**(8D)**
**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.