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Strategies to Improve Protein Expression and Solubility: Lessons from the Structural Genomics of Plasmodium. Sujata Sharma, Jocelyne Lew, Peter Loppnau, Farrell Mackenzie, Anthony Semesi, Adelinda Yee, Structural Genomics Consortium, Univ. of Toronto, 200 Elizabeth St. Toronto, ON M5G2C4 Canada.

Malaria is the most devastating parasitic disease in the world; it kills more than a million people every year. Due to rise in drug resistant strains, there is an urgent need for new antimalarials. The complete sequence of genome of *Plasmodium falciparum*, causative agent of one of the most lethal forms of malaria in humans should facilitate functional and structural genomics efforts with a hope to find new and more effective drug targets against malaria.

The plasmodium genome is ~80% AT rich and its proteins are encoded by codons that are rarely used in *E. coli*. These features have presented difficulties for structural biologists who need to express recombinant proteins in *E. coli*. We have carried out a pilot structural proteomics study on 96 unique targets from *P. falciparum*. A very low percentage of proteins from *P. falciparum* were produced in soluble form when expressed in *E. coli*. Incremental increases in the success rate were achieved by manipulating bacterial strains, through the addition of tRNAs and by studying orthologous proteins from other Plasmodia. In total, these methods improved the recovery of soluble protein 3 fold suggesting a strategy that can be applied to other systems.