TITLE: *Paracoccidioides* species present distinct fungal adherence to epithelial lung cells and promote different IL-8 secretion levels

AUTHORS: Almeida, B. R.; Barros, B. C. S. C.; Alcantara C. & Suzuki, E.

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

ABSTRACT:

Fungi that belong to the genus *Paracoccidioides* are the etiologic agents of paracoccidioidomycosis, a human systemic mycosis, which occurs in Latin America. Epithelial cells are the first cells that interact with these fungi and can respond appropriately by secreting inflammatory mediators such as cytokines and chemokines. In this work, we observed that yeasts of different isolates of *Paracoccidioides brasiliensis* (Pb18 and Pb03) and *Paracoccidioides lutzii* (Pb01) distinctly promoted IL-8 cytokine secretion by epithelial cells. Pb18 isolate promoted the highest IL-8 level secretion, followed by Pb03 that induced intermediate levels, and Pb01 that promoted the lowest levels of this cytokine. In addition, we verified that direct contact between yeasts and A549 epithelial cells is important for IL-8 secretion only when these cells were infected with Pb03 isolate. We also found that these fungi secrete components that can promote IL-8 secretion by epithelial cells. Regarding adhesion of yeasts to pulmonary epithelial cells A549, we also observed that the different *Paracoccidioides* isolates adhered in a distinct way. The highest percentage of A549 cells with adhered yeasts was observed with *P. lutzii*. We verified that all *Paracoccidioides* isolates induced an increase of α3 and α5 integrins expression in A549 cells and, by using interfering RNA, we observed that the integrin silencing in A549 promoted a reduction of *P. lutzii* adhesion, which suggests the involvement of integrins in this event. In this way, the data shown here helps to understand *Paracoccidioides*-host interaction studies. We emphasize the importance of this topic since paracoccidioidomycosis is a neglected disease and association between the clinical pattern of this mycosis and different species of *Paracoccidioides* still needs to be determined.

Keywords: *Paracoccidioides*; epithelial cell; cytokine; adhesion; integrin

Development Agency: CNPq, CAPES and FAPESP