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Physiological regulation of heritable protein aggregation

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Ordered protein aggregates (amyloids) and their transmissible forms (prions) are associated with a variety of neurodegenerative disorders, which can be studied using yeast as a model. In yeast and other fungi, prions control heritable traits. Prion formation and loss are modulated by environmental and physiological conditions, including nutrient limitation and heat stress. Our data show that propagation of yeast prions is controlled by the same cytosolic chaperones that are responsible for the protection of yeast cells against proteotoxic stress. Yeast prions are adjusted to physiological levels of chaperone proteins and hijack the cellular stress defense machinery for their own propagation. Chaperones of the ribosome associated complex, which are involved in proper folding of a nascent polypeptide, antagonize initial prion formation. During stress, the decrease in overall translational activity is accompanied by a relocation of the ribosome associated chaperones into the cytosol, resulting in the impairment of a prion-like propagation of misfolded proteins. Cellular asymmetric segregation apparatus, controlling the asymmetry of mitotic division, influences maintenance and properties of self-perpetuating protein aggregates both during recovery from stress and in the process of replicative aging. Overall, this intimate relationship with the protein quality control machinery of the cell plays a key role in the processes of prion formation and propagation in yeast.

Biography

Rebecca L Howie is pursuing a PhD at Georgia Tech in the School of Biological Sciences, with a focus on protein misfolding. Before becoming a full-time graduate student, she worked at the CDC as part of the National Antimicrobial Resistance Surveillance Team in the Enteric Diseases Laboratory Branch for over six years, studying antimicrobial resistance in foodborne pathogens. Prior to her work at CDC, she worked in anti-bioterrorism as a contractor in the Asymmetric Threat Protection Division at Tyndall AFB, FL.

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