413 induces apoptosis in the Colo-205 cells, but not in HCC1954 cells. XL413 is effective DDK inhibitors in vitro, with IC50 of 22.7 nM. XL413 is defective in inhibiting DDK-dependent Mcm2 phosphorylation in HCC1954 cells but is effective in Colo-205 cells[2].

XL413 (100 mg/kg, p.o.) shows excellent plasma exposures in mice and possesses good PK properties. XL413 (10, 30, or 100 mg/kg, p.o.) is well tolerated at all the doses, with no significant body weight loss[1].

References:
[1]. Koltun ES, et al. Discovery of XL413, a potent and selective CDC7 inhibitor. Bioorg Med Chem Lett. 2012 Jun 1;22(11):3727-31.
[2]. Sasi NK, et al. The potent Cdc7-Dbf4 (DDK) kinase inhibitor XL413 has limited activity in many cancer cell lines and discovery of potential new DDK inhibitor scaffolds. PLoS One. 2014 Nov 20;9(11):e113300.

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