IGS DHD

SFB 635
Posttranslational control of protein function

Seminars in Genetics and Molecular Cell Biology

Claes Andreasson
Cell Biology, Wenner-Gren Institute,
Stockholm

Nucleotide exchange factors - cellular regulators of Hsp70 function

Hsp70 chaperones are abundant factors that play essential roles in many important processes by facilitating protein folding or conformational transitions. Currently we lack an understanding of the *in vivo* regulation and role of Hsp70s in the eukaryotic cellular chaperone network. Nucleotide exchange factors (NEFs) that previously have been described as mere catalysts of the Hsp70 ATPase activity have just recently emerged as key regulators of Hsp70 function.

Yeast cells carry all three classes of Hsp70 NEFs present in eukaryotes and we study the functions of these factors using a combination of biochemistry, cell biology and genetics. Specifically, we have focused on the NEF Fes1, a homologue of mammalian HspBP1. Fes1 appears to play a key role in maintaining protein homeostasis (proteostasis) in the cell. Deletion of *FES1* results in a massive and constitutive induction of the heat shock response, suggesting that misfolded proteins accumulate in *fes1*Δ cells. Consistent with this notion *fes1*Δ induces strong synthetic phenotypes when combined with mutations in the structural genes encoding Hsp70 or the protein disaggregase Hsp104. Furthermore, *fes1*Δ cells are hypersensitive to protein misfolding conditions such as elevated temperature and the presence of the arginine analogue canavanine. Taken together, our results indicate that Fes1 plays a key role in eukaryotic proteostasis, either by directly participating in *de novo* protein folding or by clearing misfolded proteins from the cytoplasm via proteasomal degradation.

Tuesday, November 15, 2011 at 5.00 p. m.

Institute for Genetics,
Zülpicher Str. 47 a, Lecture hall, 4th floor

Host: Jürgen Dohmen, Institute for Genetics,
University of Cologne

www.sfb635.uni-koeln.de