Overexpression of Full-length but Not N-terminal Truncated Isoform of Microtubule-associated Protein (MAP) 1B Accelerates Apoptosis of Cultured Cortical Neurons

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β-amyloid (Aβ) is presumed to play a pathogenic role in Alzheimer’s disease (AD). However, there is an imperfect correlation between Aβ deposition and neuronal loss or dementia. To clarify neuronal responses to Aβ, Aβ-induced gene expression in cultured cortical neurons was analyzed by differential display followed by Northern blotting. Here we report that nonaggregated or aggregated Aβ induced microtubule-associated protein 1B (MAP1B) mRNA, especially the alternative transcript containing exon 3U, before disruption of the cell membrane by Aβ. An alternative transcript containing exon 3U is translated into an N-terminal truncated shorter isoform of MAP1B. Transfection experiments reveal that overexpression of this isoform does not accelerate neurite outgrowth or apoptosis of cortical neurons. In contrast, overexpression of MAP1B fragments containing the N-terminal 126 amino acids promoted neurite outgrowth and neuronal apoptosis. These results suggest that Aβ does not induce deleterious full-length MAP1B directly, but overexpression of full-length MAP1B might act as an effector of cell death in neurodegenerative disorders related to cytoskeletal abnormalities.

The accumulation of β-amyloid (Aβ) plaques and neurofibrillary tangles and neuronal loss in the neocortex are hallmarks of Alzheimer’s disease (AD). Pathological studies of Down’s syndrome have indicated that deposition of Aβ throughout the neocortex is the earliest event among the three lesions seen in the AD neocortex (1). Moreover, mutations in the three genes associated with familial AD cause increases in Aβ production (2), and Aβ has a toxic effect on cultured neuronal cells via an increase in reactive oxygen species production and/or activation of specific immediate-early genes (3, 4). These observations indicate that Aβ may play an important role in the pathogenesis of AD. However, about half of non-demented aged individuals have Aβ plaques in the neocortex (5–7), and transgenic mice expressing mutant human amyloid precursor protein (APP) with V171F or K670N/M671L develop Aβ plaques in the neocortex progressively with age (8, 9) but do not show neuronal loss in the neocortex (10, 11). These contradictory findings in vitro and in vivo suggest that Aβ induces not only molecules that activate the cell death pathway but also molecules that protect neurons from Aβ toxicity in the neocortex.

To begin to understand the molecular mechanisms of Aβ toxicity and the protective response of neurons against Aβ, we applied the method of RNA differential display to isolate the genes implicated in Aβ toxicity or protective responses to Aβ. The results presented here demonstrate that nonaggregated or aggregated Aβ induces MAP1B mRNA, especially the alternative transcript containing exon 3U. Transfection experiments of MAP1B isoforms in cultured cortical neurons indicated that full-length MAP1B but not the alternative MAP1B isoform resulted in the acceleration of neuronal death.

EXPERIMENTAL PROCEDURES
Cell Culture—Cerebral cortices dissected from day E17 embryonic rats were dissociated by incubation with 0.08% trypsin/0.008% DNase I at 37 °C for 10 min and passed through a 62-μm nylon mesh. The cells (4 × 10⁶ cells/dish or 4.5 × 10⁶ cells/dish, respectively) were seeded in 96-well plates or 6-cm dishes, both of which were precoated with gelatin-polyornithine, and were cultured for 7 days in MEM with 5% fetal bovine serum and 10 μM β-mercaptoethanol.

