

Product Data Sheet

Product Name: BC-LI-0186

Cat. No.: GC50572

Chemical Properties

Cas. No. 695207-56-8

SMILES CC(C1=C(N(N(C2=CC=C(S(=O)(NCCOC3=CC=CC=C3)=O)C=C2)C1=O)C)C

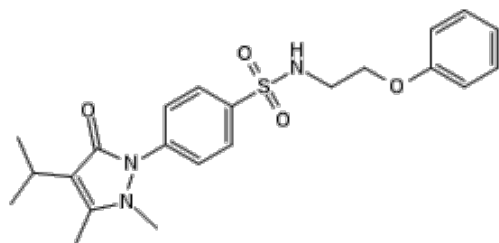
Formula C₂₂H₂₇N₃O₄S M.Wt 429.54

Solubility Soluble 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 SW620 cells (human colon cancer cell line)

Preparation Method SW620 cells were maintained in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) at 37°C, 5% CO₂. Cells were treated with BC-LI-0186 at concentrations ranging from 0.1 to 20 μM for 24 hours.

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

Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com

Address: 10292 Central Ave. #205, Montclair, CA, USA

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Reaction
Conditions 0.1-20 μ M; 24h.

Applications BC-LI-0186 selectively inhibited leucine-dependent mTORC1 signaling by disrupting the LRS-RagD interaction, leading to dose-dependent suppression of S6K phosphorylation (IC_{50} =81.4nM). BC-LI-0186 induced apoptosis via cleavage of PARP and caspase-3, with an EC_{50} of 62nM for cell death. The compound also blocked lysosomal localization of LRS and Raptor, suppressing mTORC1 activation without affecting LRS catalytic activity.

Animal experiment [2]:

Animal models LSL K-ras G12D mice (lung cancer model)

Preparation Method Mice were intraperitoneally administered BC-LI-0186 (20mg/kg, twice daily) for 5 days per week over 2 weeks. Tumor progression was monitored via microcomputed tomography (μ CT) before and after treatment. Lung tissues were harvested for histopathological and immunohistochemical analysis post-treatment.

Dosage form 20mg/kg; i.p.; twice daily for 2 weeks.

Applications BC-LI-0186 significantly suppressed tumor growth by approximately 40%, comparable to cisplatin. BC-LI-0186 induced apoptosis via increased activated caspase-3 expression in tumor tissues and inhibited mTORC1 signaling, evidenced by reduced phosphorylation of S6 and AKT.

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References:

- [1] Kim JH, Lee C, Lee M, et al. Control of leucine-dependent mTORC1 pathway through chemical intervention of leucyl-tRNA synthetase and RagD interaction. Nat Commun. 2017 Sep 29;8(1):732.
- [2] Kim EY, Lee JG, Lee JM, et al. Therapeutic effects of the novel Leucyl-tRNA synthetase inhibitor BC-LI-0186 in non-small cell lung cancer. Ther Adv Med Oncol. 2019 May 19;11:1758835919846798.

Background

BC-LI-0186 is a potent and highly selective inhibitor of the interaction between leucyl-tRNA synthetase (LRS) and Ras-related GTP-binding protein D (RagD), with an IC_{50} value of 46.11 nM ^[1-2]. By competitively binding to the RagD interaction site on the LRS protein, BC-LI-0186 specifically disrupts the LRS – RagD interaction and induces apoptosis in cancer cells. BC-LI-0186 is primarily used in cancer-related research^[3-4].

In vitro, treatment of SW620 colon cancer cells with BC-LI-0186 ($0.1\text{--}20\mu\text{M}$) for 24 hours. BC-LI-0186 significantly inhibited leucine-induced S6K phosphorylation and blocked the interaction between LRS and RagD, thereby suppressing mTORC1 signaling activation and ultimately inducing cancer cell apoptosis^[1]. In C2C12 myoblasts, treatment with BC-LI-0186 ($4\mu\text{M}$) for 72 hours. BC-LI-0186 disrupted LRS – RagD binding, relieved mTORC1-mediated suppression of the IRS1-PI3K-Akt pathway, and significantly promoted myogenic differentiation^[5].

In vivo, in an LSL K-ras G12D mouse lung cancer model, BC-LI-0186 (20mg/kg ; intraperitoneal injection; 5 days per week for 2 weeks) significantly reduced tumor volume, increased expression of activated caspase-3 in tumor tissue, and inhibited phosphorylation of the mTORC1 signaling markers pS6 and pAKT^[6]. In a BALB/c nude mouse H460 cell xenograft model, BC-LI-0186 (20mg/kg ; i.p.; 5 days per week for 2 weeks) combined with trametinib (1mg/kg ; oral; 5 days per week) synergistically suppressed tumor growth, decreased the tumor volume increase rate, enhanced activated caspase-3 expression in tumor tissue, and inhibited pMEK and pS6 signaling pathway activation without causing significant body weight changes^[7].

References:

- [1] Kim JH, Lee C, Lee M, et al. Control of leucine-dependent mTORC1 pathway through chemical

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- [2] Choi H, Son JB, Kang J, et al. Leucine-induced localization of Leucyl-tRNA synthetase in lysosome membrane. Biochem Biophys Res Commun. 2017 Nov 18;493(2):1129-1135.
- [3] Kim JH, Jung K, Lee C, et al. Structure-based modification of pyrazolone derivatives to inhibit mTORC1 by targeting the leucyl-tRNA synthetase-RagD interaction. Bioorg Chem. 2021 Jul;112:104907.
- [4] You JS, Karaman K, Reyes-Ordoñez A, et al. Leucyl-tRNA Synthetase Contributes to Muscle Weakness through Mammalian Target of Rapamycin Complex 1 Activation and Autophagy Suppression in a Mouse Model of Duchenne Muscular Dystrophy. Am J Pathol. 2024 Aug;194(8):1571-1580.
- [5] Son K, You JS, Yoon MS, et al. Nontranslational function of leucyl-tRNA synthetase regulates myogenic differentiation and skeletal muscle regeneration. J Clin Invest. 2019 Apr 15;129(5):2088-2093.
- [6] Kim EY, Lee JG, Lee JM, et al. Therapeutic effects of the novel Leucyl-tRNA synthetase inhibitor BC-LI-0186 in non-small cell lung cancer. Ther Adv Med Oncol. 2019 May 19;11:1758835919846798.
- [7] Lee SH, Kim EY, Han JM, et al. Combination of the LARS1 Inhibitor, BC-LI-0186 with a MEK1/2 Inhibitor Enhances the Anti-Tumor Effect in Non-Small Cell Lung Cancer. Cancer Res Treat. 2023 Jul;55(3):851-864.

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