

Fragmented Population Structure of *Plasmodium falciparum* in a Region of Declining Endemicity

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Background. The population genetic structure of *Plasmodium falciparum* differs between endemic regions, but the characteristics of a population recently fragmented by effective malaria control have been unknown.

Methods. Genotypic analysis of 10 microsatellite loci widely separated in the parasite genome was conducted on 288 *P. falciparum* isolates from 8 foci in Malaysian Borneo, a region in which malaria incidence has been progressively reduced.

Results. Within all *P. falciparum* foci, moderate levels of allelic diversity were found, but levels of multilocus linkage disequilibrium were extremely variable. The population with the highest proportion of mixed-clone infections also had the highest allelic diversity and nonsignificant linkage disequilibrium. In contrast, several populations showed evidence of clonal expansion, and one offshore island population had exceptionally high levels of linkage disequilibrium. Genetic differentiation between many populations was very high and strongly associated with the geographical distance between them.

Conclusions. High levels of differentiation and contrasting population structure among *P. falciparum* populations in Malaysian Borneo indicate that they are genetically independent. This supports the feasibility of individually eradicating the remaining *P. falciparum* foci.

The protozoan parasite *Plasmodium falciparum* is the most important eukaryotic pathogen in humans, being responsible for ~1 million deaths each year [1]. The parasite is haploid for most of its life cycle but reproduces sexually during a brief diploid stage, after which meiotic recombination occurs with a high crossover rate [2]. Globally, *P. falciparum* is known to exhibit a mosaic of population genetic characteristics, apparently correlated with local levels of endemicity and transmission intensity [3]. For example, levels of allelic diversity, parasite outcrossing, and gene flow are generally high in African populations, low in South American pop-

ulations, and intermediate in Southeast Asian populations [3–6]. The majority of malaria cases reported in Malaysia occur in Sabah and Sarawak, 2 states separated from Peninsular Malaysia by the South China Sea and located in the northern part of the island of Borneo [7] (figure 1). The most prevalent species of human malarial parasite in Malaysia is *P. falciparum*, for which the reported annual incidence in Sabah has been reduced drastically (from 30,999 reported cases in 1995 to 3052 reported cases in 1999), whereas in Sarawak the number of cases has been more stable but low (<1000 cases/year) ([7] and Sarawak Vector-Borne Diseases Control Programme, unpublished data). Data on the entomological inoculation rate in Sabah or Sarawak are currently unavailable. Malaria has been controlled in Malaysian Borneo by use of a combination of insecticide residual spraying, distribution of insecticide-treated bed nets, reduction of mosquito breeding sites, and employment of trained microscopists in remote endemic regions to diagnose and treat malaria cases. Thus, *P. falciparum* now tends to occur in discrete foci in Malaysia. The low level of human migration between regions of endemism, because of the moun-

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