THE IL-33/ST2 AXIS MODULATES LIVER PATHOLOGY AND INFLAMMATION DURING *Trypanosoma cruzi* EXPERIMENTAL INFECTION

Maria Eduarda Fernandes Soares[1], Marcelo Eduardo Cardozo[1], Jorge Lucas Nascimento Souza[1], Isabela de Brito Duval[1], Ana Rafaela Antunes Porto[1], Fernando Bento Rodrigues Oliveira[2], Mayra Fernanda Ricci[2], Lívia Fernandes Dias Santana[2], Laura Lis De Oliveira Santos[2], Luiza Pinheiro Silva[2], Chiara Cássia Oliveira Amorim[1], Tatyane Martins Cirilo[1], José Bryan Rihs[1], Izabela Souza[1], luisa Vitor Braga do Amaral[1], Gabriela Gomes Monteiro lemos[1], Geovanni Dantas Cassali[3], Luisa Mourão Magalhães[1], Lilian Lacerda Bueno[1], Fabiana Simão Machado[2], Ricardo Toshio Fujiwara[1].

[1]Department of Parasitology, Belo Horizonte, Minas Gerais, Brasil, [2]Department of Biochemistry and Immunology, Belo Horizonte, Minas Gerais, Brasil, [3]Department of Pathology, Belo Horizonte, Minas Gerais, Brasil

Chagas disease (CD) is a neglected tropical disease that affects millions of people worldwide. The etiologic agent, *Trypanosoma cruzi*, leads to impairment of multiple organs, including the liver. The pathology of CD primarily results from the host immune response against the parasite. Recent studies indicate that interleukin-33 (IL-33) plays a key role in various inflammatory diseases. IL-33 is rapidly released into the extracellular space upon tissue injury or necrosis and exerts its biological effects by binding to its receptor, ST2. Whether IL-33 has protective or detrimental effects depends on the immune mechanisms underlying each disease. To investigate the impact of IL-33/ST2 signaling, female BALB/c wild-type (WT) and ST2 knockout ($ST2^{-/-}$) mice were intraperitoneally infected with 1,000 blood trypomastigotes of the *T. cruzi* Y strain. During the acute phase, WT-infected mice developed anemia, characterized by reduced hemoglobin, hematocrit, and erythrocyte counts, whereas $ST2^{-/-}$ infected mice exhibited leukocytosis, primarily driven by monocytes, along with thrombocytosis and increased macroplatelet production. $ST2^{-/-}$ mice also showed heightened hepatic macrophage activity, accompanied by elevated ALT and albumin levels, indicating liver damage. Histological analysis confirmed exacerbated hepatic inflammation, with increased inflammatory foci and hemorrhagic areas in $ST2^{-/-}$ infected mice. In the chronic phase, $ST2^{-/-}$ infected mice exhibited persistent hepatic inflammation, with increased eosinophil and macrophage activity. ALT and albumin levels remained elevated in $ST2^{-/-}$ mice, despite no significant differences in AST levels among infected groups, suggesting sustained liver dysfunction. Collectively, our findings indicate that the IL-33/ST2 axis plays a role in regulating chronic liver damage and inflammation. Understanding the role of the IL33/ST2 axis may pave the way for new therapeutic strategies to mitigate the damage during *T. cruzi* infection.

Keywords: Chagas disease; Hepatic Immune Response; IL-33/ST2 pathway

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