Designing a novel multi-epitope cocktail vaccine candidate for Lymphatic Filariasis: An immuno-informatics approach

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ABSTRACT

Background: Lymphatic filariasis is a neglected tropical disease (NTD) affecting more than 657 million people in 39 countries across the world. A multi-epitope prophylactic/therapeutic vaccination targeting filarial defense proteins would be invaluable in achieving the current goal of LF elimination.

Method: In this study, a combination of immunomics and immune-informatics was applied to construct a multi-epitope vaccine candidate. The antigenic proteins were identified by immune blotting against different categories of *Wuchereria bancrofti*-infected LF sera.

Result: The major antigenic proteins were heat shock protein 70, Tubulin beta chain, Enolase, Galectin, and 14-3-3 zeta. The five antigens were combined together to construct a multi-epitope vaccine after predicting the linear B-cell and T-cell epitopes of individual antigens. A three-dimensional model of the candidate vaccine was predicted, followed by refinement, and was validated using RAMPAGE and PROCHECK servers. A Toll-like receptor (TLR) agonist, a 50S ribosomal subunit of *Mycobacterium tuberculosis*, was included in the candidate vaccine to enhance vaccine immunogenicity. The docking of the chimeric peptide vaccine against the TLR5 resulted in high binding efficiency for the docked complex. The in silico immune simulation provided a significant increase in $CD4^+$ T-cell and $CD8^+$ T-cell populations.

Conclusion: In summary, the recombinant putative vaccine showed high immunogenicity which could be experimentally validated in the future for the development of a potent LF vaccine. Furthermore, by employing multi-epitope structures and constructing a cocktail vaccine for LF, this study has the potential to represent an important milestone in the development of an anti-filarial vaccine.

INTRODUCTION

More than 657 million people in 39 countries are affected with Lymphatic Filariasis (LF). LF is a debilitating and profoundly disfiguring disease. Antioxidant proteins like Superoxide dismutase, Glutathione-S-transferase, and Glutathione peroxidase downregulate the host immune response and prolong the survival of parasites. Hence, these antioxidant proteins are considered major targets for immunotherapeutic interventions. The World Health Organization has recognized LF as the second most common cause of long-term and irreversible impairment (WHO, 2024).

MATERIALS AND METHODS

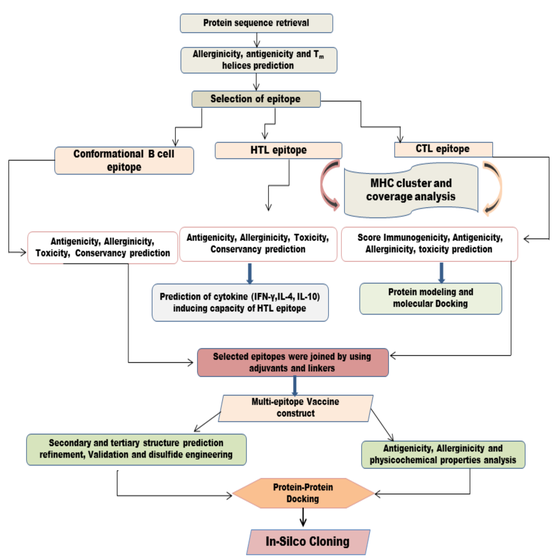

Fig. 1. Flowchart of vaccine development and its cloning

Table: Predicted B-cell epitopes, CTL epitopes and HTL epitopes.

Proteins	B-cell epitope	Cytotoxic T-Lymphocyte epitope	Helper T-Lymphocyte epitope
HSP 70	ELSGIPPAPRGVPQIEVTFD KVQVEYKGETKTFTPEEISS	KTSETFTTY QSDMKHWPF YSDNQPGVL	DEAVAYGAAVQAAIL SLGIETAGGVMTALI DSGAIAGLNVLRIIN
Tubulin beta chain	DEHGVQPDGTYKGDSDLQIE TADEEGDLQEGESEYIEQEE WYTGEGMDEMEFTEAESNMN	VSDVVLEPY LSARDAAAY NMNDLVSEY QIERINVYY ACDPRHGRY QVQNKNSSY	HFFMPGFAPLSARDA FFMPGFAPLSARDAA RLHFFMPGFAPLSAR LHFFMPGFAPLSARD PRLHFFMPGFAPLSA FMPGFAPLSARDAAA MPGFAPLSARDAAAY MSSFSVVPSPKVSDV PGFAPLSARDAAAYR SSFSVVPSPKVSDVV IMSSFSVVPSPKVSD RFPRLHFFMPGFAPLS IMSSFSVVPSPKVS
Enolase	PIYDSRGNPTV VDLTTDKG	AMDCAASEY NTAIATAGY TGDQMMEIY	KGIFRAAVPSGASTG SEIYHYLKAEIKKRY DKGIFRAAVPSGAST EIYHYLKAEIKKRYG MQEFMIMPIGASSFS GIFRAAVPSGASTGV QEFMIMPIGASSFSE GSEIYHYLKAEIKKR IYHYLKAEIKKRYGL
Galectin	SYPIPYRSQLQEKIEPGQTL GNWGNEEREGKIPFEKGVGA	HLSIDGDLY MSDQRSYPI	KIPFEKGVGADLKIV GKIPFEKGVGADLKI PFEKGVGADLKIVN
14-3-3 zeta	LEKQQMVKEYREKVEKELRD YKNVVGARRSSWRVISSIEQ	ALNYSVFFY VADAGQRAY KLAEQAERY	KGDYYRYLAEVASGD MKGDYYRYLAEVASG

