

## PROTEOME ANALYSIS OF THE CAUSATIVE AGENT OF CHAGAS DISEASE: *TRYPANOSOMA CRUZI*

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The identification of new targets for chemotherapeutic and vaccine approaches is a major challenge in the control of Chagas disease. Proteomic approach constitutes an excellent tool in order to identify molecular markers. We generated highly reproducible 2D maps from *T. cruzi*, and the identified proteins were grouped into functional categories. We could identify proteins expected to be expressed in different subcellular compartments and accomplishing different cellular functions in the parasite. Several spots were identified as  $\beta$ - and  $\alpha$ -tubulin, but several had smaller apparent molecular weights, suggesting that small tubulins could play a functional role *in vivo*. A second approach was the analysis of metacyclogenesis process, which is triggered by nutritional stress. The proteomic study of metacyclogenesis showed that most of the proteins were present in the epimastigote and trypomastigote stages. However, the major differences between maps were at the isoelectric point level, indicating a relevant role of post-translational modifications. Finally, a third approach was the study of oxidative stress responses, taking into account that parasites are challenged with oxidative species during cell invasion. The treatment of parasites with biological oxidants allowed us to detect proteins involved in **antioxidant responses**. We focused our work in the trypanothione system, particularly the tryparedoxin peroxidase, that was expressed and purified, showing peroxidase and peroxynitrite activity. The resolution of its structure was done, giving us clues about kinetic mechanisms and drug design.