Elucidating a Novel Pathway Underlying Yeast Prion Replication: Atg17 and the Essentiality of Specific Genes in Yeast Prion Propagation

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Prion proteins are associated with neurodegenerative diseases, causing normal cellular proteins to fold abnormally in a rapidly progressive manner. Studying the genes required for yeast prion formation and propagation can help reveal the mechanisms that drive mammalian prion diseases and may reveal the key to future treatments in a safe manner. In this study, I utilized previously gathered Saturated Transposon Analysis in Yeast (SATAY) data. Here, we first explore the formation of yeast prions in environmental stress and identify genes necessary for yeast prion propagation. Interestingly, my results revealed a more influential factor than the environment: yeast prion polymorphisms or strains. The polymorphic impact on gene essentiality became the second part of my study. SATAY data analysis of these polymorphisms and their impact on four targeted gene groupings revealed that out of the four groupings (139 genes per polymorphism), the autophagy gene group is of most interest for future research. Surprisingly, our data also indicated that only one gene, Atg17, was universally essential for all polymorphisms of yeast prions to propagate. Notably, upon further analysis, Atg17 interacted with another complex essential for the yeast prions in this study, the Snx4-Snx41 complex. My results suggest the presence of a heretofore unreported essential pathway for yeast prion formation and propagation involving Atg17 and the Sx4-Snx41 complex in yeast, not only providing insight into the mechanisms that drive prion diseases but also elucidating a potential pathway of interest to study and focus treatments on in the future of neurodegenerative disease research.

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