Plasmodium falciparum epigenome: A distinct dynamic epigenetic regulation of gene expression

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Abstract

Epigenetic mechanisms have been proposed to play major role in gene expression in a range of organisms. However, little is known about epigenetic regulations in *Plasmodium falciparum*, the causative agent of malaria. To elucidate stage-specific epigenetic regulations in *P. falciparum*, we performed genome-wide mapping of various histone modifications, nucleosomes and RNA Polymerase II and integrated them with other publicly available data. Further to understand the differences in transcription regulation in *Plasmodium* and its host, human, we contrasted their histone modifications, which suggest that transcription initiation and elongation are distinct in *Plasmodium.* Our comprehensive analysis also suggests that most of the chromatin is poised, and many genes produce anti-sense RNA from their 3'end in the malaria parasite. Interestingly, we found that H3K36me2 acts as a global repressive mark in *Plasmodium* and gene regulation is achieved by the ratio of activation marks to H3K36me2. This novel mechanism of gene regulation is supported by the fact that knockout of SET genes (responsible for H3K36 methylation) lead to higher expression of least expressed genes with highest H3K36me2 in wild-type conditions. Moreover, clonally variant multicopy genes, which are involved in virulence and pathogenicity, are mostly poised and marked by a unique set of activation (H4ac) and inactivation (H3K9me3) marks within the gene body and around it. Thus, our study reveals unique plasticity in the epigenetic and transcriptional regulation in *Plasmodium falciparum* which can influence parasite virulence and pathogenicity.