MOLECULAR CHAPERONES IN THE PATHOGENESIS OF ALzheimer DISEASE

Z. Milicevic¹, V.S. Bajic², B. Spremo Potparevic³

¹Laboratory for Molecular Biology and Endocrinology, Institute for Nuclear Sciences Vinca, ²Institute of Biomedical Research, Galenika a.d., ³Institute of Physiology, Faculty of Pharmacy, Belgrade, Serbia

Neurodegeneration, a result of multiple dysregulatory events, is a lengthy multistep process manifested by accrual of mutant variants and abnormal expression, posttranslational modification and processing of certain proteins. Whereas enhanced Hsp90 affinity for mutated or functionally deregulated client proteins has been observed for several oncoproteins, it is unknown whether Hsp90 plays a similar role for neuronal proteins and thus maintains and facilitates the transformed phenotype in neurodegenerative diseases. Hsp90 in the particular case of Alzheimer's disease (cerebral cortex, hippocampus) was analyzed by Western blotting and immunohistochemistry (ABC, APAAP) with mAbs H 9010 and AC88. Antibody 5282 was used to establish the pattern of deposition of amyloid β proteins. Hsp90 antibody specifically identified the chaperone in complex with amyloid β species. Significant or extensive staining for Hsp90 was found in both amyloid (fibrillar) and preamyloid (nonfibrillar) diffuse deposits in AD cases. Expression of Hsp90 in amyloid lesions suggests a general participation of these molecules in Alzheimer's disease pathology. The presence of Hsp90 in the preamyloid lesions supports the notion that molecular chaperones may play a role in the early steps of fibrillogenesis. These facts support the relevance of therapeutic strategies targeting Ab production and neurotoxicity. An open question remains whether a common principle is governing cancer and neurodegenerative diseases.