Roles of sulfotopes from glycoproteins and sulfatides in *Trypanosoma cruzi*, the agent of Chagas disease

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INTRODUCTION

***Trypanosoma cruzi*, the causative agent of Chagas disease (ChD), contains a major antigen, cruzipain (Cz). Its C-terminal domain (C-T), bears several post-translational modifications The presence of sulfated oligosaccharides was demonstrated in Cz, in a minor antigen with serine-carboxypeptidase activity (SCP), and in sulfatides.**

MATERIALS & METHODS

Native SCP and Cz were co-purified from Concanavalin-A affinity columns. The Cz-SCP was desulfated, ascribing the cross-reactivity between both molecules to the presence of sulfated groups, separated by SDS-PAGE and used as immunogens prior and after desulfation treatment. Similar assays were performed with the synthetic epitope Glc*N*Ac-6-SO3coupled to BSA and with passive transference of IgG antibodies specific for sulfotopes to demonstrate sulfotopes input in immunopathogenesis. *In vivo* effects of sodium chlorate on Cz-sulfation and tissue damage in C-T-immunized-mice muscle-tissues were evaluated to verify their participation in infection. Flow citometry was used to demonstrate immunomodulation effects and ELISA for the determination of the IgG2 human antibody levels specific for sulfotopes

RESULTS

1-Sulfate-bearing glycoproteins in *T. cruzi* are targets of specific immune responses. *T. cruzi* chronically-infected-subjects mount specific humoral immune responses to sulfated-Cz. In absence of infection, mice immunized with C-T- but not desulfated C-T, showed surprising ultrastructural heart pathological effects.

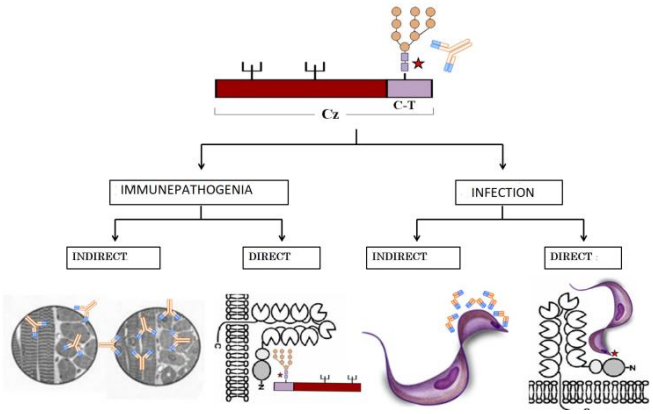
2-The synthetic anionic sugar conjugate Glc*N*Ac-6-SO3 mimics the N-glycan-linked sulfated epitope (sulfotope) humoral response.

3-The participation of sulfotopes in the immunomodulation by host-parasite interaction *via* sialic-acid-Ig-like-specific-lectins (Siglec) binding to sulfosialylated glycoproteins as well as in the parasite infection process has been reported.

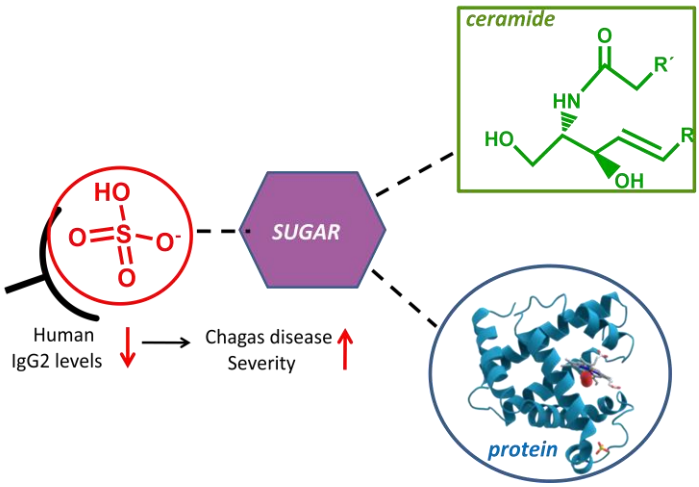
4- Recent evidences involved to sulfotopes and their specific antibodies in the immunopathogenesis and infection processes of the experimental ChD.

5- *T. cruzi* sulfotopes are antigenic independently of the sulfated-glycoconjugate type (Acosta et al, 2008, 2012). IgG2 human antibody levels specific for sulfotopes are inversely correlated with ChD severity.

SCHEMES



Scheme 1. Participation of sulfotopes and their specific antibodies in the immunopathogenia by directioning the tendency of the immunonogical host response when faced up with the parasite, and the mechanisms of invasion and virulence of the parasite during the acute phase of ChD infection



Scheme 2. ELISA sera IgG2 levels of chronically *T. cruzi*-infected individuals from mild disease displayed higher levels of IgG2 antibodies specific for sulfated glycoconjugates compared with those in more severe forms of the disease.

CONCLUSION

Ongoing assays indicate that antibodies specific for sulfotopes might play a role as predictors of stability from early stages of chronic ChD and might be considered biomarkers of human ChD progression.

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