

Product Data Sheet

Product Name: Lats-IN-1

Cat. No.: GC61527

Chemical Properties

Cas. No. 1424635-83-5

SMILES O=C(C1=CNC2=NC=CC=C12)/N=C(SC=C3)/N3CC4=CC=CC=C4

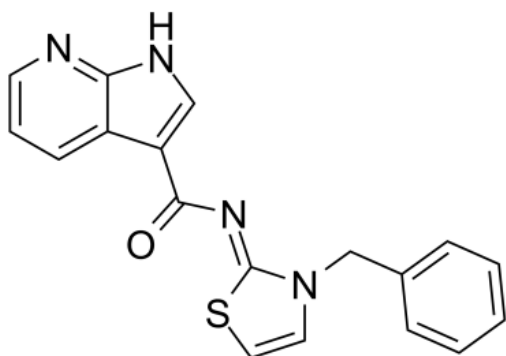
Formula $C_{18}H_{14}N_4OS$ M.Wt 334.39

Solubility DMSO: 83.33 mg/mL (249.20 mM) 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

Kinase experiment [1]:

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The LATS-IN-1 kinase assay uses an in vitro kinase activity detection method, using recombinant Lats1 and Lats2 proteins containing the main kinase domain, and STK1 peptides known to be phosphorylated by them as substrates.

Preparation Method Gradient concentrations of LATS-IN-1 are added under different ATP concentrations (10, 50, 250 μ M). After the reaction system is configured, incubate for 1h. The degree of substrate phosphorylation is detected by fluorescence or FRET and the IC₅₀ value is calculated.

Reaction Conditions 0.01nM-1 μ M; 1h

Applications The IC₅₀ of TRULI against Lats1/2 is 0.2nM at 10 μ M ATP, and the IC₅₀ increases accordingly with increasing ATP concentration, TRULI is an ATP-competitive Lats kinase inhibitor.

Cell experiment [1]:

Cell lines HEK293A cells

Preparation Method HEK293A cells were plated overnight in 96-well culture plates at a density of 50,000 cells per well in the medium described above. To start the assay, new serum-free medium with 10 μ M LATS-IN-1 was added to the cells, which were then incubated for 24h at 37 °C.

Reaction Conditions 10 μ M; 24h

Applications Lats-IN-1 inhibits YAP phosphorylation and promotes YAP nuclear translocation, activating its downstream transcriptional activity.

Animal experiment [2]:

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Animal models Myocardial infarction (MI) mice models

Preparation Method The mice in the Sham + Lats-IN-1 group and the MI + Lats-IN-1 group were administered intraperitoneally with Lats-IN-1 (1mg/kg) dissolved in corn oil on the first day after myocardial infarction surgery, while the mice in the Sham + Vehicle group and the MI + Vehicle group were given corn oil. Following a period of 2 weeks post-MI, the mice were anesthetized and subsequently sacrificed to facilitate the collection of heart tissues for subsequent examinations and analyses.

Dosage form 1mg/kg; ip; 14d

Applications Lats-IN-1 treated mice had higher ejection fraction (EF%) and fractional shortening (FS%) than those treated with the vehicle.

References:

- [1]. Kastan N, Gnedeva K, Alisch T, et al. Small-molecule inhibition of Lats kinases may promote Yap-dependent proliferation in postmitotic mammalian tissues. *Nature communications*. 2021 May 25; 12(1): 3100.
- [2]. Shen H, Wang Q, Liu B, et al. Lats-IN-1 protects cardiac function and promotes regeneration after myocardial infarction by targeting the hippo pathway. *Frontiers in Pharmacology*. 2024 Oct 3; 15: 1463465.

Background

LATS-IN-1 is an inhibitor of LATS1 and LATS2 ($IC_{50} = 2nM$ for both). Lats-IN-1 inhibits core Hippo pathway kinases and activates downstream effector molecules YAP/TAZ, which translocate to the nucleus, driving expression of genes that promote cell proliferation and survival. Lats-IN-1 is primarily used to treat tissue regeneration and degenerative diseases [1-4].

