Transcriptional landscape of *Paracoccidioides brasiliensis*: an isolate presenting no dimorphism shift

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Paracoccidioidomycosis, a systemic mycosis of significant medical importance, endemic to Latin America, is caused by thermodimorphic fungi of *Paracoccidioides* species complex. The infection is thought to be contracted by inhalation of fungal propagules and the disease is triggered by the dimorphic shift from conidial to the yeast phase at body temperature. We selected from a clinical isolate of *Paracoccidioides brasiliensis* (Pb339; ATCC32069) under pressure of 400 µg of sulfamethoxazole an isolate that presents no dimorphic shift (YRT, Yeast at Room Temperature). By integrating experimental and computational information the systems biology approach aims at generating new insights to underlying complex dimorphism and virulence mechanisms of *P. brasiliensis*. Here, for the first time we apply advanced next-generation sequencing (Illumina RNASeq) in order to investigate of two temperature-regulated states across the reference isolate Pb339 and the defective isolate YRT. In terms of RNA sequencing we found $5x10^8$ reads (PE 2x100, Q Phred ≥25), mapping $3{,}2x10^8$ to a reference genome. Estimates of FPKM values (fragments per kilobase of exon per million aligned fragments) were well-correlated between biological replicates. PbB339 yeast and mycelial phases have distinct transcriptomes presenting 248 and 802 differentially expressed gene, respectively. Oxidative stress pathways were the most enriched. The transcriptome of the defective isolate YRT changes dramatically compared to yeast and mycelia transcriptomes of the reference isolate. The defective YRT at 37ºC and PBB339 isolate at yeast phase share a similar transcriptional profile, showing 462 up regulated genes. The oxidative and protein synthesis pathways were over-represented. However, at room temperature YRT transcriptome identified 387 differentially expressed genes when compared with M phase in the same conditions. Oxidative stress pathways were also enriched. Additionally, co-factor binding, ABC transporters and Kinase pathways were found to be over-represented. We uncovered 125 genetic variants (SNP/Indel) in YRT isolate, of which 2 were non-synonymous substitutions and 4 were potentially associated to loss of function. The first mutations for MAPK3 e TAO3/PAG1 genes are involved with mycelial growth regulation in pathogenic fungi. Loss of function related to USP protein (universal stress protein) were found with one hypothetical gene presenting tetratricopeptide repeats and glycosil transferase domains involved with response to environmental and dimorphism phenomena, tRNA2 thiolation and APG9 autophagy function. Here we present the only PbB339 Y and M phase-specific transcriptomes carried out by RNASeq as well as for a dimorphism defective isolate. These analyses will provide new information about thermal dimorphism and morphogenesis currently underexplored in *Paracoccidioides.*