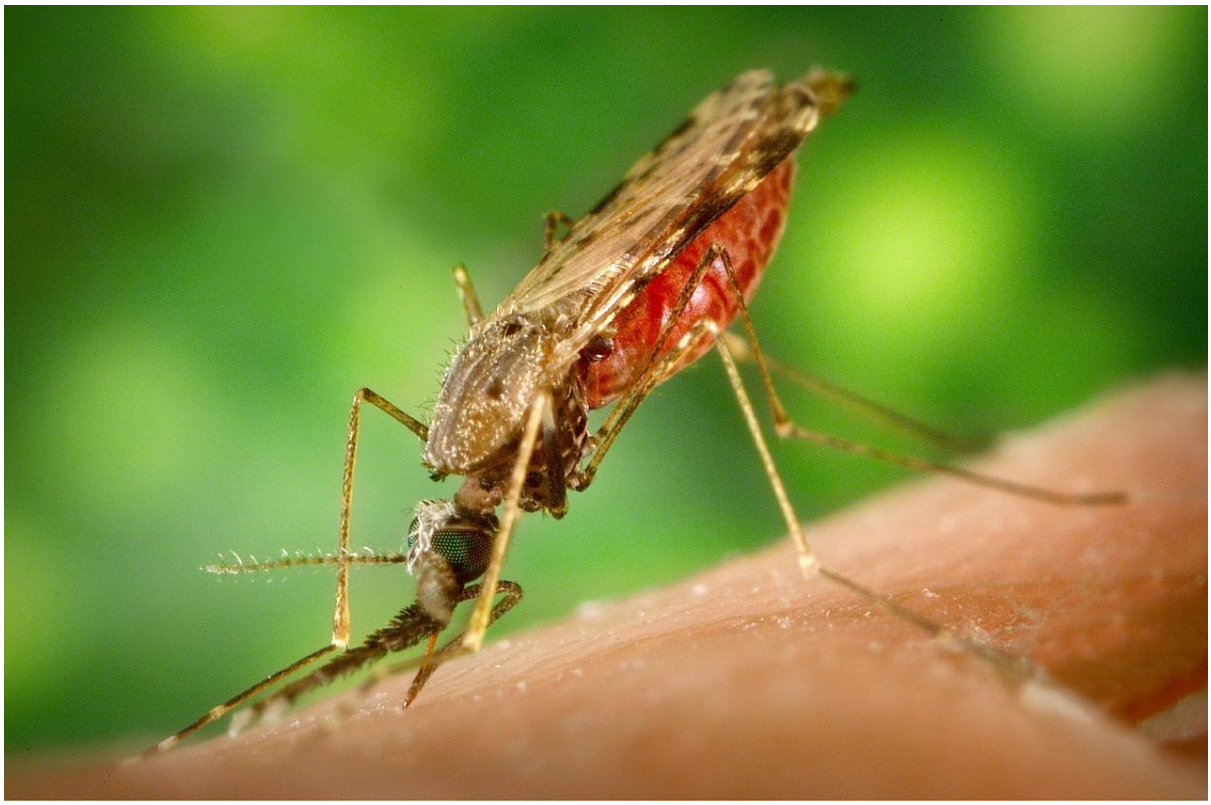
DBT-CDFD study could help fight malaria better

New Delhi, Jan 10: A laboratory at DBT- Centre for DNA Fingerprinting and Diagnostics (DBT-CDFD), Hyderabad has been studying acyl-CoA-binding proteins from the malaria parasite Plasmodium falciparum and its host-humans. They had earlier shown that the antimalarial drug-Mefloquine inhibits the binding of acyl-CoAs to acyl-CoA-binding proteins of Plasmodium falciparum (PfACBP749) and human (hACBP).



In their current studies, they have used molecular dynamics simulation and other computational approaches to investigate the differences in stabilities of mefloquine–PfACBP749 and mefloquine–hACBP complexes. The stability of mefloquine in the binding cavity of PfACBP749 is lower than its stability in the binding pocket of hACBP. Although the essential tyrosine residues (tyrosine-29 and tyrosine-32 of hACBPandtyrosine-30 and tyrosine-33 of PfACBP749)do mediate the initial binding of mefloquine to the proteins through π-stacking interactions, additional temporally longer interactions between mefloquine and aspartate-22 and methionine-25 of hACBP contribute to a stronger interaction of mefloquine to hACBP. The higher fluctuation of mefloquine-binding residues of PfACBP (PfACBP749) contributes to the instability of mefloquine interaction in the binding cavity of the protein.

On the other hand, in the mefloquine-bound state, the stability of hACBP protein is lower than the stability of PfACBP749. It arises from the helix-to-coil transition of the N-terminal hydrophobic region of hACBP that has a destabilizing effect upon the protein's structure. It

causes the induction of aggregation properties in the hACBP in the mefloquine-bound state. In conclusion, our studies have revealed the mechanistic features that affect the differential dynamic stabilities of mefloquine-bound PfACBP749 and hACBP proteins.

Contact Person& Contact Details: Akash Ranjan, Staff Scientist VII (Chief Scientist) and Head, Computational and Functional Genomics Group &Computational Biology and Bioinformatics Services Group, Email: akash@cdfd.org.in

Link: http://www.cdfd.org.in/