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ProductInformation

ANTI-BACE-1 (EE-17)
Developed in Rabbit
Affinity Isolated Antibody

Product Number **B 0681**

Product Description

Anti-BACE-1 (EE-17) is developed in rabbit using a synthetic peptide corresponding to the N-terminal region of human BACE-1 (amino acids 46-62, with C-terminally added lysine) conjugated to KLH as immunogen. This sequence is identical in rat BACE-1, highly conserved in mouse BACE-1 (single amino acid substitution), and is not found in BACE-2 homologue. Anti-BACE-1 (EE-17) is affinity-purified using the immunogen peptide immobilized on agarose.

Anti-BACE-1 (EE-17) recognizes human BACE-1 (broad band at 60-75 kDa). Applications include immunoblotting. Staining of BACE-1 in immunoblotting is specifically inhibited with BACE-1 immunizing peptide (human, amino acids 46-62, with C-terminally added lysine).

Alzheimer's disease is characterized by the progressive formation in the brain of insoluble amyloid plaques and vascular deposits composed primarily of the amyloid-β peptide (Aβ).[1] It has been suggested that Aβ plays a central role in Alzheimer's disease pathogenesis. Formation of Aβ requires proteolytic cleavage of the β-amyloid precursor protein (APP) by two proteases, β-secretase and γ-secretase.[2, 3] Cleavage by β-secretase at the amino-terminus of Aβ, between residues 670 and 671 of APP, leads to the generation and extracellular release of APPs-β, an approximately 100 kDa soluble N-terminal fragment, and a membrane-associated C-terminal fragment bearing the complete Aβ domain. Cleavage of the C-terminal fragment by γ-secretase, which appears to be identical to the presenilins, leads to the formation of Aβ.[4, 5] The membrane-associated aspartic protease BACE-1 (β-site APP cleaving enzyme, Asp2 or memapsin 2) has been identified as β-secretase.[6-10] A close homologue was also identified and termed BACE-2, Asp1, DRAP or memapsin 1.[9-11]

BACE-1 constitutes the predominant β-secretase activity in human brain tissue.[6, 10] It is highly expressed in neurons, the major site of Aβ generation, while BACE-2 is widely expressed in peripheral tissues.[10, 11] Overexpression of BACE-1 leads to increased β-secretase activity while displaying appropriate cleavage site specificity for APP. The Swedish double mutations of APP, K670N, and M671L, found in early-onset Alzheimer's disease, are immediately adjacent to the APP BACE-1 cleavage site and increase the efficiency of β-secretase activity compared to wild-type APP.[6-8, 10] BACE-1 is localized within the Golgi and endosomal compartments, among the several intracellular sites where Aβ is thought to be produced. BACE-1 appears to be synthesized as an inactive pro-enzyme. Pro-BACE-1 is predominantly located within the endoplasmic reticulum.[12] It is co-translationally modified by N-glycosylation and further maturates by complex glycosylation as well as removal of its prodomain by furin-like proteases.[12-15] Pro-BACE-1 cleavage appears to occur immediately before full maturation and transport to the Golgi and endosomal systems.[12] BACE-1 is also localized to the plasma membrane, cycling between the cell membrane and the endosome. Phosphorylation of BACE-1 within its C-terminal domain appears to regulate the retrieval of reinternalized BACE-1 from the endosome.[16]

Reagent

Anti-BACE-1 (EE-17) is supplied as a solution in 0.01 M phosphate buffered saline, pH 7.4, containing 1% BSA and 15 mM sodium azide.

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 prolonged storage, freeze in working aliquots at –20 °C. Repeated freezing and thawing is not recommended. Storage in "frost-free" freezers is also 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 minimum working dilution of 1:1,000 is determined by immunoblotting, using a whole cell extract of HEK293 cell line stably transfected with human BACE-1.
Note: In order to obtain best results in different techniques and preparations we recommend determining optimal working dilutions by titration test.

References

1. Selkoe, D.J., Nature, **399 (suppl)**, A23 (1999).
2. Kang, J., et al., Nature, **325**, 733 (1987).
3. Haas, C., and Selkoe, D.J., Cell, **75**, 1039 (1993).
4. De Strooper, B., et al., Nature, **391**, 387 (1998).
5. Haas, C., and De Strooper, B., Science, **286**, 916 (1999).
6. Vassar, R., Science, **286**, 735 (1999).
7. Yan, R., et al., Nature, **402**, 533 (1999).
8. Sinha, S., et al., Nature, **402**, 537 (1999).
9. Hussain, I., et al., Mol. Cell. Neurosci., **14**, 416 (1999).
10. Lin, X., et al., Proc. Natl. Acad. Sci. USA, **97**, 1456 (2000).
11. Bennett, B.D., et al., J. Biol. Chem., **275**, 20647 (2000).
12. Capell, A., et al., J. Biol. Chem., **275**, 30849 (2000).
13. Bennett, B.D., et al., J. Biol. Chem., **275**, 37712 (2000).
14. Huse, J.T., et al., J. Biol. Chem., **275**, 33729 (2000).
15. Creemers, J.W., et al., J. Biol. Chem., **276**, 4211 (2001).
16. Walter, J., et al., J. Biol. Chem., **276**, 14634 (2001).

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