

EFFECT OF PROSTAGLANDINS ON THE PRODUCTION OF H₂O₂ AND CYTOKINES THAT MODULATE THE FUNGICIDAL ACTIVITY OF HUMAN MONOCYTES AGAINST *Paracoccidioides brasiliensis*

THESIS. A. P. Bordon submitted this dissertation for her Masters in Tropical Diseases at Botucatu School of Medicine, São Paulo State University – UNESP, Botucatu, São Paulo, Brazil, 2005.

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ABSTRACT: Human monocytes lack fungicidal activity against high virulent strains of *Paracoccidioides brasiliensis*, the etiological agent of paracoccidioidomycosis, even after IFN- γ activation. However, monocytes treated with indomethacin (INDO) or INDO plus IFN- γ effectively killed this fungus, suggesting an inhibitory role of prostaglandins in this process. Thus, the purpose of this work was to test if this regulatory effect of prostaglandin was associated with alterations on H₂O₂ production and/or on modulatory cytokines levels, such as TNF- α , IL-10, and IL-6. Peripheral blood monocytes obtained from 10 healthy donors were incubated for 18 hours in the presence or absence of IFN- γ , INDO, or IFN- γ plus INDO, and further challenged with a high virulent strain of *P. brasiliensis* (Pb18) for 4 hours. Then, the monocytes cultures were evaluated for H₂O₂ release and fungicidal activity calculated by counting the colony forming units after plating. Moreover, on supernatants of the same cultures, TNF- α , IL-10, IL-6, and PGE₂ concentrations were evaluated by ELISA. Monocytes treated with INDO or INDO plus IFN- γ presented higher fungicidal activity associated with the release of higher levels of H₂O₂ and TNF- α , but lesser levels of PGE₂, when compared to nontreated cells. However, the levels of IL-10 and IL-6 were similar between treated and nontreated cells. The results suggest that human monocytes when challenged with high virulent strains of *P. brasiliensis* produce prostaglandins that inhibit the fungicidal activity of these cells by reducing H₂O₂ and TNF- α levels.

KEY WORDS: cytokines, H₂O₂, monocytes, *Paracoccidioides brasiliensis*, prostaglandins, paracoccidioidomycosis.

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