Product Data Sheet

Product Name: CCT241533
Cat. No.: GC18053

Chemical Properties

Cas. No.	1262849-73-9		
Chemical Name	(E)-4-fluoro-6-(4-((4-(2-hydroxypropan-2-yl)pyrrolidin-3-yl)amino)-6,7-dimethoxyquinazolin-2(1H)-ylidene)cyclohexa-2,4-dienone		
SMILES	CC(C1CNCC1NC2=N/C(NC3=CC(OC)=C(OC)C=C32)=C4C=C(F)C=CC\4=O)(O)C		
Formula	$C_{23}H_{27}FN_4O_4$	M.Wt	442.48
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	CCT241533		

Protocol

Cell experiment [1]:

Cell lines	HeLa and HT-29 cells
Preparation method	Soluble in DMSO. General tips for obtaining a higher concentration: Please warm the tube at 37℃ for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20℃ for several months.

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

Product Data Sheet

Reaction Conditions	2.2 μmol/L for HeLa cells, 1.7 or 3 μmol/L for HT-29 cells; 24 hrs
Applications	In the presence of CCT241533, HeLa (2.2 μmol/L CCT241533) and HT-29 cells (1.7 μmol/L CCT241533) exhibited enhanced sensitivity to AG14447. In HeLa cells, the combination of CCT241533 (3 μmol/L) and Olaparib showed significant potentiation.

References:

[1]. Anderson VE, Walton MI, Eve PD, Boxall KJ, Antoni L, Caldwell JJ, Aherne W, Pearl LH, Oliver AW, Collins I, Garrett MD. CCT241533 is a potent and selective inhibitor of CHK2 that potentiates the cytotoxicity of PARP inhibitors. Cancer Res. 2011;71(2):463-72.

Background

CHK2 is a checkpoint kinase involved in the ATM-mediated response to double-strand DNA breaks. Inhibitors of CHK2 may increase the efficacy of genotoxic cancer therapies. CCT241533 has been identified and characterized as a novel CHK2 kinase inhibitor.

In vitro: CCT241533 inhibits CHK2 with an IC50 of 3 nmol/L and shows minimal cross-reactivity against a panel of kinases at 1 mmol/L. CCT241533 did not potentiate the cytotoxicity of a selection of genotoxic agents in several cell lines [1]. Moreover, as the most potent CHK2 inhibitor identified in the series, CCT241533 shows potent selectivity (63-fold) over CHK1 and low hERG inhibition (hERGIC50=22 μM) [2].

In silico: X-ray crystallography confirmed that CCT241533 bound to CHK2 in the ATP pocket. Overall, the binding mode was found to be very highly conserved relative to previous compounds, with all of the key hydrogen bond interactions maintained. The

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA

potency gained with CCT241533 therefore appears to be due to the presence of the two methoxy substituents occupying the solvent exposed region of the enzyme, and contributions from the isopropyl alcohol substituent, which may participate in a second intramolecular hydrogen bond to the quinazoline exocyclicNH [2].

Clinical trial: No clinical data are available.

References:
[1] Anderson VE, Walton MI, Eve PD, Boxall KJ, Antoni L, Caldwell JJ, Aherne W, Pearl LH, Oliver AW, Collins I, Garrett MD. CCT241533 is a potent and selective inhibitor of CHK2 that potentiates the cytotoxicity of PARP inhibitors. Cancer Res. 2011;71(2):463-72.
[2] Caldwell JJ, Welsh EJ, Matijssen C, Anderson VE, Antoni L, Boxall K, Urban F, Hayes A, Raynaud FI, Rigoreau LJ, Raynham T, Aherne GW, Pearl LH, Oliver AW, Garrett MD, Collins I. Structure-based design of potent and selective 2-(quinazolin-2-yl)phenol inhibitors of checkpoint kinase 2. J Med Chem. 2011;54(2):580-90.