Treatment with Aβ Peptides—For treatment with nonaggregated Aβ peptide, Aβ-(1–42) (Bachem) was dissolved at 250 μM in 0.05 N HCl, filtered through a 0.45-μm membrane filter, diluted with MEM with N2 supplement (MEM-N2), and neutralized. The nonaggregated Aβ peptide was added to the 7-DIV cultures at a concentration of 5 μM immediately after preparation. For treatment with aggregated Aβ peptide, Aβ-(1–42) was dissolved at 250 μM in 0.05 N HCl, neutralized, and incubated at 37 °C for 4 days. The aggregated peptide suspension was diluted with MEM-N2 and added to the 7 DIV cultures at a concentration of 5 μM. Neuronal viability was determined by an MTT assay (12) and trypan blue exclusion.

mRNA Differential Display—Poly(A)⁺RNA from cultured rat neurons was isolated using an Amersham Biosciences Micro mRNA purification kit. Reverse transcription was carried out using AMV reverse transcriptase XL (Life Sciences) and the two three-base-anchored oligo(dT) primers (T11), GG, CG, or AA. PCR amplification was performed with the three oligo(dT) primers in combination with 24 arbitrary primers (Display Systems Biotech) in the presence of [32P]dCTP. PCR products were electrophoresed on Gene Gel Clean (Amersham Biosciences) and exposed to the imaging plate of a Fuji Bioimage analyzer BAS 2500. cDNAs were eluted from differentially displayed bands, amplified with the same primer sets described above, and cloned into a pCR2.1 vector (Invitrogen).

Northern Blot Analysis—Aliquots of 1 μg of poly (A)⁺RNA were denatured, electrophoretically fractionated on a 1.4% agarose/formaldehyde gel, and transferred to a nylon membrane. Hybridization was performed in the solution containing cloned cDNA labeled with [32P]dCTP using a random labeling kit (Roche Molecular Biochemicals). Radioactivities of the bands were measured using a Fuji Bioimage analyzer BAS 2500.
cDNA Library Screening—A 64-bp cDNA fragment obtained by the differential display method was used to screen 4 × 10^5 colonies from a SuperScript Rat Neuronal Cell cDNA Library (Invitrogen). The corresponding DNA was sequenced using a Taq cycle sequencing kit (Takara) with a fluorescence autosequencer ABI377.

**RT-PCR of MAP1B**—RT-PCR analysis was carried out according to the method of Kutschera et al. (1996) (13). Briefly, first-strand cDNA was synthesized from poly(A)^+ RNA of cultured rat neurons using SuperScript II and random hexamers (Invitrogen). PCR was carried out with EOLGase Enzyme Mix (Invitrogen). For amplification of regular transcripts of rat MAP1B, the upstream primer was nucleotides 169–190 (accession no. U52985) (14), which are located in exon 1 of MAP1B. For amplification of alternative transcripts containing exon 3U (accession no. AF035827) and 3A (accession no. AF035829), the upstream primers were nucleotides 98–74 and 58–34, respectively (13). The downstream primer was nucleotides 684–660, which are located in exon 5 of MAP1B (accession no. X60370) (15) for all amplifications. PCR products were electrophoretically fractionated on a 1.4% agarose gel and transferred to a nylon membrane. A cDNA probe of MAP1B for authenticated rat MAP1B cDNA. The full-length transcript and the additional 24 h.

**Immunoblotting**—Cells were harvested 20 h after transfection, extracted with radiolabeled precipitation assay (RIPA) buffer containing 2 mM EDTA and proteinase inhibitors, and centrifuged 20 min at 14,000 rpm at 4 °C. Cell lysates were analyzed by SDS-PAGE (a 3–10% acrylamide linear gradient gel). After the proteins were transferred to Immobilon, a Myc-tag was detected with anti-Myc-tag antibodies (MBL International) by the enhanced chemiluminescence method.

**RESULTS**

**Time Course of Aβ Neurotoxicity**—The neurotoxicity of Aβ-(1–42) to rat cortical neurons was assessed by the MTT reduction or the trypan blue exclusion. A significant decrease in MTT reduction was detected after 3 h of either nonaggregated or aggregated Aβ-(1–42) treatment (p < 0.001 or p < 0.05, respectively) and continued until at least 48 h of treatment (Fig. 1A), whereas the neuronal viability assessed by trypan blue exclusion began to decrease at 6 h of treatment with either nonaggregated or aggregated Aβ (p < 0.05) (Fig. 1B). After the addition of nonaggregated Aβ peptide, the neuronal viability continuously decreased for at least up to 48 h; however, the decrease in neuronal viability reached a plateau at 24 h after treatment with aggregated Aβ peptide. These results indicate that the decline in metabolic activity induced in neurons by Aβ treatment occurs before the disruption of the plasma membrane and that nonaggregated Aβ is more toxic than aggregated Aβ.

