

## Proteins Involved on TGF- $\beta$ -pathway are Up-regulated During the Acute Phase of Experimental Chagas Disease

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**INTRODUCTION:** Studies developed by our group have shown the involvement of TGF- $\beta$  in Chagas heart disease, with elevated plasma levels and activated TGF- $\beta$  cell signaling pathway as remarkable features of patients in the advanced stages of this disease. Imbalance in synthesis and degradation of extracellular matrix components is the basis of pathological fibrosis and TGF- $\beta$  is considered as one of the key regulators of this process. **OBJECTIVES:** In the present study, we investigated the activity of the TGF- $\beta$  signaling pathway, including receptors and signaling proteins activation in the heart of animals experimentally infected with *Trypanosoma cruzi* during the period that mimics the acute phase of Chagas disease. **MATERIALS AND METHODS:** Male Swiss mice were infected intraperitoneally with  $10^4$  bloodstream trypomastigotes. At 8, 15, 24 and 27 dpi a group of mice were euthanized to remove the heart for further analysis. TGF- $\beta$ 1 and collagen gene expression were analyzed by qPCR. TGF- $\beta$  receptors and signaling proteins activation were analyzed by immunoblotting. Collagen deposition was confirmed by Masson's trichrome. Measurement of TGF- $\beta$  in serum samples was performed using a TGF- $\beta$ 1 ELISA kit. **DISCUSSION AND RESULTS:** We observed that infected animals presented increased expression of TGF- $\beta$  receptors. Overexpression of receptors was followed by an increased phosphorylation of Smad2/3, p38 and ERK. Furthermore, we correlated these activities with cellular factors involved in the fibrotic process induced by TGF- $\beta$ . We observed that the expression of collagen, fibronectin and CTGF were increased in the heart of infected animals on 15 dpi. Correlated with the increased TGF- $\beta$  activity, we found that serum levels of total TGF- $\beta$  were significantly higher during infection. **CONCLUSION:** Taken together, our data suggest that the commitment of the heart associates with increased activity of TGF- $\beta$  pathway and expression of its main components. Our results, confirm the importance of this cytokine in the development and maintenance of cardiac damage caused by *T. cruzi* infection.

Keyword: TGF- $\beta$ , *T. cruzi* infection and Chagas disease  
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