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产品名称：KU-60019
产品别名：KU-60019

生物活性：

Description	KU-60019 is an improved ATM kinase-specific inhibitor with IC50 of 6.3 nM.	
IC_{50} & Target	ATM	DNA-PKcs
	6.3 nM (IC_{50})	1.7 μM (IC_{50})
In Vitro	KU-60019 is an improved analogue of KU-55933. KU-55933 has an IC50 of 13 nM and Ki of 2.2 nM in vitro and is highly specific for the ATM kinase using a panel of 60 protein kinases. KU-60019 is an improved inhibitor of the ATM kinase with an IC50 of 6.3 nM, approximately half that of KU-55933. The IC50 values for DNA-PKcs and ATR are 1.7 and >10 μM, respectively, almost 270-and 1600-fold higher than for ATM. KU-60019 is 10-fold more effective than KU-55933 at blocking radiation-induced phosphorylation of key ATM targets in human glioma cells. In human U87 glioma cells, KU-55933 completely inhibits phosphorylation of p53 (S15) at 10 μM but not at 3 μM, whereas γ-H2AX levels are only partly reduced with 10 μM 1 h after irradiation. By comparison, 3 μM KU-60019 completely inhibits p53 phosphorylation and partial inhibits at 1 μM[1].	
In Vivo	Despite PTEN-deficient control tumors reaching a 4-fold increase in size before PTEN wild-type controls, KU-60019-treated PTEN-deficient tumors display a statistically significant slowing in growth. This growth inhibition is especially evident at the start of the experiment (days 5-12) just after KU-60019 is administered (days 1-5)[2].	

Solvent&Solubility

In Vitro:

DMSO : ≥ 30 mg/mL (54.78 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	1.8259 mL	9.1296 mL	18.2592 mL
	5 mM	0.3652 mL	1.8259 mL	3.6518 mL
	10 mM	0.1826 mL	0.9130 mL	1.8259 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: ≥ 2.5 mg/mL (4.56 mM); Clear solution

此方案可获得 ≥ 2.5 mg/mL (4.56 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 (4.56 mM); Clear solution 此方案可获得 ≥ 2.5 mg/mL (4.56 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。
References	[1]. Golding SE, et al. Improved ATM kinase inhibitor KU-60019 radiosensitizes glioma cells, compromises insulin, AKT and ERK prosurvival signaling, and inhibits migration and invasion. Mol Cancer Ther. 2009 Oct;8(10):2894-902. [2]. McCabe N, et al. Mechanistic Rationale to Target PTEN-Deficient Tumor Cells with Inhibitors of the DNA Damage Response Kinase ATM. Cancer Res. 2015 Jun 1;75(11):2159-65.

实验参考：

Cell Assay	Cell growth is determined by AlamarBlue. U1242 cells are serially diluted, allowed to attach for 6 h and then exposed to KU-60019 at 3 μM. At days 1, 3 and 5 after seeding, AlamarBlue is added to the medium to the recommended final concentration. Plates are incubated for 1 h at 37°C and fluorescence determined on a FluoroCount plate reader (excitation 530 nm, emission 590 nm) and values taken as a measure of cell growth[1].
Animal Administration	Mice[2] Cells (3×10^7) are implanted into male Fox Chase Severe Combined Immunodeficiency (SCID) mice. Administration of Doxycycline is started when tumors reach 100 mm^3 in volume and is performed every 48 hours up to removal of the animal from the experiment. Forty-eight hours after PTEN induction, animals are administered KU-60019 (100 mg/kg) for 5 consecutive days and measured until they reach a target 400 mm^3 volume. Measurements of tumor volume and body weight took place every 3 days using calipers.
References	[1]. Golding SE, et al. Improved ATM kinase inhibitor KU-60019 radiosensitizes glioma cells, compromises insulin, AKT and ERK prosurvival signaling, and inhibits migration and invasion. Mol Cancer Ther. 2009 Oct;8(10):2894-902. [2]. McCabe N, et al. Mechanistic Rationale to Target PTEN-Deficient Tumor Cells with Inhibitors of the DNA Damage Response Kinase ATM. Cancer Res. 2015 Jun 1;75(11):2159-65.