

TITLE: Interaction of β 1 integrin and Toll-like receptors in *Paracoccidioides brasiliensis*-infected A549 epithelial cells

AUTHORS: Barros B.C.S.C., Suzuki E.

INSTITUTION: Departamento de Microbiologia, Imunologia e Parasitologia - Escola Paulista de Medicina - Universidade Federal de São Paulo (EPM-UNIFESP)

INTRODUCTION: The thermodimorphic fungus *Paracoccidioides brasiliensis* is one of the etiologic agents of paracoccidioidomycosis, the most prevalent systemic mycosis in Latin America. Infection by this pathogen is acquired through inhalation of fungal propagules, which once in the lungs, they convert to yeast forms that interact with epithelial cells, resulting in the activation of signaling pathways and then, modulating the host innate immune response. By forming a structural barrier, pulmonary epithelial cells are one of the first defense mechanisms against inhaled particles and microorganisms. In addition, several groups have demonstrated that different microorganisms promote cytokine release and expression of several receptors in epithelial cells. Among these receptors, Toll-like receptors (TLRs) are able to recognize specific pathogen-associated molecular patterns (PAMPs) in microorganisms. Some research groups have shown that TLRs can collaborate with integrins, receptors formed by α and β subunits that can modulate signal transduction pathways responsible for cytoskeletal organization, cell proliferation, adherence, differentiation and migration. In this study, we verified the interaction between TLR2/TLR4 with β 1 integrin in pulmonary epithelial A549 cells in the presence of *P. brasiliensis* yeasts. **MATERIAL AND METHODS:** A549 cells were incubated with live yeasts of *P. brasiliensis* for 24 hours. Protein expression of TLR2, TLR4 and β 1 integrin in A549 cells was analyzed by Western-blot. In addition, immunoprecipitates were obtained from A549 cell protein extracts by incubating with anti-TLR2 and TLR4 antibodies. These immunocomplexes were submitted to SDS-PAGE and TLRs and β 1 integrin interaction was analyzed by Western blot. **RESULTS:** It was verified an increase of TLR2 and TLR4 expression in A549 cells after infection with *P. brasiliensis*. In addition, it was observed that β 1 integrin interacts with both TLRs. **CONCLUSIONS:** Taking together, these results suggest that *P. brasiliensis* yeasts are able to modulate β 1 integrin, TLR2 and TLR4 expression in pulmonary epithelial cells, and moreover, this fungus promotes interaction between TLRs and β 1 integrin. **Supported by:** FAPESP, CNPq and CAPES.

Keywords: *Paracoccidioides brasiliensis*, Integrins, Toll-like Receptors, Epithelial Cells, Infection.