IMMUNOPATHOLOGY AND IMMUNOMODULATION OF CARDIOMYOPATHY IN THE CHAGAS' DISEASE. M.B.P. Soares, J.O. Mengel, R.R. Santos. Laboratory of Immunopharmacology – Gonçalo Moniz Research Center/FIOCRUZ; Department of Immunology, ICB/USP.

To study the role of autoreactivity in the pathogenesis of the myocardium heart lesions in Chagas' disease, we have generated a CD4+ T cell line by repeated in vitro antigenic stimulation of purified splenic CD4+ T lymphocytes from chronically *T. cruzi*-infected mice (Colombian strain). These T cells
proliferate in the presence of soluble heart antigens and syngeneic feeder cells or in co-cultures with irradiated splenic syngeneic feeder cells and fetal heart cells. The lymphocytes originating the cell line appears to have resulted from the in vivo expansion of T.cruzi-reactive lymphocytes, since the line was activated in vitro by T.cruzi lysates, in addition to heart antigens. The cell line could also destroy and stop the beating fetal heart cell-clusters in vitro when co-cultured with irradiated splenic syngeneic feeder cells and fetal heart cells. In vitro antigen stimulation of the cell line showed a Th1 cytokine profile, with production of high levels of IFN-and IL-2 and absence IL-4, IL-5 or IL-10. In addition, in situ injection of these cells into well established heart transplants induce the cessation of heart beating. Adoptive transfer of the cells to BALB/c nude mice caused 100% mortality of recipients after 1-2 months, compared to controls which received normal CD4+ T cells. Histological studies revealed the presence of multifocal mononuclear infiltrates in their hearts similar to those observed during the chronic phase of T.cruzi infection. No significant alterations were observed in the hearts of BALB/c nude mice transferred with ConA-activated splenic cells. Finally, BALB/c mice vaccinated with mytomycin-treated T cell line developed milder cardiac disease after challenge with T.cruzi, compared to mice immunized with normal splenocytes, suggesting immunotherapies as possible methodologies for treatment or prevention of chronic Chagas’ cardiomyopathy.