

## SUMMARY OF THESIS\*

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**BASTOS, Sueli Fátima de** – Eficiência imunodiagnóstica de seis proteínas do *Trypanosoma cruzi* obtidas pela tecnologia do DNA recombinante, na Doença de Chagas. São Paulo, 1998. (Dissertação de Mestrado – Instituto de Ciências Biomédicas da Universidade de São Paulo).

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American trypanosomiasis or Chagas' disease is usually diagnosed by serological assays, with variable diagnostic efficiency and complex interpretation, needing constant reappraisal. Here, we study the diagnostic efficiency of six recombinant antigens of *Trypanosoma cruzi* (H49, JL7, A13, B13, JL8 and 1F8) obtained by the DNA recombinant technology and expressed as fusion products with glutathione S-transferase (GST), in the immunodiagnosis of Chagas' disease by ELISA, comparing with *T. cruzi* epimastigotes extract as a standard assay.

The initial standardization, performed in 101 Brazilian samples, from chronic chagasic patients (45) and non-chagasic ones (56), allow the determination of the reactivity threshold (cut-off), sensitivity and specificity of each recombinant antigen ELISA. Specificity was also confirmed using 237 samples from non-chagasic patients or with several others diseases. The diagnostic efficiency from the 6 recombinant antigens were determined in 247 samples from chagasic patients and 20 non-chagasic controls from three endemic Brazilian regions (Virgem da Lapa-

MG, and hinterlands of Paraíba and Piauí), with clinical, serological and parasitological proofs. Occasional regional variation was determined in samples from chronic chagasic patients from 9 countries from both South America (Argentina, Bolivia, Brazil, Chile, Colombia and Venezuela) and Central America (El Salvador, Guatemala and Honduras).

Positivity of the several antigens varied between 79% to 100%, depending from each region or antigen, with specificity ranging between 0.962-0.996, with higher discrepancies in samples from Colombia and Venezuela, suggesting that the use of recombinant antigens in Chagas' disease serology must take account of regional variations both from agent and patients.

This study also concludes that *T. cruzi* recombinant proteins should always be used in serology assays as association of at least two antigens to achieve maximal sensitivity, once they already had high levels of specificity.

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**ARRUK**, Viviana Galimberti - Fina especificidade da resposta imune a antígenos peptídicos múltiplos (MAPs) contendo epítomos T e B da proteína CS de *Plasmodium falciparum* de indivíduos naturalmente expostos à malária no Brasil. São Paulo, 1999. (Dissertação de Mestrado - Instituto de Ciências Biomédicas da Universidade de São Paulo).

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### FINE SPECIFICITY OF IMMUNE RESPONSES TO MULTIPLE ANTIGEN PEPTIDES CONTAINING T AND B EPITOPES OF *PLASMODIUM FALCIPARUM* CS PROTEIN FROM BRAZILIAN INDIVIDUALS NATURALLY EXPOSED TO MALARIA

Circumsporozoite protein (CSP) was the first antigen identified that play a role in malaria immunity and it is a highly candidate for inclusion in a multiantigen subunit vaccine against falciparum malaria.

We have analyzed the cellular (T-cell proliferation) and antibody (detection of IgG and IgM antibodies by ELISA) immune responses to a multiple antigen peptide (MAP) (T1B)<sub>4</sub> of *P. falciparum* CSP from individuals naturally exposed to malaria in Brazil. The MAP (T1B)<sub>4</sub> is constructed with the immunodominant epitope of B-cell, (NANP)<sub>3</sub> covalently linked to T-cell epitope, T1, (DPNANPNVDPNANPNV). We also analyzed the immune response to MAPs of monoepitopes (B<sub>4</sub> and (T1)<sub>4</sub>) and linear peptides, T1B and B.

The greatest T-cell proliferation frequencies were obtained with the MAPs (T1)<sub>4</sub> (47%) and (T1B)<sub>4</sub> (36.4%) which contain the epitope T1. IgG antibodies were significantly more frequent to MAPs (T1B)<sub>4</sub> (44.8%) and B<sub>4</sub> (33.3%) which contain the epitope B; conversely IgM antibodies

frequency to different peptides were not significantly.

Based on MAPs results with the MAPs, we chose the T-cell proliferation response to (T1)<sub>4</sub> as a cellular response pattern, and IgG antibodies response to (T1B)<sub>4</sub> as an antibody response pattern. Thus, the frequency of responders cellular and/or antibody, was 66.7% significantly greater than non-responders ( $P=0.0003$ ).

The results of the T and B cell responses to T1 and B epitopes were complementary, and satisfactory, since the studied population live in an area with unstable transmission of malaria.

These data confirm those got in American studies with animals and volunteers MAP (T1B)<sub>4</sub> immunized. Both of them suggest that this construction can act presenting the antigen on individuals that have never gotten malaria or as a booster in the immune response of individuals naturally exposed, prompting greater antibody levels than the ones of natural infection.

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