**MAP1B Was Induced by Either Nonaggregated or Aggregated Aβ-(1–42) Treatment before Neuronal Death**—To identify Aβ-responsive genes by differential display RT-PCR before the disruption of the cell membrane by Aβ, we compared RNA fingerprinting patterns from neurons exposed to Aβ-(1–42) (5 μM) for 3 h with those from control neurons. Most of the bands observed in this screening using 72 primer pairs showed the same patterns in control neurons and in neurons treated with nonaggregated or aggregated Aβ. A cDNA band obtained with the primer set T11G and upstream primer no. 13 (5′-TGGAT-TGGTC-3′) showed an increase in the neurons treated with either nonaggregated or aggregated Aβ (Fig. 2A). This band
Fig. 2. Differential display screening of rat cortical neurons treated with nonaggregated or aggregated Aβ-(1–42) for 3 h. Poly(A)^+ RNA extracted from cortical neurons treated for 3 h with nonaggregated or aggregated Aβ-(1–42) (final concentration 5 μM) was used either for differential display RTPCR screening (A) or Northern blot analysis (B). A, amplified ^32P-labeled PCR products using the primer set T11GG and 5'-TGGATTGGTC-3'/H11032 were separated by electrophoresis. The arrow shows the selected band, i132. B, cDNAs were eluted from the band selected in panel A, reamplified, and used as probes for Northern blotting. One microgram of the same poly(A)^+ RNA samples were electrophoresed, transblotted to a nylon membrane, and hybridized with i132 probe and a glyceraldehyde-3-phosphate dehydrogenase (GAPDH) probe. CNT, control.

contained a 64-bp cDNA (clone i132). Northern blot analysis using clone i132 as a probe confirmed the differential expression in Aβ-treated neurons (Fig. 2B). By iterative screening of a nerve cell cDNA library using the clone i132 as a probe, a cDNA (3.572 kb) was identified as the 3'-untranslated region of MAP1B (accession no. AF115776). Alternative MAP1B Transcript Containing Exon 3U Was Up-regulated in Cortical Neurons Treated with Either Nonaggregated or Aggregated Aβ-(1–42)—The MAP1B gene is transcribed into three different transcripts, i.e. a regular transcript containing exons 1–7 and two alternative transcripts containing either exon 3U or 3A and 3–7 (13). RT-PCR using 5'-specific primers located in exon 1, 3U, and 3A and a common 3'-primer located in exon 5 followed by Southern blot hybridization using a MAP1B-specific probe showed that only the transcript containing exon 3U increased in neurons treated with either nonaggregated or aggregated Aβ-(1–42) for 3 h (Fig. 3B). Northern blot analysis confirmed the significant induction of the alternative transcript containing exon 3U in cortical neurons treated with nonaggregated or aggregated Aβ-(1–42) for 3 h (Fig. 3C). The mRNAs of microtubule-associated proteins other than MAP1B were also analyzed by Northern blotting. However, neither MAP1A nor β-tubulin mRNA were not affected by treatment with nonaggregated or aggregated Aβ-(1–42) for 3–24 h (Fig. 3C).

