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ProductInformation

Anti-Aph-1aL
Developed in Rabbit, Affinity Isolated Antibody

Product Number **A 9603**

Product Description

Anti-Aph-1aL is developed in rabbit using a synthetic peptide encoding amino acids 246-265 located at the C-terminus of human Aph-1aL, conjugated to KLH, as immunogen. This sequence is identical in mouse Aph-1aL and is not found in Aph-1aS and Aph-1b. The antibody is affinity-purified using the immunizing peptide immobilized on agarose.

The antibody recognizes Aph-1aL (30 kDa). Additional bands at ~46 kDa and 20 kDa may be observed in some cell extracts, which may represent Aph-1aL aggregation and degradation products, respectively. Applications include immunoblotting. Staining of Aph-1aL in immunoblotting is specifically inhibited with the Aph-1aL immunizing peptide (human, amino acids 246-265).

The γ-secretase complex is an unusual high molecular weight (500-600 kDa) multimeric aspartyl protease responsible for the intramembrane cleavage of a variety of type I transmembrane proteins including the β-amyloid precursor protein (β-APP), and the developmental signaling receptor Notch/Glp-1.[1,2] γ-Secretase is intimately associated with the pathogenesis of Alzheimer's disease because β-amyloid is generated by the γ-secretase-mediated cleavage of β-APP. This proteolytic activity is also essential for the proper functioning of the Notch receptor, and additional substrates require γ-secretase-mediated processing to release the signaling moieties. Genetic and biochemical data have revealed that this protease complex consists of the presenilin (PS1, PS2) heterodimer, a highly glycosylated form of nicastrin (Nct) and the gene products Aph-1 and Pen-2.[3-6] Aph-1 consists of several isoforms including Aph-1aS (247 amino acids), Aph-1aL (265 amino acids) and Aph-1b (258 amino acids), containing seven predicted membrane-spanning domains.[7] Aph-1 physically interacts with PS1 and Nct and is necessary for γ-secretase activity. Aph-1 interacts with the immature species of nicastrin (iNct, 110 kDa) forming a stable intermediate, early in the assembly of the γ-secretase complex, prior to the addition of PS and Pen-2.[8] RNAi-mediated reduction in Aph-1 levels leads to reduction of PS1 levels, accumulation of β-APP-C-terminal fragments (β-APP-CTFs), and reduced production of β-APP and Notch-intracellular domain (S3/NICD).[7,9] In cells coexpressing PS1, Aph-1 and Nct, full-length PS1 accumulates to high levels and is stable.[10] Upon coexpression of Pen-2, the levels of PS1 are significantly reduced, concomitant with an elevation in levels of PS1 fragments over endogenous levels, and a marked accumulation of β-APP-CTFγ, suggesting that Aph-1 and Nct are necessary for stabilization of full-length PS1 and that Pen-2 is critical for proteolytic cleavage of stabilized PS1.

Reagent

The product is provided as a solution in 0.01 M phosphate buffered saline, pH 7.4, containing 15 mM sodium azide as a preservative.

Antibody concentration: approx. 2.0 mg/ml

Precautions and Disclaimer

Due to the sodium azide content a material safety data sheet (MSDS) for this product has been sent to the attention of the safety officer of your institution. Consult the MSDS for information regarding hazardous and safe handling practices.

Storage/Stability

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

Product Profile

A working concentration of 2-4 µg/ml is determined by immunoblotting using a whole extract of human kidney 293 cells transfected with human Aph-1aL.

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

References

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