Analysis of the Glycerol Kinase gene in Plasmodium falciparum

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Malaria is one of the most virulent forms of disease with an annual mortality rate of >2 million people worldwide. Knowledge of the Plasmodium falciparum parasite needs to be expanded and despite efforts in the sequencing and gene annotation of the P. falciparum genome, characterization of proteins and metabolic pathways are required to fully understand the parasite. P. falciparum is devoid of a pathway for cholesterol biosynthesis; instead all newly synthesized membrane lipids are based on a glycerol backbone or glycerolipid. This suggests that the gluconeogenesis enzyme, glycerol kinase (GK), may have an essential role in the growth and development of the parasite. GK catalyzes the ATPdependant phosphorylation of glycerol to glycerol-3-phosphate, which is one of the precursors for the synthesis of glycerolipids and membrane biogenesis. The P. falciparum sequence obtained from PlasmoDB shows that the parasite enzyme consists of an A/T-rich 1506bp sequence with no introns. Bioinformatic analysis using the EMBOSS Pairwise Alignment tool shows that P. falciparum GK is 38.7% identical to the human enzyme and several residues at the active site are conserved, implying an active enzyme. However, several differences in key residues indicate that the enzyme may serve as a possible drug target. To characterize the P. falciparum GK, DNA was extracted from FCR-3 P. falciparum and the full length GK gene was amplified via PCR and ligated into the pGEX4T2 vector for expression studies. Elucidation of the functional and kinetic requirements of the enzyme will increase our understanding of the metabolism of P. falciparum.