MAP1B Fragment Containing N-terminal 126 Amino Acids Induced Apoptosis in Cortical Neurons—MAP1B is a minor component of paired helical filaments found in Alzheimer’s disease brains (16–19) and also of cortical Lewy bodies in Parkinson’s disease (20, 21). It is not known which isoforms, full-length MAP1B or shorter isoforms (MAP1B Δ126), are involved in the formation of paired helical filaments or Lewy bodies. To investigate which isoforms of MAP1B are responsible for the degeneration of neurons, we examined the effects of overexpression of MAP1B fragments on neurite sprouting and neuronal apoptosis. Because the indistinguishable electrophoretic mobility between full-length MAP1B (MAP1B-(1–2459)) and MAP1B Δ126 (MAP1B-(127–2459)) makes it difficult to examine the expression of each MAP1B isoform in transfected neurons by Western blotting, MAP1B fragments MAP1B-(1–1367) and MAP1B-(127–1367), both of which were tagged with c-Myc epitope, were generated and expressed in

Fig. 3. An alternative MAP1B transcript containing exon 3U was up-regulated in cortical neurons treated with either nonaggregated or aggregated Aβ-(1–42) for 3 h. A, schematic representation of regular and alternative transcripts of rat MAP1B. Exons are shown by boxes with the exon number. B, RTPCR analysis followed by Southern blot hybridization of three MAP1B transcripts in cortical neurons treated with nonaggregated (Non) or aggregated (Agg) Aβ-(1–42) for 3 h. Aliquots of first-strand cDNA from poly(A)^+ RNA were subjected to PCR using the same downstream primer located in exon 5 and the upstream primers in exon 1, 3U, or 3A (the positions of primers are illustrated as bars in panel A). Southern blot hybridization was carried out using an MAP1B-specific probe. The fragments showed the expected size for the regular transcript containing exons 1–5 (515 bp), the alternative transcript containing exons 3U to 5 (435 bp), or the alternative transcript containing exons 3A to 5 (395 bp). CNT, control. C, Northern blot analysis of regular MAP1B, an alternative MAP1B transcript containing exon 3U, MAP1A, α-, and β-tubulin in cortical neurons treated with nonaggregated or aggregated Aβ-(1–42). One microgram aliquots of poly(A)^+ RNA extracted from cortical neurons treated with either nonaggregated or aggregated Aβ-(1–42) for 3, 6, and 24 h were electrophoresed, transblotted to a nylon membrane, and hybridized with specific probes. Data are mean ± S.D. of three experiments. **, p < 0.01; ***, p < 0.001 by analysis of variance (ANOVA) and the post hoc test compared with untreated control.
6-DIV cortical neurons. Fragments MAP1B-(1–1367) and MAP1B-(127–1367) were detectable with anti-Myc antibodies and an authentic MAP1B antibody, AA6. The expression of exogenous MAP1B proteins was confirmed by Western blotting (Fig. 4B) and immunocytochemistry (Fig. 4C and D) using an antibody against c-Myc. As shown, both the construct encoding amino acids 1–1367 and the one encoding 127–1367 gave rise to a protein band with a different size. Both proteins expressed in cortical neurons were larger than those deduced from the predicted amino acid sequence (152 or 138 kDa, respectively), as was full-length MAP1B (280–300 kDa in SDS-PAGE but 269 kDa deduced from the predicted amino acid sequence). Immunofluorescence double staining for c-Myc and MAP1B indicated that transfected neurons expressed both MAP1B fragments with distribution patterns similar to that of endogenous MAP1B (Fig. 4C). The transfection efficiencies of constructs MAP1B-(1–1367) or MAP1B-(127–1367) were 4.5% or 2.7%, respectively, indicating that the lower level of fragment MAP1B-(127–1367) expression in Western blot reflects, in part, the lower transfection efficiency of construct MAP1B-(127–1367) in cortical neurons.

