产品名称：**MK-4101**
产品别名：**MK-4101**

生物活性：		
Description	MK-4101 is a Smoothened (SMO) antagonist (IC_{50} of 1.1 μM for 293 cells) and also a potent inhibitor of the hedgehog pathway (IC_{50} of 1.5 μM for mouse cells; IC_{50} of 1 μM for KYSE180 oesophageal cancer cells). MK-4101 has robust antitumor activity that inhibits tumor cell proliferation and induces extensive apoptosis[1]	
IC_{50} & Target	IC50: 1.1 μM (293 cells); 1.5 μM (mouse cells); 1 μM (KYSE180 oesophageal cancer cells)[1]	
In Vitro	MK-4101 inhibits Hh signaling both in a reporter gene assay in an engineered mouse cell line with an **IC_{50}** of 1.5 μM, and in human KYSE180 oesophageal cancer cells with an **IC_{50}** of 1 μM. MK-4101 displaces a fluorescently-labeled cyclopamine derivative from 293 cells expressing recombinant human SMO with an **IC_{50}** of 1.1 μM, implying that the compound binds to SMO. MK4101 also inhibits the proliferation of medulloblastoma cells derived from neonatallyirradiated $Ptch1^{-/+}$ mice in vitro with an **IC_{50}** of 0.3 μM[1] MK-4101 (10 μM; 60 hours, 72 hours; medulloblastoma or BCC cells) treatment shows cell cycle arrest with a nearly complete disappearance of the S phase subpopulation, a prominent increase of the G1 population and, to a minor extent, of the G2 population[1] MK-4101 (10 μM; medulloblastoma or BCC cells) treatment significantly reduces cyclin D1 protein and accumulation of cyclin B1 protein[1]	
	Cell Cycle Analysis[1]	
	Cell Line:	Medulloblastoma or BCC cells
	Concentration:	10 μM
	Incubation Time:	60 hours, 72 hours
	Result:	Showed cell cycle arrest.
	Western Blot Analysis[1]	
	Cell Line:	Medulloblastoma or BCC cells
	Concentration:	10 μM
	Incubation Time:	
	Result:	Significant reduction of cyclin D1 protein and accumulation of cyclin B1 protein.
In Vivo	MK-4101 (40-80 mg/kg; oral administration; for 3.5 weeks; CD1 nude female mice) treatment shows tumor growth inhibition (40 and 80 mg/kg) and tumor regression at the highest dose (80 mg/kg). MK-4101 treatment shows a dose-dependent down-regulation of Gli1 mRNA. The maximum effect for tumor inhibition and hedgehog pathway downregulation is achieved at 80 mg/kg[1].	
	Animal Model:	5-weeks old CD1 nude female mice with medulloblastoma/BCC cells[1]
	Dosage:	40 or 80 mg/kg once a day, 80 mg/kg twice a day
	Administration:	Oral administration; for 3.5 weeks
	Result:	Showed tumor growth inhibition (40 and 80 mg/kg) and tumor regression at the highest dose (80 mg/kg).
	In Vitro: **DMSO : ≥ 50 mg/mL (101.32 mM)** * "≥" means soluble, but saturation unknown.	

<table>
<tr><td rowspan="5">Solvent&Solubility</td><td rowspan="4">Preparing Stock Solutions</td><td>Solvent / Mass / Concentration</td><td>1 mg</td><td>5 mg</td><td>10 mg</td></tr>
<tr><td>1 mM</td><td>2.0265 mL</td><td>10.1323 mL</td><td>20.2647 mL</td></tr>
<tr><td>5 mM</td><td>0.4053 mL</td><td>2.0265 mL</td><td>4.0529 mL</td></tr>
<tr><td>10 mM</td><td>0.2026 mL</td><td>1.0132 mL</td><td>2.0265 mL</td></tr>
<tr><td colspan="5">*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: ≥ 2.5 mg/mL (5.07 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (5.07 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (5.07 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (5.07 mM，饱和度未知) 的澄清溶液。
以 1 mL 工作液为例，取 100 μL 25.0 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: ≥ 2.5 mg/mL (5.07 mM); Clear solution
此方案可获得 ≥ 2.5 mg/mL (5.07 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 25.0 mg/mL 的澄清 DMSO 储备液加到 900 μL 玉米油中，混合均匀。</td></tr>
<tr><td>References</td><td colspan="4">[1]. Filocamo G et al. MK-4101, a Potent Inhibitor of the Hedgehog Pathway, Is Highly Active against Medulloblastoma and Basal Cell Carcinoma. Mol Cancer Ther. 2016 Jun;15(6):1177-89.</td></tr>
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