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Patterns of nucleotide and haplotype diversity at *ICAM-1* across global human populations with varying levels of malaria exposure

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Abstract

Malaria is one of the strongest selective pressures in recent human evolution. African populations have been and continue to be at risk for malarial infections. However, few studies have re-sequenced malaria susceptibility loci across geographically and genetically diverse groups in Africa. We examined nucleotide diversity at *Intercellular adhesion molecule-1* (*ICAM-1*), a malaria susceptibility candidate locus, in a number of human populations with a specific focus on diverse African ethnic groups. We used tests of neutrality to assess whether natural selection has impacted this locus and tested whether SNP variation at *ICAM-1* is correlated with malaria endemicity. We observe differing patterns of nucleotide and haplotype variation in global populations and higher levels of diversity in Africa. Although we do not observe a deviation from neutrality based on the allele frequency distribution, we do observe several alleles at *ICAM-1*, including the *ICAM-1*^{Kilifi} allele, that are correlated with malaria endemicity. We show that the *ICAM-1*^{Kilifi} allele, which is common in Africa and Asia, exists on distinct haplotype backgrounds and is likely to have arisen more recently in Asia. Our results suggest that correlation analyses of allele frequencies and malaria endemicity may be useful for identifying candidate functional variants that play a role in malaria resistance and susceptibility.