EVALUATION OF MACROPHAGES AND T CELLS ACTIVITY IN MURINE EXPERIMENTAL MODELS OF HIGH AND LOW ANTIBODY-PRODUCERS (SELECTION IV-A) INFECTED WITH Paracoccidioides brasiliensis

THESIS. C. C. Pedigone submitted this thesis for her Masters in Tropical Diseases at Botucatu School of Medicine, São Paulo State University, UNESP, Botucatu, São Paulo, Brazil, 1998.

Advisor: Professor Sílvio Luis de Oliveira

ABSTRACT: The goal of this work was to evaluate the activity of macrophages and T cells in murine experimental models of paracoccidioidomycosis using High (H) and Low (L) antibody-producer mice of the IV-A selection, and to explain the differences in the pattern of pulmonary lesions showed by both strains. Animals were intravenously infected with 18 strains of P. brasiliensis (2.0 x 105 yeast/animal) and sacrificed after 3 days, and 1, 2, and 4 weeks. The following parameters were observed: recovery of viable fungi from pulmonary lesions; lymphocytes proliferative response to Concanavalin A (Con A); INF-γ determination in the serum and in the supernatant of spleen cells culture; and H2O2, NO, and TNF-α release by peritoneal macrophages. HIV-A mice had a higher recovery of viable fungi from the lung in the beginning of the infection (3 days and 1 week) when compared with LIV-A. This was inverted in the last periods of time, and LIV-A showed a higher recovery of fungi. With regards to the lymphocytes proliferative response, there was a positive association between the higher recovery of fungi in the HIV-A strain and the lower proliferative response only after 3 days and 1 week. Higher levels of INF-γ were remarkably related to lower recovery of fungi in the HIV-A animals. With respect to the activation state of macrophages, the higher production of H2O2 in the HIV-A strain after 3 days was associated to a control of the fungi multiplication in the lung. On the other hand, the decrease in this metabolite production in the LIV-A strain was associated to an increase in the recovery of fungi. NO production was increased in HIV-A strain when these animals showed lower recovery of fungi, but this association cannot be made in the LIV-A. Another indicative of macrophage activation was TNF-α production. This cytokine level was high in the beginning of the infection in both strains. However, this increase cannot be associated to a possible control of fungi multiplication, mainly in the HIV-A strain, when the increase of this cytokine was associated to a higher fungi recovery. Thus, the higher levels of TNF-α showed by the infected animals, when compared to controls, were considered as a parameter of macrophage activation and not as a regulatory cytokine involved in fungi multiplication. Our results show the important role of INF-γ in the defense mechanisms against P. brasiliensis.

KEY WORDS: Paracoccidioides brasiliensis, Biozzi mice, immune response.

CORRESPONDENCE TO: SÍLVIO LUÍS DE OLIVEIRA, Departamento de Microbiologia e Imunologia, Instituto de Biociências, UNESP, Campus de Botucatu, 18618-000, Botucatu, SP, Brasil, Email: oliveira@ibb.unesp.br