Gene Regulatory Network Modeling for Mycelium-to-Yeast Transition of *Paracoccidioides brasiliensis*

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Recent advances in systems biology are focused on uncovering the mechanisms underlying the establishment and maintenance of cell states. Gene regulatory networks (GRNs) models have allowed to clarify complex interactions between large numbers of genes and identify genes involved in modulation of different cell phenotypes. Networks can be mapped as a graph whose nodes are associated with genes (or groups of genes) and edges depict the relation between the nodes. In this work, we have applied a GRN approach to analyze transcriptional data of *Paracoccidioides brasiliensis* cells going through mycelium-to-yeast transition. *Paraccocidioides* spp. (Pb) is a human pathogenic fungus responsible for paracoccidiodomycosis (PCM), the most prevalent systemic mycosis in Latin America. The pathogenicity of Pb have been seen closed related to its dimorphic transition once the shift from mycelium to the yeast form is essential for infection. The experimental data (GEO, accession no.: GSE3238) monitor the gene expression of 4692 genes at several time points (5, 10, 24, 48, 72 to 120h) after a temperature shift (26° to 37°C) comprising the mycelium-to-yeast conversion. After preprocessing of control genes and biological replicates, genes with similar expression profiles were grouped in an optimum number of clusters (Nc=431). Intra-cluster averages of the expression level we used to model the GRN dynamics by a fist order Markov model, where the future state depends linearly on the present state and on external perturbation. This approach allows the identification of regulatory genes mainly involved into the known phenotypic states and the environmental-cue effectors considering the transition between states. After analyzing the data, we described 20 genes with important regulatory activity for mycelium-to-yeast transition, whose three are up- or down-regulated by temperature. Among the genes coding for proteins with known function, we found proteins related to pro synthesis of cell wall and basal metabolism of the fungus.