SOUTENANCE de THESE

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« Structural Modelling and Characterization of Target Specifics of Trypanosoma cruzi, Etiologic agent of Chagas Disease »

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BIBLIOTHEQUE

According to the World Health Organization, 21 Latin American countries are endemic for Chagas disease, affecting 10 million people. Chagas' disease, caused by the protozoan Trypanosoma cruzi (T. cruzi), is a parasitic illness endemic mostly in Latin America and particularly in Brazil. Despite many experimental studies, there is no efficient treatment against Chagas disease, and the search for new therapeutic targets specific to T. cruzi is critical for drug development. In my thesis, I have revisited 41 protein sequences proposed by the analogous enzyme pipeline, and found that it is possible to provide structures for 33 T. cruzi sequences with clear homologs or analogs in H. sapiens and likely associated with trypanothione reductase, cysteine synthase and ATPase functions, and structures for sequences specific to T. cruzi and absent in H. sapiens associated with 2,4-dienoyl-CoA reductase, and leishmanolysin activities. The implications of our structures refined by atomistic molecular dynamics (monomer or dimer states) in their in vitro environments (aqueous solution or membrane bilayers) are discussed for drug development and suggest that all protein targets, except cysteine synthase, merit further investigation.