Small Molecules

XAV939

WNT pathway inhibitor; Inhibits TNKS1 and TNKS2

Catalog # 72672 1 mg
72674 10 mg

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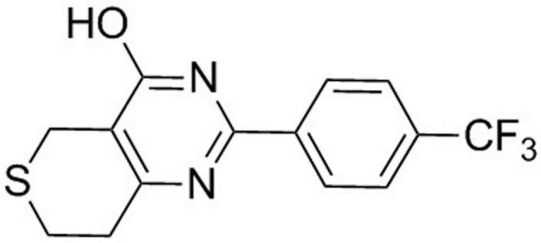
Product Description

XAV939 is an inhibitor of WNT signaling. WNT proteins are small secreted proteins that are active in embryonic development, tissue homeostasis (Clevers), and tumorigenesis (Polakis; Reya et al.). WNT proteins bind to receptors on the cell surface, initiating a signaling cascade that leads to β-catenin accumulation and downstream gene transcription. The WNT signaling pathway is regulated through degradation of the downstream effector, β-catenin, via a complex consisting of the tumor suppressor, APC, AXIN, and glycogen synthase kinase 3 (GSK3). AXIN is the concentration-limiting factor for this degradation complex. Initially identified as telomere-associated proteins (Smith), tankyrases promote AXIN ubiquitination, possibly through poly-ADP-ribosylation (PARsylation; Huang et al.). XAV939 is a potent, small molecule inhibitor of tankyrase (TNKS) 1 and 2 (IC_{50} = 11 and 4 nM, respectively; Huang et al.). By inhibiting TNKS activity, XAV939 increases the protein levels of the AXIN-GSK3β complex and promotes the degradation of β-catenin in SW480 cells (Huang et al.), thereby inhibiting WNT pathway downstream actions.

Molecular Name:	XAV939
Alternative Names:	Not applicable
CAS Number:	284028-89-3
Chemical Formula:	$C_{14}H_{11}F_3N_2OS$
Molecular Weight:	312.3 g/mol
Purity:	≥ 98%
Chemical Name:	2-[4-(trifluoromethyl)phenyl]-1,5,7,8-tetrahydrothiopyrano[4,3-d]pyrimidin-4-one
Structure:	

Properties

Physical Appearance:	A crystalline solid
Storage:	Product stable at -20°C as supplied. Protect from prolonged exposure to light. Stable as supplied for 12 months from date of receipt.
Solubility:	· DMSO ≤ 6.4 mM For example, to prepare a 1 mM stock solution in DMSO, resuspend 1 mg in 3.20 mL of fresh 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

DIFFERENTIATION
· Induces cardiomyogenesis in mesoderm progenitor cells derived from mouse embryonic stem cells (Wang et al.).
· In combination with the SMAD inhibitors LD193189 (Catalog #72146) and SB431542 (Catalog #72232), promotes induction of forebrain fates in human pluripotent stem cell lines (Maroof et al.).
CANCER RESEARCH
· Inhibits colony formation of APC-deficient, β-catenin-dependent DLD-1 colorectal cancer cells (Huang et al.).

References

Clevers H. (2006) Wnt/beta-catenin signaling in development and disease. Cell 127(3): 469–80.
Huang S-MA et al. (2009) Tankyrase inhibition stabilizes axin and antagonizes Wnt signalling. Nature 461(7264): 614–20.
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Polakis P. (2000) Wnt signaling and cancer. Genes Dev 14(15): 1837–51.
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Smith S. (1998) Tankyrase, a poly(ADP-ribose) polymerase at human telomeres. Science 282(5393): 1484–7.
Wang H et al. (2011) Cardiac induction of embryonic stem cells by a small molecule inhibitor of Wnt/β-catenin signaling. ACS Chem Biol 6(2): 192–7.

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