Characterizing the Folding of the C-Terminal Amyloid Precursor Protein

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The human Amyloid Precursor Protein (APP) is vital to the development of Alzheimer's Disease. The beta peptides of APP, in particular Aβ42, accumulate into intercellular plaques in the brain that inhibit neuron function. We hypothesize that the C-Terminal 42 residues of APP bind to motor proteins. As such, the elucidation of APP-C42 behavior is vital to better understand the disease. In this project, we obtained the membrane-spanning APP C99 NMR structure (C-terminal 99 residues of APP) from the Sanders' lab at Vanderbilt University. We then truncated the structure to the last 42 residues, resulting in APP-C42 Utilizing the Amber software package, we ran two 3.5 microsecond unrestrained molecular dynamics simulations on the TIP3P-solvated and neutralized APP-C42 molecule. We used RMSD as well as secondary and tertiary structure analyses to evaluate the simulations and produce starting conformations for further studies. The occurrence of a C-terminal alpha helix was consistent throughout both simulations, a previously unidentified motif that could have significant implications in future research. Several other helices were observed throughout the simulations across the peptide. With these results we are able to fully characterize the secondary structures and some tertiary structures in the human APP-C42 peptide.