Structural Implications of C-terminal regions of alpha-synuclein.

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The aggregation and fibrillization of \( \alpha \)-synuclein, a major component of Lewy Bodies (LB), is an important event in the development of Parkinson’s Disease (PD). Although the mechanisms of protein conformational changes of \( \alpha \)-synuclein leading to amyloid fibrils are largely investigated, the function of \( \alpha \)-synuclein in vivo is not yet clearly elucidated. Protein sequence analysis has shown that C-terminal regions \( \alpha \)-synuclein has amino acid sequence similarities to \( \alpha \)-crystallin and other small heat shock proteins (sHSPs). Based on its primary sequence analysis and highly flexible conformation, we have investigated the functional similarity of \( \alpha \)-synuclein to sHSPs. In our experiments, \( \alpha \)-synuclein could inhibit the aggregation of various \( E. \ coli \) cellular proteins during heat stress and C-terminal deletion mutants could not provide any protection to these cellular proteins. \( \alpha \)-Synuclein could also protect the catalytic activity of model enzymes during cold stress. In addition, we have shown that expression of \( \alpha \)-synuclein was able to confer a cellular tolerance to \( Escherichia \ coli \) against thermal- and oxidative-stress. Interestingly, extracellular addition of \( \alpha \)-synuclein could also protect HEK 293 cells against oxidative stress. It is suggested that C-terminal regions might have a role in regulation of this protective function through ligand binding. In conclusion, our results suggest that \( \alpha \)-synuclein, like other small heat shock proteins, could protect cellular proteins from thermal and oxidative damage, which finally leads to resistances to thermal- and oxidative-tolerance to cells.