Immune protection against *Trypanosoma cruzi* induced by TcVac1 vaccine in a murine model using an intradermal/electroporation protocol

Wael Hegazy-Hassan[1*], José Guillermo Estrada-Franco[1], José Antonio Zepeda-Escobar[1], Laucel Ochoa García[1,2], J. M. Eloy Contreras-Ortíz[1], Esvieta Tenorio-Borroto[1], Alberto Barbabosa-Pliego[1], José Esteban Aparicio-Burgos[3], Juan Carlos Vázquez-Chagoyán[1*]

[1]Centro de Investigación y Estudios Avanzados en Salud Animal, Facultad de Medicina Veterinaria y Zootecnia, Universidad Autónoma del Estado de México, Toluca, México.

[2]Laboratorio Estatal de Salud Pública del Instituto de Salud del Estado de México, Toluca, México.

[3]Escuela Superior de Apan, Universidad Autónoma del Estado de Hidalgo, Carretera Apan-Calpulalpan, Km. 8, Chimalpa Tlalayote s/n, Colonia Chimalpa, Apan, Hidalgo, México. C. P. 43900.

hegazi_wael@yahoo.com, joseestradaf@hotmail.com, zpepito@hotmail.com, ochuaglau@yahoo.com.mx, joshekawa@hotmail.com, esvieta@gmail.com, abarbabosa@yaho.com.mx, jcvch@yahoo.com.

Abstract

The development of vaccines against Chagas disease during the past years have provided a partial control of *Trypanosoma cruzi* infection. GPI-anchored *T. cruzi* genes are conserved in all *T. cruzi* life cycle stages and were tested as vaccine candidates in previous studies, they elicited humoral and cellular mediated immune responses and controlled parasitemia in mice. Herein we tested multi-component DNA-prime/DNA-boost vaccine

(TcVac1) which comprises two plasmids encoding GPI-anchored genes (TcG2 and TcG4) from *Trypanosoma cruzi*; two plasmids encoding adjuvant cytokines (IL12 and GM-CSF). To identify the best route of vaccine application in BALB/c mouse model, two vaccination protocols were compared; a) intradermal injection/electroporation (IDE), b) intramuscular injection (IM). Humoral immune response was evaluated through assessing titers of anti-TcG2 and TcG4 IgG and IgG subtypes (IgG1, IgG2a and IgG2b) antibodies through ELISA assay, using recombinant TcG2 and TcG4 as sensitizing antigens. Evaluation of immune cellular response was assessed through a lymphocyte proliferation assay, after exposure of vaccinated mice splenocytes to the studied antigens. Finally, histopathological and common clinical signs were carried on for vaccinated and infected mice groups. Results demonstrated higher antibody titers for IDE mice groups with a switch from a Th1 (IgG2b/IgG1>1) to Th2 (IgG2b/IgG1<1) immune profile from pre- to post-infection experimental periods, as well as a higher lymphocyte proliferation favoring IDE> IM mice groups. Histopathological evaluation of experimental mice hearts showed areas of myocardial necrosis and degenerative changes associated with severe inflammatory cell infiltrates for control infected mice groups to slight or moderate infiltrates for vaccinated-infected groups. In conclusion electroporation technique enhances the TcVac1 vaccine uptake leading to high specific immune response in both pre- and post-infection periods compared to the intramuscular technique.

Key words

Trypanosoma cruzi; TcVac1; Electroporation; Chagas Disease; Mice model.