

Abstract

The way malaria parasites are transmitted in space will have an influence on their genetic relationships. It can be expected that parasites collected within close geographic distances of each other would be more closely related than those across large geographic distances. Further to this, because malaria transmission is focal and heterogeneous in space, then the genetic relatedness between malaria parasites in these foci of malaria transmission would be greater within tightly clustered regions. Thus, using the level of genetic relatedness of these parasites would reveal how they are transmitted not only within these foci but at different geographic settings. This knowledge would offer insight on how malaria control methods can be effectively disseminated. In field settings malaria infections are polyclonal and each of the clones represented within these infections occur at different proportions. With the aid of genetic markers such as single nucleotide polymorphisms (SNPs) or microsatellites, parasite clonal genotypes can be identified. In this study, the genetic markers of choice are SNPs. Using a method that can quantify these SNPs representing the different clones occurring at different proportions in an isolate, then each of the clonal genotypes can be determined. Microsatellites were also used as additional markers in the study. In this thesis, 1. Genetic markers (SNPs) across the *P. falciparum* genome were identified (Chapter 3); 2. Pyrosequencing™ was validated as a technique that would enable the identification of each genetically distinct clone represented in an infection by assigning proportions to the SNPs representing each genetically distinct clone and enabling the identification of parasite clonal genotypes in every isolate analysed. This was validated using laboratory prepared clone mixtures of *P. falciparum*. In addition; the progeny from a cross derived from genetically characterised 3D7 and HB3 isolates was analysed in preparation for the analysis of the field isolates (Chapter 4). , 4. In Chapter 5, field isolates were tested and clonal genotypes identified using both SNPs and microsatellites. A detailed population genetic analysis was also performed and finally in Chapter 6, evidence for correlation between the genetic relationships of these parasites and geographic distance was investigated. The results from field isolates summarised in this thesis were from analysis of 54 isolates; 7 samples collected from Cameroon, 13 from Kenya and 34 from Mali. The data consists of 13 SNPs analysed by Pyrosequencing™ and 8 microsatellites. 84 clonal genotypes were identified by both genetic markers from the analysed isolates. Analysis of both SNPs and microsatellites revealed that microsatellites were more informative than the SNPs based on the observed allelic

richness and heterozygosity (genetic diversity) across all loci analysed. The overall F_{ST} value was 0.061 using SNPs and 0.043 by microsatellites analysis. These values were low but consistent with what is typically observed in African *P. falciparum* populations. Finally, analyses of the combined data set revealed that no statistically significant levels of spatial autocorrelation existed within the studied parasite populations. However, there was evidence of within host mixed parasite infections exhibiting a high level of genetic relatedness compared to between host infecting clones.