

# Small Molecules

LY411575

Notch pathway inhibitor; Inhibits  $\gamma$ -secretase

Catalog # 72792  
72794

5 mg  
25 mg



Scientists Helping Scientists™ | WWW.STEMCELL.COM

TOLL FREE PHONE 1 800 667 0322 • PHONE +1 604 877 0713

INFO@STEMCELL.COM • TECHSUPPORT@STEMCELL.COM

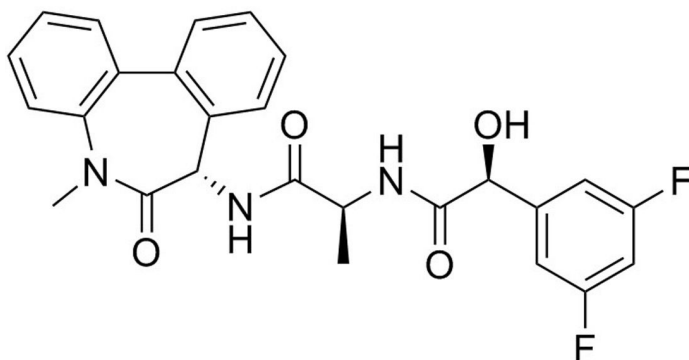
FOR GLOBAL CONTACT DETAILS VISIT OUR WEBSITE

## Product Description

LY411575 is a cell-permeable  $\gamma$ -secretase inhibitor ( $IC_{50} = 0.14$  nM) that has been shown to block Notch activation in vitro at 500  $\mu$ M (Curry et al.; Czirr et al.).  $\gamma$ -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:	$\geq 98\%$
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

Physical Appearance:	A crystalline solid
Storage:	Product stable at $-20^{\circ}C$ as supplied. Protect from prolonged exposure to light. Stable as supplied for 12 months from date of receipt.
Solubility:	· Absolute ethanol $\leq 60$ mM · DMSO $\leq 60$ mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 1 mg in 209 $\mu$ L 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  $-20^{\circ}C$ . 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.
- 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.

## Related Small Molecules

For a complete list of small molecules available from STEMCELL Technologies, visit [www.stemcell.com/smallmolecules](http://www.stemcell.com/smallmolecules) or contact us at [techsupport@stemcell.com](mailto:techsupport@stemcell.com).

STEMCELL TECHNOLOGIES INC.'S QUALITY MANAGEMENT SYSTEM IS CERTIFIED TO ISO 13485. PRODUCTS ARE FOR RESEARCH USE ONLY AND NOT INTENDED FOR HUMAN OR ANIMAL DIAGNOSTIC OR THERAPEUTIC USES UNLESS OTHERWISE STATED.

Copyright © 2017 by STEMCELL Technologies Inc. All rights reserved including graphics and images. STEMCELL Technologies & Design, STEMCELL Shield Design, and Scientists Helping Scientists are trademarks of STEMCELL Technologies Canada Inc. All other trademarks are the property of their respective holders. While STEMCELL has made all reasonable efforts to ensure that the information provided by STEMCELL and its suppliers is correct, it makes no warranties or representations as to the accuracy or completeness of such information.