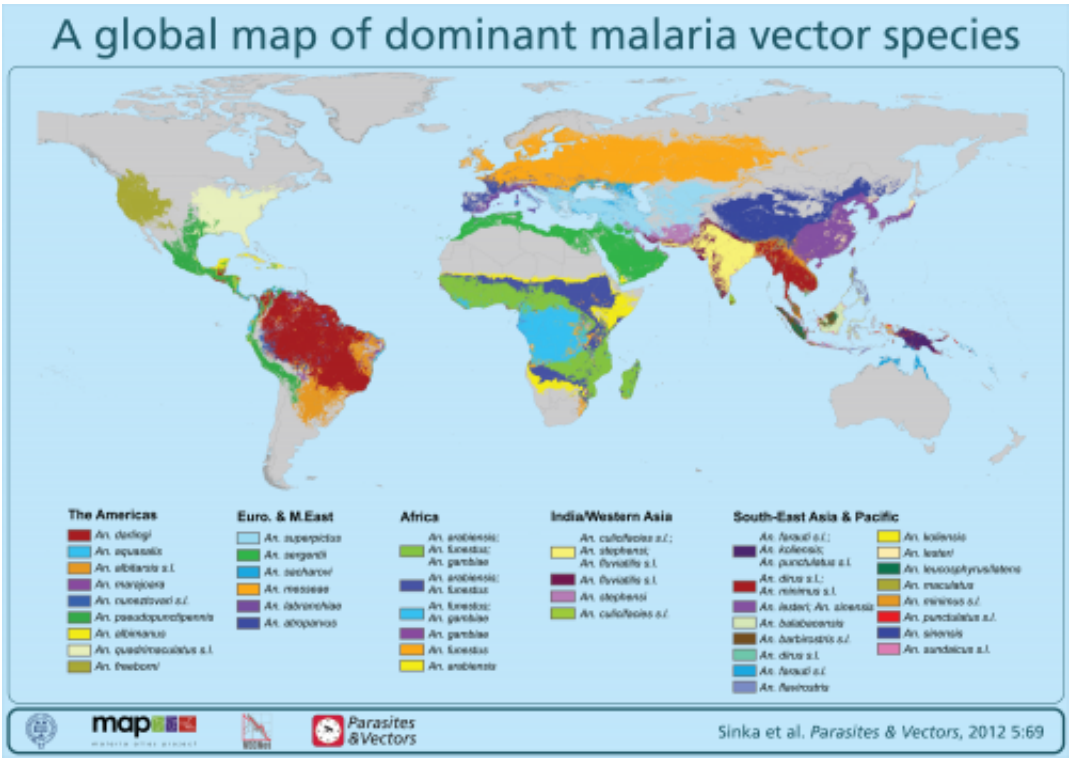
Malaria in the Americas presents a complex picture

July 11 2013



The anopheles mosquito is the vector carrying malaria around the globe, but as this map illustrates, there are many varieties within the anopheles genus. Credit: The Biodesign Institute at Arizona State University

(Phys.org) —Human migrations – from the prehistoric epoch to the present day – have extended cultures across the globe. With these travelers have come unwanted stowaways: mosquito-borne parasites belonging to the Plasmodium species – a group responsible for malaria,

worldwide.

As part of a team of collaborators from 10 countries, Ananias Escalante, a researcher at Arizona State University's Biodesign Institute, has been tracking the tenacious global spread of one of these malarial parasite species: Plasmodium vivax, the most prevalent cause of malaria in many countries outside of Africa. In a new study, this international team explores the genetic diversity of P. vivax in the Americas and other areas of the world.

"The strongest results from the study are that the populations of this parasite in the Americas are highly diversified," Escalante says. The analysis further found that, contrary to most existing assumptions, some genetic lineages in the Americas are very old, though they may not have originated in the New World. Much of this genetic diversity had been missed in previous surveys, due to insufficient sampling of large regions of the continent.

The new findings – which recently appeared in the journal *Molecular Biology and Evolution*, co-authored by ASU researchers Jesse Taylor and Maria A. Pacheco, together with a team of collaborators from 12 institutions – undermine earlier assumptions about the low genetic diversity of P. vivax across the Americas and raise new questions about the time of arrival and events leading to its New World introduction.

