

TITLE: INVOLVEMENT OF NEUTROPHILS IN THE MODULATION OF THE IMMUNE RESPONSE IN BALB/C MICE VACCINATED WITH THE P10 PEPTIDE COMBINED WITH THE CATIONIC LIPID DODAB IN EXPERIMENTAL PARACOCCIDIOIDOMYCOSIS

AUTHORS: DIAS, L.S.¹; SILVA, L.B.R.²; TABORDA, C.P.^{1,2}

INSTITUTION: 1. DEPARTMENT OF MICROBIOLOGY, INSTITUTE OF BIOMEDICAL SCIENCES, UNIVERSITY OF SÃO PAULO, SÃO PAULO-SP-BRAZIL (Av. Prof. Lineu Prestes, 1374 - Butanta, São Paulo - SP, 05508-900) 2. INSTITUTE OF TROPICAL MEDICINE OF SÃO PAULO/LIM 53 DEPARTMENT OF DERMATOLOGY FM- UNIVERSITY OF SÃO PAULO, SÃO PAULO-SP-BRAZIL (Av. Dr. Enéas de Carvalho Aguiar, 470 - Jardim America, São Paulo - SP, 05403-000)

ABSTRACT

Paracoccidioidomycosis (PCM), a systemic mycosis and endemic in several Latin American countries, mainly in Brazil, Colombia, Argentina and Venezuela, is an important public health problem. Although there is treatment, it is prolonged and cases of relapse are common. In this sense, the development of new therapeutic approaches, such as vaccines, is extremely important. In addition, it is imperative to understand the participation of different cell populations in the immune response triggered by the vaccine. Thus, the aim of this work was to evaluate the participation of neutrophils in the immune response induced by a vaccine using an experimental murine model in paracoccidioidomycosis. We infected BALB/c mice with 3×10^5 of yeasts of *P. brasiliensis* by intratracheal route and then after 15 days of infection the animals were vaccinated with peptide P10 associated with lipid cationic DODAB. The vaccination schedule was composed by three doses (one dose/week), and 7 days after the last vaccine the animals were sacrificed and the lungs evaluated for fungal load, cytokine profile, inflammation and fibrosis. In addition, one of the experimental groups was submit to passive administration of Gr-1 monoclonal antibody (clone RB6/8C5) twenty-four hours before each immunization. This antibody was used to deplete the neutrophils and this effect was lasted for up to 48 hours. We observed that the therapeutic vaccine reduced the pulmonary neutrophils influx and the fungal load when compared to the control group (animals infected not treated). The lungs of these animals have a preserved parenchyma with a few granulomas and free of fibrosis. The cytokine profile of this animals show a cellular type immune response with augmented levels of IL-12, IFN- γ and TNF- α and low levels of IL-4. However, when the neutrophils were depleted 24 hours of each treatment the vaccine effectiveness was completely lost. The animals show lungs with fungal dissemination and the cytokine production was affected too. In conclusion, these founds seems indicate that the neutrophils are extremely important to ensure the immune response triggered after each vaccine treatment. However, we still can not rule out that this effect may involve non-neutrophil Gr-1 + cells.

Keywords: *Paracoccidioides brasiliensis*, Neutrophils, Vaccine, Paracoccidioidomycosis, P10.

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