Malaria parasite in the Americas is more genetically diverse than previously thought

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Credit: CDC

The populations found in the Americas of *Plasmodium vivax*, one of the main human malaria parasites, are as genetically diverse as those found in Southeast Asia, where malaria transmission is much more frequent.

Because *P. falciparum*, the predominant species of malaria parasite, displays low genetic diversity in the Americas compared with other

regions, scientists believed the same was true for P. vivax. This belief is mistaken, according to a study by researchers at the University of São Paulo (USP) in Brazil, in collaboration with colleagues from Rio de Janeiro, Uruguay and the United Kingdom. The results were published in *PLOS Neglected Tropical Diseases*.

Principal investigator for the study, Marcelo Urbano Ferreira stated that the study presented surprising results. "The discovery that populations of *P. vivax* in the Americas are more diverse than populations of *P. falciparum* was surprising. If we accept the hypothesis that both *P. falciparum* and *P. vivax* came to the Americas after European colonization, we would expect to find similar levels of genetic diversity in both species, as they would have undergone an intense population squeeze during their 'migration' to the New World. However, this is simply not the case," said, the Brazilian scientist, a professor in the Parasitology Department of the Biomedical Science Institute at the University of Sao Paulo (ICB-USP).

The study of *P. vivax*'s genetic diversity in the Americas seeks clues to the origin of the many lineages or populations found on the continent.

Upon arriving in the Americas, *P. vivax* appears to have retained much more of its existing diversity, as in Africa for example, than *P. falciparum*.

"A possible explanation is that the populations of *P. vivax* that came to the Americas originated in a wider geographical area, including Africa, Europe and perhaps Asia, than the populations of *P. falciparum* that came here, as these were predominantly African, but this has yet to be demonstrated," Urbano Ferreira said. The investigator coordinates the Thematic Project intitled "Scientific bases for residual malaria elimination in the Brazilian Amazon", supported by the São Paulo Research Foundation - FAPESP.

Ancient lineages may have come to the Americas, and depending on the magnitude of the migration (the number of individuals involved), they may have lost little diversity on the way.

Some lineages may have come to Brazil in the nineteenth century with immigrants from Italy and Spain, where malaria was endemic until the mid-twentieth.

"The diversity of *P. vivax* in Brazil is substantial, given more than 300 years of slave trading, one of the ways the parasite migrated. However, it entered Brazil in many ways at different times, not least in the nineteenth century with the first wave of immigrants," said Thaís Crippa de Oliveira, a PhD student at ICB-USP and first author of the article published in *PLOS Neglected Tropical Diseases*.

Methodology

Blood samples were collected from patients in Northwest Brazil, more precisely in the cities of Acrelândia and Remansinho, near the border with Peru and Bolivia. Brazil accounts for 37% of all malaria cases reported in the Americas. All nine patients were found to be infected with *P. vivax*.

The parasites in the samples were separated, and their nuclear DNA was isolated and subjected to whole-genome sequencing. To place these sequences in a regional context, the researchers performed whole genome sequencing of 75 other clinical isolates of *P. vivax* from Brazil (2), Peru (23), Colombia (31) and Mexico (19) obtained via international gene banks.

All this material was analyzed in search of single-nucleotide polymorphisms (SNPs), widely used as markers of differentiation and in this case capable of establishing diversity among the parasites sampled.

The study showed that the genetic diversity found in Brazil's *P. vivax* population is similar to that found in other countries of the Americas.

The analysis of *P. vivax*'s nuclear genome sequence was performed using three populations from the Americas. "For now, we have genome data for parasites from only four countries in the Americas. Even within each country, we don't have a representative sample," Urban Ferreira said. "Many lineages are undoubtedly circulating in the Americas, far more than three, but owing to the intense genetic recombination to which most of them are exposed these lineages aren't stable. Genetic recombination quickly creates new 'recombinant' variants that circulate on the continent. It's highly likely that clonal lineages aren't being transmitted along several generations of parasites."

"This research is a work in progress," Urbano Ferreira said. "So far, the available data, both ours and those of other research groups, suggests P. vivax came to the Americas from Africa, Europe and Asia. It's also possible there was a contribution from Oceania, but this needs to be confirmed," Urbano Ferreira said. "Mitochondrial genomes are very useful in these studies, but we certainly need more complete nuclear genomes to make more definitive inferences."

According to the researcher, it would simplistic to assume that all the genetic diversity found in the populations of these parasites in the Americas today has come about in the past 500 years. This would be the case only if the migration had involved a "founder effect", i.e., if only one or very few lineages had come to the continent and all the parasites currently alive on the continent were descendants of those first lineages.

"Mitochondrial genomes are very useful in these studies, but we certainly need more complete nuclear genomes to make more definitive inferences," stresses Urbano Ferreira.

The researchers are now working on a new sample collected by Urbano Oliveira from a single community during 12 months of study.

Whole-genome sequencing of these parasites will enable them to evaluate the levels of genetic variation in populations of P. vivax over time and infer some of the mechanisms that contribute to such variation, including migration and recombination.

More information: Thais C. de Oliveira et al, Genome-wide diversity and differentiation in New World populations of the human malaria parasite Plasmodium vivax, *PLOS Neglected Tropical Diseases* (2017). DOI: 10.1371/journal.pntd.0005824

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