Product Data Sheet

Product Name: TC LPA5 4
Cat. No.: GC15808

Chemical Properties

Cas. No.	1393814-38-4		
Chemical Name	5-(3-chloro-4-cyclohexylphenyl)-1-(3-methoxyphenyl)-1H-pyrazole-3-carboxylic acid		
SMILES	COC1=CC=CC(N2C(C3=CC(Cl)=C(C4CCCCC4)C=C3)=CC(C(O)=O)=N2)=C1		
Formula	$C_{23}H_{23}ClN_2O_3$	M.Wt	410.89
Solubility	<41.09mg/ml in DMSO	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	TC LPA5 4		

Protocol

Cell experiment [1]:

Cell lines	DLD-1 cells
Preparation Method	DLD-1 cells were seeded at a density of 3000 cells per well into the wells of 96-well plates and cultured in 5 % fetal bovine serum (FBS)-DMEM medium under 21 % and 1 % O_2 conditions for 3 days. Cells were treated with LPA (1μM) for 30min, followed by treatment with AM966 and TC LPA5 4 at concentrations of 0, 0.1 and 1μM, respectively for 3 days. Then, the cell viability was analyzed.

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Reaction Conditions	0, 0.1 and 1μM; 3 days
Applications	TC LPA5 4 treatment significantly enhanced the cell viability of DLD-1 cells in a dose-dependent manner.

Animal experiment [2]:

Animal models	BALB/C-nu/nu mice
Preparation Method	BALB/C-nu/nu mice, aged 4-5 weeks, were housed in sterile cages under laminar airflow hoods in a specific pathogen-free room with a 12-hour light and 12-hour dark schedule. The mice were fed autoclaved chow and water ad libitum. A total of 1×10^7 CGTH-W3 cells were transplanted s.c. into the flank of the nude mice. When the tumor volume reached 100mm^3, the mice were randomly assigned into control and treatment groups. Control groups were given vehicle, and treatment groups received TC LPA5 4 administration (10mg/kg; i.p.) 5 times a week for 2 weeks. The sizes of the tumors were measured twice per week.
Dosage form	10mg/kg; 5 times a week for 2 weeks; i.p.
Applications	TC LPA5 4 treatment significantly inhibited CGTH-W3 xenograft growth in mice.

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References:
[1] Yamamoto M, Takai M, Yashiro N, et al. The role of LPA receptor signaling in modulating cellular responses of colon cancer cells co-cultured with lymphoid endothelial cells under hypoxic stress[J]. Tissue and Cell, 2024, 91: 102528.
[2] Zhao W J, Zhu L L, Yang W Q, et al. LPAR5 promotes thyroid carcinoma cell proliferation and migration by activating class IA PI3K catalytic subunit p110β[J]. Cancer Science, 2021, 112(4): 1624-1632.

Background

TC LPA5 4 is a potent LPA5-selective receptor antagonist and a heparanase inhibitor with IC_{50} values of 0.8μM and 10μM, respectively[1]. TC LPA5 4 can enhance anti-tumor activity and inhibit metastasis by inhibiting LPAR5 and autotaxin in immune cell types[2]. TC LPA5 4 has been widely used in the development of combined therapies to inhibit the progression of multiple myeloma[3].

In vitro, TC LPA5 4 treatment at 1μM for 3 days at a 21% oxygen concentration significantly promoted the growth of DLD-1 cells[4]. The 4-hour treatment with 1μM TC LPA5 4 significantly reduced the maximum respiratory capacity enhancement of LPA-

mediated effector CD8 T cells, without affecting the basal respiratory capacity[5]. Treatment of 0.5μM TC LPA5 4 for 16 hours significantly stimulated the motility of HT1080 cells[6].

In vivo, TC LPA5 4 treatment via intraperitoneal injection at a doe of 10mg/kg (5 times a week) for 2 weeks significantly inhibited CGTH-W3 xenograft growth in mice[7].

References:
[1] Zhang Y, Xiong M, Chen Z, et al. Design principle of heparanase inhibitors: A combined in vitro and in silico study[J]. ACS Medicinal Chemistry Letters, 2024, 15(7): 1032-1040.
[2] Lee S C, Dacheux M A, Norman D D, et al. Regulation of tumor immunity by lysophosphatidic acid[J]. Cancers, 2020, 12(5): 1202.
[3] Zhou X, Yang Y, Hu X, et al. Identification of LPAR1/LPAR5 as novel GPCR partners of GPRC5D for the efficient CAR-T therapy of multiple myeloma[J]. Blood, 2023, 142: 4679.
[4] Yamamoto M, Takai M, Yashiro N, et al. The role of LPA receptor signaling in modulating cellular responses of colon cancer cells co-cultured with lymphoid endothelial cells under hypoxic stress[J]. Tissue and Cell, 2024, 91: 102528.
[5] Turner J A, Fredrickson M A, D'Antonio M, et al. Lysophosphatidic acid modulates CD8 T cell immunosurveillance and metabolism to impair anti-tumor immunity[J]. Nature Communications, 2023, 14(1): 3214.
[6] Takahashi K, Minami K, Otagaki S, et al. Lysophosphatidic acid receptor-2 (LPA2) and LPA5 regulate cellular functions during tumor progression in fibrosarcoma HT1080 cells[J]. Biochemical and biophysical research communications, 2018, 503(4): 2698-2703.
[7] Zhao W J, Zhu L L, Yang W Q, et al. LPAR5 promotes thyroid carcinoma cell proliferation and migration by activating class IA PI3K catalytic subunit p110β[J]. Cancer Science, 2021, 112(4): 1624-1632.