



**Parasitus**  
Revista de la Sociedad  
Argentina de Protozoología

Vol. 2 (2023) - ISSN 2953-5751

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## Foto de Portada

*Trichomonas vaginalis* (azul) conectados por citonemas (naranja) observados por microscopía electrónica de barrido.

**Créditos:** Nehuen Salas (INTECH, CONICET-UNSAM, Argentina), Antonio Pereira Neves (Instituto Aggeu Magalhães, Brasil) y Natalia De Miguel (INTECH, CONICET-UNSAM, Argentina).

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## SIMPOSIO X: Inmunología

### Moving forward with antigen-specific T cell response in Chagas disease: deciphering the immunopeptidome landscape in *Trypanosoma cruzi* infection

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T lymphocyte-mediated immune response against *Trypanosoma cruzi* (*T. cruzi*), the parasite causing Chagas disease, is relevant for both parasite control and disease pathogenesis. Therefore, the study of T cells results crucial to the understanding of the immune response in patients and thus contribute to the development of therapies and/or vaccines. However, many challenges are faced when attempting to identify T cell epitopes that can be used for diagnostic or preventive purposes. The complexity of the parasite-host interactions added to the large *T. cruzi* proteome and the diversity of human leukocyte antigen (HLA) haplotypes in humans hamper the characterization of T cell-activating epitopes, with high population coverage. To date, only a limit number of *T. cruzi* T cell antigens have been described and only a small proportion of HLA population diversity has been covered. To facilitate this issue, we profiled the repertoire of HLA class I and class II-bound peptides presented by human monocyte-derived macrophages infected or not with *T. cruzi*. Herein we purified HLA-peptide complexes from infected and uninfected cells and characterized the peptide ligands using LC/MS. For this subset of peptides, the binding to HLA class I and II alleles from THP-1 haplotype was predicted by using MHCmotifDecon1.1, NetMHCpan

4.1a and NetMHCIIpan 4.2 algorithms based on artificial neural network trained with empirical HLA binding and immunopeptidomics data. Our approach allowed us to identify 66 *T. cruzi* encoded ligands originating from 37 proteins, many of them outside TS proteins and with intracellular localization. Additionally, results showed no difference in length between *T. cruzi* and uninfected host ligands, thus suggesting that the parasite does not alter antigen processing and presentation machinery in the host cell. For *T. cruzi* source proteins, 8-12-mer and 12-21-mer peptides were extracted for HLA class I and II, respectively. Binding to a set of 19 HLA-A, 28 HLA-B, 19 HLA-C molecules prevalent in Latin America and 28 HLA-DRB1 alleles, 13 HLA-DPA1/DPB1 and 36 HLA-DQA1/DQB1 haplotypes were predicted using NetMHCpan 4.1 and NetMHCIIpan 4.1 methods, respectively. Finally, we selected 2 sets of 50 peptides each, 19 amino acid residues long, with optimal allelic (and potential *T. cruzi* strain genomic variation) coverage by using PopCover 2.0 method spanning all HLA alleles previously tested. Those peptides will be validated by evaluating T cell response in chronic Chagas disease patient samples. As far as we know, this study represents the most comprehensive immunopeptidomic dataset available for *T. cruzi* to date. This knowledge holds great promise for understanding adaptive immune activation in chronic Chagas disease and for direct rational discovery of T cell antigens.

### Infeción por *T. cruzi*: estudio de la respuesta inmune y desarrollo de nuevas terapias

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La persistencia de *T. cruzi* en los tejidos y la ausencia de daño previo a la aparición de síntomas durante la infección, sugieren la modulación de la respuesta inmune hacia un perfil incapaz de erradicar al patógeno. Estudios previos de nuestro equipo de trabajo