Product Name: LY2603618

Chemical Properties

Product Name: LY2603618
Cas No.: 911222-45-2
M.Wt.: 436.3
Formula: C18H22BrN5O3
Synonyms: N/A
Chemical Name: 1-[5-bromo-4-methyl-2-[[2S]-morpholin-2-yl]methoxy]phenyl]-3-(5-methylpyrazin-2-yl)urea
Canonical SMILES: CC1=CC=C(C=C1Br)NC(=O)NC2=NC(N=C2)COC3CNCCO3
Solubility: ≥43.6mg/mL in DMSO with gentle warming
Storage: Store at -20°C
General tips: For obtaining a higher solubility, please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Shopping Condition: Evaluation sample solution: ship with blue ice
All other available size: ship with RT, or blue ice upon request

Biological Activity

Targets: Cell Cycle/Checkpoint
Pathways: Chk
Description: LY2603618 is a novel small molecular checkpoint kinase 1 (Chk1) inhibitor that has direct anti-tumour effect [1], as well as desensitizing tumour cell against DNA-damaging chemotherapy treatment [2].
Checkpoint kinase 1 (Chk1) is a type of kinase that coordinates damaged-DNA repair [1]. Some tumour cells have been found to possess over-regulated populations of Chk1 that desensitize the cell from DNA-targeting chemotherapy, promoting tumour proliferation [3].
LY2603618 inhibits Chk1 by competing with ATP molecules [2]. In A549 and H1299 non-small cancer cell lines, lethal concentration of LY2603618 (10 µM) not only resulted in cell proliferation arrest (increase population of cell at G2/M phase from 13% to 38%) but also directly DNA damage, the latter of which was indicated by the increasing occurrence of H2AX phosphorylation[1].

In vivo, experiment was carried out to determine the combining effect of LY2603618 with other chemotherapy[2]. In mice xenograft model that inculated with Calu-6 lung cancer cell, combining administration of injected gemcitabine 150 mg/kg and orally uptake LY2603618 (200 mg/kg) resulted in increased DNA damage of tumour, as was demonstrated by a 2-fold increase in Chk1 s345 phosphorylation in comparison with mice treated with gemcitabine alone[2].

Reference:

Protocol

Cell experiment:

Cell lines HeLa cervical cancer cells, Calu-6 non-small cell lung cancer cells, HT29 and HCT-116 colon cancer cells

Preparation method The solubility of this compound in DMSO is >21.8mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Reacting conditions

Applications Treatment with 1250 nM LY2603618 resulted in a clear decrease in the G1 population and an increase in late S-phase cells. Cells treated with 5000 nM LY2603618 were predominantly found in the S-phase peak with a DNA content intermediate between 2 and 4N. LY2603618 induced DNA damage and arrested DNA synthesis while increasing the number of cells expressing an early marker of mitosis. LY2603618 treated cells lacked normal mitotic cells. An increased proportion of LY2603618 treated cells stained for pH3(S10) and were arrested in an abnormal prometaphase relative to the control cells. LY2603618 increased the potency of gemcitabine in p53-mutant HT-29 cells, but not in p53 WT HCT-116 cells
**Animal experiment [3]:**

<table>
<thead>
<tr>
<th>Animal models</th>
<th>Female Harlan athymic nude mice bearing Calu-6 xenografts</th>
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</thead>
<tbody>
<tr>
<td>Dosage form</td>
<td>Oral administration, 200 mg/kg</td>
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<tr>
<td>Applications</td>
<td>LY2603618 effectively inhibited the activation of Chk1 but not ATR by gemcitabine in Calu-6 tumor xenografts.</td>
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<td>Other notes</td>
<td>Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.</td>
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</table>

**Reference:**


**Product Citations**


**Caution**

**FOR RESEARCH PURPOSES ONLY.**

**NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.**

Specific storage and handling information for each product is indicated on the product datasheet. Most ApexBio products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Short-term storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.