

Product Data Sheet

Product Name: DUBs-IN-2

Cat. No.: GC17125

Chemical Properties

Cas. No. 924296-19-5

Chemical Name (E)-9-(ethoxyimino)-9H-indeno[1,2-b]pyrazine-2,3-dicarbonitrile

SMILES CCO/N=C1C2=CC=CC=C2C3=C\1N=C(C(C#N)=N3)C#N

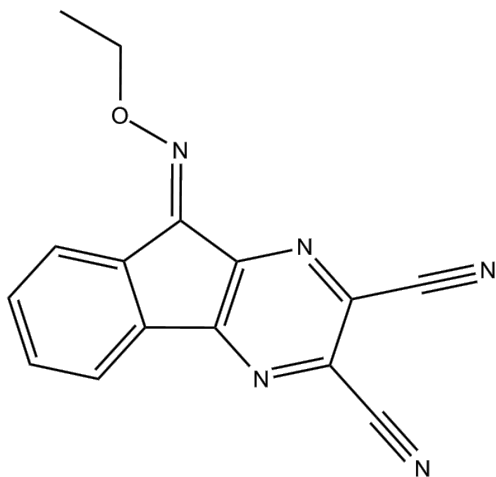
Formula $C_{15}H_9N_5O$ M.Wt 275.26

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 BGC-823 cells

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

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Preparation Method BGC-823 cells were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum, and were maintained in a humidified incubator at 37°C and 5% CO₂. 4×10^3 cells were inoculated into a 96-well plate, with 100μl of culture medium added to each well. After culturing in the incubator for 72 hours with different concentrations of DUBs-IN-2 (0.01, 0.1, 1, 10, and 100μM), cell viability was detected by the MTT assay.

Reaction Conditions 0.01, 0.1, 1, 10, and 100μM; 72h

Applications DUBs-IN-2 treatment inhibited the viability of BGC-823 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models Male nude mice

Preparation Method Male nude mice (6 weeks old) were raised in a standard sterile environment, had free access to food and water, and the light/dark cycle was 12 hours. 100μl of the culture medium containing H1975 (4×10^6) cells was mixed with 100μl of Matrigel and subcutaneously implanted into the posterior abdominal region of each mouse. When the tumor volume of the mice reached approximately 100mm³, 5 days of intraperitoneal injection of DUBs-IN-2 (1mg/kg) was administered weekly for 6 weeks. The tumor volume was measured weekly, and on the last day of the experiment, the tumor was removed for immunohistochemical analysis.

Dosage form 1mg/kg; 5 times a week for 6 weeks; i.p.

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Applications DUBs-IN-2 significantly reduced the tumor volume and downregulated the expression of phosphorylated EGFR, ERBB3 and c-MET in the tumor tissues of mice.

References:

- [1] Sun J, Shen D, Gao Y, et al. Down-regulation of USP8 suppresses HER-3 positive gastric cancer cells proliferation[J]. OncoTargets and therapy, 2020: 7973-7984.
- [2] Byun S, Lee S Y, Lee J, et al. USP8 is a novel target for overcoming gefitinib resistance in lung cancer[J]. Clinical cancer research, 2013, 19(14): 3894-3904.

Background

DUBs-IN-2 is a highly selective and membrane-permeable inhibitor for USP8 with IC₅₀ value of 0.28μM [1]. DUBs-IN-2 can activate the NF-κB signaling pathway by inhibiting the activity of USP8, thereby upregulating MHC-I expression [2]. DUBs-IN-2 has been widely used as an anti-cancer agent, effectively inhibiting the progression of colon cancer, lung cancer and prostate cancer[3].

In vitro, DUBs-IN-2 treatment for 3 days significantly inhibited the proliferation of HGC-27 cells, BGC-823 cells, and MGC-803 cells, with IC₅₀ values of 0.72μM, 0.921μM, and 1.219μM, respectively [4]. Treatment with 2μM DUBs-IN-2 for 6 hours markedly reduced the protein levels of NICD and HES1 in MDA-MB-231 cells[5]. Treatment with 10μM DUBs-IN-2 for 24 hours remarkably reduced the mRNA levels of Proopiomelanocortin (Pomc) and the protein level of EGFR in AtT-20 cells[6].

In vivo, DUBs-IN-2 was administered intraperitoneally at a dose of 1mg/kg (5 times per week) for 6 consecutive weeks, which significantly reduced the tumor volume of H1975 cell-xenograft of mice, and downregulated the expressions of phosphorylated EGFR, ERBB3 and c-MET in the tumor tissues[7]. Continuous intraperitoneal injection of 0.2mg/kg/day dose of DUBs-IN-2 for two consecutive weeks can protect the pulmonary hypertension (PH) rat model from the occurrence and development of experimental PH[8].

References:

- [1] Tsefou E, Ketteler R. Targeting deubiquitinating enzymes (DUBs) that regulate mitophagy via direct or indirect interaction with Parkin[J]. International Journal of Molecular Sciences, 2022, 23(20):

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[2] Hsu S K, Chou C K, Lin I L, et al. Deubiquitinating enzymes: potential regulators of the tumor microenvironment and implications for immune evasion[J]. Cell Communication and Signaling, 2024, 22(1): 259.

[3] Qin B, Chen X, Wang F, et al. DUBs in Alzheimer's disease: mechanisms and therapeutic implications[J]. Cell Death Discovery, 2024, 10(1): 475.

[4] Sun J, Shen D, Gao Y, et al. Down-regulation of USP8 suppresses HER-3 positive gastric cancer cells proliferation[J]. OncoTargets and therapy, 2020: 7973-7984.

[5] Shin S, Kim K, Kim H R, et al. Deubiquitylation and stabilization of Notch1 intracellular domain by ubiquitin-specific protease 8 enhance tumorigenesis in breast cancer[J]. Cell Death & Differentiation, 2020, 27(4): 1341-1354.

[6] Kageyama K, Asari Y, Sugimoto Y, et al. Ubiquitin-specific protease 8 inhibitor suppresses adrenocorticotrophic hormone production and corticotroph tumor cell proliferation[J]. Endocrine journal, 2020, 67(2): 177-184.

[7] Byun S, Lee S Y, Lee J, et al. USP8 is a novel target for overcoming gefitinib resistance in lung cancer[J]. Clinical cancer research, 2013, 19(14): 3894-3904.

[8] Jutant E M, Chelgham M K, Ottaviani M, et al. Central role of ubiquitin-specific protease 8 in leptin signaling pathway in pulmonary arterial hypertension[J]. The Journal of Heart and Lung Transplantation, 2024, 43(1): 120-133.

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