

A Transcriptomic Atlas of Acute Stress Response to Low pH in Multiple *Issatchenkia orientalis* Strains

Background/Objective

Issatchenkia orientalis is a promising non-model yeast for biofuel and product production because it has high stress tolerance to low pH, heat, and other chemicals toxic to microorganisms used in processing lignocellulosic biomass. Little is known about its specific mechanisms of its pH tolerance, limiting the ability to genetically engineer it to produce products. In this study, comparative transcriptomics analysis, followed by a multi-pronged bioinformatics analysis, was performed on *I. orientalis* to study potential mechanisms of pH tolerance in this species.

Approach

The transcriptomes of twelve *I. orientalis* strains with varying acid stress tolerances, six tolerant and six susceptible, were profiled after exposure to various pH conditions. Genes whose expression response were similar in tolerant strains but not in susceptible strains, or vice versa, were mapped to regulatory mechanisms by motif analysis and differential network reconstruction, and their functions identified by functional genomic analysis. Additionally, acid-specific effects on genes were tested for two organic acids, 3-hydroxypropionate (3-HP) and citramalate.

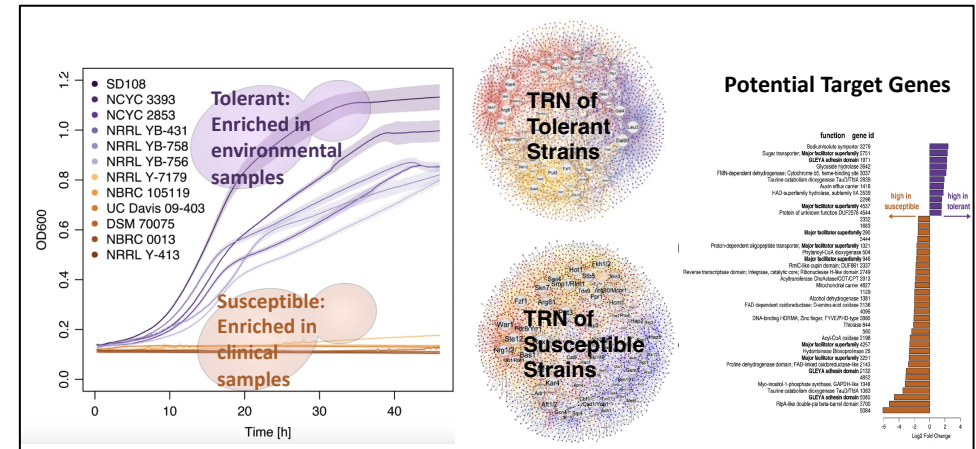
Results

Multiple regulatory mechanisms involved in tolerance to low pH were identified, including genes and transcription factors associated with energy metabolism, translation-related processes, cell wall integrity pathway, and a signaling pathway between the mitochondria and nucleus. Acid-specific effects of 3-HP and citramalate found potential roles for glycolysis and trehalose biosynthesis, specifically in response to low pH.

Significance/Impacts

This study identified potential targets for future gene editing and perturbation experiments to understand the mechanism of pH tolerance in *I. orientalis*. Future studies could explore long-term low-pH stress to elucidate the regulatory differences between acute and prolonged low-pH stress adaptations.

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Comparative transcriptomic analysis to associate potential target genes with low-pH tolerance and to reconstruct transcriptional regulatory networks (TRNs) for tolerant and susceptible strains.