Molecular Modelling of *Leishmania major* Telomerase RNA Binding Domain (TRBD) Shows Tertiary Structure Conservation but specific Aminoacid Substitutions in motifs involved on TER binding

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INTRODUCTION: Parasites of the *Leishmania* genus are the causative agents of leishmaniasis, a spectrum of diseases that have no effective control or available treatment. Therefore, new approaches to treat these diseases are being explored. Due to their role in genomic stability, telomeres are considered potential targets for the development of new therapies against leishmaniasis. Telomeres are maintained by the telomerase ribonucleoprotein complex which is minimally composed by the protein component TERT and TER, the RNA component. The interaction between these components is vital for telomerase action. Both components have been characterized in *Leishmania*, but none information is available about their structure and interactions. **OBJECTIVES:** To elucidate LmTERT tridimensional structure and the dynamic of interactions between LmTERT and LmTER, and between LmTERT and telomeric DNA. **MATERIAL AND METHODS:** In this work we generated an *in silico* model of the RNA binding domain (TRBD) of LmTERT using threading techniques and molecular dynamics simulations. In addition, LmTERT TRBD, TEN and RT domains were cloned to be expressed in a heterologous system in order to obtain recombinant proteins. **RESULTS AND DISCUSSION:** Structural comparisons of LmTERT *in silico* model and crystallographic structures of TRBDs from different eukaryotes show conservation on LmTERT tertiary structure. However, LmTERT has aminoacid substitutions specific to the *Leishmania* genus that are located in motifs involved in TER binding in other organisms. This suggests that the dynamics of interaction between LmTERT and TER might be different in *Leishmania*. Currently, we are obtaining recombinant proteins of separated LmTERT domains in order to perform *in vitro* protein: RNA and protein: DNA interaction assays. **CONCLUSION:** The characterization of the interactions between the *Leishmania* telomerase complex components might reveal the nature of these interactions and the physiological importance of the complex. Finally, these results can also provide insights about the evolution of the eukaryotic telomerase.

Keywords: *Leishmania*, Telomerase, Molecular Dynamics, Protein-RNA Interaction, Protein-DNA Interaction.

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