Product Data Sheet

Product Name: TD139
Cat. No.: GC19350

Chemical Properties

Cas. No.	1450824-22-2		
SMILES	O[C@H]([C@@H](N1N=NC(C2=CC=CC(F)=C2)=C1)[C@H]([C@@H](CO)O3)O)[C@@H]3S[C@H]4[C@@H]([C@@H](N5N=NC(C6=CC=CC(F)=C6)=C5)[C@H]([C@@H](CO)O4)O)O		
Formula	$C_{28}H_{30}F_2N_6O_8S$	M.Wt	648.64
Solubility	DMSO : 50 mg/mL (77.08 mM);Ethanol : ≥ 3.33 mg/mL (5.13 mM);Water : < 0.1 mg/mL (insoluble)	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	TD139		

Protocol

Cell experiment [1]:

Cell lines	Mice Primary Alveolar Epithelial Cells
Preparation Method	Primary alveolar epithelial cells from wild-type (WT) mice were plated and treated with transforming growth factor (TGF)-β1 in the presence or absence of 10 μM TD139
Reaction Conditions	10 μM TD139

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Applications	TD139 blocked TGF-β1-induced phosphorylation of β-catenin. TD139 reduced TGF-β1-induced translocation of β-catenin to the nucleus, and most β-catenin was retained on the cell surface.

Animal experiment [1]:

Animal models	C57/Bl6 mice
Preparation Method	Mice were given bleomycin intratracheally and then saline or 10 μg TD139 was instilled into the lungs on Days 18, 20, 22, and 24 and lungs were harvested on Day 26
Dosage form	10 μg TD139 on Days 18, 20, 22, and 24
Applications	In the lungs of WT mice treated with TD139 there was marked reduction in fibrosis and β-catenin activation accompanied by decreased galectin-3 expression. TD139 produced a significant decrease in total lung collagen, TD139 also decreased β-catenin activation in vivo as quantified, galectin-3 inhibition via TD139 can block the active fibrotic phase after bleomycin-induced lung injury.

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References:

[1]. Mackinnon AC, Gibbons MA, Farnworth SL, Leffler H, Nilsson UJ, Delaine T, Simpson AJ, Forbes SJ, Hirani N, Gauldie J, Sethi T. Regulation of transforming growth factor-β1-driven lung fibrosis by galectin-3. Am J Respir Crit Care Med. 2012 Mar 1;185(5):537-46. doi: 10.1164/rccm.201106-0965OC. Epub 2011 Nov 17. PMID: 22095546; PMCID: PMC3410728.

Background

TD139 is a novel high-affinity inhibitor of the galectin-3 carbohydrate binding domain (Kd = 14 nM)[6].The antifibrotic potential of TD139 centres around the inhibition of the recruitment and expansion of Gal-3-secreting macrophages that drive local myofibroblast activation[7].

In Mice Primary Alveolar Epithelial Cells ,TD139 blocked TGF-β1-induced phosphorylation of β-catenin. TD139 reduced TGF-β1-induced translocation of β-catenin to the nucleus, and most β-catenin was retained on the cell surface[3].TD139 has been shown pre-clinically to exhibit effects on all of the key IPF cell types: modulating macrophage phenotype/Gal-3 expression and fibroblast activation, reducing the effects of key profibrotic growth factors that act on myofibroblasts, and inhibiting epithelial–mesenchymal transition[5,6].

In the lungs of WT mice treated with TD139 there was marked reduction in fibrosis and β-catenin activation accompanied by decreased galectin-3 expression. TD139 produced a significant decrease in total lung collagen, TD139 also decreased β-catenin activation in vivo as quantified, galectin-3 inhibition via TD139 can block the active fibrotic phase after bleomycin-induced lung injury[3].In mice, Inhibition of Gal3 by TD139 prevented the expression of proinflammatory cytokines in microglia, TD139 treatment ameliorated

the clinical and histological manifestations of EAU[2].TD139 also suppressed microvascular thrombosis to protect the heart from myocardial ischaemia-reperfusion injury in ApoE-/- mice[1].

In clinical trials,TD139 is safe and well tolerated in healthy subjects and IPF patients. It was shown to suppress Gal-3 expression on bronchoalveolar lavage macrophages and, in a concerted fashion, decrease plasma biomarkers associated with IPF progression[4].

References:
[1]: Chen Y, Fu W, et,al. Galectin 3 enhances platelet aggregation and thrombosis via Dectin-1 activation: a translational study. Eur Heart J. 2022 Feb 15:ehac034. doi: 10.1093/eurheartj/ehac034. Epub ahead of print. PMID: 35165707.
[2]: Liu Y, Zhao C, et,al. Galectin-3 regulates microglial activation and promotes inflammation through TLR4/MyD88/NF-kB in experimental autoimmune uveitis. Clin Immunol. 2022 Mar;236:108939. doi: 10.1016/j.clim.2022.108939. Epub 2022 Feb 1. PMID: 35121106.
[3]: Mackinnon AC, Gibbons MA, et,al. Regulation of transforming growth factor-β1-driven lung fibrosis by galectin-3. Am J Respir Crit Care Med. 2012 Mar 1;185(5):537-46. doi: 10.1164/rccm.201106-0965OC. Epub 2011 Nov 17. PMID: 22095546; PMCID: PMC3410728.
[4]: Hirani N, MacKinnon AC, et,al. Target inhibition of galectin-3 by inhaled TD139 in patients with idiopathic pulmonary fibrosis. Eur Respir J. 2021 May 27;57(5):2002559. doi: 10.1183/13993003.02559-2020. Erratum in: Eur Respir J. 2022 Apr 14;59(4): PMID: 33214209; PMCID: PMC8156151.
[5]: N. Hirani, L. Nicol, A.C. et,al. TD139, A Novel Inhaled Galectin-3 Inhibitor for The Treatment of Idiopathic Pulmonary Fibrosis (IPF). Results from The First in (IPF) Patients Study., QJM: An International Journal of Medicine, Volume 109, Issue suppl_1, September 2016, Page S16, https://doi.org/10.1093/qjmed/hcw127.003
[6]: Delaine T, Collins P, et,al. Galectin-3-Binding Glycomimetics that Strongly Reduce Bleomycin-Induced Lung Fibrosis and Modulate Intracellular Glycan Recognition. Chembiochem. 2016 Sep 15;17(18):1759-70. doi: 10.1002/cbic.201600285. Epub 2016 Aug 12. PMID: 27356186.
[7]: MacKinnon AC, Farnworth SL, et,al. Regulation of alternative macrophage activation by galectin-3. J Immunol. 2008 Feb 15;180(4):2650-8. doi: 10.4049/jimmunol.180.4.2650. PMID: 18250477.

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