The Genome of the Zoonotic Malaria Parasite Plasmodium simium Reveals Adaptions to Host-switching

O-5. The Genome of the Zoonotic Malaria Parasite *Plasmodium simium* Reveals Adaptions to Host-switching

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Plasmodium simium, a malaria parasite of non-human primates in the Atlantic forest region of Brazil was recently shown to cause zoonotic infections in humans. Phylogenetic analyses based on of six *P. simium* isolates from humans and two isolates from brown howler monkeys revealed that *P. simium* is monophyletic within the broader diversity of South American *Plasmodium vivax*, consistent with the hypothesis that *P. simium* first infected non-human primates as a result of a host-switch of *P. vivax* from humans. Very low levels of genetic diversity within *P. simium* and the absence of *P. simium*-*P. vivax* hybrids suggest that the *P. simium* population emerged recently with a subsequent period of independent evolution in Platyrrhini monkeys. We find that *Plasmodium* Interspersed Repeat (PIR) genes, *Plasmodium* Helical Interspersed Subtelomeric (PHIST) genes and Tryptophan-Rich Antigen (TRAg) genes in *P. simium* are divergent from *P. vivax* orthologues and are enriched for non-synonymous single nucleotide polymorphisms, consistent with the rapid evolution of these genes. Analysis of genes involved in erythrocyte invasion revealed several notable differences between *P. vivax* and *P. simium*, including large deletions within the coding region of the Duffy Binding Protein 1 (DBP1) and Reticulocyte Binding Protein 2a (RBP2a) genes of *P. simium*. Sequence analysis of *P. simium* isolates from non-human primates (NHPs) and zoonotic human infections revealed a deletion of 38 amino acids in DBP1 present in all human-derived isolates, whereas NHP isolates were multi-allelic at this locus. We speculate that these deletions in key erythrocyte invasion ligands along with other significant genetic changes may have facilitated zoonotic transfer to humans. NHPs are a reservoir of parasites potentially infectious to humans that must be considered in malaria eradication efforts. The *P. simium* genome is an important resource for understanding the mechanisms of malaria parasite zoonoses.