

Chagas108- Genetic vaccination against chronic experimental *Trypanosoma cruzi* infection

Araújo AF^a, Oliveira G^b, Machado AV^c, Dominguez M.R.^a, Bruna-Romero O^d, Soares MB^e, Rodrigues MM^a.

^aCentro de Terapia Celular e Molecular (CTCMol), Unifesp, São Paulo - Brazil. ^bLab. Biologia Celular, IOC, Fiocruz, Rio de Janeiro - Brazil. ^cCentro de Pesquisas René Rachou, Fiocruz, Minas Gerais - Brazil. ^dDepto. Microbiologia, ICB, UFMG, Minas Gerais - Brazil. ^eCentro de Pesquisas Gonçalo Moniz, Fiocruz, Salvador - Brazil.

Introduction: In the last 15 years evidence supported by a number of experimental studies provided that genetic vaccination elicited protective immunity against acute infection with *T. cruzi*. The present work evaluated the prophylactic and therapeutic vaccination against experimental chronic infection. **Materials and Methods:** F1 (BALB/cXC10) inbred mice were primed intramuscularly with plasmid DNA and subsequently boosted 21 days later with replication defective recombinant human type 5 adenovirus. Plasmids and adenoviruses contained the genes of *T. cruzi* TS or ASP-2. In addition, we used during priming a plasmid containing the gene of the murine IL12 (pIL-12). Immune responses were estimated two weeks after the last immunizing dose. The immunological analyzes were performed by ELISPOT assay and intracellular staining (ICS), using as stimulus the CD8 epitopes TS-Epi (IYNVGQVSI H2-K_d restricted) and VNHRFTLV (H2-K_b restricted). Mice were challenged with 10³ bloodstream trypomastigotes of the Brazil or Colombian strain of *T. cruzi*. We evaluated daily parasitemia, survival, ECG, and serum CKMB. **Results:** Immunization elicited strong CD8⁺ T cells mediated immune response. Most cells were multifunctional expressing surface CD107a, IFN- γ presence of pIL-12 during priming improved the CD8 immune responses. In the case of prophylactic vaccination, following challenge with Brazil or Colombian strains, we observed a significant reduction in the peak parasitemia of immunized animals when compared to control mice (p<0.01 in all cases). The presence of pIL-12 further reduced the parasitemia (p<0.01). ECG (cardiac alteration) and serum CKMB were significantly reduced in all vaccinated animals challenged with Colombian strain when compared to control mice. We are currently evaluating the results of the prophylactic vaccination with the Brazil strain and the therapeutic vaccination with the Colombian and Brazil strains. **Conclusions:** Our preliminary results show that prophylactic genetic vaccination with *T. cruzi* genes encoding TS and ASP-2 impacts favorably the chronic experimental infection with Colombian strain of *T. cruzi*. **Supported by:** FAPESP, INCTV (CNPq) and FAPEMIG. **E-mail:** mrodrigues@unifesp.br