产品名称：CP-466722
产品别名：CP466722

生物活性：

Description	CP-466722 is a rapidly reversible inhibitor of ATM, with an IC_{50} of 4.1 μM, and has no effects on PI3K or closely related PI3K-like protein kinase (PIKK) family members.
IC_{50} & Target	ATM
	4.1 μM (IC_{50})
In Vitro	CP-466722 (CP466722, 6-10 μM) inhibits IR-induced ATM kinase activity, and the inhibition can be rapidly and completely reversed. CP466722 (6, 10 μM) inhibits p53 induction and ATM-dependent phosphorylation in mouse cells, but CP466722 fails to inhibit ATR activity and ATR-dependent phosphorylation of Chk1. CP466722 (6 μM) disrupts ATM-dependent cell cycle checkpoints in cells[1]. CP466722 (1 μM) completely inhibits ATM-dependent phosphorylation in MCF7 cells. CP466722 (10 μM) reduces pKAP1 phosphorylation in MCF7 cells, with an IC50 of 0.41 μM. CP466722 (10 μM) inhibits both pATM and pKAP1 signals[2]. CP-466722 (CP466722, 5-50 μM) inhibits proliferation of SKBr-3 cancer cells more strongly than MCF-7 cancer cells. CP466722 (10 μM) also slightly increases proportions of MCF-7 and SKBr-3 cells in the G1 phase after treatment for 48 hours[3].
Solvent&Solubility	***In Vitro:***
	DMSO : 7 mg/mL (20.04 mM; Need warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.8625 mL	14.3123 mL	28.6246 mL
	5 mM	0.5725 mL	2.8625 mL	5.7249 mL
	10 mM	0.2862 mL	1.4312 mL	2.8625 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。

References	[1]. Rainey MD, et al. Transient inhibition of ATM kinase is sufficient to enhance cellular sensitivity to ionizing radiation. Cancer Res. 2008 Sep 15;68(18):7466-74. [2]. Guo K, et al. Development of a cell-based, high-throughput screening assay for ATM kinase inhibitors. J Biomol Screen. 2014 Apr;19(4):538-46. [3]. Węsierska-Gądek J, et al. Interactions Between Ataxia Telangiectasia Mutated Kinase Inhibition, Poly(ADP-ribose) Polymerase-1 Inhibition and BRCA1 Status in Breast Cancer Cells. J Cancer Prev. 2014 Jun;19(2):125-36.

实验参考：

Cell Assay	Cells are plated in triplicate (40,000 cells/plate), incubated as required before culture media and trypsinsed cells are combined and viability determined: Vi-CELL™ XR cell viability analyzer[1].
	To screen for small molecule inhibitors of ATM kinase activity, an in vitro kinase assay is carried out, and an ELISA assay developes which measures the phosphorylation status of the ATM downstream target p53. Recombinant GST-p53(1-101) and full-length Flag-tagged ATM & ATR are purified for use in the ELISA and in vitro kinase assays. Briefly, Nunc 96 well Maxisorp plates are coated

Kinase Assay	overnight (4°C) with 2 μg of purified, recombinant GST-p53(1-101) in PBS. All subsequent incubations are performed at room temperature. The plates are washed (0.05% v/v-Tween/PBS) before addition of purified recombinant full-length ATM kinase (30-60 ng) in a final volume of 80 μL of reaction buffer (20 mM HEPES, 50 mM $NaCl_2$, 10 mM $MgCl_2$, 10 mM $MnCl_2$, 1 mM DTT and 1 μM ATP) in the presence or absence of compound. Compounds including CP-466722 (10 μM) are added to plates in duplicate and the kinase assay is incubated (90 min). Plates are washed (0.05% v/v-Tween/PBS), blocked (1 h, 1% w/v-BSA/PBS) and rinsed before anti-Phospho(Ser15)-p53 antibody (1:1000/PBS) is added to the plates and incubated (1 h). To reduce non-specific binding plates are washed (0.05% v/v-Tween/PBS) prior to incubation (1 h) with HRP-conjugated goat anti-rabbit IgG secondary antibody (1:5000/PBS). Secondary antibody that is linked to the phosphorylated GST-p53(1-101) protein is detected with TMB substrate reagent. Plates are developed (15-30 min) and the reaction is stopped (1M H_2SO_4 final concentration) before absorbance is determined (λ450 nm). Compounds that inhibit ATM kinase activity in ELISA assays, are characterized with respect to inhibition of ATM/ATR kinases using in vitro kinase assays. Western blotting using the anti-Phospho(Ser15)-p53 antibody is used as a readout of ATM/ATR inhibition [1]
References	[1]. Rainey MD, et al. Transient inhibition of ATM kinase is sufficient to enhance cellular sensitivity to ionizing radiation. Cancer Res. 2008 Sep 15;68(18):7466-74. [2]. Guo K, et al. Development of a cell-based, high-throughput screening assay for ATM kinase inhibitors. J Biomol Screen. 2014 Apr;19(4):538-46. [3]. Węsierska-Gądek J, et al. Interactions Between Ataxia Telangiectasia Mutated Kinase Inhibition, Poly(ADP-ribose) Polymerase-1 Inhibition and BRCA1 Status in Breast Cancer Cells. J Cancer Prev. 2014 Jun;19(2):125-36.