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Annual Congress on

Mycology and Fungal Infections

November 16-17, 2017 Atlanta, Georgia, USA

Prion-like properties of a yeast g protein receptor involved in regulation of mating

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G-protein-coupled receptors (GPCRs) are integral membrane proteins that initiate responses to extracellular stimuli by mediating ligand-dependent activation of cognate heterotrimeric G proteins. Ste18 is a gamma-subunit of a G-protein receptor that is conserved in evolution and plays a key role in a variety of cellular processes, including pheromone-signaling pathway that is crucial for the yeast mating. We demonstrate that Ste18 possess prion-like properties. Upon overproduction, Ste18 forms detergent-resistant amyloid-like aggregates and promotes formation of [*PSI*$^+$], a prion isoform of Sup35/eRF3. Ste18 mutants, defective in anchoring to plasma membrane, are not able to form detergent-resistant aggregates or induce [*PSI*$^+$] prion, while a mutant, deficient in signal transduction but not in membrane anchoring, is able to do so. These data show that prion-like properties of Ste18 depend on its association with a membrane and resemble our previous results for another protein, Lsb2 (see Chernova et al., 2017 *Cell Reports* 18: 751-761), whose prion properties depend on association with a peripheral actin cytoskeleton. Our findings emphasize the significance of a specific intracellular location for prion formation. Ste18 is short-lived, ubiquitinated, and degraded by a proteasome. Levels of Ste18 protein are increased when proteasome function is impaired, suggesting that Ste18 may form aggregates in response to proteotoxic stress when proteasome is malfunctioning Potential involvement of prion-like aggregation in regulation of G-protein dependent signaling and yeast mating will be discussed in the light of our data and recent developments, suggesting the role of protein aggregation in diseases and in regulation of some biological processes.

Biography

Tatiana Chernova received her PhD in Microbiology from Institute of Agricultural Microbiology, Academy of Agricultural Sciences, Pushkin, St. Petersburg, Russia in 1986, and performed postdoctoral studies at University of Illinois (Chicago, USA) and Winship Cancer Center, Emory University School of Medicine (Atlanta, USA). She is an Assistant Professor at Department of Biochemistry, Emory University School of Medicine (Atlanta, USA). She has published 27 peer-reviewed papers, that are cited 2050 times, with typically more 100 citations per year in the last 10 years. Her expertise is in protein postranslational modifications (including ubiquitination), misfolding and degradation, yeast prions and glycobiology.

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