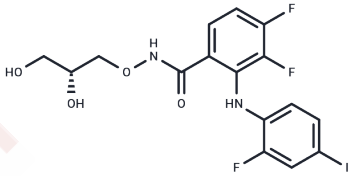
Data Sheet (Cat.No.T6189)

TargetMol

Mirdametinib

Chemical Properties



CAS No. : 391210-10-9

Formula: C16H14F3IN2O4

Molecular Weight: 482.19

Storage: Keep away from direct sunlight,Keep away from moisture
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Mirdametinib (PD325901) is an MEK inhibitor (IC50=0.33 nM) with selective, non-ATP-competitive, and oral activity. Mirdametinib exhibits antitumor activity by inhibiting p-ERK1/2 expression and inducing apoptosis.
Targets(IC50)	Apoptosis,MEK,Autophagy
In vitro	**METHODS**: Eleven human melanoma cell lines were treated with Mirdametinib (0.1-1000 nM) for 72 h, and cell counts were determined using the trypan blue exclusion test. **RESULTS**: Mirdametinib (IC50=20-50 nM) effectively inhibited the growth of human melanoma cell lines with BRAF mutations (M14/A375P/A375M/A375SM/ME10538/ME4686/JR8) or without BRAF mutations (ME4405/ME13923). ME8959 both have wild-type BRAF and are slightly more resistant to Mirdametinib-mediated growth inhibition (IC50≥100 nM). [1] **METHODS**: Papillary thyroid carcinoma (PTC) cell lines K2 and TPC-1 were treated with Mirdametinib (0.1-1000 nmol/L) for 1-96 h. Target protein expression levels were detected by Western Blot. **RESULTS**: Mirdametinib effectively inhibited the phosphorylation of ERK1/2 in various PTC cell lines. [2]
In vivo	**METHODS**: To assay antitumor activity in vivo, Mirdametinib (20-25 mg/kg, 80 mmol/L citric buffer (pH 7)) was administered by gavage to Athymic Ncr-nu/nu mice harboring PTC tumors K2 or TPC-1 five times per week for three weeks. **RESULTS**: Mirdametinib completely inhibited tumor growth in mice inoculated with PTC cells K2 harboring BRAF mutations and significantly reduced tumor growth in mice inoculated with PTC cells TPC-1 harboring RET/PTC1 rearrangements. [2] **METHODS**: To assay anti-tumor activity in vivo, Mirdametinib (1.6-25 mg/kg, 0.5% hydroxypropylmethylcellulose + 0.2% Tween 80 in water) was administered orally to mice bearing mouse colorectal cancer tumor CT26 once daily for fourteen days. **RESULTS**: Mirdametinib significantly inhibited pERK levels in tumors. [3]
Kinase Assay	Incorporation of 32P into myelin basic protein (MBP) is assayed in the presence of a glutathione S-transferase fusion protein containing p44MAP kinase (GST-MAPK) and a glutathione S-transferase protein containing p45MEK (GST-MEK). The assay solution contained 20 mM HEPES, pH 7.4, 10 mM MgCl2, 1 mM MnCl2, 1 mM EGTA, 50 mM [γ-32P] ATP, 10 mg GST-MEK, 0.5 mg GST-MAPK and 40 mg MBP in a final volume of 100 mL.

Kinase Assay	Reactions are stopped after 20 minutes by addition of trichloroacetic acid and filtered through a GF/C filter mat. 32P retained on the filter mat is determined using a 1205 Betaplate [1].
Cell Research	A cell death detection enzyme-linked immunosorbent assay was used per the manufacturer's instructions. Briefly, 4 × 10^4 cells were plated in 24-well plates in triplicate the day before treatment. PTC cells were treated with 0.1 μmol/L PD0325901 for 96 hours. Cells treated with 1 μmol/L staurosporine served as positive controls for apoptosis. At the end of treatment, cells were lysed using the lysis buffer provided in the kit for 30 minutes at room temperature and then centrifuged in 24-well plates. Lysates (20 μL of supernatant) were transferred to streptavidin-coated wells and incubated for 2 hours at room temperature with two antibodies (biotin-labeled anti-histone antibody and peroxidase-conjugated anti-DNA antibody). After the wells were washed three times, the samples were incubated with peroxidase substrate (ABTS) and the amount of colored product was determined spectrophotometrically at 405 nm. The background was measured at 490 nm [2].
Animal Research	Athymic Ncr-nu/nu mice were obtained from the National Cancer Institute at ages 6 to 8 weeks and housed for at least 1 week after arrival. Mice (10–14 per group) were anesthetized s.c. with a cocktail (100 μL/10 g body weight of 10 mg/mL ketamine and 1 mg/mL xylazine). K2 and TPC-1 cells stably infected with a retrovirus expressing luciferase (5 × 105 cells in 5 μL RPMI1640 medium) were inoculated into the thyroid gland, and the mice were monitored weekly for tumor growth by Xenogen (IVIS 200 imaging system) using Living Image 3.0 software. One week after inoculation, PD0325901 was dissolved in 80 mmol/L citric buffer (pH 7) by sonication and given to mice daily by oral gavage (20–25 mg/kg) for 3 weeks (5 consecutive days/week). Mice were sacrificed only due to tumor burden or loss of 20% of body weight. Tumor sizes were measured with calipers and tumor volume (V) was calculated by the formula (V = length × width × depth). Control mice were given 80 mmol/L citric buffer (pH 7) alone. All in vivo experiments were done at least twice [2].

