SUMMARY AND CONCLUSION

Work described in this study primarily falls into two categories: 1) Identification of epitopes and mimotopes in a selected target protein of *P. falciparum* and testing their vaccine potential in *in vitro* assays and *in vivo* mouse model. 2) Identification and characterization of target protein/sequence, peptide and its analogues for testing their application in arresting malaria parasite growth *in vitro* and in mouse model.

1. **Identification of vaccine candidates:** The monoclonal antibody B6 (mAbB6), cross reactive to RhopH3 of both *P. berghei* and *P. falciparum* parasites and inhibits *in vitro* growth of *P. falciparum*, identified its epitope in 1-147 aa region of RhopH3. B cell epitope analysis by ABCPred and BCPREDS and T-cell epitopes analysis by IEDB revealed that this N-terminal region of *P.berghei* (Pb) and *P.falciparum* (Pf) RhopH3 is rich in both B and T cell epitopes, some of which are overlapping and also conserved in these species. Synthetic peptide, corresponding to one such region i.e. $PfRhopH3_{64-84}$, was able to induce, as such or conjugated to KLH, a high titer antibodies which cross reacted with both $PfRhopH3_{64-84}$ and $PbRhopH3_{64-84}$ polypeptides thus demonstrating the immunogenicity of epitope(s) conserved in both species. Interestingly, antibodies, so generated, inhibited *in vitro* growth of *P. falciparum*. However, immunization with this polypeptide could not induce protection in mouse model against *P. berghei* infection. This may be due to either poor T cell response, as indicated by splenocyte proliferation assay or suboptimal conditions used for testing *in vivo* efficacy. On the other hand, immunizations with phage peptides R1P16 and C3P1, screened on parasite growth inhibitory mAbs B6 and C3 reactive to PbRhopH3 and PbMSP1 respectively, were able to induce protective immunity against *P.berghei* infection in mice. The level of protection achieved was ~50% and ~25% in R1P16 and C3P1immunized mice respectively. Interestingly, the protected mice, after 90 days of recovery, when rechallenged with *P. berghei*, did not develop parasitemia again. This demonstrated that the protective response was inclusive of memory response. Thus R1P16 and C3P1 peptides can be putative candidates for vaccine development in malaria.

2. **Identification of drug candidates:** The recombinant B-subunit protein of V-ATPase showed ATP hydrolysis and point mutations of D283A (walker B motif residue) and D364A (conserved residue) reduced the activity by more than 50%, indicating importance of aspartate residues in B-subunit function. The surface structure showed that both walker motifs are in close proximity

suitable for ATP binding and stabilization. Also, other key residues like arginine (R384), sine (Y373, Y355), and aspartic acid (D366) are accessible for ATP binding and ilization. Parasite growth inhibitory ATPase13 peptide, one among several peptides ened using recombinant B-subunit, was found effectively taken up specifically by *P. iparum* infected erythrocytes, particularly to parasite nuclear location. This indicated that the parasitic activity of this peptide can be enhanced by loading it with antimalarial cargo. her, structural analysis of ATPase13 peptide and using the pepMMsMIMIC, number of ogues of this peptide were identified. These compounds, already approved by Food and Drug ninistration (FDA), USA, have earlier been reported for their therapeutic applications in other ases. Importantly, when tested for their antimalarial activity, *in vitro* and *in vivo*, meticillin, ıetocin and nelfinavir were found to be antimalarial, albeit to different levels. As these are ady approved drugs, it would be easier and useful to take these leads for antimalarial drug elopment.