

## PRODUCTION OF PROSTAGLANDINS AND LEUKOTRIENES BY

*Paracoccidioides brasiliensis*

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*Paracoccidioides brasiliensis* is the causative agent of paracoccidioidomycosis, the most prevalent deep mycosis in Latin America. Production of eicosanoids, including prostaglandins and leukotrienes, during fungal infections is theorized to play a critical role on fungal survival and/or growth as well as on host immune response modulation. Host cells are one source of these mediators; however another potential source may be the fungus itself. The purpose of our study was to assess whether *P. brasiliensis* strains with different degree of virulence (Pb18, Pb265, PbBT79, Pb192) produce both, prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) and leukotriene B<sub>4</sub> (LTB<sub>4</sub>). Moreover, we asked if *P. brasiliensis* can use exogenous sources of arachidonic acid (AA), as well as metabolic pathways dependent on cyclooxygenase (COX) and lipoxygenase (5-LO ) enzymes, for PGE<sub>2</sub> and LTB<sub>4</sub> production, respectively. Finally, a possible association between these eicosanoids and fungus viability was assessed. We demonstrated, using ELISA assays, that all *P. brasiliensis* strains, independently of their virulence, produce high PGE<sub>2</sub> and LTB<sub>4</sub> levels after a 4-hour culture, which were reduced after 8 hours. However, in both culture times, higher eicosanoids levels were detected when culture medium was supplemented with exogenous AA. Differently, treatment with indomethacin, a COX inhibitor, or MK886, a 5-LO inhibitor, induces a reduction on PGE<sub>2</sub> and LTB<sub>4</sub> levels, respectively, as well as in fungus viability. The data provide evidence that *P. brasiliensis* is able to metabolize either endogenous or exogenous AA by pathways that depend on COX and 5-LO enzymes for producing, respectively, PGE<sub>2</sub> and LTB<sub>4</sub> that are critical for its viability.

**KEY WORDS:** arachidonic acid, eicosanoids, leukotrienes, *Paracoccidioides brasiliensis*, prostaglandin.

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