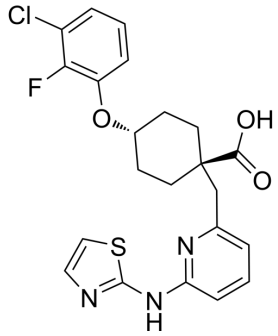
MK-5108

Cat. No.:	HY-13252
CAS No.:	1010085-13-8
Molecular Formula:	$C_{22}H_{21}ClFN_3O_3S$
Molecular Weight:	461.94
Target:	Aurora Kinase; Autophagy
Pathway:	Cell Cycle/DNA Damage; Epigenetics; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 1 year -20°C 6 months



SOLVENT & SOLUBILITY

In Vitro

DMSO : 12.5 mg/mL (27.06 mM; ultrasonic and warming and heat to 60°C)

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

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 0.5% MC >> 0.5% Tween-80
   Solubility: 6.67 mg/mL (14.44 mM); Suspended solution; Need ultrasonic
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.25 mg/mL (2.71 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.25 mg/mL (2.71 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.25 mg/mL (2.71 mM); Clear solution

BIOLOGICAL ACTIVITY

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 IC_{50} 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 IC_{50} values between 0.16 and 6.4 μM[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	The Aurora-A assay reaction is conducted in the presence of 20 μM ATP, 25 μM Tetra-Kemptide, 1.0 μCi per well [γ-^{33}P]-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 IC_{50} values of MK-5108 are determined in the presence of different concentrations of ATP. Then, the IC_{50} value is plotted as a function of ATP concentration to analyze the effect of ATP concentration on the IC_{50} value of MK-5108[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	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 IC_{50} values are determined from those curves[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Patent. US20180263995A1.
- Technical University of Munich. 24.01.2018.

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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

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