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Proteomic and Network Analysis Characterize Stage-Specific Metabolism in Trypanosoma cruzi

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Trypanosoma cruzi is a Kinetoplastid parasite of humans and is the cause of Chagas disease, a potentially lethal condition affecting the cardiovascular, gastrointestinal, and nervous systems of the human host. Constraint-based modeling has emerged in the last decade as a useful approach to integrating genomic and other high-throughput data sets with more traditional, experimental data acquired through decades of research and published in the literature.

We present a validated, constraint-based model of the core metabolism of *Trypanosoma cruzi* strain CL Brener. The model includes four compartments (extracellular space, cytosol, mitochondrion, glycosome), 51 transport reactions, and 93 metabolic reactions covering carbohydrate, amino acid, and energy metabolism. In addition, we make use of several replicate high-throughput proteomic data sets to specifically examine metabolism of the morphological form of *T. cruzi* in the insect gut (epimastigote stage).

This work demonstrates the utility of constraint-based models for integrating various sources of data (e.g., genomics, primary biochemical literature, proteomics) to generate testable hypotheses. This model represents an approach for the systematic study of *T. cruzi* metabolism under a wide range of conditions and perturbations, and should eventually aid in the identification of urgently needed novel chemotherapeutic targets.

Key words: metabolism, human pathogens, proteomics, cell modeling