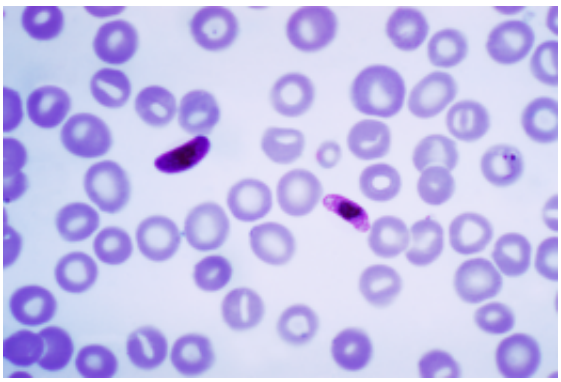
Study shows Plasmodium falciparum emerged earlier than thought and gives clues to how deadly parasites arise

May 21 2018



This photomicrograph of a blood smear contains a macro- and microgametocyte of the Plasmodium falciparum parasite. Credit: Wikipedia.

The evolutionary path of the deadliest human malaria parasite, *Plasmodium falciparum*, has been revealed for the first time. This parasite is a member of a parasite family called the Laverania that only infect the great apes including humans, chimpanzees and gorillas. Scientists from the Wellcome Sanger Institute and their collaborators from the French National Centre for Scientific Research, French National Research Institute for Sustainable Development (IRD), and the International Centre for Medical Research of Franceville, Gabon, estimate that *Plasmodium falciparum* emerged as a human-specific parasite species earlier than previously thought.

The results, published today (21 May) in *Nature Microbiology* provide estimated dates at which branches in the evolutionary tree for the Laverania family of malaria parasites diverged, and give clues as to how deadly parasites emerge.

Nearly half of the world's population is at risk of malaria and more than 200 million people are infected each year. The disease caused the deaths of almost half a million people globally in 2016, predominantly children under the age of five.

To discover how *Plasmodium falciparum* evolved, a team of scientists from the Sanger Institute and their collaborators sequenced and studied the genomes of all known malaria parasites in the Laverania family.

Plasmodium falciparum is the only parasite from this group that has successfully adapted to transfer from gorillas to infect humans, and subsequently spread all over the world.

The key challenge of this study was obtaining malaria parasites. The team used blood samples taken from orphaned chimpanzees and gorillas, as part of routine health checks in sanctuaries and nature reserves in Gabon.

Dr. Franck Prugnolle, co-lead author from the MIVEGEC Laboratory in France and the International Centre for Medical Research of Franceville, Gabon, said: "We had to work with tiny blood samples taken from these protected species as part of health check-ups. Even then, there were so few parasites present that we had to devise strategies to amplify the material to obtain good quality genomes."

Scientists discovered that the evolutionary lineage leading to *Plasmodium falciparum* emerged 50,000 years ago, but did not fully diverge as a human-specific parasite species until 3,000 to 4,000 years ago.

Dr. Matt Berriman, co-lead author from the Wellcome Sanger Institute, said: "We sequenced the genomes of all known species in a family of malaria parasites that gave rise to the deadliest form of human malaria. We estimated when *Plasmodium falciparum* and its relatives diverged and found evidence that the recent expansion of modern humans created the home in which the parasites irreversibly evolved into a human-specific form."

The researchers analysed the genomes of the malaria parasites in the Laverania family tree and discovered a chain of events that led to the emergence of *Plasmodium falciparum*.

Dr. Thomas Otto, co-first author now based at the University of Glasgow, said: "Using the parasites' genomic data, we constructed their family tree and identified major genetic events that led to their emergence. The movement of a single cluster of genes was an early crucial event that enabled the malaria parasites to infect the red blood cells of a new host species. After reconfiguring and fine-tuning the repertoires of genes that interact with the host and the vector, the parasites were able to establish long term, transmissible infections in humans."

More information: Thomas D. Otto et al, Genomes of all known members of a Plasmodium subgenus reveal paths to virulent human malaria, *Nature Microbiology* (2018). DOI: 10.1038/s41564-018-0162-2

Provided by Wellcome Trust Sanger Institute