Title:	Amyloid regulation and phase separation of a yeast prion domain
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Keywords:	Amyloid prion domain phase separation
Issue Date:	Apr-2022
Publisher:	IISER Mohali
Abstract:	Adenosine triphosphate (ATP) is the cellular energy currency that provides energy for multiple cellular processes and drives biological machinery, including the chaperones involved in protein quality control (PQC). Apart from its indirect roles in the PQC via operating the chaperones, recent studies suggested the direct molecular role of ATP in protein homeostasis by controlling amyloid formation and dissolution of preformed amyloids. Several attempts were made to understand the chemical nature of ATP-protein interactions that govern the genesis of amyloids and their dissolution; however, the impact of such events in the cell-to-cell amyloid transmission remains largely uncharacterized. Here, in this in vitro study to understand the role of ATP in prion-like amyloid colonization using the intrinsically disordered domain of a yeast prion Sup35 by utilizing an amalgamation of biophysical and biochemical tools, we discerned that high concentrations of ATP accelerated the amyloid aggregation with the help of magnesium. Additionally, we recapitulated disaggregation of preformed amyloids in a wide range of ATP concentrations ranging from nanomolar to millimolar. In addition to the kinetic alteration, the amyloids generated in the presence of high concentrations of ATP showed remarkable compactness in the amyloid core resulting in minimal disaggregation by ATP itself that limits the number of transmissible seeds. Intriguingly, in low concentrations, ATP gave rise to such amyloids that showed no seeding potential, indicating a possible alternative anti-prion strategy in this concentration regime. Our study shed light on two distinct strategies that can restrict amyloid propagation depending on the cellular ATP concentrations. Further, to understand the role of ATP in regulating material states and phase transition of liquid-like droplets, we tried to standardize the protocol for liquid-liquid phase separation of an intrinsically disordered prion domain of Sup35.
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