

**S009** Systems biology of protein secretion in *Saccharomyces cerevisiae*: mapping of global regulatory structures  
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The yeast *Saccharomyces cerevisiae* serves as an important eukaryotic model organism, both in the elucidation of molecular mechanisms underlying many different diseases and in the production of drugs, food products, industrial chemicals, and fuels. The secretory pathway, responsible for processing a third of all synthesized protein, has been studied extensively by reductionist approaches, but until recently, tools for systemic study of the pathway have been inadequate. Here we undertook a global analysis of the protein secretion pathway in *S. cerevisiae*. First we reconstructed the complete network involved in protein secretion. This network was used as a scaffold for integrated analysis of transcriptome data. The secretory pathway was queried by various disturbances to identify significant molecular pathways involved in maintaining homeostasis. The disturbances, (1) recombinant secretion of human insulin and  $\alpha$ -amylase proteins, and (2) deletion of the Unfolded Protein Response (UPR) transcription factor *HAC1*, caused significant physiological changes that could be mapped to different stress pathways. Through our analysis, we propose a holistic model for coping with secretory pathway stress including both endoplasmic reticulum folding processes, as well as, downstream compensation mechanisms. This model should be useful as a scaffold for understanding protein secretion in higher eukaryotic cells and in the analysis of protein folding-related disease.