Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad - 500107

Students' Annual Seminar

Fragment-based search to identify novel binding sites of PfRh5 protein

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The most severe form of human malaria is caused by the Plasmodium falciparum (P falciparum) parasite. The current estimates suggest that in 2018 there were over 228 million clinical cases leading to 405,000 deaths worldwide. Artemisinin-based combination therapies (ACTs) are the mainstay treatments for P falci-parum malaria and have led to substantial decline in the number of malaria-related deaths. However, the recent emergence of drug resistant strains in Southeast Asia region threatens to reverse this progress. Currently, there are no other drugs or vaccines available to address this issue. We aim to systematically understand the parasite invasion process in molecular level with the goal of identifying potential peptide or protein therapeutics against malaria. Among the PfRh family proteins, responsible for red blood cell invasion process, the PfRh5 has been found to be the crucial ligand that binds to the host receptor basigin through the formation of a ternary complex with two other parasitic proteins called Ripr and CyRPA. In this study, we used decoy search strategy to find out the possible binding sites of PfRh5 using chemically synthesized rationally designed PfRh5 peptide fragments and parasite growth inhibition assays. We also chemically stabilized the secondary structure of the active peptide fragment(s) to increase their efficacy. We believe this strategy will allow us to identify novel protein-protein interaction(s) targets, potential peptide inhibitors and vaccine candidates against malaria.

References:

Volz, J. C.; Yap, A.; Sisquella, X.; Thompson, J. K.; Lim, N. T. Y.; Whitehead, L. W.; Chen, L.; Lampe, M.; Tham, W. H.; Wilson, D.; et al. Essential Role of the PfRh5/PfRipr/CyRPA Complex during Plasmodium Falciparum Invasion of Erythrocytes. Cell Host Microbe 2016, 20 (1), 60–71.

Monday, Feb 10th 2020

9:30 AM (Tea/Coffee at 9:15 AM)

Seminar Hall, TIFR-H