To examine the effect of overexpression of MAP1B fragments on neurite extension, cortical neurons transfected with constructs MAP1B-(1–1367) or MAP1B-(127–1367) were enzymatically removed from dishes, re-plated onto gelatin-polyornithine-coated dishes, and cultured for 6 h. As shown in Fig. 5A, overexpression of fragment MAP1B-(1–1367) in cortical neurons shifted the peak of neurite length to a longer range. The average neurite lengths of MAP1B-(1–1367) expressing (63.1 ± 1.3 μm) and MAP1B-(127–1367) expressing neurons (54.9 ± 1.0 μm) were significantly different (p < 0.0001). To examine the effect of overexpression of MAP1B fragments on neuronal apoptosis after serum withdrawal, cortical neurons expressing MAP1B-(1–1367) or MAP1B-(127–1367) and showing DNA fragmentation were visualized by immunostaining with anti-Myc antibodies and Hoechst 33342, and the percentage of apoptotic neurons relative to the total number of transfected neurons was determined. Fig. 5B shows that the overexpression of MAP1B-(1–1367) in neurons induced a significantly higher level of apoptosis than that of MAP1B-(127–1367) or untransfection.

To confirm the apoptotic properties of the MAP1B isoform containing the N-terminal 126 amino acid fragment, full-length or shorter isoforms (MAP1B Δ126), both of which were tagged with the c-Myc epitope, were expressed in 6-DIV cortical neurons, and their effects on neuronal apoptosis were assessed after serum withdrawal. Fig. 6 shows that neurons expressing full-length MAP1B were more sensitive to serum withdrawal than those expressing MAP1B Δ126 or untransfected neurons. These results indicate that overexpression of the MAP1B fragment containing the N-terminal 126 amino acids in cortical neurons may make neurons vulnerable to apoptotic signals.

**DISCUSSION**

MAP1B is expressed abundantly in the fetal or neonatal brain (22–24) but negligibly in the adult brain except in areas with greater plasticity potential. MAP1B is highly associated with neurofilibrillary tangles and senile plaque neurites in Alzheimer’s disease (16–19). The re-expression of developmentally regulated proteins such as MAP1B and CRMP2 (25) in the AD neurons may contribute to the aberrant neuritic sprouting process in the AD brain (26). Two different possible explanations for this are that the aberrant sprouting may be a neuronal response to neurodegeneration or activated glial cells at the end stage of the disease or that the aberrant sprouting may be induced by the deposition of Aβ or plaque-associated molecules at an early stage before neurodegeneration. The aberrant axonal growth in the vicinity of amyloid plaques in APP-trans
neurofibrillary tangles and se-
itive isoforms still remains unknown. RT-PCR analysis of
neurons transfected with different MAP1B isoforms were calcu-
neurons expressing fragment MAP1B-(1–1367) was almost similar to that in neurons expressing
neurons expressing fragment MAP1B-(1–1367) was 3.5-fold higher than that in neurons expressing
neurons expressing fragment MAP1B-(1–1367). The immunofluores-
centrity of the MAP1B epitope as recognized by mono-
cans using human brain poly(A)⁺ RNA did not reveal which transcript was up-regulated in the AD brain be-
cause of the low quality of the postmortem poly(A)⁺ RNA for
neurons. We demonstrated that overexpression of
lysing organelle transport as a specific feature; full-length MAP1B may promote neurite sprout-
genic mice, which develop amyloid plaques but not neuronal
deleterious. In agreement with our finding that the alternative
overexpression of MAP1B transcripts using human brain poly(A)⁺ RNA did not reveal which transcript was up-regulated in the AD brain because of the low quality of the postmortem poly(A)⁺ RNA for
neurons resulting in good growth of neurites and acceleration of neuronal death. It is unlik-
neurons expressing MAP1B-(1–1367) and MAP1B-(126–1367). Thus, the susceptibility of
MAP1B-expressing neurons to death may be an isoform-specific feature; full-length MAP1B may promote neurite sprouting and neuronal death, but the alternative isoform may not be deleterious. In agreement with our finding that the alternative isoform of MAP1B does not accelerate neuronal death, a recent report indicated that up-regulation of the MAP1B alternative isoform in heterozygotes of MAP1B-deficient mice does not cause any overt abnormalities in the nervous system (28). The isoform-specific deleteriousness of MAP1B appeared to be analogous to the expression of certain τ isoforms in specific tauopat-
thelial transport as τ does (30).
As expected from the aberrant axonal sprouting before neurodegeneration in APP transgenic mice (27), Aβ indeed induced
a developmentally regulated protein, an alternative isoform of MAP1B. However, this isoform of MAP1B did not accelerate neuronal death when it was overexpressed in cultured cortical neurons. It should not be ruled out that non-Aβ components of plaque amyloid, e.g., heparan sulfate proteoglycan, apoprotein E, agrin, and CLAC-P/collagen type XXV (31–34), might be responsible for inducing full-length MAP1B. Recent reports suggested that MAP1B may play a role in the pathogenesis of neurodegenerative disorders related to cytoskeletal abnormalities. The high level of MAP1B in Lewy bodies indicates that overexpression of MAP1B might be involved in the formation of Lewy bodies (21). Mutations of gigaxonin induce giant axonal neuropathy via loss of gigaxonin-MAP1B light chain interactions (35). MAP1B, whose isoforms are not clearly defined, is up-regulated in the immediate-early phase of apoptosis in cerebellar granule neurons deprived of potassium and serum (36). These observations suggest that common cell death signal(s) among neurodegenerative disorders related to cytoskeletal abnormalities might stimulate the expression of full-length MAP1B, which might act as an effector of cell death (37). Further studies to identify molecules that induce full-length MAP1B should contribute to our understanding of the role of MAP1B in neurodegeneration.