In HEK293A cells, LATS-IN-1 (10 μ M, 24h) inhibits phosphorylation of YAP1 in serum-starved HEK293A cells ($EC_{50} = 510$ nM) [1]. In K562 cells, LATS-IN-1 (30 μ M, 48h) significantly reduces the

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number of K562 colonies in the colony formation assay [5]. In human embryonic stem cells, LATS-IN-1 (30 μ M, 24h) inhibition of the Hippo Pathway Promotes Growth of ATM-Knockout human embryonic stem cells and of Their Derived NPCs [6]. In MCF-7 cells, the proliferation and migration ability of MCF-7 cells was significantly restored after LATS-IN-1 (30 μ M, 24h) inhibited the Hippo signaling [7]. In LX2 cells, Lats-IN-1 (5 μ M, 24h) was supplemented, expression of YAP and α -SMA was increased in Ctrl (scrambled)-siRNA-transfected LX2 cells [8].

In a subcutaneous xenograft tumor mouse model of 4T1 cells, LATS-IN-1 (10mg/kg, sc, 7d) increases xenograft tumor growth [7]. In myocardial infarction mice models, Lats-IN-1 (1mg/kg, ip, 14d) treated mice had higher ejection fraction (EF%) and fractional shortening (FS%) than those treated with the vehicle [9]. In lumbar spine instability surgery mice modes Lats-IN-1 (3mg/kg, ip, 56d) treated mice showed less pores or remodeling related signs in the cartilage endplate, with abundant Collagen II expression and rare Collagen X expression [10]. In vascular smooth muscle cell-specific Ddr1 knockout mice, Lats-IN-1 (0.5mg/kg, ip, 7d) abolishes the effect of DDR1-IN-1 on the inhibition of YAP activation [11].

References:

- [1]. Kastan N, Gnedeva K, Alisch T, et al. Small-molecule inhibition of Lats kinases may promote Yap-dependent proliferation in postmitotic mammalian tissues. *Nature communications*. 2021 May 25; 12(1): 3100.
- [2]. Cai X, Warburton C, Perez OF, et al. Hippo signaling modulates the inflammatory response of chondrocytes to mechanical compressive loading. *bioRxiv*. 2023 Jun 11.
- [3]. Boopathy GT, Hong W. Role of hippo pathway-YAP/TAZ signaling in angiogenesis. *Frontiers in cell and developmental biology*. 2019 Apr 10; 7: 49.
- [4]. Ohnishi Y, Masui A, Suezawa T, et al. Screening of factors inducing alveolar type 1 epithelial cells using human pluripotent stem cells. *Stem cell reports*. 2024 Apr 9; 19(4): 529-544.
- [5]. Klaihmon P, Lorthongpanich C, Kheolamai P, et al. Inhibition of LATS kinases reduces tumorigenicity and increases the sensitivity of human chronic myelogenous leukemia cells to imatinib. *Scientific Reports*. 2024 Feb 18; 14(1): 3993.
- [6]. Viner-Breuer R, Golan-Lev T, Benvenisty N, et al. Genome-Wide Screening in Human Embryonic Stem Cells Highlights the Hippo Signaling Pathway as Granting Synthetic Viability in ATM Deficiency. *Cells*. 2023 May 29; 12(11): 1503.
- [7]. Chen Y, Li J, Pu L, et al. DNAJB4 suppresses breast cancer progression and promotes tumor

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immunity by regulating the Hippo signaling pathway. Discover Oncology. 2023 Aug 7; 14(1): 144.

[8]. Xie L, Chen H, Zhang L, et al. JCAD deficiency attenuates activation of hepatic stellate cells and cholestatic fibrosis. Clinical and Molecular Hepatology. 2024 Jan 8; 30(2): 206.

[9]. Shen H, Wang Q, Liu B, et al. Lats-IN-1 protects cardiac function and promotes regeneration after myocardial infarction by targeting the hippo pathway. Frontiers in Pharmacology. 2024 Oct 3; 15: 1463465.

[10]. Li H, Tang Y, Liu Z, et al. Lumbar instability remodels cartilage endplate to induce intervertebral disc degeneration by recruiting osteoclasts via Hippo-CCL3 signaling. Bone Research. 2024 May 30; 12(1): 34.

[11]. Liu J, Wang J, Liu Y, et al. Liquid-liquid phase separation of DDR1 counteracts the hippo pathway to orchestrate arterial stiffening. Circulation Research. 2023 Jan 6; 132(1): 87-105.

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