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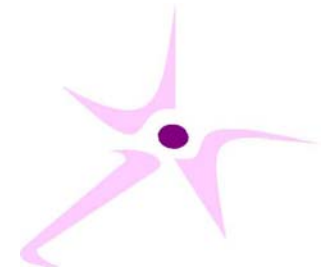
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Vedecí pracovníci NIU SAV na medzinárodnej
vedeckej konferencii, Štokholm 2002



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Truncated Tau is Intimately Involved in Formation of PHF

Lubica Vechlerova¹, Peter Kontsek², Rostislav Skrabana³, Eva Kontsekova⁴, Khalid Iqbal⁵, Michal Novak⁶

¹Institute of Neuroimmunology, Slovak Academy of Sciences, Bratislava, Slovakia; ²Axon Neuroscience, Vienna, Austria; ³New York State Institute for Basic Research in Developmental Disabilities, New York, USA

ABSTRACT

Pathological tau forms (PHF) are neurofibrillary tangles found in Alzheimer's disease brain tissues. It has been shown that PHFs are composed of full length and truncated phosphorylated tau species. Our aim was to evaluate the role of truncated tau forms in PHF formation. The neurofibrillary tangles in transgenic mice were subjected to various pathological modifications of tau associated with PHF formation... (text continues)

INTRODUCTION

The major constituents of pathological AD lesions (neurofibrillary tangles, neuritic plaques, synaptic loss and dystrophic neurites) is neurofibrillary tangle protein, tau. Tau is a microtubule associated protein that binds to the tails of paired helical filaments (PHF). PHFs are composed of full length and truncated phosphorylated tau species. Truncation effectively modifies the physiological function of tau and promotes its assembly into pathological structures... (text continues)

MATERIALS AND METHODS

AD brain tissues and healthy age-matched control brains were used for preparation of tau extracts. Brain tissue from cortex of 1293 AD and transgenic at 4, 12, 24 and 36 months of age was homogenized (10% in RNeasy lysis buffer) in a RNeasy lysis buffer... (text continues)

RESULTS

Outline of special tau forms preparation
1. Isolation and purification of tau (Cation exchange column)
2. Separation of tau forms (Size-exclusion column)

Fig. 1. Size-fractionation of tau protein from AD brain tissue...

Fig. 2. Long forms of tau protein ('AL' fraction) were not able to form PHF in vitro. The AT fraction was concentrated, dialyzed and incubated for 20 hours at 4°C. The mixture was centrifuged and both pellet and supernatant were analyzed for the presence of tau protein and PHF-like structures. Purified antibody DC25 and phosphorylation dependent antibody PHF1 were used. The major amount of AT tau protein remained in the supernatant (top panel). Only AT tau was found in pellet (P band). As expected, phosphorylated AL tau forms were not able to assemble into PHF-like structures (Fig. 3a, top P). (P - pellet, S - supernatant after incubation and centrifugation of AL samples)

Fig. 3. The proteins in 'AT' fraction formed PHF-like structures in vitro. The AT fraction was prepared as described above for 'AL' samples. Pellet and supernatant were analyzed using the specific antibodies DC25 and PHF1. Analysis of the pelleted tau protein (P) showed typical tau-associated PHF pathology. Truncated forms of tau protein together with long forms assembled into high-molecular weight PHF-like structures. Associated tau forms were phosphorylated (Fig. 3a, top P) and in the pelleted tau protein PHF-like structures.

CONCLUSION

1. Tau proteins isolated from Alzheimer's brain disease could be separated into two major categories 'AL' (full length tau) and 'AT' (full length and truncated tau).
2. 'AT' tau - consisting of truncated forms of tau protein and long forms assembled into high-molecular weight complexes that under EM showed typical tau-like structures.
3. The expression of human truncated tau in rats induced the formation of PHF-like structures.
4. Truncated tau is essential for formation of PHF-like structures and for neurofibrillary degeneration (for details see poster Zilka et al.).

Fig. 4. Immunoblot analysis of tau protein in AD, 24M, 36M and 48M transgenic mice.

Vedecká prednáška Prof. Khalida Iqbala (USA) na
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