

Product Information

Anti-Nicastrin

produced in rabbit, IgG fraction of antiserum

Catalog Number **N1660**

Product Description

Anti-Nicastrin is produced in rabbit using as immunogen a synthetic peptide corresponding to the C-terminus of human nicastrin (amino acids 693-709) conjugated to keyhole limpet hemocyanin (KLH). This sequence is identical in mouse nicastrin. Whole antiserum is purified to provide an IgG fraction of antiserum

Anti-Nicastrin recognizes human nicastrin (110 kDa) by immunoblotting. Staining of nicastrin in immunoblotting is specifically inhibited with nicastrin immunizing peptide.

Nicastrin is a type I transmembrane glycoprotein (709 amino acids) that interacts with both presenilin-1 (PS1) and presenilin-2 (PS2). It has a key role in the regulation of presenilin-mediated cleavage of the β -amyloid precursor protein (β -APP) and Notch/GLP-1.¹⁻³ PS1 and PS2 are functional components of separate high molecular weight complexes found in the endoplasmic reticulum (ER) and Golgi apparatus.⁴⁻⁶ In addition to nicastrin and PS1 holoprotein, α and β -catenins are also found in this complex. PS1 and PS2 are essential for the unusual form of proteolytic cleavage that occurs within the transmembrane domain of several proteins including β -APP, Notch, and Ire1p.⁷⁻⁹ Evidence suggests that PS1 and PS2 possess the γ -secretase proteolytic activity that is necessary for the production of the neurotoxic A β peptide. In addition, the intramembrane proteolysis of β -APP is increased in missense mutations in the presenilins associated with familial Alzheimer's disease (FAD), resulting in overproduction of the A β peptide.^{10,11}

Nicastrin binds to β -APP and its C-terminal α - and β -cleaved forms and is able to modulate the production of A β peptide.¹ Missense mutations in a conserved hydrophilic domain of nicastrin increases A β peptide secretion. Deletions in this domain inhibit A β production.

Nicastrin binds to the membrane-tethered form of Notch and is essential for the intramembrane cleavage of Notch to generate Notch intracellular domain (NICD), which is involved in intracellular signaling.^{12,13} It has been suggested that nicastrin binds substrates of presenilin/ γ -secretase complexes or modulates γ -secretase activity.

Suppression of nicastrin expression in *C. elegans* embryos induces a subset of *notch/glp-1* phenotypes similar to those induced by simultaneous null mutations in both presenilin homologues of *C. elegans* (*sel-12* and *hop-1*).¹ Thus, increasing evidence indicates that both nicastrin and presenilins are necessary components for the intramembrane proteolysis of proteins such as β -APP and Notch, and implicates a direct role for nicastrin in the pathogenesis of Alzheimer's disease and in the regulation of Notch signaling *in vivo*.

Reagent

Solution in 0.01 M phosphate buffered saline, pH 7.4, containing 15 mM sodium azide.

Precautions and Disclaimer

This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

Storage/Stability

For continuous use, store at 2-8 °C for up to one month. For prolonged storage, freeze in working aliquots at -20 °C. Repeated freezing and thawing, or storage in frost-free freezers, is not recommended. If slight turbidity occurs upon prolonged storage, clarify the solution by centrifugation before use. Working dilutions should be discarded if not used within 12 hours.

Product Profile

Immunoblotting: a minimum working antibody dilution of 1:1,000 is recommended using a whole cell extract of the HEK293 cell line stably transfected with human nicastrin.

Note: In order to obtain the best results using different techniques and preparations, we recommend determining the optimal working dilutions by titration.

References

1. Yu, G., et al., *Nature*, **407**, 48 (2000).
2. Schenk, D., et al., *Nature*, **407**, 34 (2000).
3. Sisodia, S.S., et al., *Science*, **289**, 2296 (2000).
4. Yu, G., et al., *J. Biol. Chem.*, **273**, 16470 (1998).
5. Nishimura, M., et al., *Nature Med.*, **5**, 164 (1999).
6. De Strooper, B., et al., *J. Biol. Chem.*, **272**, 3590 (1997).
7. De Strooper, B., et al., *Nature*, **391**, 387 (1998).
8. Song, W., et al., *Proc. Natl. Acad. Sci. USA*, **96**, 6959 (1999).
9. Niwa, M., et al., *Cell*, **99**, 691 (1999).
10. Scheuner, D., et al., *Nature Med.*, **2**, 864 (1996).
11. Citron, M., et al., *Nature Med.*, **3**, 67 (1997).
12. Hu, Y., et al., *Dev. Cell*, **2**, 69 (2002).
13. Lopez-Schier, H., and Johnston, D.S., *Dev. Cell*, **2**, 79 (2002).

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