Adsorption and Surface-mediated Aggregation of Disordered Protein Tau at Model Surfaces

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Abstract

Introduction: The adsorption and aggregation of an intrinsically disordered soluble protein, tau, into insoluble filaments are a defining hallmark of many neurodegenerative diseases, commonly referred to as tauopathies. The macromolecular environment, including the presence of surfaces such as the cell membrane, and the presence of macromolecules in a crowded environment, has been implicated in the aggregation of tau protein. **Methods:** In this study we employ a combination of biophysical techniques to study the adsorption and aggregation of a wild type and several mutations of tau protein at model surfaces. A quartz crystal microbalance with dissipation was used to monitor the adsorption of different tau species at nanomolar concentrations, mimicking the in vivo situation, to surfaces with different surface charge, wettability and softness, while atomic force microscopy was utilized to obtain direct visualization of the proteins at these different surfaces. **Results and discussion:** Our results show that the adsorption of different tau protein mutants to phospholipid covered surfaces of different fluidity indicated tau protein oligomers can lead to destabilization or disintegration of lipid bilayers. Such disintegration may be the cause of observed cell death in several tauopathies.

Conclusion: Hydrophobic amino acid sequences in the microtubule binding region were the leading force driving the adsorption of tau proteins to different surfaces.

Keywords: Tauopathies, Quartz Crystal Microbalance with Dissipation, Atomic Force Microscopy, Lipid Bilayer, Aggregation

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