

FUNGICIDAL ACTIVITY OF MULTINUCLEATED GIANT CELLS INDUCED “IN VITRO” BY INTERFERON-GAMMA AND *Paracoccidioides brasiliensis* ANTIGEN

THESIS. M. P. P. do Nascimento submitted this dissertation for her Masters in Tropical Diseases at Botucatu School of Medicine, São Paulo State University, UNESP, Botucatu, São Paulo, Brazil, 2004.

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ABSTRACT: Multinucleated giant cells (MGC) are a common feature of granulomas that occur in chronic infectious diseases such as tuberculosis and paracoccidioidomycosis. This study investigated the *in vitro* formation of MGC derived from human monocytes of healthy individuals, stimulated with recombinant human interferon-gamma (IFN- γ), *P. brasiliensis* antigens (PbAg), and a conditioned medium obtained from supernatant of Concanavalin A-stimulated mononuclear cells (CM-ConA). Fungicidal activity of monocytes and monocyte-derived MGC challenged with *P. brasiliensis* strain (Pb18) was also evaluated. Peripheral blood monocytes obtained from healthy individuals were cultured for three days with or without stimulus such as: IFN- γ (300 IU/ml), CM-ConA or PbAg (100ug/ml). The fusion index and the percentage of MGC formation were determined after cell fixing and May-Grumwald-Giensa staining. Fungicidal activity of monocytes and monocyte-derived MGC were evaluated 4h after co-culture of monocytes with Pb18 strain in a ratio of 50:1 monocyte-fungus, by plating in BHI-agar and determining the viable fungi recovery. The results demonstrated that IFN- γ enhanced the generation of MGC in a dose-dependent pattern, being the fusion index and the percentage of MGC formed significantly higher than those observed with CM-ConA and PbAg stimulation. This effect was eliminated by addition of anti-IFN- γ monoclonal antibodies to the cultures. Both monocytes and monocyte-derived MGC induced *in vitro* by IFN- γ had the ability to kill the fungus, being the results significantly higher than those observed in control cells cultured without stimulus. The PbAg incubation also led to lower viable fungi recovery in monocytes and MGC cultures. Together, these data suggest that IFN- γ and PbAg are good stimuli for MGC generation and activation, and in fungicidal activity induction of these cells against *P. brasiliensis*.

KEY WORDS: multinucleated giant cells, interferon-gamma, fungicidal activity, *Paracoccidioides brasiliensis*

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