

## Product Information

### Anti-Amyloid Precursor Protein, N-Terminal produced in rabbit, IgG fraction of antiserum

Catalog Number **A8967**

Synonym: Anti- APP

#### Product Description

Anti-Amyloid Precursor Protein, N-Terminal is produced in rabbit using as immunogen a synthetic peptide NVQNGKWSDPSGTK corresponding to the N-terminal region of human APP<sub>695</sub> (amino acids 46-60) conjugated to KLH. This sequence is identical in rat and mouse APP<sub>695</sub> and the isoforms APP<sub>751</sub> and APP<sub>770</sub>. Whole antiserum is fractionated and then further purified by ion-exchange chromatography to provide the IgG fraction of antiserum that is essentially free of other rabbit serum proteins.

Anti-Amyloid Precursor Protein, N-Terminal recognizes APP<sub>695</sub>, APP<sub>751</sub> and APP<sub>770</sub> (95-100 kDa) and APP cleavage products (60 kDa), by immunoblotting. Staining of the APP bands by immunoblotting is specifically inhibited by the APP immunizing peptide.

The antibody may be used for the localization of AAP by immunoblotting and detection of neurite plaques in human Alzheimer's Disease (AD) brain by immunohistochemistry.

Alzheimer's Disease is characterized by deposition of amyloid in the central nervous system, in neurite plaques and on cerebral vasculature. The principal constituent of amyloid deposits is the  $\beta$ -amyloid peptide ( $\beta$ A4, A $\beta$ , A4) a 42-43 amino acid (4.2 kDa) fragment that is a cleavage product of the amyloid precursor proteins (APPs).<sup>1,2</sup> APPs are members of a large family of transmembrane glycoproteins widely distributed in many tissues. APPs three major isoforms, APP<sub>695</sub>, APP<sub>751</sub> and APP<sub>770</sub> (calculated MW 79-87 kDa), are derived from alternative splicing of common precursor mRNA. Both APP<sub>751</sub> and APP<sub>770</sub> contain a 56 amino acid domain that is highly homologous to the Kunitz family of serine protease inhibitors (KPI domain), whereas APP<sub>695</sub> lacks this insert.<sup>3</sup> APP<sub>695</sub> is preferentially expressed in the central nervous system,

while APP<sub>751</sub> and APP<sub>770</sub> are more abundant in peripheral tissues.<sup>4</sup> APPs undergo post-translational processing including N- and O-glycosylation, phosphorylation and sulfation. The function of APPs is unknown and the mechanisms underlying APP processing are not completely understood. Mutations in the APP gene are linked with rare forms of autosomal dominant familial Alzheimer's Disease (FAD). These mutations result in increased production of A $\beta$ . In Alzheimer's Disease, APP is thought to be internalized and degraded by an endosomal-lysosomal pathway to yield amyloidogenic peptides.<sup>5</sup>  $\beta$ -Amyloid is cytotoxic causing neuronal damage and degeneration *in vitro* and *in vivo*.<sup>6,7</sup>  $\beta$ -Amyloid peptide induces cytotoxic oxidative stress, formation of reactive oxygen intermediates (ROI), promotes microglia activation, astrocytosis and microgliosis<sup>8,9,10</sup> and it is therefore thought to play a central role in the neuropathology of AD.

#### Reagent

Supplied in 0.01 M phosphate buffered saline, pH 7.4, containing 15 mM sodium azide as a preservative.

#### 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 extended storage freeze in working aliquots. 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.

### **Product Profile**

**Immunohistochemistry:** a minimum working dilution of 1:200 is determined using formalin-fixed, paraffin-embedded, formic acid-treated sections of human Alzheimer's Disease (AD) brain.

**Immunoblotting:** a minimum working dilution of 1:1,000 is determined using rat brain cytosolic S1 fraction or supernatant of 293T cells secreting APP.

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

### **References**

1. Goldgaber, D., et al., *Science*, **235**, 877 (1987).
2. Tanzi, R.E., et al., *Science*, **235**, 880 (1987).
3. Tanzi, R.E., et al., *Nature*, **331**, 528 (1988).
4. Tanaka, S., et al., *Biochem. Biophys. Res. Commun.*, **165**, 1406 (1989).
5. Golde, T.E., et al., *Science*, **255**, 728 (1992).
6. Yankner, B.A., et al., *Science*, **245**, 417 (1989).
7. Johnson-Wood, K., et al., *Proc. Natl. Acad. Sci. USA*, **94**, 1550 (1997).
8. Hensley, K., et al., *Proc. Natl. Acad. Sci. USA*, **91**, 3270 (1994).
9. Games, D., et al., *Nature*, **373**, 523 (1995).
10. Yan, S.D., et al., *Nature*, **382**, 685 (1996).

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