Small Molecules

SAG

Hedgehog pathway activator;
Activates Smoothened (SMO)

Catalog # 73412 1 mg
73414 10 mg

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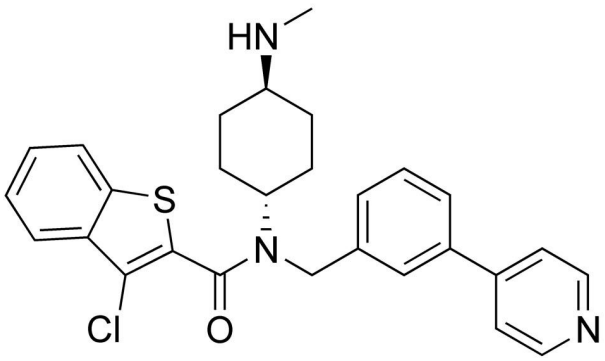
Product Description

SAG (Smoothened Agonist) is a chlorobenzothiophene-containing compound which acts as an activator of the G protein-coupled receptor Smoothened (SMO, EC_{50} = 3 nM; Chen et al.) SMO is a component of the Hedgehog signaling pathway, which is translocated to the primary cilium after stimulation of the Patched receptor by Hedgehog family ligands, leading to pathway activation. SAG activates SMO via direct binding to the heptahelical bundle (Kd = 59 nM), stabilizing a specific conformation of SMO in cilia and leading to increased downstream gene expression (Rohatgi et al.). SAG abrogates cyclopamine inhibition of SMO, indicating that it acts downstream of cyclopamine (Frank-Kamenetsky et al.; Chen et al.; Lewis & Krieg).

Molecular Name:	SAG
Alternative Names:	Smoothened Agonist
CAS Number:	912545-86-9
Chemical Formula:	$C_{28}H_{28}ClN_3OS$
Molecular Weight:	490.1 g/mol
Purity:	≥ 98%
Chemical Name:	3-chloro-N-[trans-4-(methylamino)cyclohexyl]-N-[[3-(4-pyridinyl)phenyl]methyl]-benzo[b]thiophene-2-carboxamide
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. For product expiry date, please contact techsupport@stemcell.com.
Solubility:	· DMSO ≤ 40 mM · Absolute ethanol ≤ 40 mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 204 µL of DMSO. Prepare stock solution fresh before use. Information regarding stability of small molecules in solution has rarely been reported, however, as a general guide we recommend storage in DMSO at -20°C. Aliquot into working volumes to avoid repeated freeze-thaw cycles. The effect of storage of stock solution on compound performance should be tested for each application. Compound has low solubility in aqueous media. For use as a cell culture supplement, stock solution should be diluted into culture medium immediately before use. Avoid final DMSO concentration above 0.1% due to potential cell toxicity.

Published Applications

MAINTENANCE AND SELF-RENEWAL
· Induces proliferation and survival of neuronal and glial precursors in vitro and in vivo (Bragina et al.).
· Prevents glucocorticoid neurotoxicity in Math1-Cre, SmoM2 transgenic mice (Heine et al.).
· Rescues cerebellar size and behavioral phenotypes in the Ts65Dn mouse model of Down Syndrome (Das et al.).
DIFFERENTIATION
· Improves neuronal differentiation of human induced pluripotent stem cells (Mak et al.).

References

Bragina O et al. (2010) Smoothened agonist augments proliferation and survival of neural cells. Neurosci Lett 482(2): 81–5.
Chen JK et al. (2002) Small molecule modulation of Smoothened activity. Proc Natl Acad Sci 99(22): 14071–6.
Das I et al. (2013) Hedgehog agonist therapy corrects structural and cognitive deficits in a Down syndrome mouse model. Sci Transl Med 5(201): 201ra120.
Frank-Kamenetsky M et al. (2002) Small-molecule modulators of Hedgehog signaling: identification and characterization of Smoothened agonists and antagonists. J Biol 1(2): 10.
Heine VM et al. (2011) A Small-Molecule Smoothened Agonist Prevents Glucocorticoid-Induced Neonatal Cerebellar Injury. Sci Transl Med 3(105): 105ra104.
Lewis C & Krieg PA. (2014) Reagents for developmental regulation of Hedgehog signaling. Methods 66(3): 390–7.
Mak SK et al. (2012) Small molecules greatly improve conversion of human-induced pluripotent stem cells to the neuronal lineage. Stem Cells Int 2012: 140427.
Rohatgi R et al. (2009) Hedgehog signal transduction by Smoothened: pharmacologic evidence for a 2-step activation process. Proc Natl Acad Sci U S A 106(9): 3196–201.

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