# THE IMPACT OF SARS-COV2 CO-INFECTION ON CHRONIC CHAGAS DISEASE IN A MURINE MODEL: SOCS-2 AS A THERAPEUTIC MOLECULE

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**Abstract**

The balance of the immune response (IR) is essential for the survival of Trypanosoma cruzi and the host during the acute phase of Chagas disease (CD). Infection with Sars-cov2 can cause an unbalanced immune response associated with systemic damage in its host. Suppressor cytokine signaling (SOCS) 2 is an important regulatory protein of the innate and adaptive response, but its role during chronic infection by CD and betacoronavirus MHV-3 (virus that mimics Sarscov-2 in a murine model) is unknown. Our objective was to evaluate the role of SOCS2 during chronic CD, acute MHV3 infection and chronic CD/acute MHV3 co-infection in a murine model. C57BL/6 (WT) and SOCS-2 (KO) animals were infected with trypomastigote forms (Y strain), and after reaching chronic CD (100 days), they were co-infected or not with MHV-3. We performed clinical, physiological, histopathological, immunobiochemical, parasitism and microbiota analyses. Our data demonstrated a systemic alteration in all infections, but mainly in the groups coinfected with betacoronavirus, where cardiac and pulmonary dysfunctions occurred, associated with fibrotic processes in the tissue, and a higher viral load detected in SOCS2 KO mice when compared to WT counterparts. In addition, reduced mucus production and muscle degeneration were observed in the colon due to high parasitism and dysbiosis. SOCS2 deficiency also resulted in lung and intestinal tissue with a higher pro-inflammatory profile, increasing TNF, IFN-g and reducing IL-10 production by innate and adaptive immune cells. In summary, SOCS-2 is essential to modulate the immune response and the progression of pathogenesis, especially in coinfection with betacoronavirus MHV-3 in the chronic phase of CD, being a possible therapeutic target not only in CD but also in Sarscov-2 infections. Financial support: INCT-Dengue and Host Microorganism Interaction, Fapemig, Capes and Cnpq.

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