Product Data Sheet

Product Name: WAY 316606
Cat. No.: GC15661

Chemical Properties

Cas. No.	915759-45-4		
Chemical Name	5-(benzenesulfonyl)-N-piperidin-4-yl-2-(trifluoromethyl)benzenesulfonamide		
SMILES	C1CNCCC1NS(=O)(=O)C2=C(C=CC(=C2)S(=O)(=O)C3=CC=CC=C3)C(F)(F)F		
Formula	$C_{18}H_{19}F_3N_2O_4S_2$	M.Wt	448.48
Solubility	≥ 44.8 mg/mL in DMSO with ultrasonic, ≥ 6.26 mg/mL in EtOH with ultrasonic and warming	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	WAY 316606		

Protocol

Cell experiment [1]:

Cell lines	Mouse bone marrow-derived macrophage

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Preparation Method	Mouse bone marrow-derived macrophages were seeded (8×10^3 cells/well) and treated with Macrophage-colony stimulating factor (M-CSF) (30ng/mL) and receptor activator of nuclear factor-κB ligand (RANKL) (50ng/mL) for 5 days until osteoclasts matured. Indicated concentrations of WAY 316606 (0, 6.25, 12.5 and 25μM) were used to treat cells for another 5 days. After that, cells were removed from the surface of bovine slices. The resorption pits were captured using a scanning electron microscope, then ImageJ software was used to quantify the area of bone resorption.
Reaction Conditions	0, 6.25, 12.5 and 25μM; 5 days
Applications	WAY 316606 significantly inhibited osteoclastogenesis induced by RANKL in a dose-dependent manner within mouse bone marrow-derived macrophage.

Animal experiment [2]:

Animal models	C57BL/6J mice
Preparation Method	A complete transection injury was made at a distance of 5mm proximal to the trapezium of the sciatic nerve in C57BL/6J mice mice. After the injury, the nerve ends at the proximal and distal ends were reconnected using 6-0 sutures. After suturing the wound, the mice were returned to the cages. For sFRP1 inhibition treatment, WAY 316606 (0.5μM, 5μL) and LPS (15mg/kg) were injected into different mice via intraneural injection, and the control group mice received PBS injections. The nerve injections of WAY 316606 and PBS were repeated every 3 days for 2 weeks. After collecting the mice, they were killed with carbon dioxide, then their cervical dislocation was performed, and the sciatic nerve was cut with scissors for analysis.

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Dosage form	0.5μM/5μL; every 3 days for 2 weeks; intraneural injection
Applications	WAY 316606 treatment significantly promoted the axon regrowth of transected nerves in mice.

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References:
[1] Ma Q, Wang S, Xie Z, et al. The SFRP1 Inhibitor WAY?316606 Attenuates Osteoclastogenesis Through Dual Modulation of Canonical Wnt Signaling[J]. Journal of Bone and Mineral Research, 2020, 37(1): 152-166.
[2] Yao X, Kong L, Qiao Y, et al. Schwann cell-secreted frizzled-related protein 1 dictates neuroinflammation and peripheral nerve degeneration after neurotrauma[J]. Cell Reports Medicine, 2024, 5(11).

Background

WAY 316606 is a potent inhibitor of Secreted Frizzled-Related Protein I (sFRP-1), with an IC_{50} value of 0.5μM[1]. WAY 316606 can regulate the activation of Wnt signaling

pathway by inhibiting sFRP-1 activity, and is used as a key regulator to modulate osteoclastogenesis and bone resorption[2]. WAY 316606 can be used as a hair growth promoter in human hair follicle organ models to induce hair growth in humans[3].

In vitro, WAY 316606 treatment at 2μM for 72 hours stimulated the proliferation of human neural stem cells, and increased the activity of the Wnt pathway[4]. Treatment with 2μM WAY 316606 for 7 days significantly increased mineralization and the expression of mineralization-related genes in periodontal ligament fibroblasts, and improved mineral homeostasis[5]. Treatment with 2μM WAY 316606 for 12 hours can partially alleviate the growth inhibition of U251 cells induced by H_2O_2 (1 mM; 12 hours), reduce cell apoptosis, and increase cell viability[6].

In vivo, WAY 316606 treatment (0.5μM/5μL) via intraneural injection per 3 days for 2 weeks significantly promoted the axon regrowth of transected nerves in mice following nerve transection[7]. In female Sprague-Dawley rats, WAY 316606 exhibited high plasma clearance (77mL/min/kg) following a single intravenous bolus dose (2mg/kg)[8].

References:
[1] Moore W J, Kern J C, Bhat R, et al. Modulation of Wnt signaling through inhibition of secreted frizzled-related protein I (sFRP-1) with N-substituted piperidinyl diphenylsulfonyl sulfonamides[J]. Journal of medicinal chemistry, 2009, 52(1): 105-116.
[2] Ma Q, Wang S, Xie Z, et al. The SFRP1 Inhibitor WAY-316606 Attenuates Osteoclastogenesis Through Dual Modulation of Canonical Wnt Signaling[J]. Journal of Bone and Mineral Research, 2020, 37(1): 152-166.
[3] Hawkshaw N J, Hardman J A, Haslam I S, et al. Identifying novel strategies for treating human hair loss disorders: cyclosporine A suppresses the Wnt inhibitor, SFRP1, in the dermal papilla of human scalp hair follicles[J]. PLoS biology, 2018, 16(5): e2003705.
[4] Donega V, van der Geest A T, Sluijs J A, et al. Single-cell profiling of human subventricular zone progenitors identifies SFRP1 as a target to re-activate progenitors[J]. Nature communications, 2022, 13(1): 1036.
[5] Gopinathan G, Foyle D, Luan X, et al. The Wnt antagonist SFRP1: a key regulator of periodontal mineral homeostasis[J]. Stem cells and development, 2019, 28(15): 1004-1014.
[6] Xing Z, Ni Y, Zhao J, et al. Hydrogen peroxide-induced secreted frizzled-related

protein 1 gene demethylation contributes to hydrogen peroxide-induced apoptosis in human U251 glioma cells[J]. DNA and cell biology, 2017, 36(5): 347-353.
[7] Yao X, Kong L, Qiao Y, et al. Schwann cell-secreted frizzled-related protein 1 dictates neuroinflammation and peripheral nerve degeneration after neurotrauma[J]. Cell Reports Medicine, 2024, 5(11).
[8] Bodine P V N, Stauffer B, Ponce-de-Leon H, et al. A small molecule inhibitor of the Wnt antagonist secreted frizzled-related protein-1 stimulates bone formation[J]. Bone, 2009, 44(6): 1063-1068.

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