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| Title: | Biophysical Studies on the Misfolding and Aggregation of Human B2-Microglobulin and a Yeast Prion Determinant |
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| Abstract: | Protein misfolding and aggregation resulting in amyloid formation are associated with a large number of human diseases including Alzheimer disease, Parkinson disease, Transmissible Spongiform Encephalopathies, Huntington disease, Frontotemporal dementia, and Amyotrophic lateral sclerosis. Various studies on deciphering the mechanism of protein aggregation indicate that the partial unfolding of the native structure of a protein is one of the major driving forces for amyloid formation. Therefore, it is necessary to understand how certain conditions perturb the protein structure and which regions of the protein are more prone to aggregation under stress conditions. Further, polymorphism is an important property of amyloid fibrils in which a single protein/ peptide give rises to amyloid fibrils with diverse morphologies and structures complicating the disease pathology. The cause of amyloid polymorphism is still under investigation. From various studies, it is suggested that environment stress caused by a change in pH or oxidative stress or poor quality control can affect the fibril formation and morphologies. To address these questions, we have used human β2-microglobulin (β2m) to study the effect of pH on protein structure unfolding and effect of salt on amyloid fibril morphology. We have also used well-characterized strains of yeast [PSI+] prion to study the structural differences and the role of water in two distinct strains. The details of studies are described in the following chapter. |
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