

Small Molecules

SAG

Hedgehog pathway activator;
Activates Smoothed (SMO)

Catalog # 73412
73414

1 mg
10 mg



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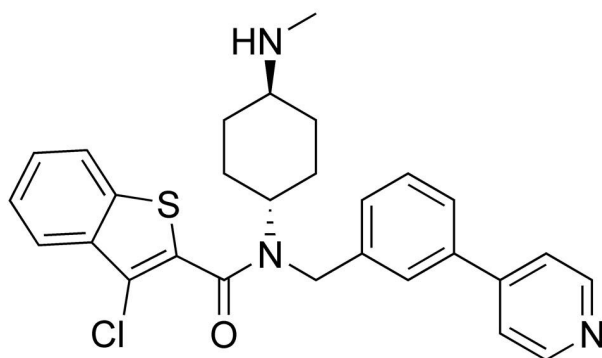
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Product Description

SAG (Smoothed Agonist) is a chlorobenzothiophene-containing compound which acts as an activator of the G protein-coupled receptor Smoothed (SMO, $EC_{50} = 3 \text{ nM}$; 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 ($K_d = 59 \text{ nM}$), 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 (Chen et al.; Frank-Kamenetsky et al.; Lewis & Krieg).

Alternative Names:	Smoothed Agonist
CAS Number:	912545-86-9
Chemical Formula:	$C_{28}H_{28}ClN_3OS$
Molecular Weight:	490.1 g/mol
Purity:	$\geq 98\%$
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. As a precaution, STEMCELL recommends storing all small molecules away from direct light. For long-term storage, store with a desiccant. Stable as supplied for 12 months from date of receipt.
Solubility:	<ul style="list-style-type: none">· DMSO $\leq 40 \text{ mM}$· Absolute ethanol $\leq 40 \text{ mM}$ 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) Smoothed agonist augments proliferation and survival of neural cells. *Neurosci Lett* 482(2): 81–5.
- Chen JK et al. (2002) Small molecule modulation of Smoothed activity. *Proc Natl Acad Sci USA* 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 Smoothed agonists and antagonists. *J Biol* 1(2): 10.
- Heine VM et al. (2011) A small-molecule Smoothed 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 Smoothed: pharmacologic evidence for a 2-step activation process. *Proc Natl Acad Sci USA* 106(9): 3196–201.

Related Small Molecules

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