# CP-466722

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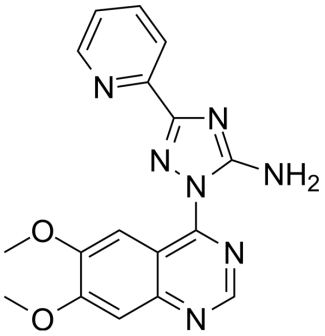
| **Cat. No.:** | HY-11002 |
| **CAS No.:** | 1080622-86-1 |
| **Molecular Formula:** | $C_{17}H_{15}N_7O_2$ |
| **Molecular Weight:** | 349.35 |
| **Target:** | ATM/ATR |
| **Pathway:** | Cell Cycle/DNA Damage; PI3K/Akt/mTOR |
| **Storage:** | Powder -20°C 3 years<br>4°C 2 years<br>In solvent -80°C 2 years<br>-20°C 1 year |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : 1 mg/mL (2.86 mM; Need ultrasonic)

| 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 | --- | --- | --- |
| | 10 mM | --- | --- | --- |

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

## BIOLOGICAL ACTIVITY

**Description**

CP-466722 is a rapidly reversible inhibitor of ATM, with an $IC_{50}$ of 0.41 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 $IC_{50}$ 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].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

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| **Kinase Assay** [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 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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Cell Assay** [1] | 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].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## CUSTOMER VALIDATION

- Nat Commun. 2018 Oct 8;9(1):4139.
- Biochem Pharmacol. 2021 Jun 7;114648.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Harvard Medical School LINCS LIBRARY

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## 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]. W?sierska-G?dek 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.





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