

LY411575

Notch pathway inhibitor; Inhibits γ -secretase

Catalog #72792 5 mg

Catalog #72794 25 mg

Product Description

LY411575 is a cell-permeable γ -secretase inhibitor ($IC_{50} = 0.14$ nM) that has been shown to block Notch activation in vitro at 500 μ M (Curry et al.; Czirr et al.). γ -Secretase is a multi-subunit aspartyl protease that regulates signaling pathways by proteolytically cleaving substrates, thereby abrogating or releasing signaling molecules. Notch is a transmembrane receptor that plays a key role in cell fate decisions including cell proliferation, differentiation, and apoptosis.

CAS Number: 209984-57-6

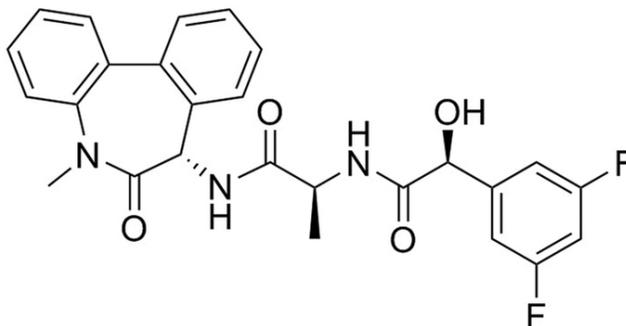
Chemical Formula: $C_{26}H_{23}F_2N_3O_4$

Molecular Weight: 479.5 g/mol

Purity: $\geq 98\%$

Chemical Name: (2S)-2-[[[(2S)-2-(3,5-difluorophenyl)-2-hydroxyacetyl]amino]-N-[(7S)-5-methyl-6-oxo-7H-benzo[d][1]benzazepin-7-yl]propanamide

Structure:



Properties

Product Format:	A crystalline solid
Stability and Storage:	Product stable at -20°C as supplied. As a precaution, STEMCELL recommends storing all small molecules away from direct light. Stable as supplied for 12 months from date of receipt.
Preparation:	<ul style="list-style-type: none"> • DMSO \leq 2 mM • Methanol \leq 2 mM <p>For example, to prepare a 1 mM stock solution in DMSO, resuspend 5 mg in 10.43 mL of DMSO. Warm the vial at 37°C with intermittent sonication or vortexing.</p> <p>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.</p> <p>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.</p>

Published Applications

DIFFERENTIATION

- Promotes neuronal differentiation of neural progenitor cells derived from mouse embryonic stem cells (Abranches et al.; Aranha et al.).
- Promotes goblet cell differentiation in mouse intestine and cultured colonic organoids (Okamoto et al.; Yui et al.).
- Induces hair cell differentiation from inner ear stem cells in vitro, and transdifferentiation of supporting cells into hair cells in vivo (Bramhall et al.; Mizutari et al.).
- Causes premature differentiation of Her4positive progenitor cells into neurons in zebrafish (Dirian et al.).

CANCER RESEARCH

- Induces apoptosis in primary and immortalized Kaposi's sarcoma cells (Curry et al.).

References

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- Bramhall NF et al. (2014) Lgr5-positive supporting cells generate new hair cells in the postnatal cochlea. *Stem Cell Reports* 2(3): 311–22.
- Curry CL et al. (2005) Gamma secretase inhibitor blocks Notch activation and induces apoptosis in Kaposi's sarcoma tumor cells. *Oncogene* 24 (42): 6333–44.
- Czirr E et al. (2007) Insensitivity to Abeta42-lowering nonsteroidal anti inflammatory drugs and gamma-secretase inhibitors is common among aggressive presenilin1 mutations. *J Biol Chem* 282(34): 24504–13.
- Dirian L et al. (2014) Spatial regionalization and heterochrony in the formation of adult pallial neural stem cells. *Dev Cell* 30(2): 123–36.
- Mizutari K et al. (2013) Notch inhibition induces cochlear hair cell regeneration and recovery of hearing after acoustic trauma. *Neuron* 77(1): 58–69.
- Okamoto R et al. (2009) Requirement of Notch activation during regeneration of the intestinal epithelia. *Am J Physiol Gastrointest Liver Physiol* 296(1): G23–35.
- Yui S et al. (2012) Functional engraftment of colon epithelium expanded in vitro from a single adult Lgr5+ stem cell. *Nat Med* 18(4): 618–23.

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