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Antigenic diversity in Plamodium falciparum: cause and consequences

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ABSTRACT

The var multi-gene family of Plasmodium falciparum encodes the highly polymorphic variant surface proteins PfEMP1 and is involved in immune evasion through clonal antigenic variation. These proteins are also important virulence factors that mediate cytoadhesion of parasitized red blood cells to a variety of host receptors, causing sequestration in vital organs, including the brain and the placenta. Acquisition of variant-specific antibodies against PfEMP1 correlates with protection against severe disease and appears to follow a particular order. The relationship between acquired protection, gene expression and infection outcome is therefore at the centre of malaria epidemiology and disease pathology but complicated by the modular genetic architectures of var genes and their multi-phenotypic assembly within each parasite repertoire. Using an evolutionary framework in conjunction with sequence and gene transcription analysis it is shown how evolutionary trade-offs optimising parasite fitness and immune evasion at both the within-host and between-host level might have shaped the domain architecture of var genes and can explain the non-random distribution of var genes within the genome and parasite population.

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