



GÖTEBORGS UNIVERSITET

On the Role of Actin in Yeast Protein Quality Control

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Abstract

Every cell is equipped with a protein quality control system to ensure the proper function of proteins. This is essential for both cell maintenance and the generation of new and healthy cells. In this thesis, the budding yeast *Saccharomyces cerevisiae* is used as a model to study both spatial quality control and the management of the protein involved in Huntington's disease. The role of the actin cytoskeleton in both these processes has been the special focus of the thesis.

Earlier studies established a role for the histone deacetylase Sir2 and the actin cytoskeleton in the asymmetrical inheritance of damaged proteins by the mother cell, as cells either lacking *SIR2* or subjected to a transient collapse of the actin cytoskeleton, fail in this segregation process. In this thesis the protein disaggregase Hsp104, the polarisome complex, and the molecular chaperone CCT were identified as additional factors having important functions in the asymmetric segregation of damaged proteins. CCT is an essential, cytosolic folding machine, vital for the production of native actin. The actin folding capacity of CCT appears to be regulated by Sir2. Without this regulation the cell suffers from a reduction in native actin molecules, which could affect the integrity of actin cytoskeletal structures. The polarisome complex ensures actin polymerization at the bud tip and the establishment of a retrograde actin cable flow from the bud to the mother. Our data show that the presence of a functional actin cytoskeleton allows for Hsp104, associated with protein aggregates, to use the actin cytoskeleton as a scaffold and prevent the inheritance of damaged and aggregated proteins by the daughter. The retention of damaged protein within the mother cell is important for the rejuvenation of the daughter cell, as a daughter being born with increased damage suffer from a reduced life span.

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Keywords: Protein quality control, actin, protein aggregate, segregation, polarisome, CCT, huntingtin, text removed from public version