产品名称：MK-5108 (VX-689)
产品别名：MK-5108 (VX-689)

生物活性：

Description	MK-5108 is a highly potent and specific inhibitor of Aurora A kinase with an IC_{50} value of 0.064 nM.
IC_{50} & Target	Aurora A
	64 pM (IC_{50})
In Vitro	MK-5108 inhibits Aurora-A activity with an IC50 value of 0.064 nM in an ATP-competitive manner. It shows robust selectivity against the other family kinases Aurora-B (220-fold) and Aurora-C (190-fold). MK-5108 also exhibits high selectivity for Aurora-A over other protein kinases. MK-5108 inhibits the growth of 14 cell lines with IC50 values between 0.16 and 6.4 μM[1].
In Vivo	MK-5108 treatments at 15 and 30 mg/kg results in significant tumor growth inhibition in the HCT116 tumor model. MK-5108 is well tolerated at both doses, with minimal reduction in body weight. MK-5108 also exhibits significant antitumor activity in nude rats bearing SW48 tumors. MK-5108 at 15 and 45 mg/kg causes dose-dependent tumor growth inhibition with a %T/C of 35% and 7% at day 10, and 58% and 32% at day 27, respectively. MK-5108 is well tolerated in nude rats, with no body weight reduction and moderate effect on blood cells[1].
Solvent&Solubility	***In Vitro:***

DMSO : 12.5 mg/mL (27.06 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1648 mL	10.8239 mL	21.6478 mL
	5 mM	0.4330 mL	2.1648 mL	4.3296 mL
	10 mM	0.2165 mL	1.0824 mL	2.1648 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: ≥ 1.25 mg/mL (2.71 mM); Clear solution

此方案可获得 ≥ 1.25 mg/mL (2.71 mM，饱和度未知) 的澄清溶液。

以 1 mL 工作液为例，取 100 μL 12.5 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: ≥ 1.25 mg/mL (2.71 mM); Clear solution

此方案可获得 ≥ 1.25 mg/mL (2.71 mM，饱和度未知) 的澄清溶液。

	以 1 mL 工作液为例，取 100 μL 12.5 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: ≥ 1.25 mg/mL (2.71 mM); Clear solution 此方案可获得 ≥ 1.25 mg/mL (2.71 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 12.5 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。
References	[1]. Shimomura T, et al. MK-5108, a highly selective Aurora-A kinase inhibitor, shows antitumor activity alone and in combination with docetaxel. Mol Cancer Ther. 2010 Jan;9(1):157-66.

实验参考：

Cell Assay	Cells are seeded in 96-well plates then incubated overnight. A medium containing MK-5108, docetaxel, or DMSO control is added and is incubated for 72 h. The cell population densities are then measured by the WST-8 colorimetric assay using a SpectraMax Plus384 plate reader. Concentration response curves are generated to give the decrease in cell population density in MK-5108– and docetaxel-treated samples relative to DMSO-treated control. Growth inhibition IC50 values are determined from those curves[1].
Animal Administration	Rats: After 8 d, MK-5108 is suspended in 0.5% methyl cellulose/0.24% SDS and orally administered twice daily for 14 d. SW48 cells are suspended in 50% Matrigel/50% PBS and s.c. transplanted into the side flank of nude rats. After 7 d, MK-5108 is suspended in 0.5% methyl cellulose/0.24% SDS and orally administered twice daily for 2 d/wk for 3 wk. In a HeLa-luc and ES-2 dual flank xenograft model, HeLa-luc or ES-2 cells are suspended in 50% Matrigel and 50% PBS, and s.c. transplanted into the right or left side flank of nude rats. After 8 d, vehicle (5% ethanol-saline) or 7.5 mg/kg docetaxel is injected i.v. MK-5108 is orally administered twice daily for 2 d 24 h after the docetaxel injection. The volume of each tumor is determined from the tumor diameter[1].
Kinase Assay	The Aurora-A assay reaction is conducted in the presence of 20 μM ATP, 25 μM Tetra-Kemptide, 1.0 μCi per well [γ-33P]-ATP, 0.1 ng per well Aurora-A in 50 mmol/L Tris-HCl (pH 7.4), 15 mmol/L Mg(OAc)2, and 0.2 mmol/L EDTA at 30°C for 40 min. To investigate the inhibition mode of MK-5108 for Aurora-A, the IC50 values of MK-5108 are determined in the presence of different concentrations of ATP. Then, the IC50 value is plotted as a function of ATP concentration to analyze the effect of ATP concentration on the IC50 value of MK-5108[1].
References	[1]. Shimomura T, et al. MK-5108, a highly selective Aurora-A kinase inhibitor, shows antitumor activity alone and in combination with docetaxel. Mol Cancer Ther. 2010 Jan;9(1):157-66.