Computational identification of signalling pathways in *Plasmodium falciparum*

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Abstract

Malaria is one of the world's most common and serious diseases causing death of about 3 million people each year. Its most severe occurrence is caused by the protozoan *Plasmodium falciparum*. Reports have shown that the resistance of the parasite to existing drugs is increasing. Therefore, there is a huge and urgent need to discover and validate new drug or vaccine targets to enable the development of new treatments for malaria. The ability to discover these drug or vaccine targets can only be enhanced from our deep understanding of the detailed biology of the parasite, for example how cells function and how proteins organize into modules such as metabolic, regulatory and signal transduction pathways. It has been noted that the knowledge of signalling transduction pathways in *Plasmodium* is fundamental to aid the design of new strategies against malaria. This work uses a linear-time algorithm for finding paths in a network under modified biologically motivated constraints. We predicted several important signalling transduction pathways in *Plasmodium falciparum*. We have predicted a viable signalling pathway characterized in terms of the genes responsible that may be the PfPKB pathway recently elucidated in *Plasmodium falciparum*. We obtained from the FIKK family, a signal transduction pathway that ends up on a chloroquine resistance marker protein, which indicates that interference with FIKK proteins might reverse *Plasmodium falciparum*from resistant to sensitive phenotype. We also proposed a hypothesis that showed the FIKK proteins in this pathway as enabling the resistance parasite to have a mechanism for releasing chloroquine (via an efflux process). Furthermore, we also predicted a signalling pathway that may have been responsible for signalling the start of the invasion process of Red Blood Cell (RBC) by the merozoites. It has been noted that the understanding of this pathway will give insight into the parasite virulence and will facilitate rational vaccine design against merozoites invasion. And we have a host of other predicted pathways, some of which have been used in this work to predict the functionality of some proteins.