产品名称：

4-(4-chlorobenzyl)-1-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)piperidin-4-amine

产品别名：**CCT128930**

生物活性：

Description	CCT128930 is a potent and selective inhibitor of Akt2 (IC_{50} 6 nM) with 28-fold selectivity over the closely related PKA kinase (IC_{50} 168 nM), as well as 20-fold selectivity over p70S6K (IC_{50} 120 nM).

IC_{50} & Target

Akt2	p70S6K	PKA	Autophagy
6 nM (IC_{50})	120 nM (IC_{50})	168 nM (IC_{50})	

In Vitro

CCT128930 exhibits marked antiproliferative activity and inhibits the phosphorylation of a range of Akt substrates in multiple tumor cell lines in vitro, consistent with Akt inhibition. CCT128930 causes a G1 arrest in *PTEN*-null U87MG human glioblastoma cells, consistent with Akt pathway blockade. CCT128930 is a potent ATP-competitive Akt inhibitor, which is initially screened at 10 μM against a panel of kinases representative of the human protein kinome. In view of the potential of ATP-competitive inhibitors to cross-react with the closely related AGC class of kinases, the IC_{50} of CCT128930 against selected AGC kinases is determined. The GI_{50} values of CCT128930 for growth inhibition are 6.3 μM±2.2 (n=3) for U87MG human glioblastoma cells, 0.35 μM±0.11 (n=4) for LNCaP human prostate cancer cells, and 1.9 μM±0.80 (n=5) for PC3 human prostate cancer cells, all of which are *PTEN*-deficient human tumor cell lines [1].

In Vivo

The pharmacokinetics of CCT128930 after a single dose of 25 mg/kg are shown. Following i.v. administration, CCT128930 reaches a peak concentration of 6.4 μM in plasma and is eliminated with a relatively short half-life, high volume of distribution and rapid clearance, giving an $AUC_{0-\infty}$ of 4.6 μMh. Following i.p. administration, the peak plasma drug concentration is 4-fold lower and the plasma clearance is similar to that observed i.v..The corresponding $AUC_{0-\infty}$ is 1.3 μMh, giving an i.p. bioavailability of 29% [1].

Solvent&Solubility

In Vitro:

DMSO : 36.67 mg/mL (107.27 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.9253 mL	14.6267 mL	29.2535 mL
	5 mM	0.5851 mL	2.9253 mL	5.8507 mL
	10 mM	0.2925 mL	1.4627 mL	2.9253 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

In Vivo:

请根据您的实验动物和给药方式选择适当的溶解方案。以下溶解方案都请先按照 **In Vitro** 方式配制澄清的储备液，再依次添加助溶剂：

——为保证实验结果的可靠性，澄清的储备液可以根据储存条件，适当保存；体内实验的工作液，建议您现用现配，当天使用； 以下溶剂前显示的百分比是指该溶剂在您配制终溶液中的体积占比；如在配制过程中出现沉淀、析出现象，可以通过加热和/或超声的方式助溶

1.请依序添加每种溶剂： 10% DMSO→40% PEG300 →5% Tween-80 → 45% saline

Solubility: ≥ 2.75 mg/mL (8.04 mM); Clear solution

	此方案可获得 ≥ 2.75 mg/mL (8.04 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 400 μL PEG300 中，混合均匀；向上述体系中加入 50 μL Tween-80，混合均匀；然后继续加入 450 μL 生理盐水定容至 1 mL。 2.请依序添加每种溶剂： 10% DMSO→ 90% (20% SBE-β-CD in saline) Solubility: ≥ 2.75 mg/mL (8.04 mM); Clear solution 此方案可获得 ≥ 2.75 mg/mL (8.04 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 20% 的 SBE-β-CD 生理盐水水溶液中，混合均匀。 3.请依序添加每种溶剂： 10% DMSO →90% corn oil Solubility: ≥ 2.75 mg/mL (8.04 mM); Clear solution 此方案可获得 ≥ 2.75 mg/mL (8.04 mM，饱和度未知) 的澄清溶液，此方案不适用于实验周期在半个月以上的实验。 以 1 mL 工作液为例，取 100 μL 27.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
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.

实验参考：

Cell Assay	All cell lines are grown in their recommended culture medium, supplemented with 10% fetal bovine serum at 37°C in 5% CO_2 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 GI_{50} values are derived [1].
Animal Administration	Mice [1]. *PTEN*-null U87MG human glioblastoma cells (2×10^6) 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 (5×10^6) 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 mm^3 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.
Kinase Assay	Profiling against 50 different human kinases is carried out using 10 μM CCT128930 at an ATP concentration equivalent to the K_m for each enzyme. All other enzyme assays are performed [1].
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.