

Product Data Sheet

Product Name: PTC-209

Cat. No.: GC15725

Chemical Properties

Cas. No. 315704-66-6

Chemical Name N-(2,6-dibromo-4-methoxyphenyl)-4-(2-methylimidazo[1,2-a]pyrimidin-3-yl)-1,3-thiazol-2-amine

SMILES CC1=C(N2C=CC=NC2=N1)C3=CSC(=N3)NC4=C(C=C(C=C4Br)OC)Br

Formula $C_{17}H_{13}Br_2N_5OS$

M.Wt 495.19

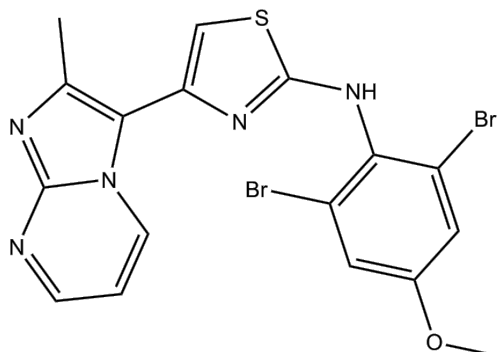
Solubility $\geq 24.75\text{mg/mL}$ in DMSO

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.

Shipping Condition Evaluation sample solution: ship with blue ice. All other available size: ship with RT, or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines various cancer cell lines: lung (LNM35, A549), breast (MDA-MB-231 and T47D), and colon (HT-29, HCT-116, and HCT8/S11)

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Preparation Method Cells were seeded at a density of 5000 cells/well into 96-well plates. After 24h, cells were treated for another 24, 48, and 72h with increasing concentrations of PTC-209 (0.01-10 μ M) in triplicate. Control cultures were treated with 0.1% DMSO (the drug vehicle).

Reaction Conditions 0.01-10 μ M PTC-209 for 24, 48, and 72h

Applications PTC-209 induced a concentration- and time-dependent decrease in the cellular viability of all cell lines tested. Lung cancer cells (LNM35 and A549) showed a higher sensitivity to PTC-209 treatment compared with breast (MDA-MB-231) and colon (HT-29) cancer cells.

Animal experiment [2]:

Animal models female nude mice, four to six weeks old

Preparation Method MDA-MB-231 cells were exposed to PTC-209, palbociclib, or combination of the two inhibitors at 5.0 μ M for 72h. Cells were then trypsinized, washed with PBS, and 2×10^6 cells were subcutaneously injected into the right left flank of female nude mice in a 100 μ L mixture (1:1 v/v of PBS/matrigel). The animals were monitored twice weekly and tumor volume was measured using caliper.

Dosage form MDA-MB-231 cells were exposed to drugs at 5.0 μ M for 72h

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Applications

PTC-209 and palbociclib significantly inhibit the growth of tumor, and combination of both drugs was more efficacious in inhibiting MDA-MB-231 tumor growth in vivo. PTC-209 and palbociclib treatments restricted the invasiveness of MDA-MB-231 cells, while combination group exhibited the most profound restricted invasion of tumor cells compared to other treatment groups and control.

References:

- [1]. Sulaiman S, Arafat K, et al. PTC-209 Anti-Cancer Effects Involved the Inhibition of STAT3 Phosphorylation. *Front Pharmacol.* 2019;10:1199. Published 2019 Oct 21.
- [2]. Elango R, Vishnubalaji R, et al. Concurrent targeting of BMI1 and CDK4/6 abrogates tumor growth in vitro and in vivo. *Sci Rep.* 2019;9(1):13696. Published 2019 Sep 23.

Background

PTC-209 is a cell-permeable BMI-1 inhibitor with an IC₅₀ of 0.5μM in HEK293T cells. PTC-209 downregulates BMI-1 protein expression by inhibiting BMI-1 transcription and impairs RING1A-mediated epigenetic regulation of H2AK119ub1. PTC-209 suppresses tumor progression by reducing the self-renewal capacity of tumor-initiating cells. PTC-209 can be used in studies related to colorectal cancer, glioblastoma, multiple myeloma, and cardiac reprogramming^[1-4].

