NATURAL SELECTION ON NUCLEOTIDE COMPOSITION OF
PLASMODIUM FALCIPARUM

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Abstract: Each year, 300 to 500 million global cases of malaria are reported. Approximately 2 million of those cases result in death, with children being disproportionately affected. Several of the *Plasmodium* species (protozoan parasites) have been found to be causative agents of malaria in humans. *Plasmodium falciparum* is considered the most fatal among the species members. *P. falciparum* has an unusual and biased nucleotide composition compared to other eukaryotic genomes. The non-coding regions of *P. falciparum* are more than 81% A-T rich. This high A-T nucleotide composition could be the result of natural selection shifting the genome for reasons currently not well understood. We conducted comparative genome analyses along with population variation analyses by comparing *P. falciparum* to its closely related sister genome, *Plasmodium reichenowi*, another species member that infects chimpanzees. By observing the rates of occurrence of fixed and polymorphic mutations that do or do not alter the A-T nucleotide composition over different classes of genomic regions, and using the principles of the McDonald-Kreitman test (MK test), we were able to test the following hypotheses: The very high A-T nucleotide composition is the result of mutation pressures and not natural selection or, natural selection is responsible for maintaining or changing the nucleotide composition. We find that natural selection is playing a role in the regulation of the A-T nucleotide composition and is fixing mutations that change the A-T nucleotide compositions faster than expected.