

## IMMUNE RESPONSE TO *Rhodococcus equi* INFECTION IN HIGH AND LOW ANTIBODY-PRODUCER MICE (SELECTION IV-A)

**THESIS.** S. C. B. Pedrini submitted this dissertation for her Masters in Tropical Diseases at Botucatu School of Medicine, São Paulo State University, UNESP, Botucatu, São Paulo, Brazil, 2003.

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**ABSTRACT:** *Rhodococcus equi* is a gram-positive, facultative intracellular bacterium, which infects macrophages and causes rhodococcal pneumonia and enteritis in foals. Recently, this agent has been recognized as an opportunistic pathogen for immunocompromised humans. Several murine experimental models have been used to study *R. equi* infection. High (H<sub>IV-A</sub>) and Low (L<sub>IV-A</sub>) Antibody (Ab)-producer mice were obtained by bidirectional genetic selection for their ability to produce antibodies against sheep and human erythrocytes (Selection IV-A). These strains also maintain their phenotypes of high and low responders for antigens other than those of the selection (multispecific effect). A higher macrophage activity in L<sub>IV-A</sub> mice has been described for several intracellular infectious agents, what could be responsible for their intense macrophage Antigen (Ag)-processing and low Ab production. Because of these differences, L<sub>IV-A</sub> mice were found to be better in triggering an effective immune response towards intracellular pathogens. The objective of this work was to evaluate the macrophage activity and to characterize the immune response of IV-A mice. H<sub>IV-A</sub> and L<sub>IV-A</sub> mice were intravenously infected with 2.0x10<sup>6</sup>CFU of *Rhodococcus equi* ATCC 33701+. With regards to bacterial clearance and survival, L<sub>IV-A</sub> mice were more resistant to virulent *R. equi* than H<sub>IV-A</sub> mice. L<sub>IV-A</sub> mice presented a higher endogenous production of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and nitric oxide (NO) by splenic, pulmonary, and peritoneal cells than H<sub>IV-A</sub> mice. This work showed that increased TNF- $\alpha$ , H<sub>2</sub>O<sub>2</sub>, and NO levels are important components of the immune response in rhodococcosis, and that the Selection IV-A maintained the multispecific effect and the polygenic control of humoral and cellular responses to *R. equi*.

**KEY WORDS:** *Rhodococcus equi*, Biozzi mice, immune response.

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