Systems Biology and Malaria

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Malaria is the cause of significant global morbidity and mortality with 300-500 million cases annually. Despite its disease burden relatively little is known about the molecular biology of the pathogen that causes malaria. For example, the completion of the genome sequence of *Plasmodium falciparum*, the species responsible for the most severe form of human malaria revealed that only ~35% of the genes code for proteins with an identifiable function. In addition, little is known about how transcription and translation are regulated. The absence of routine genetic tools for studying *Plasmodium* parasites suggests that these numbers are unlikely to change quickly if conventional, serial, biological methods are used to study the parasite. We are using high-density oligonucleotide arrays and informatic methods to study the genome of the malaria parasite with the goals of understanding how expression is regulated, functionally cataloging the genome, discovering allelic variation and identifying new therapeutic targets. We have shown that genes with highly correlated levels and temporal patterns of expression are often involved in similar functions or cellular processes suggesting that expression profiling can be used to rapidly predict function. In addition we find that there is good correlation between protein levels and transcript levels, suggesting that regulation of expression occurs transcriptionally. Analysis of whole-genome transcription patterns reveals that the chromosome is organized into regions that are transcriptionally active and transcriptionally silent in the intraerythrocytic stage of the parasite's lifecycle. Thus, both the timing and the relative level of transcription in the parasite is organized into position-dependent domains suggesting that transcription may be regulated at least partially at the level of chromatin structure.