

# The genomic signature of Fungi at the gene- and pathway-levels

Francisco Pereira Lobo, Alison Menezes, Aline Soares dos Reis

*UNIVERSIDADE FEDERAL DE MINAS GERAIS, UNIVERSIDADE FEDERAL DE MINAS GERAIS*

## Abstract

Fungi comprise a highly diverse eukaryotic taxon that plays important ecological and biotechnological roles. They can also be a threat due to their pathogenicity: fungal toxicity and drug resistance are key concerns in medicine and agriculture. Therefore, the molecular and functional characterization of fungi is both noteworthy and needed to achieve a better understanding of their modus operandi and to detect possible new targets for molecular intervention. KEGG database describes groups of homologous genes shared across genomes as Kegg Orthology groups (KO). We use the KEGG API to obtain all KO groups for each complete eukaryotic genome available, which were divided into fungi (F, 129 genomes) and non-fungi (NF, 406 genomes). To select KO groups enriched in F, we used the following strategy: 1) genome bootstrapping in both groups (100 bootstraps); 2) For each bootstrap, perform the Fisher's test, followed by FDR correction, to evaluate if a KO was more observed in F than in NF; 3) a KO is considered overrepresented in F if FDR-corrected q-values are  $< 0.05$  in 95% of the bootstraps and absent in NF. From the set of 13962 KOs found in at least one genome, 495 (3.5%) are significantly enriched in Fungi. Among the 50 most enriched KOs, we found enzymes of fungal activity as decomposers and also of metabolic activities of commercial interest. Interestingly, we also found several enzymes already targeted by antifungals, indicating our strategy also detects known druggable proteins. We also found several interesting candidates for future research that play major roles in fungal biology, such as transcriptional regulators and components of cell wall processes. We detected enriched pathways in F by computing the ratio of enriched KOs in a pathway by the total count of KOs in the same pathway. Among the pathways with the highest ratio of KOs enriched in fungal genomes we found both fungi-specific processes and fungal-specific modules within conserved eukaryotic pathways, such as DNA repair, protein synthesis and fatty acid metabolism. Mapping of KOs into specific pathways will also allow us to search for chokepoints, defined as steps that either uniquely consumes a specific substrate or uniquely produces a specific product, therefore comprising interesting targets for systemic interventions in fungal metabolism. Together, our comparative genomics analysis provides a gene- and pathway-level signature of fungal biology.

Funding:

Link to Video: