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CTLA-4 polymorphisms and anti-malarial antibodies in an endemic population of Papua New Guinea

[Hikota Osawa](#)¹⁾²⁾, [Marita Troye-Blomberg](#)³⁾, [Kenji Hirayama](#)⁴⁾, [M Francis Hombhanje](#)⁵⁾, [Takeo Tanihata](#)²⁾⁶⁾, [Rachanee Udomsangpet](#)⁷⁾, [Björkman](#)²⁾, [Takatoshi Kobayakawa](#)¹⁾ and [Akira Kaneko](#)¹⁾²⁾

1) Department of International Affairs and Tropical Medicine, Tokyo University

2) Malaria Research Laboratory, Department of Medicine, Karolinska University Hospital

3) Department of Immunology, Stockholm University

4) Department of Immunogenetics, Institute of Tropical Medicine (Nippon Medical School), Tokyo University

5) School of Medicine and Health Sciences, University of Papua New Guinea

6) Department of Epidemiology, National Institute of Public Health

7) Department of Pathobiology, Faculty of Science, Mahidol University

Abstract: In malaria endemic areas, people naturally acquire an age-dependent immunity to malaria. Part of this immunity involves anti-malarial specific antibodies. The level of malaria-specific antibodies depends not only on exposure to malaria but also on the human genetic predisposition. CTLA-4 is a costimulatory molecule that provides an inhibitory signal to suppress T-cell as well as B-cell responses. We investigated the association between malaria-specific antibody levels and CTLA-4 polymorphisms in a hyper-endemic area of Papua New Guinea (PNG), where both *P. falciparum* and *P. vivax* are prevalent. We determined *P. falciparum*/*P. vivax* specific antibody levels (total IgG, Pv-IgG, Pf-IgE, Pv-IgE) and polymorphisms in the CTLA-4 gene promoter region (A/G), the +49 exon 1 non-synonymous mutation (G/G) and the 3'-UTR (A/G). All quantified antibody levels were significantly higher in subjects > 5 years of age (n = 150) than in subjects ≤ 5 years of age (n = 39). In children ≤ 5 years of age, significant associations were detected between CTLA-4 +49 (GG/AG vs. AA) and total IgG (18.7 vs. 13.7 Mg/ml, P = 0.017) and Pv-IgE (266.6 vs. 146.5 pg/ml, P = 0.008). No significant difference was observed in subjects > 5 years old. These results suggest that CTLA-4+49 polymorphism influenced Pv-IgG and Pv-IgE levels at five years old in the studied population, which may regulate the age-dependent clinical outcomes of malaria infection.

Key words: [CTLA-4](#), [IgG](#), [IgE](#), [malaria](#), [polymorphism](#)

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