Abstract ID: - 217

Abstract Topic: - Complex traits and polygenic disorders

Abstract Title: - Prediction of immunogenic peptide ensemble and multi-subunit vaccine for Visceral Leishmaniasis using bioinformatics approaches

Presenting author name: - Sanjana Mehrotra

Presenting author institute: - Department of Human Genetics, Guru Nanak Dev University

Co-authors name: - Manu Kupani, Rajeev Kumar Pandey

Co-authors institute: - Department of Human Genetics, Guru Nanak Dev University, Amritsar, Thermo Fisher Scientific

Aims: - To design a multi-subunit epitope vaccine for Indian population by targeting antigenic secretory proteins screened from Leishmania donovani proteome using immunoinformatic tools.

Methods: - Out of 8014 proteins, 277 secretory proteins were screened for their cellular location and proteomic evidence. Through NCBI Blastp , unique fragments of the proteins were cropped, and their antigenicity was evaluated. B-cell, HTL and CTL epitopes as well as IFN-ɣ, IL-17, and IL-10 inducers were predicted, manually mapped to the fragments and common regions were tabulated forming a peptide ensemble. The ensemble was further evaluated for Class I MHC immunogenicity and toxicity. Further immunogenic peptides were randomly selected and used to design vaccine constructs. Eight vaccine constructs were generated by linking random peptides with GS linkers. Synthetic TLR-4 agonist, RS09 was used as an adjuvant and linked with construct using EAAK linkers. The predicted population coverage of constructs was ~99.8 % in Indian as well as South Asian population. The most antigenic, nontoxic, non-allergic construct was chosen for prediction of secondary and tertiary structures. The 3D structures were refined and analyzed using Ramachandran plot and Z-scores. The construct was docked with TLR-4 receptor. Molecular dynamic simulation was further done to check the stability of docked complex.

Results: - Comparative in silico immune simulation studies showed that the predicted construct elicited humoral and cell- mediated immunity in human host comparable to that elicited by Leish-F3, which is a promising vaccine candidate for human VL.

Conclusions: - The study proposes a multi-subunit vaccine which was designed using immunogenic regions mined from entire L. donovani proteome unlike most of previously reported studies, which have targeted already characterized antigenic proteins. The approach taken up to predict immunogenic ensemble is novel, to the best of our knowledge, in finding unique non- homologous segments followed by prediction of epitopes and inducers in the fragments and later manually mapping all of them to the protein fragments.

Keywords: - Comparative in silico immune simulation studies showed that the predicted construct elicited humoral and cell- mediated immunity in human host comparable to that elicited by Leish-F3, which is a promising vaccine candidate for human VL.`