SPECIFIC PHF-TAU PHOSPHORYLATION AT THR50 IS INVOLVED IN ALL DEVELOPMENTAL STAGES OF ALZHEIMER’S DISEASE

N. Ivanova¹, M. Handzusova¹, E. Kontsekova¹, M. Novak¹,²

¹Slovak Academy of Sciences, Institute of Neuroimmunology, Bratislava, Slovak Republic, ²Axon Neuroscience GmbH, Vienna, Austria

Introduction: N-terminus of tau is involved in the cascade of pathological events leading to Alzheimer’s disease (AD). Up till now, majority of identified phosphorylation sites seem to be clustered in the proline rich domain, C-terminal region and microtubule binding domain. Only a few phosphosites have been identified in N-terminal region of PHF-tau.

Aims: Limited studies have been focused on functional significance of phosphorylation as a posttranslational modification of N-terminus. The occurrence and the functional relevance of the phosphorylation site Thr50 located in the N-terminal tail of tau remained until today unexplored.

Results: By developing of monoclonal antibody (mAb) DC50 as genuine imprint of PHF-tau we obtained clear evidence, that Thr50 is phosphorylated in AD brain. Detailed epitope analysis showed, that antibody specifically recognizes phoshoepitope on PHF tau, which is created only by phosphorylated Thr50. Biochemical study of tau from AD brain showed the accumulation of phosphoepitope Thr50 in the AD -specific protein A68, considered as characteristic feature of PHF-tau. Moreover, immunohistochemical analysis revealed that this phosphoepitope rises in very early stages of neurofibrillary pathology and persists up to terminal stages. These findings indicate that phosphosite could be involved in initiation of the neurodegenerative process.

Conclusion: We conclude that the novel mAb DC50 could be successfully employed as a molecular probe that may be used for study of pathological pathway involving phosphorylation at Thr50.

This work was supported by Research grants: APVV No. 0559-07, VEGA No. 2/0151/10