Product Data Sheet

Product Name: LIT-927
Cat. No.: GC19486

Chemical Properties

Cas. No.	2172879-52-4		
SMILES	ClC1=CC=C(C(C=C(C2=CC=C(O)C(OC)=C2)N3)=NC3=O)C=C1		
Formula	$C_{17}H_{13}ClN_2O_3$	M.Wt	328.75
Solubility	DMF: 1mg/mL	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ 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	LIT-927		

Protocol

Cell experiment [1]:

Cell lines	MRL/lpr mice spleen cells
Preparation Method	Unstimulated cells (2 × 10^6 per well) sorted from the spleen of 11-13 week-old female MRL/lpr mice (2 mice per group; 2 independent experiments) were incubated with increasing concentrations of LIT-927 (0-20μM) at 37℃ for 24h and analyzed by flow cytometry.
Reaction Conditions	0, 5, 10, 20μM; 24h

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Applications	In a dose-response manner, LIT-927 down-regulated the overexpression of CD25 and CD86/B7-2 activation markers at the surface of splenic MRL/lpr $CD4^+$ T cells, and CD40 at the surface of MRL/lpr B cells.

Animal experiment [2]:

Animal models	Wistar rats with MCT-induced (60mg/kg) pulmonary arterial hypertension
Preparation Method	Young male Wistar rats received a single subcutaneous injection of MCT (60mg/kg). At Day 7, MCT-injected rats were treated for 2 weeks with daily intraperitoneal (i.p.) injections of LIT-927 (100mg/kg/day).
Dosage form	100mg/kg/day; 2 weeks; i.p.
Applications	MCT-injected rats treated with LIT-927 (100mg/kg/day) significantly reduced mPAP and TPVR, and attenuated right ventricular hypertrophy.

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References:
[1] SCHALL N, DAUBEUF F, MARSOL C, et al. A selective neutraligand for CXCL12/SDF-1? with beneficial regulatory functions in MRL/Lpr lupus prone mice[J]. Frontiers in Pharmacology, 2021, 12: 752194.
[2] BORDENAVE J, THUILLET R, TU L, et al. Neutralization of CXCL12 attenuates established pulmonary hypertension in rats[J]. Cardiovascular Research, 2020, 116(3): 686-697.

Background

LIT-927 is a highly selective and orally active C-X-C chemokine ligand 12 (CXCL12) neutraligand that effectively inhibits the interaction between the CXCL12 and its receptor CXCR4, with a binding affinity K_i value of 267nM[1]. CXCL12 is a key chemokine involved in inflammation, immune cell recruitment, and tissue homeostasis, exerting biological functions through binding to receptors CXCR4/CXCR7[2]. By blocking CXCL12, LIT-927 reduces inflammation and has been used in the treatment and research of allergic airway diseases and autoimmune disorders[3,4].

In vitro, treatment of MRL/lpr mouse splenocytes with LIT-927 (0-20μM) for 24h downregulated the overexpression of activation markers CD25 and CD86 on $CD4^+$ T cells and reduced CD40 expression on B cells in a dose-dependent manner[5]. LIT-927 (10, 30μM) treatment of human pulmonary artery smooth muscle cells (PA-SMCs) for 24h inhibited PA-SMC migration in a concentration-dependent manner[6]. LIT-927 (0.5μM) treatment of human glioblastoma U-87 MG cells for 24h suppressed temozolomide (TMZ)-induced phosphorylation of ERK and NF-κB[7].

In vivo, intranasal administration of LIT-927 (197ng/mL; 10μL) to house dust mite-

sensitized C57Bl/6 mice for 2 weeks significantly reduced respiratory symptom scores, effectively inhibited pericyte migration, and alleviated airway smooth muscle thickening[8]. Intraperitoneal injection of LIT-927 (100mg/kg/day) for 2 weeks in monocrotaline (MCT)-induced pulmonary artery hypertensive rats significantly reduced mean pulmonary arterial pressure (mPAP), total pulmonary vascular resistance (TPVR), and right ventricular hypertrophy (Fulton index)[6].

References:

[1] REGENASS P, ABBOUD D, DAUBEUF F, et al. Discovery of a locally and orally active CXCL12 neutraligand (LIT-927) with anti-inflammatory effect in a murine model of allergic airway hypereosinophilia[J]. Journal of Medicinal Chemistry, 2018, 61(17): 7671-7686.
[2] MINAMI H, NAGAHARU K, NAKAMORI Y, et al. CXCL12-CXCR4 axis is required for contact-mediated human B lymphoid and plasmacytoid dendritic cell differentiation but not T lymphoid generation[J]. The Journal of Immunology, 2017, 199(7): 2343-2355.
[3] JANSSENS R, STRUYF S, PROOST P. The unique structural and functional features of CXCL12[J]. Cellular & Molecular Immunology, 2018, 15(4): 299-311.
[4] LU L, LI J, JIANG X, et al. CXCR4/CXCL12 axis: "old" pathway as "novel" target for anti-inflammatory drug discovery[J]. Medicinal Research Reviews, 2024, 44(3): 1189-1220.
[5] SCHALL N, DAUBEUF F, MARSOL C, et al. A selective neutraligand for CXCL12/SDF-1α with beneficial regulatory functions in MRL/Lpr lupus prone mice[J]. Frontiers in Pharmacology, 2021, 12: 752194.
[6] BORDENAVE J, THUILLET R, TU L, et al. Neutralization of CXCL12 attenuates established pulmonary hypertension in rats[J]. Cardiovascular Research, 2020, 116(3): 686-697.
[7] CHIANG I T, LIU Y C, LIU H S, et al. Regorafenib reverses temozolomide-induced CXCL12/CXCR4 signaling and triggers apoptosis mechanism in glioblastoma[J]. Neurotherapeutics, 2022, 19(2): 616-634.
[8] BIGNOLD R, SHAMMOUT B, ROWLEY J E, et al. Chemokine CXCL12 drives pericyte accumulation and airway remodeling in allergic airway disease[J]. Respiratory Research, 2022, 23: 183.

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