UNVEILING THERAPEUTIC GOLD: GENOME MINING FOR *L. DONOVANI* DRUG TARGETS

Nidhi Medhi and Sandeep Swargam*

Centre for Computational Biology and Bioinformatics, Central University of Himachal Pradesh,

Shahpur (176206), Himachal Pradesh, India. E-mail: swargasms@hpcu.ac.in

ABSTRACT

Leishmaniasis is one of the most important vector borne Neglected Tropical Disease (NTD). Visceral Leishmaniasis is the most common form caused by the species of *L.donovani*. Compounds like pentavalent antimonials (Sb(V)) are used as the first option to treat the disease either directly or in combination with the second line drugs like amphotericin B (Amp B), miltefosine (MIL), methotrexate (MTX). Following each year the inefficacy of this drug is rapidly increasing the resistance of the drugs towards the disease. New potent targets are necessary to bring an improvement in the current drug available to treat the disease. In this study, we aspire to find potential novel targets against *L. donovani* strains by applying computational methods. The whole genomic data of 11 *L. donovani* strains (BPK282A1, LdCL, pasteur, MHOM/IN/1983/AG83, BHU 1220, FDAARGOS_361, FDAARGOS_360, Ld 2001, Ld 39) was gathered from NCBI FTP site by running a R script in Linux. A total of 795 genes that are conserved were extracted. Further python script was run to purify the conserved gene to find the essential proteins that was followed by unique protein pathway analysis in KEGG. Accordingly four genes (tuf, fusA, infB and fusA) were revealed to be unique. VaxiJen analysis of these three genes gave us three antigen containing genes as putative targets for future qualitative analysis. Our findings may highlight how the novel target mitigates false-positive or false-negative results and offer a suitable prospective target for further therapeutic research.

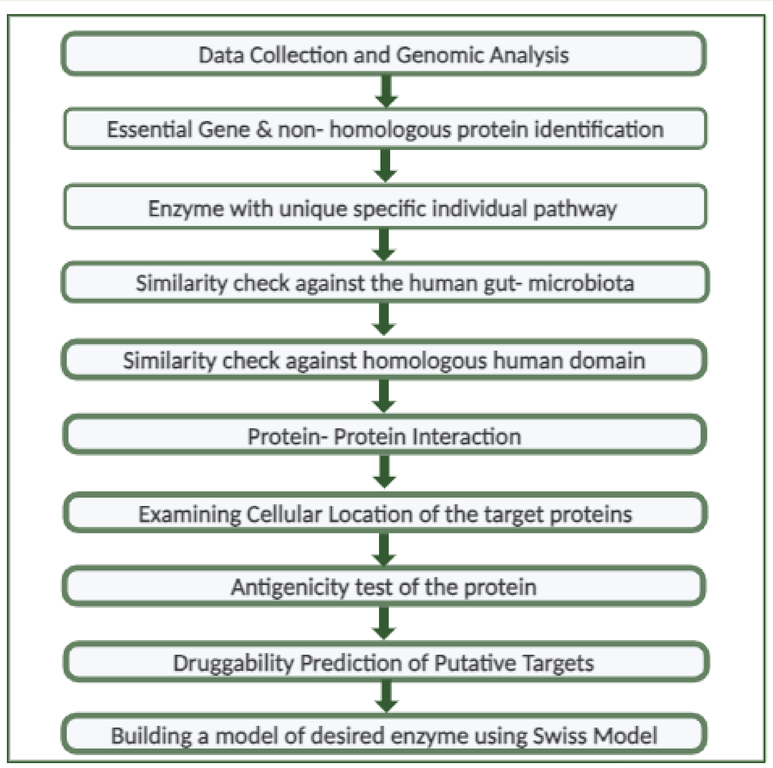
BACKGROUND

The WHO identifies 20 Neglected Tropical Diseases (NTDs), affecting over 1 million people annually, with leishmaniasis causing the highest mortality. Leishmaniasis, endemic in regions like the Middle East, Americas, and Asia is transmitted by female sand flies and caused by over 20 Leishmania species. Visceral leishmaniasis, the most lethal form, is treated with pentavalent antimonials and drugs like amphotericin B and miltefosine, but resistance is rising, especially in Bihar, India. Genomic analysis of *L. donovani* can identify new drug targets. This study aims to find conserved, essential targets distinct from human proteins to develop broad-spectrum inhibitors, addressing drug resistance and improving treatment outcomes.

AIM

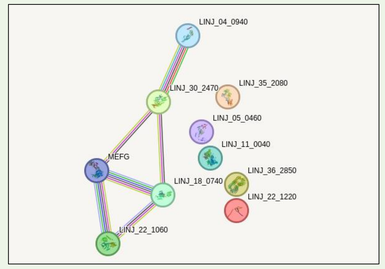
The aim of this study is to identify and validate potential drug targets in the *L.donovani* genome using computational genomic analysis to aid in the development of effective treatments for leishmaniasis.

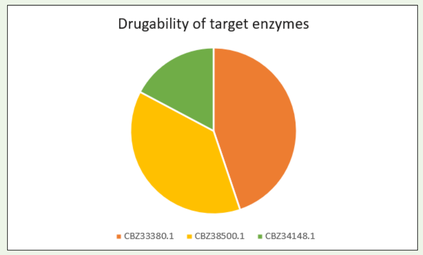
MATERIAL & METHODS



RESULTS

S. No	Analysis	No. of Proteins
1.	Size of reference genome	32.4 M
2.	No. of genes in reference genome	8032
3.	Common Conserved Gene	795
4.	Essential genes after Geptop	57
5.	Non-human homologs essential gene	38
6.	Pathogen specific enzyme	22
7.	Unique pathway specific enzyme	15
8.	Human gut microbiota non- homologous	10
9.	Human domain non- homologous	5
10.	Cytoplasmic Protein	3
11.	Antigenicity of target enzyme	3





CONCLUSION

We identified three novel drug targets for *L. donovani*: tuf, fusA, and infB. These conserved, non-human homologs gene are promising candidates for developing pathogen-specific drugs, aiding in combating drug resistance and controlling leishmaniasis in endemic regions.

REFERENCES

- Torres-Guerrero, E., Quintanilla-Cedillo, M. R., Ruiz-Esmenjaud, J., & Arenas, R. (2017). Leishmaniasis: a review. *F1000Research*, *6*, 750. https://doi.org/10.12688/f1000research.11120.1
- Vijayakumar, S., & Das, P. (2018). Recent progress in drug targets and inhibitors towards combating leishmaniasis. *Acta tropica*, *181*, 95–104. https://doi.org/10.1016/j.actatropica.2018.02.010