

Title: TLR3 IS AN ESCAPE MECHANISM OF *P. BRASILIENSIS***Authors:** Jannuzzi, G.P.¹, Kaihami, G.H.², Almeida, J.R.F.¹, R, L.M.D.¹, Almeida, S.R.¹, Ferreira, k.S.³**Institution** ¹ FCF-USP - Faculty of Pharmaceutical Sciences, University of São Paulo (Avenida Professor Lineu Prestes, 580, Butantã – São Paulo-SP), ² IQ-USP - Institute of Chemistry, University of São Paulo (Avenida Professor Lineu Prestes, 740, Butantã – São Paulo-SP), ³ ICAFAQ-UNIFESP - Institute of Environmental Sciences, Chemical and Pharmaceutical, of Federal University of São Paulo (Rua São Nicolau, 210, Diadema-SP)**Abstract:**

The paracoccidioidomycosis (PCM) is a granulomatous mycosis of nature, which preferentially compromises lung tissue, whose main etiologic agent is thermally *Paracoccidioides brasiliensis*. The immune response in this mycosis can be modulated by the action of antigen-presenting cells, especially dendritic cells (DCs), specialized in the capture, processing, and presentation of migration antigens. The recognition *P. brasiliensis* by DCs is mediated by receptors such as Toll-like receptors (TLRs), whose activation regulates the expression of costimulatory molecules and cytokine production. The role of TLRs in the response against fungi such as *Candida albicans*, *Aspergillus fumigatus* and *Cryptococcus neoformans*, is already established, but little attention has been paid to the role of TLR3. In an experimental *aspergillosis*, the TLR3 sensor function as an endogenous RNA of the fungus, contributing to the regulation of local inflammation and activation and protective memory response. Both responses were mediated by CD8⁺ T cells, whose activation was due to the action of DCs pulsed with *Aspergillus*. Given the importance of the TLR3 signaling pathway in fungal infections, this study aims to evaluate the role of this receptor in experimental paracoccidioidomycosis. Mice C57Bl/6 and TLR3 KO were infected with *P. brasiliensis*. After 30 days, we realized CFU, pulmonary cell profile, ELISA and measurement of IgG. Our findings show that TLR3 KO animals, when infected with *P. brasiliensis*, exhibited reduced pulmonary fungal burden. This result may be related directly to the increase in CD8⁺ T cells observed in the lungs of the animals, since these cells are critical for the control of pulmonary PCM. We also note increase of IFN- γ in the lungs of this animal, this cytokine is involved with the Th1 response that is protective response for PCM. Recent studies indicate that TLR3 is important receptor for the immune response in mycosis and its absence favors the fungal infection. In contrast, our preliminary findings show that in the case of PCM, the TLR3 is deleterious to the host, suggesting that activation of TLR3 can be a possible escape mechanism of *P. brasiliensis*.

Keywords: Paracoccidioidomycosis, T DC8⁺ cells, TLR3**Promotion Agency:** Capes