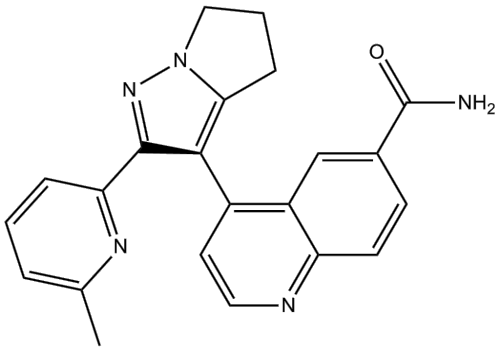
Product Data Sheet

Product Name: LY2157299
Cat. No.: GC18015

Chemical Properties

Cas. No.	700874-72-2		
Chemical Name	4-[2-(6-methylpyridin-2-yl)-5,6-dihydro-4H-pyrrolo[1,2-b]pyrazol-3-yl]quinoline-6-carboxamide		
SMILES	CC1=CC=CC(=N1)C2=NN3CCCC3=C2C4=C5C=C(C=CC5=NC=C4)C(=O)N		
Formula	$C_{22}H_{19}N_5O$	M.Wt	369.42
Solubility	≥ 18.45mg/mL 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	Hepatocellular carcinoma cells (HCC)

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Preparation Method	Seven hepatocellular carcinoma cells (HCC) lines (SK-HEP1, SK-Suni, SK-Sora, JHH6, HepG2, HuH7 and Hep3B) were incubated in serum-free medium overnight and treated with 5ng/mL of TGF-β for 1 hour followed by the addition of 1 or 10μM LY2157299 for 5 and 24h.
Reaction Conditions	1, 10μM; 5 and 24h
Applications	LY2157299 displayed potent inhibition of canonical TGF-β signalling in 6 out of 7 HCC models and selected inhibition of noncanonical pathways in several models. LY2157299 exhibited limited anti-proliferative effect only at high concentration and strong anti-invasive effect.

Animal experiment [2]:

Animal models	Sprague-Dawley male rats
Preparation Method	Acute pancreatitis group animals were administered LY2157299 intragastrically (75mg/kg) at 0 and 24h. After 48h, 0.25ml blood samples were collected and pancreas was removed.
Dosage form	75mg/kg; i.g.; 0 and 24h
Applications	LY2157299 administration alleviated the histopathological alterations of the pancreas in acute pancreatitis models by inhibiting activation of TGF-β1 signals, inducing acinar cell apoptosis and reducing proinflammatory cytokines.

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References:
[1]Serova M, Tijeras-Raballand A, Santos D C, et al. Effects of TGF-beta signalling inhibition with galunisertib (LY2157299) in hepatocellular carcinoma models and in ex vivo whole tumor tissue samples from patients. Oncotarget. 2015 Aug 28;6(25):21614-27.
[2]Liu X, Yu M, Chen Y, Zhang J. Galunisertib (LY2157299), a transforming growth factor-? receptor I kinase inhibitor, attenuates acute pancreatitis in rats. Braz J Med Biol Res. 2016 Aug 8;49(9):e5388.

Background

LY2157299 is an oral and selective TGF-β receptor type I (TGF-βRI) kinase inhibitor with an IC_{50} value of 56nM. LY2157299 specifically targets and binds to the kinase domain of TGF-βR1, thereby preventing the activation of TGF-β-mediated signaling pathways[1]. LY2157299 exhibits anticancer effects and widely applied in the treatment of various cancer types, including ovrian cancer, hepatocellular carcinoma, and neuroblastoma[2][3][4].

In vitro, LY2157299 (0, 0.1, 0.2, 0.6, 1.0, 1.5mM) treated high-grade serous ovarian cancer cells (HGSOC) for 72h inhibited TGF-β signaling characterized by the downregulation of p-SMAD2 and p-SMAD3 and also inhibited important phenotypic characteristics of HGSOC cells, including proliferation, migration, and invasion[2]. LY2157299 (0.1, 1.0, 10, and 100μM) incubated hepatocellular carcinoma cells (HCC) for 72- and 96-hour displayed limited TGF-β independent antiproliferative effects only at high concentration (100μM) and strong anti-invasive effects at 10μM[3]. LY2157299 (5μM) pretreated neuroblastoma with/without TGF-β1 (10ng/ml) for 24h showed that LY2157299 inhibited the suppressive effects of TGFβ1 on NK cells and enhanced the cytotoxicity effect against neuroblastoma cells[4].

In vivo, LY2157299 administed orally (75mg/kg, twice-daily, 7 days a week) 2 days before xenografting, then continuously for 4 weeks significantly slowed the growth of tumors in ovarian cancer cells (OVCAR8) derived xenografts (OV8-CDX) model[2]. LY2157299 administered intragastrically (75mg/kg) for 2 days (0 and 24h) alleviated the histopathological alterations of the pancreas in acute pancreatitis models by inhibiting activation of TGF-β1 signals, inducing acinar cell apoptosis and reducing proinflammatory cytokines[5]. LY2157299 injected intraperitoneally

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(150mg/kg) three times a week for 2 weeks showed a normal Hepatic Index value, a reduction of balloon-like degeneration, necrosis, inflammatory cells in the portal area and pseudolobules with thick fibrous septa in liver from fibrotic rats[6].

References:

[1]Cong L, Xia Z K, Yang R Y.Targeting the TGF-β receptor with kinase inhibitors for scleroderma therapy. Arch Pharm (Weinheim). 2014 Sep;347(9):609-15.
[2]Zhang Q, Hou X N, Evans J B, et al. LY2157299 Monohydrate, a TGF-βR1 Inhibitor, Suppresses Tumor Growth and Ascites Development in Ovarian Cancer. Cancers (Basel). 2018 Aug 7;10(8):260.
[3]Serova M, Tijeras-Raballand A, Santos D C, et al. Effects of TGF-beta signalling inhibition with galunisertib (LY2157299) in hepatocellular carcinoma models and in ex vivo whole tumor tissue samples from patients. Oncotarget. 2015 Aug 28;6(25):21614-27.
[4]Tran C H, Wan Z S, Sheard A M, et al.TGFβR1 Blockade with Galunisertib (LY2157299) Enhances Anti-Neuroblastoma Activity of the Anti-GD2 Antibody Dinutuximab (ch14.18) with Natural Killer Cells. Clin Cancer Res. 2017 Feb 1;23(3):804-813.
[5] Liu X, Yu M, Chen Y, Zhang J. Galunisertib (LY2157299), a transforming growth factor-β receptor I kinase inhibitor, attenuates acute pancreatitis in rats. Braz J Med Biol Res. 2016 Aug 8;49(9):e5388.
[6]Panzarini E, Leporatti S, Tenuzzo A B, et al. Therapeutic Effect of Polymeric Nanomicelles Formulation of LY2157299-Galunisertib on CCl4-Induced Liver Fibrosis in Rats. J Pers Med. 2022 Nov 1;12(11):1812.

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