

Product Data Sheet

Product Name: ML 349
Cat. No.: GC17889

Chemical Properties

Cas. No. 890819-86-0

Chemical Name (5,5-dioxido-4H-thieno[3,2-c]thiochromen-2-yl)(4-(4-methoxyphenyl)piperazin-1-yl)methanone

SMILES COC1=CC=C(N2CCN(C(C3=CC4=C(C(C=CC=C5)=C5S(C4)(=O)=O)S3)=O)CC2)C=C1

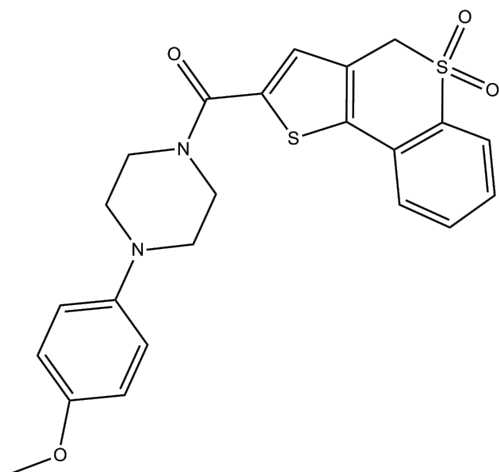
Formula $C_{23}H_{22}N_2O_4S_2$ M.Wt 454.56

Solubility 5mg/mL in DMSO, or in DMF 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]:

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Cell lines	NCM460 cells
Preparation Method	The NCM460 cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% v/v fetal bovine serum (FBS) and 1% v/v penicillin/streptomycin. The culture conditions were 37°C and 5% CO₂. The cells were pretreated with ML 349 (20μM) or DMSO for 24 hours, and then stimulated with 1μg/mL lipopolysaccharide (LPS) combined with 200μM PA and 100μM bovine serum albumin (BSA) for 24 hours. The levels of palmitoylated STAT3 were measured.
Reaction Conditions	20μM; 24h
Applications	ML 349 treatment enhanced levels of palmitoylated STAT3 in the presence of LPS-PA within NCM460 cells.

Animal experiment [2]:

Animal models	Zdhhc7-knockout mice
Preparation Method	Zdhhc7-knockout mice were raised under specific pathogen-free conditions. The mice (6-8 weeks old) were randomly divided into different groups (8 mice per group, mixed sexes). Colitis was induced by adding 3.0% DSS to the mice's drinking water. The mice were intraperitoneally injected with ML 349 solution (50mg/kg/day) for 7 days. All mice were euthanized and the distance from the cecum to the anus was measured. The colon was fixed in 4% paraformaldehyde for pathological examination.
Dosage form	50mg/kg/day for 7 days; i.p.
Applications	ML 349 treatment prevented intestinal shortening and alleviated DSS-induced colitis in mice.

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References:

- [1] Wei Y, Li J, Li J, et al. Dietary long-chain fatty acids promote colitis by regulating palmitoylation of STAT3 through CD36-mediated endocytosis[J]. Cell Death & Disease, 2024, 15(1): 60.
- [2] Zhang M, Zhou L, Xu Y, et al. A STAT3 palmitoylation cycle promotes TH17 differentiation and colitis[J]. Nature, 2020, 586(7829): 434-439.

Background

ML 349 is the active-site competitive acyl protein thioesterase 2 (APT2) inhibitor, with $K_i = 0.120\mu\text{M}$ [1]. ML 349 is a selective, reversible inhibitor of Lysophospholipase 2 (LYPLA2), with an IC_{50} value of $0.144\mu\text{M}$ [2]. ML 349 has been widely used in cell models to regulate the S-palmitoylation of proteins within the cells [3].

In vitro, ML 349 treatment at $5\mu\text{M}$ for 16 hours can restore the membrane localization and palmitoylation of multidomain scaffolding protein Scribble (Scrib), and reduce the activation of MEK in MDCK-Snail cells [4]. ML 349 pretreatment ($20\mu\text{M}$) in NCM460 cells for 24 hours reduced the effects of palmitic acid (PA) on the expression of APT2, p-STAT3, ZO-1, closure protein, BCL-2 and BAX, and upregulated the STAT3 palmitoylation level [5]. Treatment with $8\mu\text{M}$ ML 349 for 72 hours led to a slight activation of AKT in NRAS mutant-SK-MEL-2 cells, without affecting the cell viability [6].

In vivo, ML 349 treatment via intraperitoneal injection at 50mg/kg/day for 7 days prevented intestinal shortening and alleviated DSS-induced colitis in Zdhhc7-knockout mice [7]. Injecting ML 349 (5mg/kg) into the tail vein of mice for 4 hours enhanced the palmitoylation of mitochondrial antiviral signaling protein (MAVS), increased the phosphorylation of TBK1 and IRF3, inhibited the levels of VSV-GFP and VSV titer, and elevated the mRNA levels of antiviral genes during Sendai virus (SeV) infection [8].

References:

- [1] Won S J, Eschweiler J D, Majmudar J D, et al. Affinity-based selectivity profiling of an in-class selective competitive inhibitor of acyl protein thioesterase 2[J]. ACS Medicinal Chemistry Letters, 2017, 8(2): 215-220.
- [2] Adibekian A, Martin B R, Chang J W, et al. Characterization of a selective, reversible inhibitor of

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lysophospholipase 2 (LYPLA2)[J]. Probe Reports from the NIH Molecular Libraries Program [Internet], 2014.

[3] Chen B, Sun Y, Niu J, et al. Protein lipidation in cell signaling and diseases: function, regulation, and therapeutic opportunities[J]. Cell chemical biology, 2018, 25(7): 817-831.

[4] Hernandez J L, Davda D, Kit M C S, et al. APT2 inhibition restores scribble localization and S-palmitoylation in snail-transformed cells[J]. Cell chemical biology, 2017, 24(1): 87-97.

[5] Wei Y, Li J, Li J, et al. Dietary long-chain fatty acids promote colitis by regulating palmitoylation of STAT3 through CD36-mediated endocytosis[J]. Cell Death & Disease, 2024, 15(1): 60.

[6] Vujic I, Sanlorenzo M, Esteve-Puig R, et al. Acyl protein thioesterase 1 and 2 (APT-1, APT-2) inhibitors palmostatin B, ML348 and ML349 have different effects on NRAS mutant melanoma cells[J]. Oncotarget, 2016, 7(6): 7297.

[7] Zhang M, Zhou L, Xu Y, et al. A STAT3 palmitoylation cycle promotes TH17 differentiation and colitis[J]. Nature, 2020, 586(7829): 434-439.

[8] Bu L, Wang H, Zhang S, et al. Targeting APT2 improves MAVS palmitoylation and antiviral innate immunity[J]. Molecular Cell, 2024, 84(18): 3513-3529. e5.

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