

Product Information

ANTI-AMYLOID PRECURSOR PROTEIN (APP), KPI Domain Developed in Rabbit, IgG Fraction of Antiserum

Product Number **A8842**

Product Description

Anti-Amyloid Precursor Protein (APP), KPI Domain, is developed in rabbit using a synthetic peptide RAMISRWFYFDVTEGK found within the KPI domain of human APP₇₇₀ (amino acids 301-315) conjugated to BSA as immunogen. This sequence is identical in rat and mouse APP₇₇₀ and the isoform APP₇₅₁. 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 (APP), KPI Domain recognizes specifically APP₇₇₀ peptide (amino acids 301-315). Staining of the neurite plaques is specifically inhibited with APP₇₇₀ peptide (human, amino acids 301-315).

Anti-Amyloid Precursor Protein (APP), KPI Domain may be used for the 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 β -amyloid peptide (β A4, A β , A4) a 42-43 amino acids (4.2 kDa) fragment that is a cleavage product of the amyloid precursor proteins (APPs).^{1,2} APPs are members of a large family of transmembrane glycoproteins widely distributed in many tissues. APPs three major isoforms, APP₆₉₅, APP₇₅₁ and APP₇₇₀ (calculated MW 79-87 kDa), are derived from alternative splicing of common precursor mRNA. Both APP₇₅₁ and APP₇₇₀ contain a 56 amino acid domain that is highly homologous to the Kunitz family of serine protease inhibitors (KPI domain), whereas APP₆₉₅ lacks this insert.³ APP₆₉₅ is preferentially expressed in the central nervous system, while APP₇₅₁ and APP₇₇₀ are more abundant in peripheral tissues.⁴ 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 β . In Alzheimer's Disease, APP is thought to be internalized and degraded by an endosomal-lysosomal pathway to yield amyloidogenic peptides.⁵ β -Amyloid is cytotoxic causing neuronal damage and degeneration *in vitro* and *in vivo*.^{6,7} β -Amyloid peptide induces cytotoxic oxidative stress, formation of reactive oxygen intermediates (ROI), promotes microglia activation, astrocytosis and microgliosis^{8,9,10} and it is therefore thought to play a central role in the neuropathology of AD.

Reagents

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

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.

Product Profile

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

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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