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DNAJB6 Chaperone Prevents the Aggregation of Intracellular but not Extracellular Aβ Peptides Associated with Alzheimer's Disease

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Abstract : Alzheimer's disease is the most common dementia disease in the elderly. It is characterized by the accumulation of extracellular amyloid β (Aβ) peptides and intracellular hyper-phosphorylated tau protein. In addition, recent evidence indicates that accumulation of intracellular amyloid β peptides may play a role in Alzheimer's disease pathogenesis. This suggests that intracellular Heat Shock Proteins (HSP) that maintain the protein quality control in the cell might be potential candidates for disease amelioration. DNAJB6, a member of DNAJ family of HSP, effectively prevented the aggregation of poly glutamines stretches associated with Huntington's disease both in vitro and in cells. In addition, DNAJB6 was found recently to delay the aggregation of Aβ42 peptides in vitro. In the present study, we investigated the ability of DNAJB6 to prevent the aggregation of both intracellular and extracellular Aβ peptides using transfection of HEK293 cells with Aβ-GFP and recombinant Aβ42 peptides respectively. We performed western blotting and immunofluorescence techniques. We found that DNAJB6 can prevent Aβ-GFP aggregation, but not the seeded aggregation initiated by extracellular Aβ peptides. Moreover, DNAJB6 required interaction with HSP70 to prevent the aggregation of Aβ-GFP protein and its J-domain was essential for this anti-aggregation activity. Interestingly, overexpression of other DNAJ proteins as well as HSPB1 suppressed Aβ-GFP aggregation efficiently. Our findings suggest that DNAJB6 is a promising candidate for the inhibition of Aβ-GFP mediated aggregation through a canonical HSP70 dependent mechanism.

Keywords : Aβ, Alzheimer's disease, chaperone, DNAJB6, aggregation
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