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The effect of exogenous human Hsp70 treatment on neurodegeneration and aging in model mice

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Alzheimer's disease (AD) is the most prevalent neurodegenerative pathology in the growing population of elderly humans and leads eventually to dementia and death. Despite tremendous efforts, no effective treatment for AD is currently available. Molecular chaperone Hsp70 plays protective role in various neurodegenerative disorders. Various data suggest that Hsp70 and other molecular chaperones function as a complex neuroprotective system, which fails in the brains of aged people and AD patients. In special experiments, we demonstrated that eHsp70 effectively crosses the blood-brain barrier when administered intranasally. Here we have shown that chronic administration of exogenous Hsp70 (eHsp70) decreased beta-amyloid level and preserved neuron density in two mouse models of Alzheimer disease. In both cases eHsp70 restored behavior and memory disturbed by Alzheimer disease and aging. We also explored the effect of eHsp70 on neurons morphology and survival in the cortex and the hippocampus of transgenic animals. The proportion of pathologic neurons decreased drastically in Hsp70-treated animals. Therefore, Hsp70 treatment of model mice protects neurons from deterioration and death in brain areas most affected in AD patients. In conclusion, we can summarize that the intranasal administration of recombinant human Hsp70 drastically alleviates all symptoms, including memory loss, neuronal death, cellular aberrations and accumulation of the Aβ-peptide in both AD-models explored. Deep sequencing studies enabled to reveal candidate genes and signal pathways underlying beneficial effects of eHsp70 treatment. In our experiments we also demonstrated that intranasal administration of exogenous recombinant human Hsp70 can promote longevity in male but not female mice. The Hsp70 treatment also normalized the synthesis of synaptophysin in aged mice and decreased accumulation of lipofuscin which represents the marker of aging and neurodegeneration processes. Taken together, our findings establish exogenous human Hsp70 as a practical pharmacological agent for the treatment of various neurodegenerative diseases and aging.

Biography

M B Evgenev has completed his PhD from Institute of Developmental Biology, Moscow, Russia. He was Professor of Biology in 1990. He spent ten years in USA as Visiting Professor (U of John Hopkins, Baltimore, U of Arizona and Chicago University within 1990-2000 time period). He is Head of Laboratory of Molecular Basis of Biological Adaptation in Engelhardt Institute of Molecular Biology. He has published more than 140 papers in reputed journals and has been serving as an Editorial Board Member of repute in several journals.

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