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The epigenetic down regulation of *Cryptococcus neoformans* major virulence phenotypes is induced by histone deacetylases inhibitors

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The opportunistic pathogen *Cryptococcus neoformans* undergoes phenotypical changes during host infection in order to promote persistence and survival. Studies have demonstrated that such adaptations require alterations in gene transcription networks by distinct mechanisms. Drugs such as the histone deacetylases inhibitors (HDACi) Sodium Butyrate (NaBut) and Trichostatin A (TSA) can alter the chromatin conformation and have been used to modulate epigenetic states in the treatment of diseases such as cancer. In this work, we have studied the effect of NaBut and TSA on the expression of *C. neoformans* major virulence phenotypes and on the survival rate of an animal model infected with drugs-treated yeasts. Both drugs affected fungal growth at 37°C more intensely than at 30°C. HDACi also provoked the reduction of the fungal capsule expansion. Phospholipases enzyme activity decreased; mating process and melanin synthesis were also affected by both inhibitors. NaBut led to an increase in the population of cells in G2/M. Treated yeast cells, which were washed in order to remove the drugs from the culture medium prior to the inoculation in the *Galleria mellonela* infection model, did not cause significant difference at the host survival curve when compared to non-treated cells. Overall, NaBut effects on the impairment of *C. neoformans* main virulence factors were more intense and stable than the TSA effects. We propose the employment of HDACi in combination to classical antifungal drugs in experimental treatment approaches for severe cryptococcosis animal models. Furthermore, the accumulation of transcripts corresponding to eight *C. neoformans* genomic sequences presenting homology to fungal histone deacetylase genes was analyzed by qRT-PCR after yeast growth on minimal medium for 30, 60 and 180 min. Since the HD1/2 CNAG_1699, 5276, 5096 and the HOS3 CNAG_00660 genes presented the highest transcripts accumulation levels, disruption cassettes are being constructed in order to evaluate the respective mutant strains virulence phenotypes.

Biography

Marcio José Poças-Fonseca: B.Sc. in Biological Sciences (University of Brasilia-Brazil), M. Sc. in Molecular Biology (1994) and PhD in Molecular Biology from the University of Brasilia in a joint program with the Vienna University of Technology (Austria, 2000). Associate Professor at the Department of Genetics and Morphology, University of Brasilia since 1997. Post-doctoral fellow in Molecular and Microorganisms Genetics at the Institute of Chemical Engineering Vienna University of Technology from August 2006 to October 2007. Post-doctoral fellow at the Department of Microbiology of the University of Delhi South Campus (January-March 2014; November 2014 - March 2015). Expertise and focused on gene structure, function and regulation for cellulolytic and pathogenic fungi, with emphasis in epigenetics. 23 full papers in international indexed journals, 09 book chapters, 02 patents on biotechnology, 13 M.Sc. dissertations as supervisor, 03 PhD thesis as supervisor.

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