Small Molecules

DBZ

Notch pathway inhibitor; Inhibits γ-secretase

Catalog # 73092

10 mg

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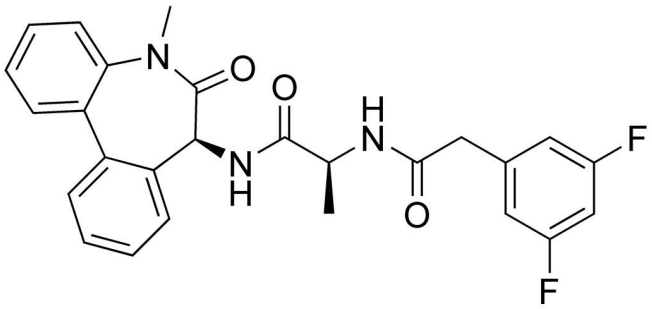
Product Description

DBZ is a diazepine inhibitor of γ-secretase, which cleaves transmembrane proteins including Notch, amyloid precursor protein (APP), and Ephrin-B2 (Borgegard et al). DBZ blocks the cleavage of Notch into its active signaling effector, Notch intracellular domain, with an IC_{50} of 1.7 nM (Milano et al.).

Molecular Name:	DBZ
Alternative Names:	Dibenzazepine; YO-01027
CAS Number:	209984-56-5
Chemical Formula:	$C_{26}H_{23}F_2N_3O_3$
Molecular Weight:	463.5 g/mol
Purity:	≥ 98%
Chemical Name:	(2S)-2-[[2-(3,5-difluorophenyl)acetyl]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 ≤ 95 mM For example, to prepare a 10 mM stock solution in DMSO, resuspend 10 mg in 2.16 mL 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°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
· Enables reprogramming of human keratinocytes to induced pluripotent stem cells in the absence of oncogenic reprogramming factors KLF4 and c-MYC (Ichida et al.).
DIFFERENTIATION
· Induces intestinal cell apoptosis and goblet cell metaplasia in rats; attenuates the reduction of Paneth cells and goblet cells caused by tuberous sclerosis 2 (TSC2) inhibition (Milano et al.; Zhou et al.).
METABOLISM
· Improves glucose homeostasis and mediates a metabolic shift toward the utilization of fat as the energy source in mice (Bi et al.).
CANCER RESEARCH
· Induces differentiation of intestinal adenomas in Apc(Min) transgenic mice (van Es et al.).
· Decreases the production of inflammatory cytokines by alloreactive T cells after bone marrow transplantation in mice, reducing the severity of graft-versus-host disease (Tran et al.).
DISEASE MODELING
· Reduces amyloid beta protein subunit (Aβ40) levels by 71% in an APP transgenic mouse model (Milano et al.).
· Reduces brain injury and improves functional outcome in an ischemia-reperfusion model of stroke in mice (Arumugam et al.).
· Attenuates renal fibrosis in a unilateral ureteral obstruction (UUO) mouse model of kidney disease (Xiao et al.).

References

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Bi P et al. (2014) Inhibition of Notch signaling promotes browning of white adipose tissue and ameliorates obesity. Nat Med 20(8): 911–8.
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Ichida et al. (2014) Notch inhibition allows oncogene-independent generation of iPS cells. Nat Chem Biol 10: 632–9.
Milano J et al. (2004) Modulation of notch processing by gamma-secretase inhibitors causes intestinal goblet cell metaplasia and induction of genes known to specify gut secretory lineage differentiation. Toxicol Sci 82(1): 341–58.
Tran IT et al. (2013) Blockade of individual Notch ligands and receptors controls graft-versus-host disease. J Clin Invest 123(4): 1590–604.
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Xiao Z et al. (2014) The Notch γ-secretase inhibitor ameliorates kidney fibrosis via inhibition of TGF-β/Smad2/3 signaling pathway activation. Int J Biochem Cell Biol 55: 65–71.
Zhou Y et al. (2015) TSC2/mTORC1 signaling controls Paneth and goblet cell differentiation in the intestinal epithelium. Cell Death Dis 6: e1631.

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