Received: 31 October 2017 | Revised: 15 December 2017 | Accepted: 16 December 2017

DOI: 10.1111/mec.14477

ORIGINAL ARTICLE

WILEY MOLECULAR ECOLOGY

Genome-wide mosaicism in divergence between zoonotic malaria parasite subpopulations with separate sympatric transmission cycles

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Funding information
H2020 European Research Council, Grant/Award Number: AdG-2011-294428; Universiti Malaysia Sarawak, Grant/Award Number: 01/(TD03)/1003/2012(01), F05/SpTDG/1447/2016/4; UK Medical Research Council, Grant/Award Number: G1100123

Abstract

Plasmodium knowlesi is a significant cause of human malaria transmitted as a zoonosis from macaque reservoir hosts in South-East Asia. Microsatellite genotyping has indicated that human infections in Malaysian Borneo are an admixture of two highly divergent sympatric parasite subpopulations that are, respectively, associated with long-tailed macaques (Cluster 1) and pig-tailed macaques (Cluster 2). Whole-genome sequences of clinical isolates subsequently confirmed the separate clusters, although fewer of the less common Cluster 2 type were sequenced. Here, to analyse population structure and genomic divergence in subpopulation samples of comparable depth, genome sequences were generated from 21 new clinical infections identified as Cluster 2 by microsatellite analysis, yielding a cumulative sample size for this subpopulation similar to that for Cluster 1. Profound heterogeneity in the level of inter-cluster divergence was distributed across the genome, with long contiguous chromosomal blocks having high or low divergence. Different mitochondrial genome clades were associated with the two major subpopulations, but limited exchange of haplotypes from one to the other was evident, as was also the case for the maternally inherited apicoplast genome. These findings indicate deep divergence of the two sympatric *P. knowlesi* subpopulations, with introgression likely to have occurred recently. There is no evidence yet of specific adaptation at any introgressed locus, but the recombinant mosaic types offer enhanced diversity on which selection may operate in a currently changing landscape and human environment. Loci responsible for maintaining genetic isolation of the sympatric subpopulations need to be identified in the chromosomal regions showing fixed differences.

KEYWORDS
adaptation, genomic divergence, host-specificity, introgression

1 | INTRODUCTION

The zoonotic malaria parasite *Plasmodium knowlesi* is a significant cause of human malaria in South-East Asia. Although long known as a malaria parasite of long-tailed and pig-tailed macaques that could potentially infect humans (Coatney, Collin, Warren, & Contacos, 1971), the first large focus of human cases was only detected approximately 15 years ago in Malaysian Borneo (Singh et al., 2004). Since then, infections