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# Mechanical and Analytical Techniques Used to Analyze Beta Sheet Formation of a Single Point Mutation for Alzheimer's Beta Amyloid Peptide

Abstract:

Amyloid diseases, such as Alzheimer's disease, are neurodegenerative disorders that have been introduced by protein misfolding into amyloid fibrils. Other similar diseases include Parkinson's, Huntington's, and Creutzfeldt-Jakob disease, which have yet to be cured effectively, are recurrently distinguished by fibrillar depositions of specific amyloid proteins. Alzheimer's β-amyloid (Aβ) peptides and α-synuclein (α-Syn) are distinctive traits of Alzheimer's disease (AD). In the extracellular region of the brain of Alzheimer's patients, the formation of amyloid plaques are formed. In multiple studies for both Aβ(1-40) and Aβ(1-42), a tendency of fibril formation has been found to start from a non-toxic monomer state that has self-assembled into a lethal fibrillar state. Additionally, the beta-amyloid peptide 1-40 and beta-amyloid 1-42, associated with the cause of Alzheimer's disease, undergoes several transformation processes resulting in structural changes in the protein shape; shifting from random coil, to alpha helical, to beta-sheet, with a range of intermediate structures in between. It is important to also examine the hair-pin region without the presence of residues 16-21. In order to study the effect on fibril formation without the "KLVFFA" region, or the sequence in the Aβ 1-40, the 22-35 sequence was chosen. Previous research conducted by Dr. Chimon Peszek has found diffusible beta sheet intermediate structures. These, in turn, could present a similar toxicity as fibrils, consequently the cause of neurodegeneration in Alzheimer's.

There are several missense mutations in the β amyloid precursor protein (APP). Among these, the Italian (E22K) point mutation lead to changes in time of fibril formation as well as solubility and toxicity of fibrils. It is believed to promote early onset of AD, prematurely producing clinical and neuropath logical features which are unchanged from those of late onset AD. The Italian mutant also has an increased level of neural toxicity. The Italian mutant is also associated with cerebral amyloid angiopathy and hemorrhagic stroke. The use of Attenuated Total Reflection Infrared Spectroscopy, ATR-IR, and Ultraviolet Visible Spectroscopy, UV-Vis, on the 22-35 sequence confirmed the formation of structures synonymous with toxic beta sheets. Discovery of more knowledge on these mutations could have a significant impact on therapeutic medicines and treatments in the near future.