Transgenic Expression of the Cancer/ Testis NY-ESO-1 Antigen by the Highly Attenuated Strain (CL-14) of *Trypanosoma cruzi*; a Novel Vaccine Vector for Immune Intervention in Cancer

JUNQUEIRA, C.1,2; Santos L. I.1,2; Galvão-Filho, B1,2; Teixeira S. M. R.1; Rodrigues, F. G.2; DaRocha, W. D.3; Chiari, E.1; Jungbluth, A. A.4; Ritter, G.4; Gnjatic, S.4, Old, L. J.4 & Gazzinelli, R. T.1,2,5

1Dep. de Bioquímica e Imunologia and Dep. de Parasitologia, ICB, UFMG, MG; 2Laboratório de Imunopatologia, CPqRR, FIOCRUZ, MG; 3Dep. de Bioquímica e Biologia Molecular, UFPR, PR, Brazil; 4Ludwig Institute for Cancer Research, New York Branch at MSKCC, USA; 5Division of Infectious Disease and Immunology, UMASS, USA.

Due to the increasing incidence of cancer around the world, the few medical interventions and none preventive treatments available, it is necessary to develop new treatments. Towards that goal, the development of antitumor vaccines becomes a promising approach to prevent and cure cancer. The present project joins the knowledge of tumor antigens, together with the precepts of immunoparasitology, to construct a new vaccine tool. It has been shown that some molecules derived from *Trypanosoma cruzi* are able to activate Toll Like Receptors, driving a Th1 phenotype. Infection with *T. cruzi* leads to induction of a strong antigen specific CD8+ T cell mediated cytotoxicity as well as IFN-γ responses. Considering the importance of a CD8+ T cell mediated immunity on host resistance to tumor growth, we evaluated the ability of live transgenic attenuated *T. cruzi* to induce specific T cell mediated immune response against the cancer/testis antigen NY-ESO-1. Transgenic *T. cruzi* expressing NY-ESO-1 was employed in vaccination protocols in mice to evaluate specific humoral, cellular, as well as antitumoral immune responses. Our data show that prophylactic vaccination is able to induce strong NY-ESO-1 specific humoral and cellular immune responses and to inhibit the growth of melanoma expressing NY-ESO-1, while therapeutic immunizations lead to tumor regression around 45% when evaluated for melanoma, fibrosarcoma and colon sarcoma. Transposing to the human model, an experiment was performed and showed that the vaccine vector, when employed in vitro presensitizations, was able to recruit CD4+ T and CD8+ T cells immune response NY-ESO-1 specific. We also searched the mechanisms involved during inhibition phenomenon driven by the transgenic parasite, and results suggest the main role of MyD88 and IL-12. In a brief statement, have been addressed here a proof of concept and regarding the good results, we face a promising scenario for the development of technologies in preventing or treating cancer.

Word Keys: Cancer vaccine; Vaccine vector; *Trypanosoma cruzi*; NY-ESO-1

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