

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

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ABSTRACT: Transforming Growth Factor-beta (TGF- β_1) 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- β_1 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- β_1 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- β_1 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- β_1 maintained the inhibitory effect on the H₂O₂ production by these cells stimulated with PMA, even in low doses of TGF- β_1 , 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- β_1 . 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- β_1 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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