PROTEOMIC PROFILING OF THE MITRAL VALVES IDENTIFIES PROTEIN TARGETS ASSOCIATED WITH IMMUNOLOGICAL PATHWAYS IN CHRONIC CHAGAS CARDIOMYOPATHY

Eula Graciele Amorim Neves, Adrien Lupieri, Abhijeet Sonawane, Ana Luiza Resende, Livia Silva Araújo Passos, Maria do Carmo Pereira Nunes, Elena Aikawa, Walderez Ornelas Dutra

Chronic Chagas Cardiomyopathy (CCC), caused by infection with the intracellular protozoan *Trypanosoma cruzi*, represents the most severe form of Chagas disease. Although CCC primarily affects the myocardium, clinical manifestations of mitral regurgitation suggest functional and structural changes in the mitral valves of affected patients. In this study, we analyzed the protein profile of mitral valves from CCC patients (n=7) using liquid chromatography coupled with mass spectrometry to identify potential targets associated with valvular immunopathology in CCC. We compared these profiles to healthy donor samples (HC, n=6) and those from patients with Idiopathic Dilated Cardiomyopathy (IDC, n=6), a cardiac condition that affects the myocardium and clinically resembles CCC. Our data showed an increased abundance of proteins involved in biological processes related to immune response activation in CCC mitral valves compared to HC. Notable proteins include PYCARD, a molecule implicated in inflammasome pathway activation; IGHG3, an immunoglobulin previously associated with the humoral immune response in Chagas disease; and the transcription factors STAT1, STAT2, and STAT5B, which are linked to cytokine-mediated inflammatory responses. Additionally, gene ontology analysis revealed associations between highly expressed molecules in CCC mitral valves and immune-related biological processes, including the humoral immune response and B cell activation. The protein expression profile observed in IDC was consistent with the less inflammatory nature of the disease; the increased abundance of proteins involved in energy metabolism and the decrease in proteins associated with immune activation may contribute to preventing immune-mediated damage to valve tissue in IDC. Our findings highlight proteins potentially involved in immunological pathways in CCC, providing new insights into the mitral valve as a target for cardiac immunopathology.

Key Words: Chronic Chagas Cardiomyopathy, Immunopathology, Proteomics

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