ORT_28 - Transforming growth factor beta neutralization reduces *Trypanosoma cruzi* infection and improves the cardiac performance: *in vitro* and *in vivo* assays

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Introduction: The antiinflammatory cytokine transforming growth factor beta (TGF-beta) plays an important role in Chagas disease, a parasitic infection caused by the protozoan *Trypanosoma cruzi*.

Objective: The aim of this study was to investigate the effect of 1D11, a neutralizing antibody to all three isoforms of TGF-beta, on *T. cruzi* infection: *in vitro* and *in vivo*.

Methodology: To this end, cardiomyocytes were seeded for 24h, incubated with trypomastigotes and treated with 1D11 (100ug/ml). C57BL/6 mice were also infected with *T. cruzi* (10^2 parasites from the Colombian strain) and, after 120 dpi, treated with 1D11(10mg/kg).

Results: In the present study, we show that addition of 1D11 greatly reduces cardiomyocyte invasion by *T. cruzi*, *in vitro*. Further, the treatment significantly reduces the number of parasites per infected cell. In a murine experimental model, the *T. cruzi*-infection altered the cardiac electrical conduction: decreasing the heart rate, increasing the PR interval and the P wave duration. The treatment with 1D11 reversed this process, improving the cardiac performance and reducing the fibrosis of the cardiac tissue.

Conclusion: Taken together, these data further confirm the major role of the TGF-beta signaling pathway in both *T. cruzi*-infection, *in vitro* and *in vivo*. The therapeutic effects of 1D11 are promising and suggest a new possibility to treat cardiac fibrosis in the chronic phase of Chagas' heart disease by TGF-β neutralization.

Keywords: Chagas disease; *Trypanosoma cruzi*; TGF-beta