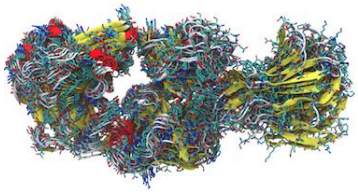

IV ASBioSim – Advanced School on Biomolecular Simulation: Protein Engineering with Rosetta, from fundamental principles to tutorials
05 to 10/May, 2019, Recife/PE, Brazil

Structural Prediction of the eIF4E and eIF4G on the *Leish*-eIF4F Complex

Luna-Aragão, M.A.; Coelho, D.F.; Bezerra, M.J.R.; Melo-Neto, O.P.; Lins, R.D.

Aggeu Magalhães Institute – IAM, Oswaldo Cruz Foundation – FIOCRUZ

Abstract: Leishmaniasis (LSM) is a neglected tropical disease that spreads via phlebotomine sandfly vectors. LSM is a parasitic disease caused by intracellular protozoa, which in humans has four clinical forms including cutaneous, diffuse-cutaneous, visceral and mucocutaneous. The LSM morbidity associated is up to 1.2 million cases distributed worldwide. On Trypanosomatids, such as *Leishmania major*, the gene expression regulation is crucial for modulating their protein synthesis in response to the environmental conditions found in different hosts. The assembly of the eIF4F complex mediates the translation initiation, this requires an interaction between eIF4E and eIF4G, two eIF4F subunits. Previous experimental studies have reported that the inhibition of eIF4E complex interrupts the life cycle of the parasite resulting in its death. These activities make the eIF4F complex a target for the treatment of LMS. The main purpose of this study is to assess the structural features of the eIF4F complex and highlight insights into its drugability. Due to the non-availability of experimental models for the referred complex, the building of theoretical models are needed. In order to overcome this limitation, structural models for the eIF4F complex of *L. major* have been built by comparative modeling and *de novo* design techniques using the Rosetta package. Molecular dynamics associated with molecular docking will be applied to elucidate and clarify details on the interactions of these proteins. The expected findings will allow the rational development of novel inhibitors to the eIF4F complex on *L. major*.

Support: CAPES/BioMol, CNPq, FACEPE, FIOCRUZ, LNCC.