

An overview of ethanol tolerance in *Saccharomyces cerevisiae* through systems biology and differential expression analysis

Ivan Rodrigo Wolf¹, Lauana Fogaça(department Of Bioprocess And Biotechnology. São Paulo State University², Leonardo Nazário de Moraes³, Rafael P. Simões⁴, Lucilene Delazari Dos Santos⁵, Rejane M. T.grotto⁶, Guilherme Targino Valente⁴

1 FCA-UNESP

2 UNESP

3 DEPARTMENT OF BIOPROCESS AND BIOTECHNOLOGY. SÃO PAULO STATE UNIVERSITY

4 UNESP - STATE USP

5 CENTER FOR THE STUDY OF VENOMS AND POISONOUS ANIMALS , SÃO PAULO STATE UNIVERSITY

6 DEPARTMENT OF BIOPROCESS AND BIOTECHNOLOGY, SÃO PAULO STATE UNIVERSITY, BOTUCATU

Abstract

The bioethanol production contributes to the sustainable development and the life's quality improvement. The main bioethanol production process is through the first generation technology, which *Saccharomyces cerevisiae* is the most widely used organism. Unfortunately, ethanol is toxic to *S. cerevisiae* in higher concentrations, limiting the bioethanol production. Tolerance to ethanol is a complex feature, and it is poorly understood, then the conventional methods have been unsuccessful in attempting to understand their mechanisms. Here we experimentally determined ethanol tolerance for five yeast strains (S288c, BY4741, BY4742, SEY6210, X2180-1A and BMA64-1A) and the unsupervised learning was used to classify the strains as high (HT) or low (LT) tolerant. RNA and proteins were further extracted for treatment (maximum ethanol exposure) and control (without ethanol exposure) conditions and submitted for sequencing and/or mass-charge quantification. The gene transcripts showing significant differences (FDR<0.05) between treatment and control were considered as differentially expressed (DE); a common set of 270 genes was found up regulated in treatment while 80 were down regulated. The extracted protein was submitted to mass spectrometry and a total of 18 protein-coding genes with fold-change>1, where considered up regulated (7 for HT, 7 for LT and 4 common to both HT and LT). Interestingly, 2 chaperones were coincidentally found up regulated in transcript and protein data. The functions of differentially expressed genes have already been observed in previous studies. However, this is the first time it was observed synergistically in one experiment. A co-expression (CoEx-net) network was created based on transcripts abundance data for each strain. Differences between CoEx-net and our previous protein-protein interaction (PPI-net) are evident considering topological characteristics as the degree, density, diameter, and assortativity; it reflects different meanings between systems biology layers analyzed. The clustering analysis

over all node degrees for each CoEx-net also showed it could be related to HT and LT strains, which clusters obey the range of ethanol tolerance. The degree differences reflect network rewiring through different strains, which can be further explored to better understanding the complex phenotype of ethanol tolerance.

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