AUTOPHAGY IN THE HUMAN PATHOGENIC FUNGUS *Paracoccidioides brasiliensis*

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Autophagy is a highly conserved eukaryotic cellular process that allows the degradation of macromolecules and organelles through the action of the lysosomal/vacuole compartments. This process is involved in many biological events such as development, differentiation and adaptation to environmental conditions. *Paracoccidioides brasiliensis*, a human pathogenic fungus, undergoes thermo-dimorphism from mycelium to yeast in the host, which is necessary for the establishment of the disease and acquisition of virulence factors. In *P. brasiliensis*, the genes involved in autophagy were identified in studies of gene expression, suggesting that this mechanism may be functional and may contribute to the differentiation of the fungus. In this work, we investigated the involvement of autophagy in dimorphism of *Paracoccidioides brasiliensis* induced by temperature rise from 25^{o}C to 37^{o}C under the effect of different drugs shown to modulate this process. We show that autophagy is basically absent in mycelia. However, the amount of autophagic vacuoles, visualized by mono-dansylcadaverine labelling, progressively increase during mycelium to yeast transition. N-ethylmaleimide, an inhibitor of autophagy, potently induces fungus death during dimorphism. Regulation of autophagy was also investigated using cyclosporin A, an inhibitor of the Ca^{2+}/calmodulin-dependent phosphatase calcineurin, which is activated during mycelium to yeast transition; and SHAM, an inhibitor of alternative oxidase, a mitochondrial enzyme important for adaptation under environmental stresses. Acknowledgements: FAPESP and CNPq. Key words: *Paracoccidioides brasiliensis*, autophagy, dimorphism.