Title:	The role of the N- terminal intrinsically disordered domain of the prion protein in liquid- liquid phase separation, membrane-binding, misfolding, and oilgomerization
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Abstract:	Conformational conversion of largely α-helical cellular prion protein to β-sheet rich scrapie isoform is associated with a range of neurodegenerative diseases classified under transmissible spongiform encephalopathies. The term “prion” was first introduced to illustrate the infectious nature of proteins namely, the protein-only hypothesis; however, additional cofactors are likely to play a role in the misfolding of the prion protein in vivo. Nucleic acids and lipid membranes have been shown to promote conformational conversion, resulting in bonafide prions. A growing body of evidence suggests the critical role of liquid-liquid phase separation (LLPS) in organizing the cellular environment; however, aberrant phase transitions have been also implicated in a wide range of neurodegenerative diseases. In this thesis, efforts were steered to understand the key molecular aspects of prion misfolding and aggregation in the presence of lipid membranes as well as to elucidate the phase behavior of the prion protein by using a diverse array of molecular biological, biochemical, and biophysical tools. In my talk, I will discuss the critical role of the N-terminal disordered domain of the prion protein in governing the phase transition and membrane-induced misfolding and oligomerization. Additionally, I will talk about the utility of surface-enhanced Raman scattering in the ultrasensitive detection of the prion protein that could have potential implications in its non-invasive detection in various biological fluids. These studies will not only improve our current understanding of prion diseases but will also provide useful insights into the "prion-like propagation" mechanism in other protein misfolding diseases.
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