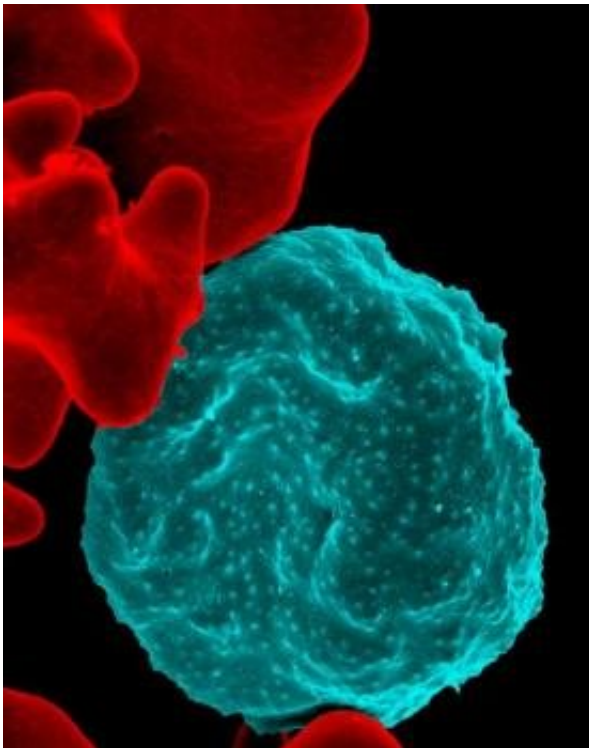


Ape parasite genomes reveal origin, evolution of leading cause of malaria outside Africa

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Colorized scanning electron micrograph of red blood cell infected with malaria parasites, which are colorized in blue. The infected cell is in the center of the image area. To the left are uninfected cells with a smooth red surface. Credit: NIAID

The genome sequences of ape parasites related to *Plasmodium vivax* (*P. vivax*), the main source of mosquito-borne malaria outside Africa, provide insights on the origin and early evolution of the human parasite.

This finding could have implications for better comprehending and eradicating malaria infection worldwide, according to new research from the Perelman School of Medicine at the University of Pennsylvania and the University of Edinburgh, published this week in the *Proceedings of the National Academy of Sciences*.

While not as deadly as malaria caused by *Plasmodium falciparum*, *P. vivax* malaria is debilitating and widespread, potentially infecting about one third of the world's population, mainly in Asia and Latin America. Most people in Africa are not at risk for infection by *P. vivax* malaria because they carry a genetic mutation that makes them resistant to this strain. However, African apes living in the wild are naturally infected with [parasites](#) that are very similar to those infecting humans. The researchers caution that it is important to monitor new cases of *P. vivax* infection in central Africa to determine whether any reflect ape-to-human transmissions.

"Chimpanzees, bonobos, and gorillas all harbor parasites that are close relatives of human *P. vivax*, but to date our knowledge of these parasites has been limited to a small number of gene fragments," said co-senior author Beatrice Hahn, MD, a professor of Medicine and Microbiology at Penn.

In this study, researchers compared almost-full-length genomes of ape parasites with sequences of *P. vivax* strains infecting humans worldwide.

"We found that ape and human parasites share near-identical genomes, differing by only two percent within the gene sequences that code for proteins," said Dorothy Loy, an MD/Ph.D. student in Hahn's lab.

After generating sequences of parasites infecting chimpanzees and gorillas, the team found that ape *P. vivax* show very different patterns of genetic diversity, compared to their human counterparts. They also

found no evidence that the ape *P. vivax* parasites discriminate which ape species they infect.

"We discovered that ape parasite strains show about 10 times more genetic diversity compared to their human-infecting counterparts," said Lindsey Plenderleith, Ph.D., from the Edinburgh team. This suggests that some time in the past the human parasites underwent a severe reduction in their population size, leading to a massive loss of genetic variation.

From an ancient population of *P. vivax* parasites, which likely infected both humans and apes in Africa, a "bottlenecked" parasite population emerged when *P. vivax* migrated with humans out of Africa. This once-small parasite population subsequently underwent a rapid population expansion as it dispersed over much of the globe, while the spread of the malaria-protective mutation eliminated *P. vivax* from people in most of sub-Saharan Africa.

Based on additional testing of certain *P. vivax* proteins associated with the parasites' ability to invade host red blood cells, the team also concluded that it is possible that ape and human strains could infect the same hosts and undergo genetic exchange if their geography overlapped.

Recently, reports of *P. vivax* infection of humans in Africa have been increasing. "Since parasites very similar to human *P. vivax* infect a large number of wild-living apes, we need to be aware that there could be spillover into humans," said co-senior author Paul Sharp, Ph.D., an evolutionary biologist at the University of Edinburgh. The team cautions that malaria monitoring programs should keep a watch to see if the genetic diversity of the ape parasites is infiltrating human-infecting strains.

More information: Dorothy E. Loy et al., "Evolutionary history of

human *Plasmodium vivax* revealed by genome-wide analyses of related ape parasites," *PNAS* (2018).

www.pnas.org/cgi/doi/10.1073/pnas.1810053115

Provided by Perelman School of Medicine at the University of Pennsylvania

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