Plasmodium falciparum protein kinase as a potential therapeutic target for antimalarial drugs development

ABSTRACT

Malaria is one of the most dangerous infectious diseases due to its high infection and mortality rates, especially in the tropical belt. Plasmodium falciparum (P. falciparum), the most virulent malaria parasite in humans, was recently reported to develop resistance against the final efficient antimalarial drug, artemisinin. Little is known about the resistance mechanisms, which further complicates the problem as a proper counteraction is unable to be taken. Hence, the understanding of drug mode of action and its molecular target is valuable knowledge that needs to be considered to develop the next generation of antimalarial drugs. P. falciparum protein kinase (Pf PK) is an attractive target for antimalarial chemotherapy due to its vital roles in all P. falciparum life stages. Moreover, overall structural differences and the presence of unique Pf PKs that are absent in human kinome, suggesting specific inhibition of Pf PK without affecting human cells is achievable. To date, at least 86 eukaryotic protein kinases have been identified in P. falciparum kinome, by which less than 40 were validated as potential targets at the erythrocytes stage. In this review, recent progress of the furthest validated Pf PKs; Pf Nek-1, Pf CDPK1, Pf CDPK4, Pf PKG, and Pf CLK-3 will be briefly discussed.