ProductInformation

ANTI-p35
Developed in Rabbit
IgG Fraction of Antiserum

Product Number **P 9489**

Product Description

Anti-p35 is developed in rabbit using a synthetic peptide corresponding to the C-terminus of the human Cdk5 regulatory subunit p35 (amino acids 192-209) conjugated to KLH (keyhole limpet hemocyanin) as immunogen. This sequence is identical in rat, mouse, and bovine p35. 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-p35 recognizes the Cdk5 regulatory subunit p35 (35 kDa). Staining of p35 in immunoblotting is specifically inhibited with p35 immunizing peptide (human, amino acids 192-209).

Cdk5 is a serine/threonine kinase with close homology to other Cdks.[1] Cdk5 is a unique Cdk, because its kinase activity can be detected mainly in post-mitotic neurons in the central nervous system (CNS).[2] Association of Cdk5 with a neuron-specific regulatory subunit p35, is critical for kinase activity.[3-5] The p35/Cdk5 kinase has been implicated in a variety of functions in the CNS, including axon outgrowth, axon guidance and fasciculation (the formation of bundles or fascicles), and proper neuronal migration during cortical development. $Cdk5^{-/-}$ mice exhibit embryonic lethality associated with disruption of the cortical laminar structures in the cerebral cortex, olfactory bulb, hippocampus, and cerebellar cortex.[6] Mice lacking p35 display defects in cortical lamination and fasciculation of axonal fibers.[7-8] Neuronal birthdate labeling by BrdU reveals an inverted pattern of cell layers in the cerebral cortex in $Cdk5^{-/-}$ and $p35^{-/-}$ mice. Mutant mice lacking either Cdk5 or p35 exhibit certain similarities with the Reelin/Dab1 (*reeler* and *scrambler/yotari*) mutant mice in the disorganization of cortical laminar structures in the brain. It has been suggested that Cdk5/p35 may contribute synergistically with Reelin/Dab1 to the positioning of cortical neurons in the developing mouse brain.[9]

Cdk5/p35 activity is also required in the mature CNS. Phosphorylation of DARPP32 by Cdk5 inhibits protein kinase A signaling and alters the response of striatal neurons to dopamine.[10] Cdk5 also phosphorylates Munc18, which in turn affects synaptic vesicle exocytosis.[11] p35/Cdk5 kinase associates with a β-catenin/N-cadherin adhesion complex in the cortex, and modulates N-cadherin-mediated aggregation in embryonic cortical neurons.[12]

Deregulation of Cdk5 activity contributes to the pathogenesis of neurodegenerative diseases such as Alzheimer's disease (AD). Deregulation of Cdk5 is caused by the accumulation of a truncated fragment of p35; (p25) produced in the brain of patients with AD.[13,14] p25 causes Cdk5 to be constitutively activated and mislocalized *in vivo*. The p25/Cdk5 kinase hyperphosphorylates tau protein and reduces the ability of tau to bind to microtubules.[15] Moreover, p25/Cdk5 causes morphological degeneration and profound apoptotic cell death of primary neurons, suggesting that the conversion of p35 to p25 is involved in the pathogenesis of AD.

Reagent

Anti-p35 is supplied as a solution in 0.01 M phosphate buffered saline, pH 7.4, containing 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 rat brain extract.

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

References

1. Meyerson, M., et al., EMBO J., **11**, 2909 (1992).
2. Tsai, L-H., et al., Development, **119**, 1029 (1993).
3. Tsai, L-H., et al., Nature, **371**, 419 (1994).
4. Lew, J., et al., Nature, **371**, 423 (1994).
5. Ishiguro, K., et al., FEBS Lett., **342**, 203 (1994).
6. Ohshima, T., et al., Proc. Natl. Acad. Sci. USA, **93**, 11173 (1996).
7. Kwon, Y.T., and Tsai, L-H., J. Comp. Neurol., **395**, 510 (1998).
8. Chae, T., et al., Neuron, **18**, 29 (1997).
9. Ohshima, T., et al., Proc. Natl. Acad. Sci. USA, **98**, 2764 (2001).
10. Bibb, J.A., et al., Nature, **402**, 669 (1999).
11. Fletcher, A.I., et al., J. Biol. Chem., **274**, 4027 (1999).
12. Kwon, Y.T., et al., Curr. Biol., **10**, 363 (2000).
13. Patrick, G.N., et al., Nature, **402**, 615 (1999).
14. Lee, M-S., et al., Nature, **405**, 360 (2000).
15. Ahlijanian, M.K., et al., Proc. Natl. Acad. Sci. USA, **97**, 2910 (2000).

ER/KAA 12/01