EFFECT OF TRANSFORMING GROWTH FACTOR BETA ON THE FUNCTIONAL ACTIVITY OF HUMAN MONOCYTES “IN VITRO” INFECTED WITH Paracoccidioides brasiliensis

THESIS: R. A. R. Martins submitted this thesis for her Doctorate in Tropical Diseases at Botucatu School of Medicine, São Paulo State University, UNESP, Botucatu, São Paulo, Brazil, 2005.

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ABSTRACT: Transforming Growth Factor-beta (TGF-β1) is a cytokine produced by cells such as macrophages and T cells having both pro- and anti-inflammatory properties depending on their environment and concentration. The aim of this study was to analyze the effect of TGF-β1 on the hydrogen peroxide (H₂O₂) release, Tumor Necrosis Factor-alpha (TNF-α) production, and fungicidal activity of human monocytes challenged with high-virulent strain of Paracoccidioides brasiliensis (Pb18). Peripheral blood monocytes from healthy individuals were preincubated with or without different concentrations (7.8 pg/ml to 500 pg/ml) of TGF-β1 for 24 h at 37°C, and then challenged with Pb18 in a ratio of 50:1 monocyte:fungus. The release of H₂O₂ by monocytes in response to Phorbol Myristate Acetate (PMA) was evaluated during and after 4h of monocyte infection with the fungus. TNF-α production by these cells was determined in supernatant cultures by enzyme immunoassay (ELISA), and fungicidal activity of monocytes against Pb18 was assessed by viable fungi recovery from 4h co-culture in Blood Heart Infusion-Agar (BHI-Agar) and counting of colony-forming units after 10 days. The results showed that monocyte incubation with TGF-β1 concentrations (31.2 pg/ml to 500 pg/ml) suppressed H₂O₂ release in a dose-dependent manner. The Pb18 infection of monocytes pretreated with TGF-β1 maintained the inhibitory effect on the H₂O₂ production by these cells stimulated with PMA, even in low doses of TGF-β1, suggesting that Pb18 may also interfere with H₂O₂ production by monocytes. These cells challenged with Pb18 produced significantly higher levels of TNF-α in comparison to monocytes not infected. However this production was inhibited when these cells were previously cultured with high concentrations of TGF-β1. On the other hand, pretreatment of monocytes with high doses of this cytokine enhanced their fungicidal activity against P. brasiliensis. Together the results suggest that exogenous TGF-β1 can exert a dual modulatory effect on monocytes infected with P. brasiliensis, when used in high concentrations. The effects are stimulatory on fungicidal activity and inhibitory on H₂O₂ release and TNF-α production.

KEY WORDS: cytokines, human monocytes, P. brasiliensis

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