Title: PROTEOME OF *HISTOPLASMA CAPSULATUM* INDUCED DURING DIMORPHIC TRANSITION

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Abstract:

Histoplasmosis is a systemic fungal disease caused by *Histoplasma capsulatum*, a dimorphic fungus that grows in the mycelial (M) form at room temperature in the environment and in the yeast (Y) form at 37°C in infected tissues. Integral to pathogenesis is the mold-to-yeast dimorphic shift. The organism grows in soil as a differentiated multicellular mold. When mold fragments or conidias are inhaled, *H. capsulatum* shifts to an undifferentiated single-cell yeast growth form in the lungs of the host. If this M-Y shift is blocked, the disease cannot progress In order to establish infection within the mammalian host, the fungus protects itself against toxic reactive oxygen species produced by cells of the immune system. This morphological change is the manifestation of several alterations in gene expression patterns that constitute a switch to a pathogenic lifestyle. However, the dimorphism and mechanisms enabling *H. capsulatum* to survive into the host is not totally elucidated. To address this deficiency, we started to define the molecular constituents of the different phases of the evolutionary life cycle of *H. capsulatum* using NanoUPLC-MS^E analysis of the proteins. Our preliminary results show that 306 proteins were differentially regulated, where 122 were preferentially induced in the mycelial phase and 184 in the yeast phase. Non-classified proteins were observed in both phases (28% in yeast phase and 36% in the filamentous phase). In the mycelial phase, the majority of proteins are involved in general metabolic activities indicating a high metabolic flexibility. Also, several enzymes related to nitrogen metabolism were induced in mycelium form. In the yeast phase was observed up regulation of enzymes related to glutamate/glutamine metabolism, as well as, production of cell wall precursors. Additionally, during yeast to mycelium transition the pathways related to alternative carbon source utilization, such as glyoxylate and methylcitrate cycles, were induced. The results indicate metabolic preferential pathways in the fungus phases.

Key words: *Histoplasma capsulatum,* proteome, dimorphism

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