

Product Information

Anti-BACE-2, N-terminus (43-60)

(Asp1; DRAP (Down region aspartic protease);
Memapsin 1)

Developed in Rabbit, Affinity Isolated Antibody

Product Number **B 7935**

Product Description

Anti-BACE-2, N-terminus (43-60) is developed in rabbit using a synthetic peptide corresponding to amino acids 43-60 near the N-terminus of human BACE-2 conjugated to KLH as immunogen. This sequence is not found in BACE-1 homologue. The antibody is affinity purified using the immunizing peptide immobilized on agarose.

Anti-BACE-2, N-terminus (43-60) recognizes human BACE-2 (52 kDa in cells transfected with BACE-2). Staining of the BACE-2 band in immunoblotting is specifically inhibited with the BACE-2 immunizing peptide (human, amino acids 43-60).

The amyloid- β peptide ($A\beta$) is a principal component of cerebral plaques in the brain of patients with Alzheimer's disease (AD). Formation of $A\beta$ involves proteolytic cleavage of the β -amyloid precursor protein (APP) by two proteases, β -secretase and γ -secretase.¹⁻³ Cleavage of APP by β -secretase, leads to the generation and extracellular release of APPs- β , a ~100 kDa soluble N-terminal fragment and intracellular C-terminal fragments (CTFs) bearing the complete $A\beta$ domain. Cleavage of the CTFs by γ -secretase, leads to the formation of $A\beta$.^{3,4} The membrane-associated aspartic protease BACE-1 (β -site APP cleaving enzyme, Asp2 or Memapsin 2) has been identified as β -secretase.⁵⁻⁸ A second homologue was also identified and termed BACE-2, (Asp1, DRAP or Memapsin 1).⁹⁻¹¹ BACE-1 and BACE-2 have similar structural organization and share 51% amino acid sequence identity. BACE-1 is highly expressed in neurons and constitutes the predominant β -secretase activity in human brain responsible for cleavage of APP at the β -cleavage site to promote $A\beta$ production. BACE-2 is expressed in the central nervous system and in many peripheral tissues, however its expression levels in neurons is substantially lower than BACE-1.^{9,10} The BACE-2 gene resides on chromosome 21 in the obligate Down's syndrome (DS) region at 21q22.3. An elevated level of

BACE-2 is observed in APP trisomic brains of DS patients, suggesting that BACE-2 may play a role in DS pathology.^{12,13} BACE-2 has also been demonstrated to cleave both wild type and Swedish mutant APP at the β -site in transfected cells.^{10,14} In addition, BACE-2 also cleaves APP at secondary sites, between Phe¹⁹-Phe²⁰ and Phe²⁰-Ala²¹ of the $A\beta$ region of APP.¹⁴ Over expression of BACE-2 in transfected cells produces intracellular CTFs, as well as increases extracellular release of APPs- β , but paradoxically reduces $A\beta$ production. The reduction of $A\beta$ formation has been attributed to the second cleavage site of BACE-2 on APP. Selective inactivation of BACE-2 by RNAi results in increased release of secreted APPs- β and $A\beta$ production,¹⁵ suggesting a role for BACE-2 in suppressing $A\beta$ production in cells expressing both BACE-1 and BACE-2.

Reagent

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

Antibody concentration: Approx. 1 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 0.5-1 µg/ml is determined by immunoblotting, using a whole extract of human HEK293 cells transfected with human BACE-2.

A working concentration of 2-4 µg/ml is determined by immunofluorescence staining of HEK293 cells transfected with human BACE-2.

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

References

1. Selkoe, D.J., Translating cell biology into therapeutic advances in Alzheimer's disease., *Nature*, **399**, A23-31 (1999).
2. Haass, C., and Selkoe, D.J., Cellular processing of β -amyloid precursor protein and the genesis of amyloid β -peptide., *Cell*, **75**, 1039-1042 (1993).
3. Esler, P.W., and Wolfe, M.S., A portrait of Alzheimer secretases--new features and familiar faces., *Science*, **293**, 1449-1454 (2001).
4. Haass, C., and De Strooper, B., The presenilins in Alzheimer's disease--proteolysis holds the key., *Science*, **286**, 916-919 (1999).
5. Vassar, R., et al., β -secretase cleavage of Alzheimer's amyloid precursor protein by the transmembrane aspartic protease BACE., *Science*, **286**, 735-741 (1999).
6. Yan, R., et al., Membrane-anchored aspartyl protease with Alzheimer's disease β -secretase activity., *Nature*, **402**, 533-537 (1999).
7. Sinha, S., et al., Purification and cloning of amyloid precursor protein β -secretase from human brain., *Nature*, **402**, 537-540 (1999).
8. Hussain, I., et al., Identification of a novel aspartic protease (Asp 2) as β -secretase., *Mol. Cell. Neurosci.*, **14**, 419-427 (1999).
9. Bennett, B.D., et al., Expression analysis of BACE2 in brain and peripheral tissues., *J. Biol. Chem.*, **275**, 20647-20651 (2000).
10. Hussain, I., et al., ASP1 (BACE2) cleaves the amyloid precursor protein at the β -secretase site., *Mol. Cell. Neurosci.*, **16**, 609-619 (2000).
11. Lin, X., et al., Human aspartic protease memapsin 2 cleaves the β -secretase site of β -amyloid precursor protein., *Proc. Natl. Acad. Sci. USA*, **97**, 1456-1460 (2000).
12. Saunders, A.J., et al., BACE Maps to Chromosome 11 and a BACE Homolog, BACE2, Reside in the Obligate Down Syndrome Region of Chromosome 21., *Science*, **286**, 1255 (1999).
13. Acquati, F., et al., The gene encoding DRAP (BACE2), a glycosylated transmembrane protein of the aspartic protease family, maps to the down critical region. *FEBS Letters*, **468**, 59-64 (2000).
14. Farzan, M., et al., BACE2, a β -secretase homolog, cleaves at the β site and within the amyloid- β region of the amyloid- β precursor protein., *Proc. Natl. Acad. Sci. USA*, **97**, 9712-9717 (2000).
15. Basi, G., et al., Antagonistic effects of β -site amyloid precursor protein-cleaving enzymes 1 and 2 on β -amyloid peptide production in cells, *J. Biol. Chem.*, **278**, 31512-31520 (2003).

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