Given that genes evolve in measurable time frames, greater diversity suggests earlier and/or multiple introductions of the pathogen. The findings in the new study stand in contrast to earlier assumptions of a recent, single introduction of P. vivax in the Americas, which were based on the limited genetic diversity previously reported. The surprising results indicate that the diversity of vivax in the Americas is comparable to Asia and Oceania, and several divergent South American sequences may indicate multiple independent introductions.

In addition to changing the predominant picture of malarial diversity in the Americas, the study has important implications for control and eradication efforts, as well as potential vaccine design. The geographic distribution of malarial diversity in the Americas was shown to be a distinct relative to Asia and Ocenania (where this malarial parasite is also highly prevalent), indicating different migrational patterns. While many Asian populations usually show wide genetic diversity, the picture is different in the Americas, where large geographic swaths may remain fairly isolated.

"The population structure we observed is, relatively speaking, good news because it means that malaria can actually be controlled or eliminated in the Pacific coast of Colombia, independently of what is happening in the Pacific coast of Peru, with only mild risk of reimportation," Escalante says. "One could envision independent malaria control programs by defining a spatial scale at which the low migration of infected humans makes the risk of reintroduction neglible."

Based on the statistical analysis of a worldwide expanded sample of complete mitochondrial genome sequences, the study estimates that the global population of P. vivax increased slowly until about 60,000 years ago. After this time it underwent rapid, exponential growth, tapering off around 10,000 years ago. Such estimates are in general agreement with known demographic histories of human migration, particularly the rapid divergence of African and European populations.

While the origins of vivax in the New World remain speculative, the study proposes two plausible models that are consistent with the data on genetic divergence and that do not exclude each other. In one scenario, ancient vivax strains may have been introduced into the Americas with pre-Colombian migrations via Beringia, 15,000 to 30,000 years ago. Alternatively, many vivax lineages in the Americas could have originated from now-extinct vivax variants from Europe or other regions.

Current theory suggests that the pathogen originally made a host switch from a non-human primate – an event that most likely occurred in Asia. The high genetic diversity of P. vivax observed in Asia and Oceania lends support to the idea. By contrast, the demographics of vivax in the Americas have received less attention and the dynamics of the new world populations remain somewhat shadowy.

Persistent and deadly

Malaria continues to cut a swath of destruction in many parts of the world. Globally, some 2.6 billion people are at risk of malarial infection and around 200 million cases occur each year, according to the World Health Organization. Some 3,000 children per day die of the disease in sub-Saharan Africa, or about one child every 30 seconds. The Americas also have been seriously impacted, though here, most cases of the disease are caused by the P. vivax parasite, as opposed to the highly virulent P. falciparum species, which reigns supreme in Africa.

While falciparum malaria remains the leading killer, vivax is the most geographically widespread malarial parasite. Due to lower mortality rates associated with P. vivax compared with P. falciparum, vivax malaria has been referred to in the past as "benign tertian malaria," though Escalante insists this is a misnomer. "People are starting to see vivax with different eyes. It's more aggressive. It may not be as aggressive as falciparum, but there's nothing benign about it."

Indeed, severe health complications associated with vivax malaria may be more common than once appreciated and include anemia, low neonatal birth weight and a dangerous decrease in the amount of platelets in the blood (a condition known as thrombocytopenia). Additionally, the complex nature of P. vivax infection makes eradication challenging. The disease is contagious very early in the infection process, increasing the probability of transmission while a patient is still pre-clinical and

symptom-free.

Thorough treatment leading to the complete elimination of the P. vivax parasite from the body requires an intense regimen of medication, lasting for 14 days. A failure in strict compliance can result in the parasite surviving in the liver and redeveloping over time to produce another full-blown bout of malaria (which may again be transmitted through mosquitoes).

A more complete understanding of P. vivax genetic diversity and its evolution are essential for improving control measures. The low local, but high regional diversity of vivax in the Americas points to low rates of gene flow between geographically distinct regions. Many of these areas are primarily agricultural, with very limited in- or out-migration of the populations. Escalante notes that this significantly improves the possibilities for malarial containment and perhaps, thorough elimination of the disease in many parts of the Americas. At the same time, the greatly expanded genetic diversity of P. vivax presents new challenges for the eventual development of a comprehensive vaccine.

More information: mbe.oxfordjournals.org/content …/06/01/molbev.mst104

Provided by Arizona State University