Molecular Modeling of the Dimensional Structure of EF-1α from *Leishmania Donovani* and its Interaction with Several Inhibitors

Mukta Rani, Manas Ranjan Dikhit, Ganesh Chandra Sahoo*, Pradeep Das

Biomedical Informatics Division, Rajendra Memorial Research Institute of Medical Sciences, Agam Kuan, Patna 800007, India

Address for correspondence:
E-mail: mukta.rani1@gmail.com

Visceral Leishmaniasis or Kala-azar is a protozoal parasitic devastating disease which takes a death toll of thousand of peoples including children. EF-1α is essential for survival of *Leishmania*, including for virulence to the mammalian host, it may be viewed as an attractive drug target. By considering the progress of computational drug designing, the structure of Elongation Factor-1 alpha (EF1-α) of *Leishmania donovani* structure was modeled using homology modeling with high accuracy based on the Yeast guanine nucleotide exchange factor eEF1B alpha K205A mutant in complex with eEF1A as a template (PDB id: 2b7C_A). EF1-α is an essential component of the eukaryotic protein biosynthesis, is a GTP-binding protein that catalyses the binding of aminoacyl-transfer RNAs to the ribosome. Multiple alignment of amino acid sequences of EF1-α protein of different species shows that all are very close to each other ranging from 77-92 sequence identity score. A hairpin of 12 amino acids was modeled that was unique to the human EF1-α protein but in *Leishmania* it is missing and it has significant opportunity to design novel, small molecule inhibitors that bind specifically to the region. The modeled structure shows acceptable Ramachandran statistics and remarkable active site residues are predicted. The quality of this model was evaluated using PROCHECK and DOPE Scores: for reliability. So know the presence of novel functional assignment of EF1-α protein by SVM revealed that along with lyases activity, it has several other novel functions e.g. iron-binding, metal-binding, copper binding, cobalt binding, zinc binding etc and has multifunctional and moonlight protein activities (one protein performing multiple independent functions). In search for a better inhibitor for EF1-α, *insilico* docking and selectivity analysis with anti-leishmanial and tetracycline compounds, has shows the presence of highest interactions with tetracycline have dock score of 80.76 and specific polar interaction with Asp35, Thr38, Lys41 and Ile73 residues, so our study provides an early insight into the structure of major drug target EF1-α, thus facilitating the inhibitor design.