

## **Dynamics of Germinal Center and Regulatory B Cells in *Leishmania amazonensis* Infection: Insights from Susceptible and Partially Resistant Mouse Models**

Hozany Praxedes<sup>1,2</sup>, Luan Firmino-Cruz<sup>1,2</sup>, Julio Souza dos-Santos<sup>1,2</sup>, Naiara C. Manhães<sup>1,2</sup>, Douglas B. de Almeida<sup>1,2</sup>, Alisson Amaral da-Rocha<sup>1,2</sup>, Igor Bittencourt<sup>1,2</sup>, João V. Paiva Romano<sup>1,2</sup>, Alessandra Márcia da Fonseca-Martins<sup>1,2</sup>, Herbert Leonel de Matos Guedes<sup>1,2</sup>

1 - Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

2 - Oswaldo Cruz Institute, Oswaldo Cruz Foundation, Rio de Janeiro, RJ, Brazil.

The role of B lymphocytes in leishmaniasis varies by parasite strain and animal model. This study examines B cell responses in BALB/c (susceptible) and C57BL/6 (partially resistant) mice after *Leishmania amazonensis* infection. Both models were infected in the ear. Early in infection, BALB/c mice developed larger lesions, though parasite loads in the ear and lymph nodes were similar. Later, BALB/c mice had more severe lesions and higher parasite loads than C57BL/6 mice. Antibody production was also analyzed. BALB/c mice showed higher IgG (early), IgG1 (early and late), and IgM (early and late) but lower IgG2b and IgG2a/c in early infection. Germinal center (GC) B cell activity was higher in BALB/c mice at both stages, suggesting enhanced antibody production.

Regulatory B (Breg) cells were also investigated. Infection induced PD-L1 expression in BALB/c B cells early on. Both models produced IL-10 in PD-L1<sup>+</sup> B cells at this stage, but at later stages, PD-L1 increased only in C57BL/6 mice, without IL-10 production. At the lesion site, PD-L1<sup>+</sup> B cells increased in both models early on, but IL-10 production was observed only in C57BL/6 mice. This phenotype disappeared in chronic infection, suggesting IL-10 is linked to peak infection. IL-10 knockout mice showed increased lesion size and parasite load at this peak. Additionally, FACS-sorted IL-10<sup>+</sup> B cells transferred into MHCII<sup>-/-</sup> mice helped control lesion progression but did not affect parasite load.

These findings underscore the role of IL-10<sup>+</sup> B cells in lesion control in C57BL/6 mice, offering insights into the immunoregulatory functions of B cells in *L. amazonensis* infection.

Supported by: CNPq, FAPERJ

Keywords: *Leishmania amazonensis*; B lymphocyte; IL-10.