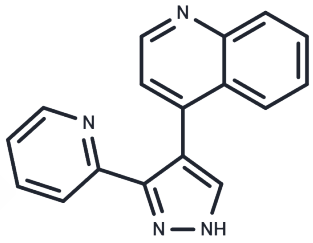
Data Sheet (Cat.No.T2048)

TargetMol

LY-364947

Chemical Properties



CAS No. : 396129-53-6

Formula: C17H12N4

Molecular Weight: 272.3

Appearance: no data available

Storage: Powder: -20°C for 3 years | In solvent: -80°C for 1 year

Biological Description

Description	LY-364947 (HTS466284) is a potent ATP-competitive inhibitor of TGFβR-I.
Targets(IC50)	MLK,Casein Kinase,RIP kinase,TGF-beta/Smad
In vitro	Administering 1 mg/kg i.p. of LY364947 significantly enhances the LYVE-1-positive regions within the tumor tissues in a BxPC3 pancreatic cancer xenograft model. Similarly, 25 mg/kg i.p. of LY364947 markedly increases LYVE-1-positive areas in a chronic peritonitis mouse model, indicating accelerated lymphangiogenesis. Additionally, LY364947 (25 mg/kg) increases p-Akt levels and decreases nuclear Foxo3a in leukemia-initiating cells in mice infected with CML.
In vivo	At a concentration as low as 0.25 μM, LY364947 enhances the xVent2-lux BMP4 response in NMuMG cells by 30%. At 2 μM, it prevents TGF-β-induced epithelial-mesenchymal transition (EMT) in NMuMG cells. A 3 μM dose of LY364947, after 24 hours of treatment, induces the expression of Prox1 and LYVE-1 in nearly all HDLECs. LY364947 promotes the nuclear export of Foxo3a and is characterized by low Smad2/3 and high Akt phosphorylation levels in leukemia-positive cells. When co-cultured with OP-9 stromal cells, LY364947 (at concentrations <20 μM) inhibits the colony-forming ability of leukemia-initiating cells. Acting as an ATP-competitive, tight-binding inhibitor, LY364947 inhibits P-Smad3 phosphorylation through TGFβR-I kinase with a Ki of 28 nM and inhibits Smad2 phosphorylation in NMuMG cells in vivo with an IC50 of 135 nM.
Kinase Assay	The IC50 of LY-364947 at different enzyme concentrations are determined by the filter-binding assay. Typically, 40 μL reactions in 50 mM HEPES at pH 7.5, 1 mM NaF, 200 μM pKSmad3(-3), and 50 mM ATP containing a titration of each inhibitor with concentrations of 1600, 800, 400, 200, 100, 50, 25, and 0 nM are incubated at 30°C for 30 min. The IC50 is calculated using a nonlinear regression method with GraphPad Prism software. The binding type is determined by plotting the correlation between enzyme concentrations and IC50 values.

Solubility Information

Solubility	DMSO: 7.5 mg/mL (27.54 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	3.6724 mL	18.3621 mL	36.7242 mL
5 mM	0.7345 mL	3.6724 mL	7.3448 mL
10 mM	0.3672 mL	1.8362 mL	3.6724 mL
50 mM	0.0734 mL	0.3672 mL	0.7345 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.

Reference

Li HY, et al. J Med Chem, 2006, 49(6), 2138-2142.
Han L, Song B, Zhang P, et al.PC3T: a signature-driven predictor of chemical compounds for cellular transition. Communications Biology.2023, 6(1): 989.
Liu S, Yan X, Guo J, et al.Periodontal ligament-associated protein-1 knockout mice regulate the differentiation of osteoclasts and osteoblasts through TGF-β1/Smad signaling pathway.Journal of Cellular Physiology.2023
Vogt J, et al. Cell Signal, 2011, 23(11), 1831-1842.
Peng SB, et al. Biochemistry, 2005, 44(7), 2293-2304.
Liu S, Yu X, Guo Q, et al.Periodontal ligament-associated protein-1 promotes osteoclastogenesis in mice by modulating TGF-β1/Smad1 pathway.Journal of Periodontology.2023
Oka M, et al. Blood, 2008, 111(9), 4571-4579.
Liu F, Zhao H, Kong R, et al. Derlin-1 and TER94/VCP/p97 are required for intestinal homeostasis. Journal of Genetics and Genomics. 2021
Naka K, et al. Nature, 2010, 463(7281), 676-680.
Li Q, Ma Y, Liu X L, et al. Anti-proliferative effect of honokiol on SW620 cells through upregulating BMP7 expression via the TGF-β1/p53 signaling pathway. Oncology Reports. 2020, 44(5): 2093-2107
Deng Y, Li L, Zhu J H, et al. COX-2 promotes the osteogenic potential of BMP9 through TGF-β1/p38 signaling in mesenchymal stem cells. Aging (Albany NY). 2021, 13(8): 11336.
Deng Y, Li L, Zhu J H, et al. COX-2 promotes the osteogenic potential of BMP9 through TGF-β1/p38 signaling in mesenchymal stem cells[J]. Aging (Albany NY) . 2021, 13(8): 11336.
Chen Q Z, Li Y, Shao Y, et al. TGF-β1/PTEN/PI3K signaling plays a critical role in the anti-proliferation effect of tetrandrine in human colon cancer cells [J]. International journal of oncology. 2017, 50(3): 1011-1021.
Li Q, Ma Y, Liu X L, et al. Anti-proliferative effect of honokiol on SW620 cells through upregulating BMP7 expression via the TGF-β1/p53 signaling pathway. Oncology Reports. 2020 Nov;44(5):2093-2107
Li Q, Ma Y, Liu X L, et al. Anti-proliferative effect of honokiol on SW620 cells through upregulating BMP7 expression via the TGF-β1/p53 signaling pathway[J]. Oncology Reports. 2020

Tel:781-999-4286 E_mail:info@targetmol.com Address:36 Washington Street,Wellesley Hills,MA 02481