RESULTS

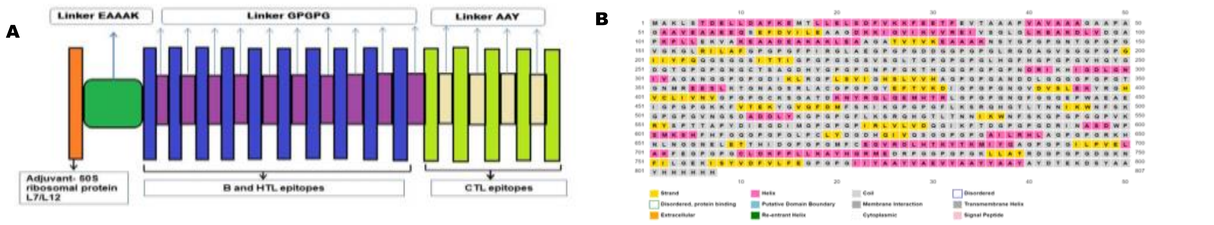

Fig.2. Structure of the desired vaccine model (A) Graphical representation of linear B-cell epitope for vaccine model. (B) Secondary structure of vaccine model, Coiled (grey), Helix (pink), and Strand (yellow) regions.

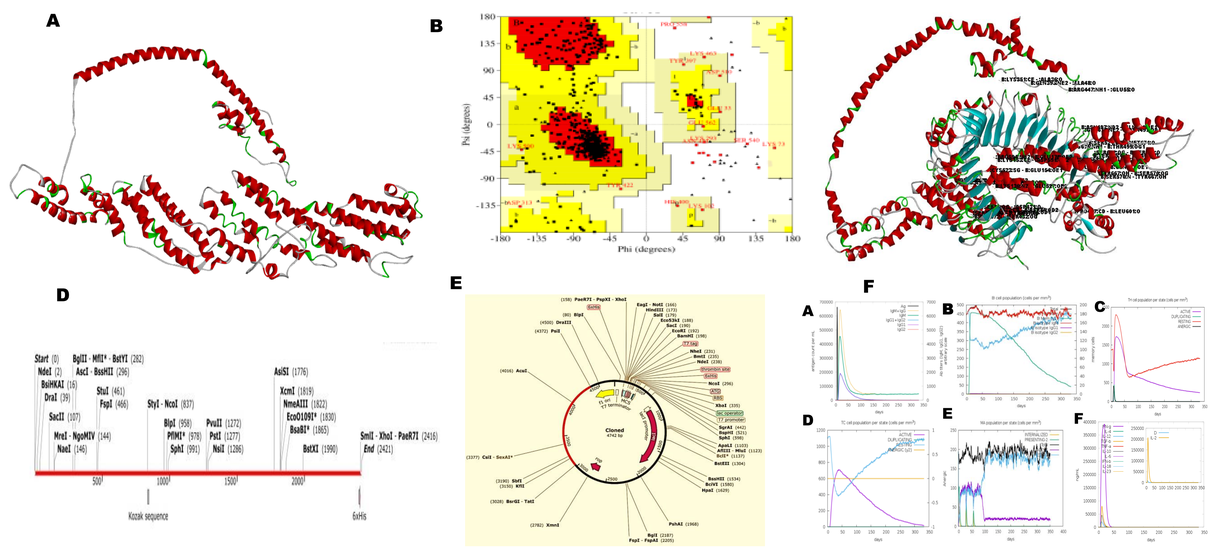

Fig. 3 (A) Tertiary structure of polypeptide vaccine. (B) Ramachandran plot analysis showing 98.2 % and 1.8 % of protein residues in favored, and disallowed (outlier) regions, respectively. (C) Interaction between TLR4 and vaccine model. (D) Insert of restriction fragment, size 2163 base-pair. (E) Final product size of cloning vector has 4742 bp, black and red regions show the vector and insert regions, respectively. The vector has a single restriction site (XcmI) and insert has two specific sites, XcmI and HindIII. (F) C-ImmSim predicted in-silico immune response production of several subclasses of immunoglobulin response of vaccine injection.

SIGNIFICANCE

The *in-silico* study, demonstrates that the multi-epitope based peptide vaccine molecule is well stable in 3D architecture and might have the potentiality to produce a strong immune response against the filarial parasite. In addition, the non-allergen vaccine model with its multi-epitope along with its antigenic form strongly supports the inductive properties to raise both humoral and cell-mediated immune responses. Though we found a strong immunogenic response in our *in-silico* study, there is still a need for in-vitro and in-vivo validation of the effective immunogenicity and host safety of the vaccine structure before human administration.

ACKNOWLEDGEMENT & REFERENCES

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