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REFERENCES
1. Wisniewski, K. E., Wisniewski, H. M., and Wen, G. Y. (1985) Ann. Neurol. 17, 279–282
2. Hardy, J. (1997) Trends Neurosci. 20, 154–159
3. Small, D. H., Mok, S. S., and Bornstein, J. C. (2001) Nat. Rev. Neurosci. 2, 595–598
4. Eustus, S., Tucker, H. M., van Rooyen, C., Wright, S., Brigham, E. F., Wogulis, M., and Rydel, R. E. (1997) J. Neurosci. 17, 7736–7745
5. Armstrong, R. A. (1994) Neurosci. Lett. 178, 59–62
6. Giannakopoulos, P., Hof, P. R., Mettler, S., Michel, J. P., and Bouras, C. (1994) Acta Neuropathol. 87, 456–468
7. Yamaguchi, H., Sugihara, S., Ogawa, A., Oshima, N., and Ibara, Y. (2001) J. Neurosci. Res. Exp. Neurol. 60, 731–739
8. Games, D., Adams, D., Alessandrini, R., Barbour, R., Berthelette, P., Blackwell, C., Carr, T., Clemens, J., Donaldson, T., Gillespie, F., Guido, T., Hagopian, S., Johnson-Wood, K., Khan, K., Lee, M., Leibowitz, P., Lieberburg, I., Little, S., Masliah, E., McConlogue, L., Montoya-Zavala, M., Mucke, L., Paganini, L., and Penniman, E. (1995) Nature 373, 523–527
9. Hsiao, K., Chapman, P., Nilsen, S., Eckman, C., Harigaya, Y., Youmkin, S., Yang, F., and Cole, G. (1996) Science 274, 99–102
10. Irizarry, M. C., McNamara, M., Fedorchak, K., Hsiao, K., and Hyman, B. T. (1997) J. Neuropathol. Exp. Neurol. 56, 965–973
11. Irizarry, M. C., Soriano, F., McNamara, M., Page, K. J., Schenk, D., Games, D., and Hyman, B. T. (1997) J. Neuropathol. Exp. Neurol. 56, 974–983
12. Manthorpe, M., Fagnani, R., Skaper, S. D., and Varon, S. (1986) Brain Res. 390, 191–196
13. Katada, T., Zauener, W., Wiche, G., and Probst, F. (1998) Genomics 49, 430–436
14. Liu, D., and Fischer, I. (1996) Gene 172, 207–208
15. Zauener, W., Kratz, J., Staunton, J., Feck, P., and Wiche, G. (1992) Eur. J. Cell Biol. 59, 46–53
16. Hasegawa, M., Arat, T., and Ibara, Y. (1990) Neuron 4, 909–918
17. Geddes, J. W., Lundgren, K., and Kim, Y. K. (1991) J. Neurosci. Res. 30, 183–191
18. Takahashi, H., Hirokawa, K., Ando, S., and Obata, K. (1991) Acta Neuropathol. 81, 626–631
19. Uitoo, L., Montejo de Garcia, E., Gomez-Ramos, P., Moran, M. A., and Avila, J. (1994) Brain Res. Brain Res. Rev. 26, 113–122
