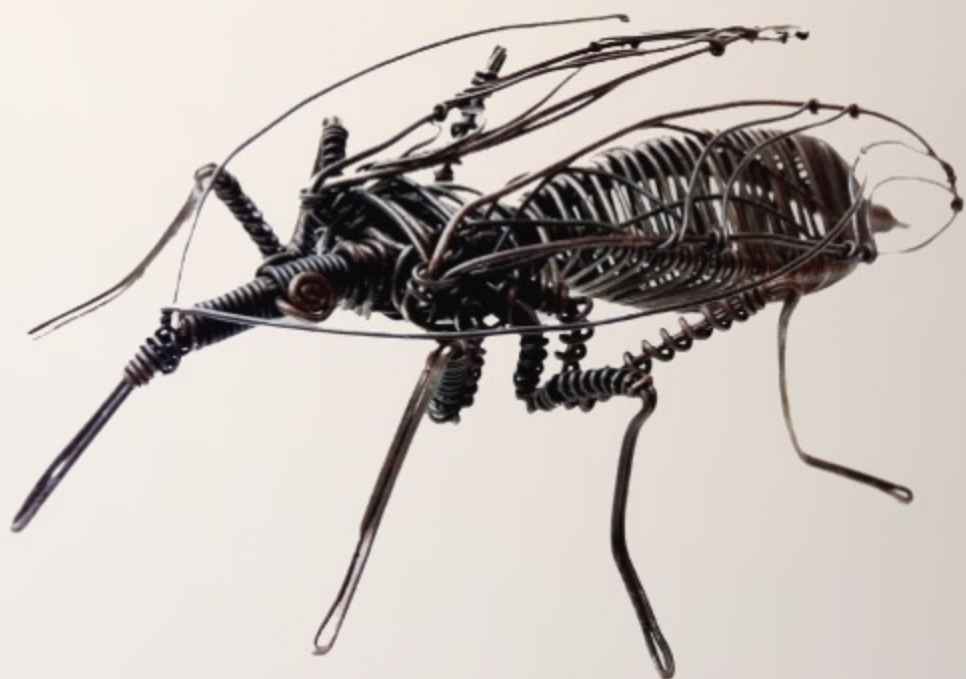


XL Annual Meeting of the Brazilian Society of Protozoology

**LI Annual Meeting on
Basic Research in
Chagas' Disease**



**Hotel Glória – Caxambu (MG), Brazil
November 10 – 12, 2025**

Abstract deadline August 5, 2025

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PROCEEDINGS

XL Meeting of the Brazilian Society of Protozoology
LI Annual Meeting on Basic Research in Chagas' Disease

Hotel Glória, Caxambu, MG, BRASIL- Caxambu
10-12 November, 2025

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TB – 018 - **Structure-Guided Discovery of Adenylosuccinate Lyase Inhibitors for Visceral Leishmaniasis**

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Visceral leishmaniasis (VL), caused by the protozoan *Leishmania donovani*, is a severe neglected tropical disease, primarily affecting vulnerable populations. Current therapeutic options present high toxicity, elevated costs, the need for hospitalization, and increasing parasite resistance, highlighting the urgent need for the development of new selective drugs. The enzyme adenylosuccinate lyase (ASL) plays a crucial role in nucleotide biosynthesis and is essential for the survival of *Leishmania* spp., since kinetoplastids, unlike humans (*HsASL*), lack the *de novo* purine synthesis pathway. Thus, ASL from *Leishmania major* (*LmASL*) and *L. donovani* (*LdASL*) represents promising targets, as their inhibition can specifically disrupt the parasite's life cycle, with potential applications against trypanosomiasis as well.

In the present study, molecular docking assays were performed using the GOLD software, screening 400 compounds from different classes (antifungals, antivirals, and antibacterials) against *LmASL* and its homologs (*HsASL* and *TbASL*). To further address this results the best-performing compounds will be subjected to co-crystallization trials and enzymatic activity assays.

The experimental methodology involved recombinant expression of *LdASL* in *Escherichia coli*, followed by biophysical characterization (DLS, SEC-MALS, CD). Biochemical evaluations (kinetic and inhibition assays) for functional validation are currently in progress. At this stage, the protein has already been successfully cloned, expressed, and purified. The next steps include further biochemical and biophysical characterization, *in vitro* screening of novel compounds and to determine antiparasitic activity, cytotoxicity, and selectivity, as well as co-crystallization and X-ray diffraction experiments to elucidate protein-inhibitor interactions.

By integrating biophysical and structural biology, biochemistry, medicinal chemistry, and molecular simulation approaches, this project aims to contribute to the discovery of innovative drug candidates against VL and to strengthen the scientific training of the researcher involved.

Supported by: Não

Keywords: Visceral Leishmaniasis;Adenylosuccinate Lyase;Drug Discovery.

TB – 019 - **Integration of vaccination schemes based on TS and TcTASV antigen families developed by two Argentine groups: Potential improvement in protection against challenge with two *Trypanosoma cruzi* strains**

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Two Argentine research groups independently developed *Trypanosoma cruzi* vaccine formulations that demonstrated strong protection in murine models. The UNL group designed a recombinant Group 1 trans-sialidase (rTS) vaccine with an ISCOMATRIX-like adjuvant (ISPA), administered in three homologous doses, achieving over 80% survival after lethal challenge with the Tulahuen strain compared to 0% in controls. The UNSAM group developed a heterologous protocol consisting of a priming dose with recombinant rTcTASV-C plus AIOH, followed by a boost with rTcTASV-C combined with recombinant baculoviruses expressing TcTASV-A in the capsid (BV::A-CAP), achieving over 90% survival against the highly virulent RA strain, compared to 0% in controls. This study evaluated two combined immunization schemes alongside the individual protocols, with experiments conducted in parallel in both laboratories using the Tulahuen and RA infection models. Cross-testing confirmed the robustness of each individual scheme. G4 (rTcTASV-C+rTS+AIOH → rTcTASV-C+rTS+BV::A-CAP) achieved the highest protection, with 100% survival versus 20% in controls (p<0.01; Tulahuen). Similar results were observed with the RA strain, where G3 (rTcTASV-C+rTS+ISPA → same → rTcTASV-C+rTS+BV::A-CAP) also reached 100% survival, and G1 (rTS+ISPA ×3) achieved 80% (vs 0% in controls). Also, mixed schemes generated the highest antibody titers against rTcTASV-C and TS and incremented vaccine antigen specific T cells. These findings demonstrate that the TS+ISPA and TASV+BV individual protocols are robust, that their integration effectively reduces parasitemia and achieves complete protection, and that comparable results across infection models highlight the strategy's consistency. The observed synergy between TS and TcTASV antigens, together with the collaborative work of both Argentine laboratories, underscores the potential of integrated vaccine strategies as a step toward an effective vaccine against Chagas disease.

Keywords: Vaccine;Chagas Disease;mixed schemes.