Behind the Cause: A Novel Role of a Natural Lipid Bilayer in Causing Alzheimer's Disease

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Alzheimer’s Paired Helical Filament (PHF) Tau is a hydrophilic, cationic, highly surface-active intrinsically disordered protein that localizes to the distal portion of axons in neurons, where it works to stabilize microtubules. It is here that Tau has been shown to aggregate, forming amyloid-ß plaques and neurofibrillary tangles that are said to cause Alzheimer’s Disease. Previously, extensive research has detailed the stages and characteristics of Tau aggregation and various synthetic causes have been proposed. However, nothing is known about the potential role of natural intracellular elements in eliciting such behavior. Thus, this novel simulation study used molecular dynamics to investigate the interaction of Tau’s microtubule assembly domain (Lys-267 to Pro-312) with an anionic surfactant 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylglycerol (POPG) lipid bilayer for times up to 12 nanoseconds. It was found that this lipid bilayer allows Tau to adopt a more stable, compact form as well as a lower conformational entropy and large structural changes that are characteristic of a protein progressing towards an aggregation state. In its aggregation state, Tau causes Alzheimer's Disease. These results illuminate an entirely new potential path in the search for a cure for Alzheimer’s Disease, as all generic drugs that are developed to date are designed to target the surface of a lipid bilayer.

Awards Won:
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