20. Gai, W. P., Blumbergs, P. C., and Blessing, W. W. (1996) Acta Neuropathol. 91, 78–81
21. Jensen, P. H., Islam, K., Kenney, J., Nielsen, M. S., Power, J., and Gai, W. P. (2000) J. Biol. Chem. 275, 21500–21507
22. Safafi, R., and Fischer, I. (1989) J. Neurochem. 52, 1871–1879
23. Schoenfield, T. A., McKerracher, L., Obar, R., and Vallee, R. B. (1989) J. Neurosci. Res. 20, 66–74
24. Garner, C. C., Garner, A., Huber, G., Kozak, C., and Matus, A. (1990) J. Neurochem. 55, 146–154
25. Yoshida, H., Watanabe, A., and Ibara, Y. (1998) J. Biol. Chem. 273, 9761–9768
26. Arendt, T. (2001) Neuroscience 102, 723–765
27. Phinney, A. L., Deller, T., Stalder, M., Callhoun, M. E., Frotscher, M., Sommer, E., Staufenbiel, M., and Jucker, M. (1999) J. Neurosci. 19, 8552–8559
28. Gonzalez-Billault, C., Demandt, E., Wandosell, F., Torres, M., Bonaldo, P., Mandelkow, E. (1998) J. Biol. Chem. 273, 52710–52718
29. Ebneth, A., Godemann, R., Stamer, K., Illenberger, S., Trinczek, B., and Lieberburg, I. (2000) J. Neurosci. Res. 61, 113–122
30. Ebneth, A., Godemann, R., Stamer, K., Illenberger, S., Trinczek, B., Lieberburg, I. (2000) J. Neurosci. Res. 61, 113–122
31. Stoykova, A., Chowdhury, K., Gruss, P., Avila, J., Sanchez, M. P. (2000) Mol. Cell. Neurosci. 16, 489–491
32. Namba, Y., Tomonaga, M., Kawasaki, H., Otomo, E., and Ikeda, K. (1991) Brain Res. 541, 163–166
33. Denahue, J. E., Berzin, T. M., Raffi, M. S., Glass, D. J., Yancopoulos, G. D., Fallon, J. R., and Stopa, E. G. (1999) Proc. Natl. Acad. Sci. U. S. A. 96, 6468–6472
34. Hashimoto, T., Wakabayashi, T., Watanabe, A., Kowa, H., Hosoda, R., Nakamura, A., Kanazawa, I., Arai, T., Takio, K., Mann, D. M., and Iwatsubo, T. (2000) EMBO J. 19, 1524–1534
35. Ding, J., Liu, J.-J., Kowal, A. S., Nardine, T., Bhattacharya, P., Lee, A., and Yang, Y. (2002) J. Cell Biol. 158, 427–433
36. Chiang, L. W., Grenier, J. M., Ettwiller, L., Jenkins, L. P., Ficenec, D., Martin, J., Jin, P., DiStefano, P. S., and Wood, A. (2001) Proc. Natl. Acad. Sci. U. S. A. 98, 2814–2819
37. Yuan, J., and Yankner, B. A. (1999) Nat. Cell Biol. 1, E44–E45
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