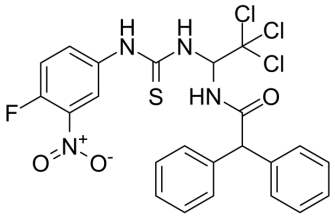
CGK733

Cat. No.:	HY-15520
CAS No.:	905973-89-9
Molecular Formula:	$C_{23}H_{18}Cl_3FN_4O_3S$
Molecular Weight:	555.84
Target:	ATM/ATR
Pathway:	Cell Cycle/DNA Damage; PI3K/Akt/mTOR
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (179.91 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	1.7991 mL	8.9954 mL	17.9908 mL
5 mM	0.3598 mL	1.7991 mL	3.5982 mL
10 mM	0.1799 mL	0.8995 mL	1.7991 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.50 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (3.74 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CGK733 is a potent ATM/ATR inhibitor, used for the research of cancer.

IC_{50} & Target

ATM ATR

In Vitro

CGK733 (4.2 ng/μL-12.5 ng/μL) enhances taxol-induced cytotoxicity in HBV-positive HCC cells. CGK733 (4.2 ng/μL) accelerates the formation of multinucleated cells and promotes the exit of mitosis in taxol-treated HBV-positive HCC cells[1]. CGK733 (10 μM) causes the loss of cyclin D1 through the ubiquitin-dependent proteasomal degradation pathway in MCF-7 and T47D breast cancer cell lines. CGK733 (0.6-40 μM) shows inhibitory activities against proliferation of LnCap prostate cancer cells, HCT116 colon cancer cells, MCF-7 and T47D estrogen receptor positive breast cancer cells, and MDA-MB436 ER

	negative breast cancer cells. Moreover, CGK733 inhibits proliferation of non-transformed mouse BALB/c 3T3 embryonic fibroblast cells. In addition, CGK733 (10 μM) inhibits MCF-7 proliferation, and the effect can not be suppressed by pan-caspase inhibition[2]. CGK733 (10 μM) results in 1.6-fold increase in ATM reporter activity in HEK-293 cells[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	CGK733 (25 mg/kg, i.p.) increases the ATM reporter activity (reports inactivation of ATM kinase activity) compared to control mice, with 2.4-fold, 3.1-fold, and 1.3-fold changes at 1, 4, and 8 hours, respectively[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	Cells are seeded in 96-well plates at a predetermined optimal cell density to ensure exponential growth for duration of the assay. After a 24 h preincubation, growth medium is replaced with experimental medium containing the appropriate drug concentrations or 0.1% (v/v) vehicle control. After a 48 h incubation, cell proliferation is estimated using the sulforhodamine B colorimetric assay and expressed as the mean ± SE for six replicates as a percentage of vehicle control (taken as 100%). Experiments are performed independently at least three times. Statistical analyses are performed using a two-tailed Student's t test. $P < 0.05$ is considered to be statistically significant[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Four to six weeks old athymic CD-1 female mice are acclimatized for at least one week before use. The mice are injected sub-cutaneously with 2×10^6 D54-ATMR cells in each flank. Tumors are allowed to grow to the size of 100-150 mm^3. Mice are injected intraperitoneally with vehicle control (DMSO), CGK-733, KU-55933 (25 mg/kg) or irradiated with 5 Gy to each flank. Bioluminescence is acquired on Xenogen IVIS Spectrum system after injecting 400 μg/100 μL of D-luciferin at baseline (-3h) as well as 1, 4, and 8 hours after drug administration[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Biomaterials. 2019 Oct;219:119377.
- Ecotoxicol Environ Saf. 2022 May 16;239:113645.
- iScience. 2023 Aug 25.
- J Mol Med (Berl). 2019 Aug;97(8):1183-1193.
- Harvard Medical School LINCS LIBRARY

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REFERENCES

[1]. Wang H, et al. CGK733 enhances multinucleated cell formation and cytotoxicity induced by taxol in Chk1-deficient HBV-positive hepatocellular carcinoma cells. Biochem Biophys Res Commun. 2012 May 25;422(1):103-8.

[2]. Alao JP, et al. The ATM and ATR inhibitors CGK733 and caffeine suppress cyclin D1 levels and inhibit cell proliferation. Radiat Oncol. 2009 Nov 10;4:51.

[3]. Williams TM, et al. Molecular imaging of the ATM kinase activity. Int J Radiat Oncol Biol Phys. 2013 Aug 1;86(5):969-77.

Caution: Product has not been fully validated for medical applications. For research use only.

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