Title: Evaluation of copper transporter CTR1 in macrophages infected by *Cryptococcus neoformans* and *Candida albicans*

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Abstract

Cryptococcus neoformans and *Candida albicans* are pathogenic yeasts that frequently cause opportunistic infections worldwide, being able to survive, proliferate and escape from macrophages. These immune cells try to avoid the microorganisms proliferation using different mechanisms, including changes in the essential metals availability, such as copper. In this way, either copper deprivation (nutritional immunity) or its accumulation may constitute antifungal strategies used by macrophages to eliminate pathogenic fungi. We aim to investigate copper homeostasis modulation during interaction between macrophages and C*. neoformans* or *C. albicans* cells (live or heat-killed) by evaluation of CTR1 expression. CTR1 is a copper transporter responsible for the modulations of this metal homeostasis in macrophages. Previous studies of our group showed that this transporter is modulated in response to infection by those yeasts, possibly following a nutritional immunity pathway. To confirm the transcriptional data, western blot, *in cell* ELISA and immunofluorescence analysis were conducted. We found that incubation of macrophages with heat-killed cells of both *C. neoformans* and *C. albicans* induced the expression of the expression of CTR1 gene in comparison to live yeast cells. Immunofluorescence experiments revealed that CTR1 can be located spread in the cell. *In cell* ELISA showed an increase at surface expression of CTR1 after incubation with *C. albicans*. These partial results suggests that presence of living *Cryptococcus neoformans* and *Candida albicans* cells leads to an alteration in expression of copper transporter, suggesting that there is a complex modulation of macrophage copper homeostasis in response to fungal pathogens. More studies are in progression to further validate these results.

Keywords: copper, copper transporters, *Cryptococcus neoformans*, *Candida albicans*.

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