INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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SHORT ABSTRACT

Malaria is a life-threatening disease caused by the protozoan parasite *Plasmodium falciparum.* Emergence of drug resistance necessitates the identification of new drug targets. PFD0975w is identified as an RIO-2 kinase in the malaria parasite, believed to play crucial roles in cell cycle coordination and ribosome maturation. Homology modeling enabled the structural characterization of the kinase and virtual screening identified several potential hits. The putative kinase was cloned, expressed and purified as a 35 KDa active enzyme capable of binding ATP. *Plasmodium* RIO-2 kinase localizes in the parasite cytosol with discrete localization during each RBC stage and a maximum expression is observed in trophozoites. The localization pattern of the enzyme is sensitive to cellular stresses. Several candidate drugs were identified and a series of synthetic molecules were designed to target this kinase. Most of the above molecules exhibit excellent antimalarial activity. The molecules are parasitocidal and disrupt the parasite's antioxidant machinery. Stress induced upon drug treatment influences the localization of the kinase within the iRBC. Studies suggest *Plasmodium* RIO-2 kinase as an essential gene capable of being an excellent antimalarial drug target. The work has also identified several promising antimalarial molecules for further drug development.