Small Molecules

LY364947

Activin/BMP/TGF-β pathway inhibitor; Inhibits ALK5

Catalog # 72592

5 mg

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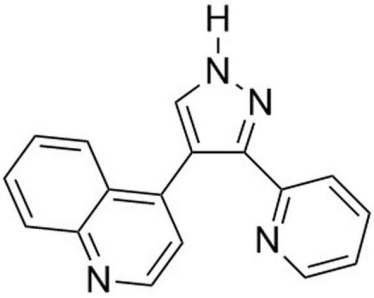
Product Description

LY364947 is a selective inhibitor of Activin/NODAL/TGFβ pathway that inhibits ALK5 (Sawyer et al.). Transforming growth factor-β (TGFβ) superfamily ligands signal through a cell surface heteromeric complex involving type I (TGFβRI) and type II (TGFβRII) receptors. Downstream signal transduction is mediated by the TGFβRI kinase domain through the phosphorylation of SMAD proteins. LY364947 is a selective inhibitor of the TGFβRI ALK5 (IC_{50} = 59 nM; Sawyer et al.). LY364947 less effectively inhibits TGFβRII (IC_{50} = 400 nM), p38 MAPK (IC_{50} = 740 nM), and mixed lineage kinase-7 (MLK-7; IC_{50} = 1,400 nM; Li et al., 2006; Sawyer et al.).

Molecular Name:	LY364947
Alternative Names:	E-616451; HTS 466284; TGF-β RI Kinase Inhibitor
CAS Number:	396129-53-6
Chemical Formula:	$C_{17}H_{12}N_4$
Molecular Weight:	272.3 g/mol
Purity:	≥ 98%
Chemical Name:	4-(3-Pyridin-2-yl)(1H)-pyrazol-4-yl quinoline
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 ≤ 3.6 mM For example, to prepare a 1 mM stock solution in DMSO, resuspend 1 mg in 3.67 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

REPROGRAMMING
· In combination with valproic acid, can replace SOX2 in reprogramming of mouse embryonic fibroblasts transduced with OCT4, KLF4 and c-MYC (Ichida et al.).
DIFFERENTIATION
· Blocks chondrogenesis induced by mechanical load in human mesenchymal stem cells (Li et al., 2010).
· Restores the hematopoietic potential of mouse para-aortic splanchnopleural cells deficient for the Evi-1 transcription factor (Sato et al.).
· Impairs definitive endoderm differentiation competence in human embryonic stem (ES) cells (Jaremko et al.).
· Blocks TGF-β-induced endothelial-to-mesenchymal transition of NMuMg mammary epithelial cells or mouse ES cell-derived endothelial cells (Peng et al.; Kokudo et al.).
CANCER RESEARCH
· Suppresses colony-forming ability of mouse and human leukemia-initiating cells cultured with OP-9 stromal cells, and, when combined with imatinib, reduces lethality in a mouse model of chronic myeloid leukemia (Naka et al.).
· Reduces invasiveness of MDA-MB-231 breast cancer cells in a matrigel invasion assay (Shiou et al.).

References

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Shiou S-R et al. (2006) Smad4-dependent regulation of urokinase plasminogen activator secretion and RNA stability associated with invasiveness by autocrine and paracrine transforming growth factor-beta. J Biol Chem 281(45): 33971–81.

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