TRYPANOSOMA CRUZI CHAPERONE HSP90 AS A TARGET FOR CHAGAS DISEASE TREATMENT

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Parasitic protozoan organisms contribute to the high burden of infectious diseases that are prevalent in both developing and developed countries and cause over a million deaths each year. *Trypanosoma cruzi*, which is the subject of our research, is the causing agent of Chagas disease, also known as American trypanosomiasis. The disease is characterized by cardiac, neurologic and digestive tract pathologies that can lead to sudden death. Although mostly widespread in Latin America, due to international immigration the disease threatens people living in other areas as well. Unwanted side effects of current drugs and the ability of parasites to quickly develop resistance mechanisms require new treatment options [1, 2].

Heat shock protein 90 (Hsp90) is a dimeric molecular chaperone, which is involved in many eukaryotic cell pathways ensuring proteostasis. The chaperone has a role in folding, maturation and degradation of select client proteins. As well as other protozoan parasites, *T. cruzi* relies on its functionality for survival, stage differentiation and adaptation to stressful conditions during infection. The fact that healthy human cells are significantly less sensitive to partial Hsp90 inhibition than parasitic protozoa makes it an attractive drug target for treatment of the Chagas disease [3, 4].

We aim to develop antiparasitic drugs based on Hsp90 inhibition. To achieve that, we first had to acquire a viable protein model for ligand binding assays. Since full length proteins are often difficult to obtain, we chose to work with isolated N-terminal domain of Hsp90, which binds ATP molecules and Hsp90-selective inhibitors of interest [5]. Fluorescence thermal shift assay was used to assess protein stability and determine binding affinities for the Hsp90 inhibitors.

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