Title: SECRETOME CHARACTERIZATION OF *PARACOCCIDIOIDES SP* DURING NITROGEN STRAVATION

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Resume:

Paracoccidioides spp is a thermodimorphic fungus that causes paracoccidioidomycosis (PCM), an endemic human systemic mycosis in Latin America. When grown in temperatures less than 28 °C the fungus grows as mycelium and as yeast form in temperatures around 37 °C. The secretome include proteins that have important functions such as cell-cell communication, adhesion, migration, differentiation, defense and virulence. Nitrogen is an important element in microorganism's nutrition that participates in the synthesis of proteins, nucleic acids and others essential biomolecules. In this vein, nitrogen uptake and metabolism are essential to growth and for fungal establishment. When nitrogen levels and sources such as glutamine and ammonia concentration are limiting, pathogenic fungus use a system of regulation called Nitrogen Catabolite Repression that induce the expression of genes encoding permeases and enzymes required for the catabolism of secondary nitrogen sources, such as formamidase. This study aims to evaluate the *Pb*01 secreted proteins regulated during the nitrogen starvation. The fungus grown in minimal medium MMcM plus and without nitrogen sources. Secreted proteins were extracted and subjected to tryptic digestion and identification by using mass spectrometry. A total of 126 proteins were identified during nitrogen depletion, which 54 were down regulated, 26 were induced and 46 were expressed constitutively. Among induced proteins, we identified molecules related to biogenesis of cellular components; amino acid metabolism; cell rescue, defense and virulence; cell fate; protein fate; energy; protein synthesis. The gamma-glutamyltranspeptidase, which is an antioxidant protein and is involved in gluthatione metabolism, was found as induced in our secretome and can serve as an alternative source of nitrogen. The protein formamidase was induced, this protein have been shown to be highly regulated in response to nitrogen levels and is related with virulence factors in *Paracoccidioides*. The study of secretome will identify possible metabolic strategies used by the fungus to adapt to the conditions encountered in the host, which will contribute to the understanding of host-parasite interaction, biology and virulence of this important pathogenic fungus.

Keywords: Starvation, metabolism nitrogen, secretome, *Paracoccidioides sp.*

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