产品名称：CCT196969
产品别名：CCT196969

生物活性：

Description	CCT196969 is a pan-Raf inhibitor, which inhibits B-Raf, $BRaf^{V600E}$ and CRAF with IC_{50}s of 0.1, 0.04, and 0.01 μM, respectively.				
IC_{50} & Target	$BRaf^{V600E}$	Braf	CRAF	LCK	SRC
	0.04 μM (IC_{50})	0.1 μM (IC_{50})	0.01 μM (IC_{50})	0.02 μM (IC_{50})	0.03 μM (IC_{50})
In Vitro	CCT196969 is a pan-Raf inhibitor with anti-SRC activity. CCT196969 is an orally available, well-tolerated B-Raf inhibitor that directly inhibits $B\text{-}Raf^{V600E}$ in cells. CCT196969 inhibits B-Raf at 100 nM and $B\text{-}Raf^{V600E}$ at 40 nM. It inhibits CRaf at 12 nM, SRC at 26 nM, and LCK at 14 nM. CCT196969 is active against melanoma and colorectal cancer cell lines that are mutant for B-Raf. CCT196969 induces caspase 3 and PARP cleavage, demonstrating that it induces apoptosis[1]				
In Vivo	CCT196969 is extremely well tolerated and does not produce any significant adverse effects in vivo. It inhibits the growth of NRAS mutant DO4 tumor xenografts in nude mice. CCT196969 inhibits ERK and SRC and induce tumor regression in a PDX from the resistant tumor without causing body weight loss in the mice[1].				

Solvent&Solubility

In Vitro:

DMSO : ≥ 32 mg/mL (62.32 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.9473 mL	9.7367 mL	19.4734 mL
	5 mM	0.3895 mL	1.9473 mL	3.8947 mL
	10 mM	0.1947 mL	0.9737 mL	1.9473 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: ≥ 2.08 mg/mL (4.05 mM); Clear solution

此方案可获得 ≥ 2.08 mg/mL (4.05 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.05 mM); Clear solution

	此方案可获得 ≥ 2.08 mg/mL (4.05 mM，饱和度未知) 的澄清溶液。 以 1 mL 工作液为例，取 100 μL 20.8 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: ≥ 2.08 mg/mL (4.05 mM); Clear solution 此方案可获得 ≥ 2.08 mg/mL (4.05 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 20.8 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Girotti MR, et al. Paradox-breaking RAF inhibitors that also target SRC are effective in drug-resistant BRAF mutant melanoma. Cancer Cell. 2015 Jan 12;27(1):85-96.

实验参考：

Cell Assay	Cultured cells are seeded into 96-well plates (2,000 cells per well). At 24 hr later, serial dilutions of the B-Raf inhibitors PLX4720 and SB590885, the MEK inhibitor PD184352, or compounds CCT241161 and CCT196969 are added. Cells are incubated for a further 72 hr, and viability is measured by CellTiter-Glo assays. Relative survival in the presence of drugs is normalized to the untreated controls after background subtraction[1].
Animal Administration	Mice: Tumors are established in female nude mice. Treatment is by oral gavage daily with vehicle (5% DMSO, 95% water), 90 mg/kg PLX4720, 20 mg/kg CCT196969, or 20 mg/kg CCT241161. All the inhibitors are administered 7 days/week, with no weekend break. Tumor size is determined by caliper measurements of tumor length, width, and depth; volume is calculated as volume = 0.5236×length×width×depth (in millimeters)[1].
References	[1]. Girotti MR, et al. Paradox-breaking RAF inhibitors that also target SRC are effective in drug-resistant BRAF mutant melanoma. Cancer Cell. 2015 Jan 12;27(1):85-96.