Small Molecules

LY411575

Notch pathway inhibitor; Inhibits γ-secretase

Catalog #	72792	5 mg
	72794	25 mg

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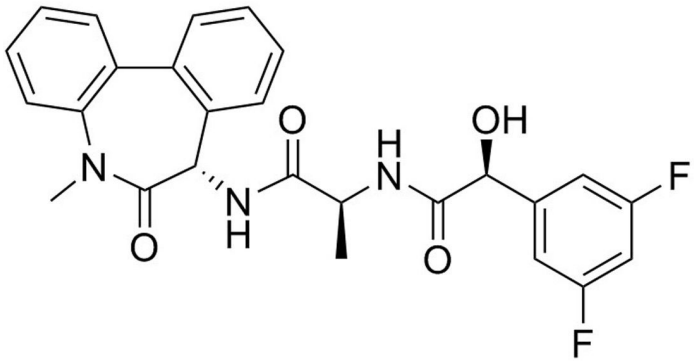
Product Description

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 µM (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.

Molecular Name:	LY411575
Alternative Names:	Not applicable
CAS Number:	209984-57-6
Chemical Formula:	$C_{26}H_{23}F_2N_3O_4$
Molecular Weight:	479.5 g/mol
Purity:	≥ 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

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 ≤ 200 µM · Absolute ethanol ≤ 200 µM · DMF ≤ 20 mM For example, to prepare a 10 mM stock solution in DMF, resuspend 1 mg in 209 µL of DMF. 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
· 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 Her4-positive 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

Abranches E et al. (2009) Neural differentiation of embryonic stem cells in vitro: a road map to neurogenesis in the embryo. PLoS One 4(7): e6286.
Aranha MM et al. (2010) Apoptosis-associated microRNAs are modulated in mouse, rat and human neural differentiation. BMC Genomics 11: 514.
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 presenilin-1 mutations. J Biol Chem 282(34): 24504–13.
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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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