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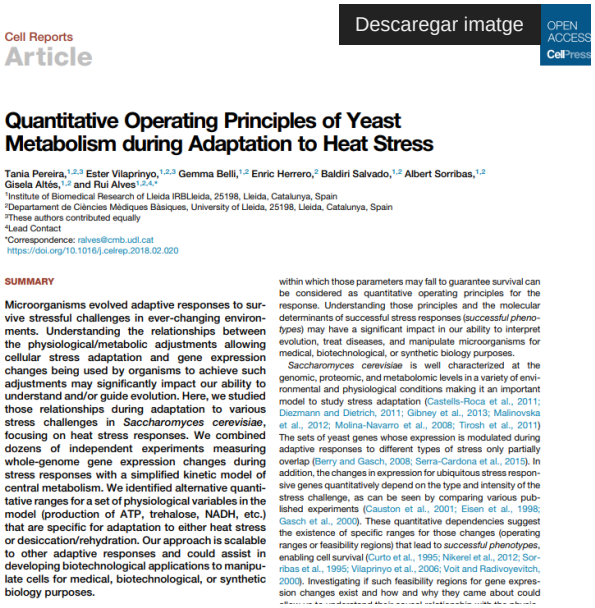
Evolution of adaptive responses in yeast. New article in Cell Report

Adaptive response

Microorganisms evolved adaptive responses to survive stressful challenges in ever-changing environments. Understanding the relationships between the physiological/metabolic adjustments allowing cellular stress adaptation and gene expression changes being used by organisms to achieve such adjustments may significantly impact our ability to understand and/or guide evolution. Here, we studied those relationships during adaptation to various stress challenges in Saccharomyces cerevisiae, focusing on heat stress responses. We combined dozens of independent experiments measuring whole-genome gene expression changes during stress responses with a simplified kinetic model of central metabolism. We identified alternative quantitative ranges for a set of physiological variables in the model (production of ATP, trehalose, NADH, etc.) that are specific for adaptation to either heat stress or desiccation/rehydration. Our approach is scalable to other adaptive responses and could assist in developing biotechnological applications to manipulate cells for medical, biotechnological, or synthetic biology purposes.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Cell Reports
Article

Quantitative Operating Principles of Yeast Metabolism during Adaptation to Heat Stress

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SUMMARY

Microorganisms evolved adaptive responses to survive stressful challenges in ever-changing environments. Understanding the relationships between the physiological/metabolic adjustments allowing cellular stress adaptation and gene expression changes being used by organisms to achieve such adjustments may significantly impact our ability to understand and/or guide evolution. Here, we studied those relationships during adaptation to various stress challenges in *Saccharomyces cerevisiae*, focusing on heat stress responses. We combined dozens of independent experiments measuring whole-genome gene expression changes during stress responses with a simplified kinetic model of central metabolism. We identified alternative quantitative ranges for a set of physiological variables in the model (production of ATP, trehalose, NADH, etc.) that are specific for adaptation to either heat stress or desiccation/rehydration. Our approach is scalable to other adaptive responses and could assist in developing biotechnological applications to manipulate cells for medical, biotechnological, or synthetic biology purposes.

within which those parameters may fall to guarantee survival can be considered as quantitative operating principles for the response. Understanding those principles and the molecular determinants of successful stress responses (*successful phenotypes*) may have a significant impact in our ability to interpret evolution, treat diseases, and manipulate microorganisms for medical, biotechnological, or synthetic biology purposes.

Saccharomyces cerevisiae is well characterized at the genomic, proteomic, and metabolomic levels in a variety of environmental and physiological conditions making it an important model to study stress adaptation (Castells-Roca et al., 2011; Diezmann and Dietrich, 2011; Gibney et al., 2013; Malinovska et al., 2012; Molina-Navarro et al., 2008; Tirosh et al., 2011) The sets of yeast genes whose expression is modulated during adaptive responses to different types of stress only partially overlap (Berry and Gasch, 2008; Serra-Cardona et al., 2015). In addition, the changes in expression for ubiquitous stress responsive genes quantitatively depend on the type and intensity of the stress challenge, as can be seen by comparing various published experiments (Causton et al., 2001; Eisen et al., 1998; Gasch et al., 2000). These quantitative dependencies suggest the existence of specific ranges for those changes (operating ranges or feasibility regions) that lead to *successful phenotypes*, enabling cell survival (Curto et al., 1995; Nikerel et al., 2012; Sorribas et al., 1995; Vilaprinyo et al., 2006; Voit and Radivoyevitch, 2000). Investigating if such feasibility regions for gene expression changes exist and how and why they came about could

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