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Biophysical studies on the effects of in vivo constituents on amyloid formation in Alzheimer's disease

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Abstract

Introduction: Alzheimer's disease (AD) is the most prevalent form of dementia which dysregulation of the amyloid-beta (Aβ) level leads to Aβ insoluble assemblies and, eventually, alternate with the normal neuronal conditions. Hence One of the grand challenges of biophysics is to understand the principles that govern formation of protein Aggregation like amyloid fibrils. So there is dire need to extend these investigations to in vivo conditions where amyloid formation is affected by a myriad of biochemical interactions.

Methods: Single molecule AFM force spectroscopy has been used to elucidate the role of cations on interpeptide interactions. moreover researchers developed a unique fluorescent assay to monitor fibril formation using to investigate pH effects on Aβ. Also Time-dependent fluorescence spectroscopic measurements carried out to investigate the fibrillation kinetics of islet amyloid polypeptide (IAPP) in the presence of different cosolvents.

Results and discussion: Histidine and lysine roots play an important role in the polymerization and growth of amyloids, and it has been found that pH below 7 have a positive effect on amyloid growth. AFM force spectroscopy revealed that Cu++ cations dramatically change the folding patent of Aβ42 within dimers. Stabilizing co-solvent hamper fibril elongation Conversely, destabilizing (urea) cosolvents leading to retardation of IAPP nuclei formation.

Conclusion: From a multitude of biophysical studies, which are mainly summarized, one knows that most, if not all of the molecules and ions composing the intra- and extracellular spaces have an influence on the thermodynamics and kinetics of amyloid aggregation. They can speed up aggregation.

Keywords: Alzheimer's, Amyloid formation, In vivo, Biophysical studies

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