MICELIUM TO YEAST DIMORPHISM OF *Paracoccidioides brasiliensis* INDUCED BY TEMPERATURE RISE REQUIRES AN EARLY AND RAPID BIOENERGETIC ADJUSTING TOWARD FUNCTIONAL MITOCHONDRIA: ROLE OF CALCINEURIN

Cláudia B. L. Campos; João Paulo T. Di Benedette, Juliana B. Santana, Marina P. Nóbrega; Francisco G. Nóbrega
Instituto de Pesquisa e Desenvolvimento, Universidade do Vale do Paraíba (UNIVAP), São José dos Campos, SP, Brazil cbcampos@univap.br

Paracoccidioides brasiliensis is a dimorphic fungus that causes paracoccidioidomycosis, a systemic mycosis prevalent in Latin America with most cases found in Brazil. The transition from mycelium to yeast is triggered by temperature rise from 25^{o}C to 37^{o}C and both virulence and pathogenicity factors necessary for human infection are expressed during this phase. We show here that mitochondria is turned on to produce energy early in the process of mycelium to yeast dimorphism, confirmed by quick shift from oligomycin-insensitive to oligomycin-sensitive respiration, enhancement of oxygen consumption, strong increase of mitochondrial transmembrane potential and increment of reactive oxygen species (ROS) generation. Cyclosporin A (CsA), an inhibitor of the Ca^{2+}/calmodulin-dependent phosphatase calcineurin, decreased both oxidative phosphorylation and ROS generation, without abolishing mitochondrial transmembrane potential or FCCP-induced uncoupling. CsA prevented dimorphism of *P. brasiliensis* and is fungistatic at 37^{o}C. Bapta-AM mimicked CsA effect, showing the role of Ca^{2+} on dimorphism and narrowing a function for calcineurin in this process. We are proposing an early role for calcineurin during mycelium to yeast transition via a fine-tuning on the production of both energy and ROS. Supported by Fapesp, CNPq. Key words: *Paracoccidioides brasiliensis*, calcineurin, mitochondria