In vitro, PTC-209 (1 or 10μM) treated U87MG and T98G glioblastoma cells and TPC-1115 and TPC-0411 primary glioblastoma cells for 2-4 days. PTC-209 downregulated BMI-1 protein and H2AK119ub1 levels, inhibited cell proliferation, and induced G0/G1 and G2/M phase arrest. PTC-209 suppressed cell migration and mesenchymal marker expression, and inhibited self-renewal and sphere-forming ability of glioblastoma stem cells^[5]. PTC-209 (1μM) pretreated mouse embryonic fibroblasts and cardiac fibroblasts for 24h. PTC-209 reduced H2AK119ub enrichment at cardiac gene loci, upregulated Gata4, Isl1, Flk1, and downregulated Col1A1 (in embryonic fibroblasts). PTC-209 downregulated chemokines, interleukins, cytokines, and related JAK/STAT3 and MAPK/ERK1-2 pathway molecules^[6].

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In vivo, PTC-209 (0.5-1mg/g per week) alone or combined with cisplatin (0.5-1mg/g per week) was intraperitoneally injected into 4NQO-induced esophageal squamous cell carcinoma model mice for 4 consecutive weeks. PTC-209 monotherapy reduced ESCC lesion numbers, and combination with cisplatin further decreased lesion numbers and inhibited tumor growth compared to monotherapy^[7]. PTC-209 (30mg/kg; once daily) was subcutaneously injected into Cal27 and FaDu head and neck squamous cell carcinoma xenograft nude mice for 15 consecutive days. PTC-209 significantly inhibited tumor growth, downregulated intratumoral Bmi1 and Ki-67 expression, and reduced CD44-positive cells^[8].

References:

- [1] Zhu M, Fan H, Deng J, et al. BMI1 Silencing Liposomes Suppress Postradiotherapy Cancer Stemness against Radioresistant Hepatocellular Carcinoma. ACS Nano. 2023 Dec 12;17(23):23405-23421.
- [2] Bolomsky A, Schlangen K, Schreiner W, et al. Targeting of BMI-1 with PTC-209 shows potent anti-myeloma activity and impairs the tumour microenvironment. J Hematol Oncol. 2016 Mar 2;9:17.
- [3] Mayr C, Wagner A, Loeffelberger M, et al. The BMI1 inhibitor PTC-209 is a potential compound to halt cellular growth in biliary tract cancer cells. Oncotarget. 2016 Jan 5;7(1):745-58.
- [4] Elango R, Vishnubalaji R, Manikandan M, et al. Concurrent targeting of BMI1 and CDK4/6 abrogates tumor growth in vitro and in vivo. Sci Rep. 2019 Sep 23;9(1):13696.
- [5] Kong Y, Ai C, Dong F, et al. Targeting of BMI-1 with PTC-209 inhibits glioblastoma development. Cell Cycle. 2018;17(10):1199-1211.
- [6] Testa G, Russo M, Di Benedetto G, et al. Bmi1 inhibitor PTC-209 promotes chemically-induced direct cardiac reprogramming of cardiac fibroblasts into cardiomyocytes. Sci Rep. 2020 Apr;10(1):7129.
- [7] Wang X, Li K, Cheng M, et al. Bmi1 Serves as a Potential Tumor-Initiating Cell Marker and Therapeutic Target in Esophageal Squamous Cell Carcinoma. Stem Cells Int. 2020 Aug;2020:8877577.
- [8] Wang Q, Li Z, Wu Y, et al. Pharmacological inhibition of Bmi1 by PTC-209 impaired tumor growth in head neck squamous cell carcinoma. Cancer Cell Int. 2017 Nov;17:107.

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