TRYPANOSOMA CRUZI PROLINE RACEMASES: POTENTIAL TARGETS FOR THE DEVELOPMENT OF A THERAPY AGAINST CHAGAS'INFECTION AND DISEASE.

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We identified a parasite B-cell mitogen, the first eukaryotic proline racemase (*Tc*PRAC), essential to *T. cruzi* viability, virulence and fate. Saturation of *Tc*PRAC catalytic site with specific inhibitors induces conformational changes of the protein precluding its interaction with B-cell ligands. Immunoprotection against parasite infection is possible by Œvaccination[1] of mice with *Tc*PRAC sub-mitogenic doses or *TcPRAC*-DNA. A signature for PRACs predicted that putative PRACs are present in other pathogens. Ongoing experiments revealed that the solubility of the PRAC inhibitor can be improved by medical chemistry. Through structural and molecular dynamic analysis of PRAC with/without its inhibitors new insights were obtained on conformational opportunities for enzyme stabilization and ligand binding; yet, calculations of the protonation state of residues of the binding site were performed and appropriate pharmacophoric/docking models were derived for further virtual screening of compound libraries. Using *PRAC*-transgenic parasites, the presence of D-proline bound to parasite peptide chains was confirmed and current proteomic approaches are in progress to identify the respective proteins in soluble and membrane *T. cruzi* extracts.

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