Solubility Information

Solubility	H2O: Insoluble, DMSO: 50 mg/mL (103.69 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 5 mg/mL (10.37 mM),Solution. *Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.0739 mL	10.3694 mL	20.7387 mL
5 mM	0.4148 mL	2.0739 mL	4.1477 mL
10 mM	0.2074 mL	1.0369 mL	2.0739 mL
50 mM	0.0415 mL	0.2074 mL	0.4148 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

Ciuffreda L, et al. Growth-inhibitory and antiangiogenic activity of the MEK inhibitor PD0325901 in malignant melanoma with or without BRAF mutations. Neoplasia. 2009 Aug;11(8):720-31.
Guo Z, Guo L, Qin J, et al. A single transcription factor facilitates an insect host combating Bacillus thuringiensis infection while maintaining fitness. Nature Communications. 2022, 13(1): 1-15.
Wan C, Huang Y, Xue X, et al.HELQ deficiency impairs the induction of primordial germ cell-like cells.FEBS Open Bio.2024
Zheng M, Zhai Y, Yu Y, et al.TNF compromises intestinal bile-acid tolerance dictating colitis progression and limited infliximab response.Cell Metabolism.2024
Ma Z, Huang X, Kuang J, et al.Cpt1a Drives primed-to-naïve pluripotency transition through lipid remodeling. Communications Biology.2024, 7(1): 1223.
Guo Z, Kang S, Sun D, et al. MAPK-dependent hormonal signaling plasticity contributes to overcoming Bacillus thuringiensis toxin action in an insect host. Nature Communications. 2020 Jun 12;11(1):3003. doi: 10.1038/s41467-020-16608-8.
Henderson YC, et al. MEK inhibitor PD0325901 significantly reduces the growth of papillary thyroid carcinoma cells in vitro and in vivo. Mol Cancer Ther. 2010 Jul;9(7):1968-76.
Barrett SD, et al. The discovery of the benzhydroxamate MEK inhibitors CI-1040 and PD 0325901. Bioorg Med Chem Lett. 2008 Dec 15;18(24):6501-4.
Kuang, Junqi, et al. SS18 regulates pluripotent-somatic transition through phase separation.. Nature Communications. 2021 Jul 2;12(1):4090. doi: 10.1038/s41467-021-24373-5.
Lin T, et al. A chemical platform for improved induction of human iPSCs. Nat Methods. 2009 Nov;6(11):805-8.
Wang W, Ren S, Lu Y, et al. Inhibition of Syk promotes chemical reprogramming of fibroblasts via metabolic rewiring and H2S production. The EMBO Journal. 2021 Jun 1;40(11):e106771. doi: 10.15252/embj.2020106771. Epub 2021 Apr 28.
Lin R, Zhai Z, Kuang J, et al. H3K27ac mediated SS18/BAFs relocation regulates JUN induced pluripotent-somatic transition. Cell & Bioscience. 2022, 12(1): 1-14
Li Y, He Y, Peng J, et al. Mutant Kras co-opts a proto-oncogenic enhancer network in inflammation-induced metaplastic progenitor cells to initiate pancreatic cancer[J]. Nature Cancer. 2020: 1-17.
Chen F, Zhang M, Feng X, et al. Discovery of a Novel Long Noncoding RNA Lx8-SINE B2 as a Marker of Pluripotency [J]. Stem Cells International. 2021, 2021.
Guo Z, Kang S, Wu Q, et al. The regulation landscape of MAPK signaling cascade for thwarting Bacillus thuringiensis infection in an insect host. PLoS pathogens. 2021, 17(9): e1009917.
Chen F, Zhang M, Feng X, et al. Discovery of a Novel Long Noncoding RNA Lx8-SINE B2 as a Marker of Pluripotency. Stem Cells International. 2021 Feb 6;2021:6657597. doi: 10.1155/2021/6657597. eCollection 2021.
Guo Z, Kang S, Sun D, et al. MAPK-dependent hormonal signaling plasticity contributes to overcoming Bacillus thuringiensis toxin action in an insect host[J]. Nature Communications. 2020, 11(1): 1-14.
Yu Y, Li X, Jiao R, et al.H3K27me3-H3K4me1 transition at bivalent promoters instructs lineage specification in development.Cell & Bioscience.2023, 13(1): 1-20.
Yang Y, Xiao L, Xue Y, et al.ZBTB7A regulates primed-to-naïve transition of pluripotent stem cells via recognition of the PNT-associated sequence by Zinc Fingers 1–2 and recognition of γ-globin– 200 gene element by Zinc Fingers 1–4.The FEBS Journal.2023