African thicket rat malaria linked to virulent human form

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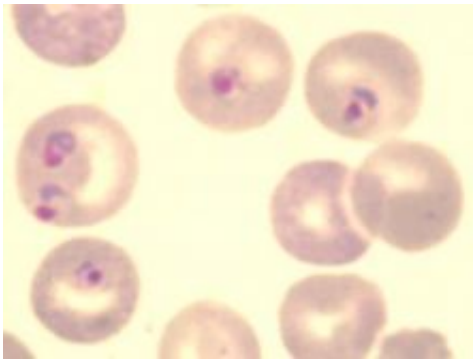

Pictured is the malarial parasite Plasmodium berghei, which is found in African thicket rats. Credit: CJ Janse

Even though the most deadly form of malaria for humans, *Plasmodium falciparum*, has been linked to malaria found in chimpanzees, this group has been fairly isolated on the malarial family tree—until now. A new phylogenetic analysis from the Sackler Institute for Comparative Genomics at the American Museum of Natural History reveals that malarial parasites found in tree-dwelling rats share a close evolutionary relationship with *P. falciparum* and *Plasmodium reichenowi*. The analysis is based on amplification of entire mitochondrial genomes of malarial parasites that use humans, rodents, birds, and lizards as their hosts.

"This is the first time that a relationship has been found between human and rodent malaria," says Susan Perkins, Assistant Curator of

Invertebrate Zoology at the Museum. "In all past studies, *P. falciparum* seemed to not be closely related to anything else but the chimpanzee parasite. But this study places it in a sister group of parasites from rodents."

The maternally inherited mitochondria of *Plasmodium* are among the smallest known in eukaryotes, containing only three protein-coding genes and a total of only about 6,000 nucleotides (the mitochondrial genomes of human and other animals are about 16,000 bases). The genome is also unusual because of its organization into linear, tandemly repeated DNA. These features allowed Perkins to take the unusual step of amplifying the entire genome in a single piece via polymerase chain reaction (PCR) and then sequence it to reconstruct the whole genome. The analysis that produced the phylogenetic tree was based on the sequences of the three protein-coding genes (a total of about 3,300 DNA characters).

The results place the malarial parasites found in African thicket rats, *P. chabaudi*, *P. berghei*,, and *P. yoelii*,, as a sister group of human and chimpanzee *P. falciparum*, and *P. reichenowi*,. This is interesting and surprising because the parasite found in African thicket rats—the only malarial parasite to be discovered first in mosquitoes and only later in a vertebrate host—is the most common laboratory model for human malarial research. The ,*P. falciparum*,-rodent group is most closely related to malarial parasites that infect humans and primates in Asia and other primates in Africa. The other clades defined by this new evolutionary tree follow previously determined evolutionary trees for malaria-causing parasites, published earlier this year by Perkins and colleagues at the University of Vermont. These other phylogenies were based on both mitochondrial and nuclear DNA.

"The link between human malaria and rodent malaria is exciting because, if they really are that closely related, our laboratory models

might be more powerful for helping to study how to fight the disease," says Perkins. She also believes that this link may include more than these species: as-yet unpublished data collected earlier in her lab found a closely related form of *,Plasmodium*, in bats from the same area, and it may be that the most virulent form of malaria jumped into humans from these other arboreal animals. "Like Ebola and SARS, this could be another example of bat-human linkage. Although the results of this study are unambiguous, they are nonetheless still based on just a very small portion of the parasite's entire DNA."

The new paper is published in the early online edition of *Mitochondrial DNA*.

Source: American Museum of Natural History