Small heat shock proteins inhibit amyloid-β protein aggregation and cerebrovascular amyloid-β protein toxicity

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Amyloid-β protein (Aβ), a 4 kDa peptide that accumulates in senile plaques and cerebral amyloid angiopathy, is involved in neuronal and cerebral vascular cell degeneration in Alzheimer's disease. Aggregation and cellular toxicity of Aβ may be affected by Aβ-associated proteins. Small heat shock proteins (sHsp) are molecular chaperones that can prevent target proteins from adopting aberrant conformations. Direct interaction between Aβ and Hsp27 and αB-crystallin have been demonstrated. It was the aim of our study to investigate if sHsps may affect aggregation of Aβ and thereby influence Aβ cytotoxicity. Aβ aggregation was studied by using Thioflavin T fluorescence, circular dichroism spectroscopy, Congo red staining, electron microscopy and atomic force microscopy. Binding affinity between sHsps and Aβ was investigated by surface plasmon resonance. Furthermore, we used our previously established model of Aβ-mediated toxicity towards cultured cerebrovascular cells to investigate the effects of sHsps on Aβ-mediated cytotoxicity. Here we demonstrated that sHsps, but especially αB-crystallin, inhibited aggregation of Aβ. αB-crystallin was also the most effective inhibitor of cerebrovascular Aβ toxicity, probably by prevention of Aβ aggregation at the cell surface by the rapid formation of protofibril-like structures. In conclusion, sHsps may regulate Aβ aggregation and serve as antagonists of Aβ thereby preventing the interaction of Aβ with vascular cells.

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