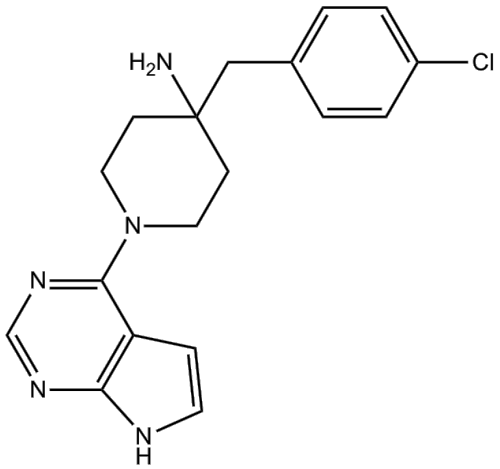
Product Data Sheet

Product Name: CCT128930
Cat. No.: GC15864

Chemical Properties

Cas. No.	885499-61-6		
Chemical Name	4-[(4-chlorophenyl)methyl]-1-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperidin-4-amine		
SMILES	C1CN(CCC1(CC2=CC=C(C=C2)Cl)N)C3=NC=NC4=C3C=CN4		
Formula	$C_{18}H_{20}ClN_5$	M.Wt	341.84
Solubility	≥ 17.1mg/mL in DMSO	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C 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



Protocol

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Address: 10292 Central Ave. #205, Montclair, CA, USA

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Kinase experiment: Profiling against 50 different human kinases is carried out using 10 μM CCT128930 at an ATP concentration equivalent to the Km for each enzyme. All other enzyme assays are performed[1].

Cell experiment: All cell lines are grown in their recommended culture medium, supplemented with 10% fetal bovine serum at 37°C in 5% CO2 and passaged for less than six months prior to replacement from early passage frozen stocks. CCT128930 and LY294002 are made up as 10mM stocks in DMSO. Cells are regularly screened for Mycoplasma using a PCR-based assay. Cells are seeded in 96-well plates and allowed to attach for 36 hours to ensure exponential growth prior to treatment. In vitro antiproliferative activity is determined using a 96-hour SRB assay, and GI50 values are derived[1].

Animal experiment: Mice[1] PTEN-null U87MG human glioblastoma cells (2×106) are injected subcutaneously (s.c.) in the right flank of 6-8 weeks old female CrTacNCr-Fox1nu mice. For HER2-positive, PIK3CA-mutant BT474 human breast cancer xenografts, cells (5×106) are administered s.c. in medium supplemented with matrigel (1:1) into the mammary fat pads of female mice implanted s.c. with estradiol pellets (0.025 mg, 90 day release) 3 days previously. Animals are randomized and treatment is started with vehicle or CCT128930 when established tumors are ~100 mm3 in mean volume. Control mice receive vehicle only (10% DMSO, 5% Tween 20, 85% saline) and treated mice received 50 mg/kg CCT128930 intraperitoneally (i.p.) daily for 5 days (U87MG human glioblastoma xenografts) or 40 mg/kg CCT128930 i.p. twice daily for 5 days (BT474 human breast cancer xenografts). Tumor size and body weight are monitored three times a week. Tumor size is evaluated by measurement of 2 orthogonal diameters with calipers and volume is calculated. At the end of the study, tumors are excised and weighed.

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References:

[1]. Yap TA et al. Preclinical pharmacology, antitumor activity, and development of pharmacodynamic markers for the novel, potent AKT inhibitor CCT128930. Mol Cancer Ther. 2011 Feb;10(2):360-71.

Background

CCT128930 is a potent, selective, novel and ATP-competitive inhibitor for AKT2 (IC50= 6 nM). It also has 28-fold and 20-fold selectivity over PKA kinase (IC50= 168 nM) and p70S6K (IC50= 120 nM), respectively.

Akt (protein kinase B) is a serine/threonine-specific protein kinase that plays a key role in multiple cellular processes such as glucose metabolism, apoptosis, cell proliferation, transcription and cell migration.

In multi tumor cell line, CCT128930 showed antiproliferative effect and blocked the phosphorylation of various Akt substrates. In PTEN-null human glioblastoma cells (U87MG), CCT128930 treatment led to a G1 arrest associated with Akt pathway suppression. [1]

In U87MG tumor xenografts, CCT128930 inhibited the phosphorylation of Akt downstream biomarkers. In U87MG, HER-2 positive and IK3CA-mutant BT474 human breast cancer xenografts, antitumor activity were recorded as tumor volume decreased. CCT128930-treated mouse whisker folliciles in vivo and human hair follicles treated ex vivo exerted prominent reduction in pThr246 PRAS40. [1]

Reference:

1. Yap TA, Walton MI, Hunter LJ et al. Preclinical pharmacology, antitumor activity, and development of pharmacodynamic markers for the novel, potent AKT inhibitor CCT128930. Mol Cancer Ther. 2011 Feb;10(2):360-71.

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