UNDERSTANDING THE STRUCTURE OF AMYLOID FIBRILS USING ATOMIC FORCE MICROSCOPY (AFM) TO DESIGN NEW THERAPEUTIC STRATEGIES FOR NEURODEGENERATIVE DISEASES

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Amyloid fibrils are misfolded proteins that are irreversible once they are formed. In human beings, there are different kinds of proteins that form into amyloid fibrils and are associated with several degenerative diseases. For example, insulin, Huntington, Amyloid β-42 and α- synuclein proteins are linked with Type-2 Diabetes, Huntington's, Alzheimer's and Parkinson's diseases, respectively. The mechanism for the misfolding and creation of the fibrils is thought to be the same for all of these proteins. Hen Egg White Lysozyme (HEWL) is a low-cost and widely recognized model protein to work with to help us understand the mechanisms of amyloid fibrillogenesis. The aim of this project is to denature the lysozyme protein using different kinds of methods, acidic and basic conditions. We will investigate the mechanisms of growth of lysozyme amyloid fibrils under these conditions over a two-week period using Atomic Force Microscopy (AFM). AFM provides a topographical image of the fibrils bound to a mica substrate. Examining the AFM images taken after different incubation times and thus at various stages of growth, will allow us to analyze their morphological parameters, such as length, width, and height, to better understand the growth mechanisms of amyloid fibrils. It is thought that a drug can be designed to be able to stop progression of the disease by removing the amyloid fibrils or preventing further buildup. Knowing the structure of the amyloid fibrils makes it possible to understand how it contributes to neurodegenerative diseases and how it could be treated with a specific drug or other therapy.

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