A NOVEL VACCINE STRATEGY FOR CHAGAS DISEASE BASED ON RNA CONTAINING SEQUENCES FROM *TRYPANOSOMA CRUZI* TRANS-SIALIDASES

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Abstract

Trans-sialidases (TS) present on the surface of *Trypanosoma cruzi* are responsible for transferring sialic acid residues from host glycoconjugates to mucins on the parasite surface, a mechanism that is related to the parasite capacity to evade the host immune system. Present in over 1000 copies in the genome parasite, only 16 TS sequences encode proteins with catalytic activity that contain amino acids repeats known as SAPA (Shed Acute Phase Antigen). In addition, SAPA domain increases the stability of the enzyme in the bloodstream, which is considered a parasite virulence factor. Previously, our group showed that immunization of mice with recombinant TS induces the development of a protective Th1 response, essential for intracellular pathogen infection control, and that the presence of SAPA repeats in the recombinant protein results in the negative modulation of this protective response. Since RNA vaccines are based on intracellular antigen synthesis and, therefore, induces a potent Th1 response, we decided to compare immunization protocols based on recombinant protein and the corresponding mRNA encapsulated into lipid nanoparticles (LNPs). Sequences of a TS gene encoding the full-length protein and a version without SAPA were cloned into a mammalian expression vector and used for mRNA synthesis using *in vitro* transcription protocols. After cell transfection, the capacity of these mRNAs to produce the antigens were evaluated by western blot using antibodies generated against the recombinant proteins. Immunization with RNA/LNP formulations containing these sequences, induces similar humoral and cellular immune responses compared to immunization with recombinant proteins, as well as similar protection against challenge with a virulent *T. cruzi* strain, as shown by parasitemia and tissue parasitism. We are currently testing different prime-boost heterologous protocols in which immunization with recombinant protein and RNA/LNP formulations are combined.

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