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TGF-Beta in Chagas disease development: Molecular insights, antifibrotic effects and, clinical utility

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The anti-inflammatory cytokine transforming growth factor beta (TGF-β) plays an important role in Chagas disease (CD), a potentially life-threatening illness caused by Trypanosoma cruzi. In this lecture Roberto Ferreira will revisit the clinical studies in CD patients combined with in vitro and in vivo experiments, presenting three main sections: an overview of epidemiological, economic, and clinical aspects of CD and the need for new biomarkers and treatment; a brief panorama of TGF-β roles and its intracellular signaling pathways, and an update of what is known about TGF-β and CD. In in vitro assays, TGF-β increases during T. cruzi infection and modulates heart cells invasion by the parasite fostering its intracellular parasite cycle. TGF-β modulates host immune response and inflammation, increases heart fibrosis, stimulates remodeling, and slows heart conduction via gap junction modulation. TGF-β signaling inhibitors reverts these effects opening a promising therapeutic approach in pre-clinical studies. CD patients with higher TGF-β1 serum level show a worse clinical outcome, implicating a predictive value of serum TGF-β as a surrogate biomarker of clinical relevance. TGF-β polymorphisms indicate that CD immunogenetics is at the base of this phenomenon. Moreover, pre-clinical studies in chronic T. cruzi infected mice proved that inhibition of TGF-β pathway improved several cardiac electric parameters, reversed the loss of connexin-43 enriched intercellular plaques, reduced fibrosis of the cardiac tissue, restored GATA-6 and Tbox-5 transcription, supporting cardiac recovery. Finally, the therapeutic effects of inhibition are promising and suggest a new possibility to treat cardiac fibrosis in the chronic phase of Chagas' heart disease by TGF-β inhibitors.

Recent Publications

1. FERREIRA, R. R.; WAGHABI, MARIANA C; BAILLY, SABINE; FEIGE, ... ARAUJO-JORGE, T. C. Chagas disease immunogenetics and the search for disease biomarkers: insights from TGF-beta studies. Frontiers in Cellular and Infection Microbiology, v. 14, p. 1, 2022.

2. ARAUJO-JORGE, TANIA C.; RIVERA, MARIA TERESA; VANDERPAS, JEAN; GARZONI, ... FERREIRA, ROBERTO R. Selenium, TGF-Beta and Infectious Endemic Cardiopathy: Lessons from Benchwork to Clinical Application in Chagas Disease. BIOMOLECULES, v. 12, p. 349, 2022.

3. WAGHABI, MARIANA C; FERREIRA, R. R.; ABREU, RAYANE DA SILVA; ... ARAUJO-JORGE, TANIA. Transforming growth factor-β as a therapeutic target for the cardiac damage of Chagas disease. MEMORIAS DO INSTITUTO OSWALDO CRUZ, v. e210395, p. 1-6, 2022.

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