Putative molecular mechanisms of anti-Alzheimer's action of the Y-box binding protein 1 (YB-1)

P.18-043-Mon

E. Grigoreva[I], D. Polyakov[I], A. Bobyliov[I], L. Ovchinnikov[I]

[I]*Institute of Protein Research, Russian academy of sciences, Pushchino, Moscow Region, Russia*

YB-1 is a multifunctional DNA/RNA-binding protein of vertebrates. It is involved in many cellular events, including proliferation, differentiation, and stress response. Using animal models of sporadic and hereditary Alzheimer's disease, it was shown that intranasal administration of this protein results in inhibition of plaque formation in the brain of animals, thereby preventing cognitive impairment. Here we propose some molecular mechanisms of putative YB-1 effect on progression of Alzheimer's disease (AD). A key role in the process is played by Aβ-peptide plaques accumulated in the interneuron space. Thioflavin T fluorescence and electron microscopy were used to show that addition of YB-1 to the Aβ-peptide inhibits formation of amyloid fibrils of the latter *in vitro*. The most pronounced inhibitory effect of YB-1 was observed at the initial stages of polymerization of the Aβ-peptide. Another AD symptom is the formation of intracellular tangles consisting of hyperphosphorylated tau-protein that has lost its ability to bind to microtubules, thus provoking microtubule destruction and disruption of mRNA transport along axons. We have compared the effects of YB-1 and tau-protein on tubulin polymerization *in vitro* and found that the stimulating effect of YB-1 is even higher than that of tau-protein. We believe that YB-1 can functionally replace the inactivated hyperphosphorylated tau-protein, thus maintaining microtubule integrity and the active mRNA transport in AD patients. This study was supported by RSF (# 14-14-00879) and RFBR (#18-04-00595).