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

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The aggregation and fibrillization of α-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 α-synuclein leading to amyloid fibrils are largely investigated, the function of α-synuclein *in vivo* is not yet clearly elucidated. Protein sequence analysis has shown that C-terminal regions α-synuclein has amino acid sequence similarities to α-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 α -synuclein to sHsps. In our experiments, α-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. α-Synuclein could also protect the catalytic activity of model enzymes during cold stress. In addition, we have shown that expression of α-synuclein was able to confer a cellular tolerance to *Escherichia coli* against thermal- and oxidative- stress. Interestingly, extracellular addition of α-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 α-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.