

## Malaria Pressure Influenced the Frequency of a Susceptible Allele of TNF-alpha Promoter Region in Vanuatu

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Tumor necrosis factor- alpha (TNF- alpha) is one of the key cytokines that influence the pathology of microbial infections. The genetic susceptibility to severe form of falciparum malaria is associated with TNF- alpha promoter gene polymorphism (TNFP alleles). In our previous study, we identified a TNFP-allele characterized by a T to C transition at position -857 (TNFP-D allele) as a strong susceptibility marker for cerebral malaria in Myanmar. To investigate whether malaria selection pressure on this susceptibility marker has influenced its prevalence, the frequency of the TNFP alleles was estimated in six islands in Vanuatu, Melanesia within the South Pacific. Within the Vanuatu archipelago there is an overall decreasing North to South cline of malaria endemicity. Of the four alleles of the TNFP gene detected, the susceptible TNFP-D allele frequency decrease corresponded to the malaria endemicity increase; TNFP-D varied from 0.55 in the lowest malarial endemicity population to 0.26 in the highest malarial endemicity population ( $r = -0.855$ ,  $p = 0.03$ ). This is the first report indicating that malaria selection pressure has selected an allele related to immunity.

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