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Fungal models for amyloids and prions

Statement of the Problem: Prions are alternatively folded self-perpetuating protein isoforms involved in a variety of biological and pathological processes. Most prions are based on self-assembled protein aggregates (amyloids). In humans, amyloids and prions are associated with important diseases, such as Alzheimer, Parkinson and Huntington diseases, and transmissible spongiform encephalopathies. In yeast and other fungi, prions are protein-based non-Mendelian elements that control heritable traits.

Methodology & Theoretical Orientation: Due to relative simplicity of cultivation procedures and availability of convenient phenotypic assays, fungi provide a great opportunity for deciphering the general mechanisms of the formation and propagation of amyloids and prions.

Findings: Yeast and fungal prions influence a variety of physiological functions. Prion formation and loss are modulated by environmental and physiological conditions. *De novo* formation of an yeast prion can be induced by a transient overproduction of a prion-forming protein. The process of prion formation includes generation of the intermediate aggregated structures, associated with cytoskeletal networks and quality control compartments. Propagation of yeast prions is controlled by the same cytosolic Hsp104/70/40 chaperone machinery that is involved in protection of yeast cells against proteotoxic stress. Chaperones fragment prion polymers thus providing oligomeric seeds for new rounds of prion propagation. Ribosome-associated chaperones antagonize prion formation and interfere with the ability of cytosolic chaperones to promote prion propagation. Chaperone and cytoskeletal machineries mediate effects of environmental stresses on prions.

Conclusion & Significance: The impact of prions on fungal biology is still underestimated. An 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. Many components of this machinery possess homologs or functional counterparts in higher eukaryotes, thus making yeast prions an excellent model for deciphering the general mechanisms of amyloid/prion formation and propagation in norm and pathology.

Biography

Yury O Chernoff is an Expert in Yeast Genetics and Molecular Biology. His major areas of research include protein biosynthesis, folding, aggregation, protein-based epigenetic inheritance, and yeast models for amyloid and prion disorders. He has demonstrated that self-perpetuating protein isoforms (prions) can be induced by transient protein overproduction and discovered the crucial role of chaperones in prion propagation. His research has also established evolutionary conservation of prion-forming properties, led to development of a yeast system for studying cross-species prion transmission, helped to establish yeast assays for aggregation and toxicity of mammalian aggregating proteins, and contributed to studying the involvement of cytoskeletal networks and protein quality control pathways in prion and amyloid phenomena. He is the Founding Editor-in-Chief of the international journal *Prion*, published by Taylor and Francis, Inc. In 2015, he has been elected a Fellow of the American Association for the Advancement of Science (AAAS).

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