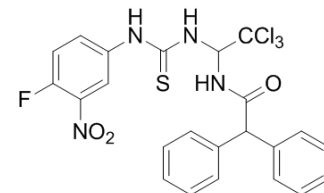


CGK733

Cat. No.:	HY-15520		
CAS No.:	905973-89-9		
Molecular Formula:	C ₂₃ H ₁₈ Cl ₃ FN ₄ O ₃ S		
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	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (179.91 mM)
 * "≥" means soluble, but saturation unknown.

Concentration	Mass		
	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

- 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
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (4.50 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

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

IC₅₀ & 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 μ M) inhibits MCF-7 proliferation, and the effect can not be suppressed by pan-caspase inhibition^[2]. CGK733 (10 μ M) 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 \pm 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 subcutaneously with 2×10^6 D54-ATMR cells in each flank. Tumors are allowed to grow to the size of 100-150 mm³. 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 μ g/100 μ L 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.
- 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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