

INTERLEUKIN-15 INCREASES *Paracoccidioides brasiliensis* KILLING BY HUMAN NEUTROPHILS

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ABSTRACT: Interleukin-15 is a pro-inflammatory cytokine produced by a wide range of different cell types, especially monocytes and macrophages, in response to infective agents, playing a crucial and modulatory role in innate and adaptive immune response. Infections by intracellular microorganisms such as some bacteria, protozoa and fungi point out the role of IL-15 in the activation of monocytes/macrophages and neutrophils, a process that represents an important defense mechanism in early periods of infection during the development of innate immune response. The aims of the present study were to evaluate the effects of IL-15 on human neutrophil fungicidal activity against a high virulent *Paracoccidioides brasiliensis* strain (Pb18) and to verify whether this activity was mediated by oxidative metabolism such as the production of superoxide anion and H₂O₂ and if it was associated with an alteration of cytokine (IL-8 and TNF- α) levels. Neutrophils from peripheral blood of healthy individuals were incubated in the presence and absence of IL-15 (12.5–250ng/ml) for 18h, at 37°C, under tension of 5% CO₂, then infected with Pb18 for 4h and evaluated for fungicidal activity, production of superoxide anion and H₂O₂, and quantification of cytokines IL-8 and TNF- α in the supernatant. Pre-incubation of neutrophils with IL-15 induced a significant increase in the fungicidal activity of such cells in a dose-dependent manner. After activation, there was an increase in the production of superoxide anion and H₂O₂ by these cells, suggesting participation of such metabolites in fungicidal activity. Catalase inhibits fungicidal activity, confirming the role of H₂O₂ in fungus killing. However, the levels of TNF- α and IL-8 were not modified after incubation with IL-15, which suggests that its role is not mediated by those cytokines. Taken together, results showed that IL-15 had a modulatory effect on human neutrophils infected *in vitro* with a high virulent strain of *P. brasiliensis*, which was characterized by an increased fungicidal activity mediated by a dependent mechanism of oxidative metabolism.

KEY WORDS: neutrophils, IL-15, *Paracoccidioides brasiliensis*, superoxide anion, H₂O₂, fungicidal activity.

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