CGK733

Cat. No.: HY-15520
CAS No.: 905973-89-9
Molecular Formula: C₂₃H₁₈Cl₃FN₄O₃S
Molecular Weight: 555.84
Target: ATM/ATR
Pathway: Cell Cycle/DNA Damage; PI3K/Akt/mTOR
Storage:
- Powder: -20°C 3 years
- Powder: 4°C 2 years
- In solvent:
  - -80°C 6 months
  - -20°C 1 month

SOLVENT & SOLUBILITY

In Vitro
- DMSO: \( \geq 100 \text{ mg/mL (179.91 mM)} \)
  * “\( \geq \)” means soluble, but saturation unknown.

<table>
<thead>
<tr>
<th>Preparing Stock Solutions</th>
<th>Solvent Concentration</th>
<th>Mass 1 mg</th>
<th>Mass 5 mg</th>
<th>Mass 10 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mM</td>
<td>1.7991 mL</td>
<td>8.9954 mL</td>
<td>17.9908 mL</td>
</tr>
<tr>
<td></td>
<td>5 mM</td>
<td>0.3598 mL</td>
<td>1.7991 mL</td>
<td>3.5982 mL</td>
</tr>
<tr>
<td></td>
<td>10 mM</td>
<td>0.1799 mL</td>
<td>0.8995 mL</td>
<td>1.7991 mL</td>
</tr>
</tbody>
</table>

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

In Vivo
- 1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
  Solubility: 2.5 mg/mL (4.50 mM); Suspended solution; Need ultrasonic
- 2. Add each solvent one by one: 10% DMSO >> 90% corn oil
  Solubility: \( \geq 2.5 \text{ mg/mL (4.50 mM)} \); Clear solution

BIOLOGICAL ACTIVITY

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

IC₅₀ & Target
<table>
<thead>
<tr>
<th>ATM</th>
<th>ATR</th>
</tr>
</thead>
</table>

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].

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].

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 2×10⁶ 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 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.

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REFERENCES


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