'Benign' malaria key driver of human evolution in Asia-Pacific

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The malaria species rampant in the Asia-Pacific region has been a significant driver of evolution of the human genome, a new study has shown. An international team of researchers has shown that *Plasmodium vivax* malaria, the most prevalent malaria species in the Asia-Pacific, is a significant cause of genetic evolution that provides protection against malaria.

Their finding challenges the widely-accepted theory that *Plasmodium falciparum*, which causes the most lethal form of malaria, is the only malaria parasite capable of driving genome evolution in humans. The study was published today in the journal PLOS Medicine.

Professor Ivo Mueller from the Walter and Eliza Hall Institute and Barcelona Centre for International Health Research (CRESIB) led the study, with colleagues from the Papua New Guinea Institute of Medical Research, Centre of Global Health and Diseases, US, and the University of Western Australia.

Malaria is a devastating parasitic disease that kills up to one million people a year. It is a major cause of poverty and a barrier to economic development. Approximately half of the world's population is at risk of malaria infection.

"Humans and malaria parasites have been co-evolving for thousands of years," Professor Mueller said. "Malaria has been a major force in the evolution of the human genome, with gene mutations that provide

humans with some protection against the disease being preserved through natural selection because they aid in survival."

Professor Mueller said the study has challenged the perception that *P. falciparum* malaria is the only malaria species that affects human genome evolution. "It has long been assumed that Plasmodium falciparum, the species that causes the most severe disease and most deaths from malaria, is the most important driver of this gene selection in humans," Professor Mueller said. "Our results suggest that *P. vivax* malaria, though until recently widely considered to be a 'benign' form of malaria, actually causes severe enough disease to provide evolutionary selection pressures in the Asia-Pacific."

Professor Mueller said that the research team was interested in whether *P. vivax* malaria might be the cause of the unusually high rates of Southeast Asian ovalocytosis (SAO), a hereditary red blood cell disorder, in the Asia-Pacific region. "SAO occurs in approximately 10 to 15 per cent of the population in parts of the South West Pacific and is caused by a hereditary mutation in a single copy of a gene that makes a red blood cell membrane protein. This is almost an absurdly high frequency when you consider that inheriting two copies of the mutation is invariably fatal, so we figured it must confer a strong advantage to the carriers," he said.

The research team looked at the incidence of *P. vivax* and *P. falciparum* infections in three studies that included a total of 1975 children in Papua New Guinea aged 0-14 years. "We found that SAO-positive children were significantly protected against *P. vivax* infection, with 46 per cent reduction of clinical disease in infants with little or no immunity, and 52-55 per cent reduction in the risk of infection in older children. We also saw a significant decrease in parasite numbers in infants and older children, which is linked to a decrease in risk of clinical disease," Professor Mueller said.

The finding could have dramatic implications for future malaria vaccine design and development, Professor Mueller said. "Studying the mechanisms that cause SAO-positive people to be protected against *P. vivax* malaria could help us to better understand the mechanics of infection and help us to identify better targets for a malaria vaccine," he said.

Provided by Walter and Eliza Hall Institute