

TITLE: MICRO-RNAS INVOLVED IN MURINE DENDRITIC CELLS RESPONSE TO *Cryptococcus neoformans* INFECTION

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ABSTRACT:

The pathogenic fungus *Cryptococcus neoformans* is one of the etiological agents of cryptococcosis, an invasive fungal infection that can spread to the central nervous system, and mainly affects immunocompromised patients. Dendritic cells play a pivotal role in the *C. neoformans* infection. These host cells recognize and phagocytose the fungus, orchestrating the innate and adaptive immune response to the infection. The immune response to microbial pathogen infections involves extensive genetic reprogramming, which is finely tuned to contain or to effectively eliminate the pathogen without causing excessive damage to the host. Micro-RNAs (miRNAs) are small regulatory RNAs involved in gene regulation mechanisms; these molecules are observed in a wide range of physiological and pathological processes controlling either messenger RNA (mRNA) stability or translation rate. Consequently, they have been identified as a crucial component in the gene regulation pathway, affecting the production and function of proteins in homeostasis and in its pathological conditions. This study focused on characterizing the profile of miRNAs expressed in bone marrow-derived dendritic cells from BALB/c mice (BMDCs) in response to *C. neoformans* infection. BMDCs were co-cultured with the B3501 strain of *C. neoformans* for 24 hours, after which the RNA was extracted for analysis of miRNA expression by *RT-qPCR array*. The expression levels of 29 miRNAs were modulated in the infected BMDCs. Out of this group, 22 miRNAs were upregulated while 7 miRNAs showed a decrease in the transcripts levels. Furthermore, the effect of miR-155 on some of BMDCs main functions in response to *C. neoformans* infection was analyzed by a loss-of-function approach –the transfection of miRNA inhibitors into the BMDCs. The miR-155-3p inhibition presented a change in BMDCs phagocytosis ability and intracellular control of the fungus. Meanwhile, the analysis of the MHCII expression in infected BMDCs, revealed an increase in the Mean Fluorescence Intensity (MFI) when miR-155-5p was inhibited. These results are pioneer in the analysis of miRNAs' participation in the dendritic cells response to *C. neoformans* infection.

Keywords: microRNAs, cryptococcosis, dendritic cells, innate immune response.

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