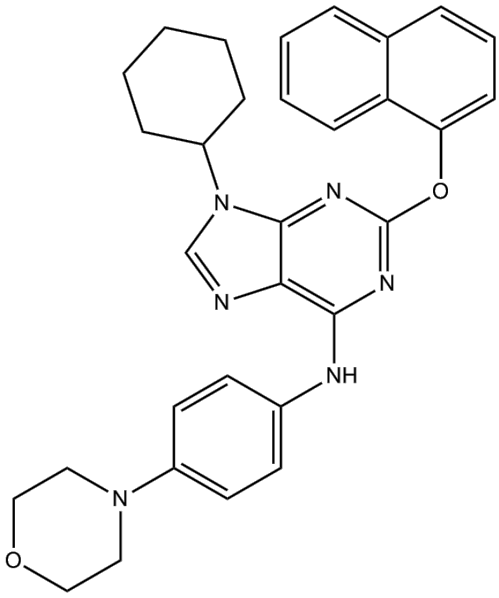
Product Data Sheet

Product Name: Purmorphamine
Cat. No.: GC15064

Chemical Properties

Cas. No.	483367-10-8		
Chemical Name	9-cyclohexyl-N-(4-morpholin-4-ylphenyl)-2-naphthalen-1-yloxypurin-6-amine		
SMILES	C1CCC(CC1)N2C=NC3=C2N=C(N=C3NC4=CC=C(C=C4)N5CCOCC5)OC6=CC=CC7=CC=CC=C76		
Formula	$C_{31}H_{32}N_6O_2$	M.Wt	520.62
Solubility	≥ 8.7mg/mL in DMSO, ≥ 1.82 mg/mL in EtOH with ultrasonic	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

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Kinase experiment[1]:	
Preparation method	Smo binding experiments were performed using BODIPY-Cyclopamine and cells overexpressing Smo. Two days after transfection of HEK 293T cells, the cells were incubated at 37 °Cfor 1 hour with DMEM medium containing BODIPY-Cyclopamine and varying concentrations of Purmorphamine (0, 1.5, or 5μM) (1 mL per well). The overexpressed Smo cells were then washed with 1xPBS buffer (1 mL per well), placed in a medium containing DAPI, observed using fluorescence microscopy, and binding detection was performed using fixed cells. Smo-overexpressing HEK293T cells were fixed at room temperature with 3% paraformaldehyde dissolved in 1 xPBS buffer (1 mL per well) for 10 minutes, then treated with 1 xPBS buffer (1 mL per well) containing 10 mm of glycerine and 0.2% sodium azide for 5 minutes with 1 xPBS buffer (1 ml per well). Cells were washed and then treated with a medium containing Purmorphamine at room temperature for 4 hours.
Reaction Conditions	0, 1.5, or 5μM Purmorphamine
Applications	Purmorphamine directly binds and activates Smoothened, blocking BODIPY-cyclopamine binding to Smo, with an IC_{50} of about 1.5 μM in HEK293T cells.
Cell experiment [2]:	

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Cell lines	C3H10T1/2 cells
Preparation method	Cells were treated with 2 μM of purmorphamine or 0.5% DMSO control for 4 days.
Reaction Conditions	2 μM purmorphamine;4 days
Applications	Purmorphamine induces osteogenesis in pluripotent mesenchymal progenitor cells.
Animal experiment [3]:	
Animal models	Male C57BL/6J mouse (HI injury)
Dosage form	10 mg/kg purmorphamine, i.p.
Applications	Purmorphamine prevents Hypoxic-Ischemic(HI)-induced brain injury.

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References:

[1]. Sinha S, Chen JK. Purmorphamine activates the Hedgehog pathway by targeting Smoothened. Nat Chem Biol. 2006 Jan;2(1):29-30. doi: 10.1038/nchembio753. Epub 2005 Nov 20. PMID: 16408088.

[2].Wu X, Walker J,et,al. Purmorphamine induces osteogenesis by activation of the hedgehog signaling pathway. Chem Biol. 2004 Sep;11(9):1229-38. doi: 10.1016/j.chembiol.2004.06.010. PMID: 15380183.

[3]. Liu D, Bai X, et,al. Purmorphamine Attenuates Neuro-Inflammation and Synaptic Impairments After Hypoxic-Ischemic Injury in Neonatal Mice via Shh Signaling. Front Pharmacol. 2020 Mar 4;11:204. doi: 10.3389/fphar.2020.00204. PMID: 32194421; PMCID: PMC7064623.

Background

Purmorphamine is the first small molecule agonist developed for Smoothened protein. Purmorphamine directly binds and activates Smoothened, blocking the binding of BODIPY-cyclopamine to Smo. Purmorphamine activates the Hedgehog(Hh) signaling pathway, resulting in up-regulation and down-regulation of its downstream target genes, including Gli1 and Patched Purmorphamine can be used to treat bone-related diseases and neurodegenerative diseases[1-2].

Purmorphamine(2 μM;4 days) induces osteogenesis in pluripotent mesenchymal progenitor cells[3]. Purmorphamine enhances osteogenic activity of human osteoblasts derived from bone marrow mesenchymal cells, Purmorphamine(1, 2 or 3 μM;21days) did not affect cell proliferation or viability, but increased ALP activity and bone-like nodule formation[4]. Purmorphamine(2 μM) had a promotive effect on adhesion, proliferation and osteogenic differentiation of human dental pulp stem cells (hDPSCs) cultured on β-TCP[5]. Purmorphamine substantially suppressed proliferation, enhanced and accelerated alkaline phosphatase activity and calcium sedimentation and increased the expression of osteopontin and osteocalcin in rat mesenchymal stem cells[6].

Purmorphamine(10 mg/kg; i.p.) prevents Hypoxic-Ischemic(HI)-induced brain injury. Purmorphamine exerted long-term protective effects upon tissue loss and improved neurobehavioral outcomes as determined at 14 and 28 days post-HI insult[7].Purmorphamine(1mg/kg; i.p.) activated Sonic hedgehog (SHH) signal to attenuate LPS-induced inflammatory response in mice[8].

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