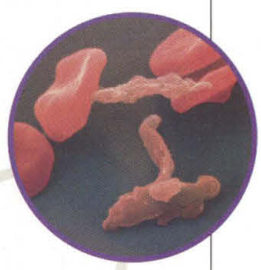
# *Anopheles gambiae* Genome: Completing the Malaria Triad

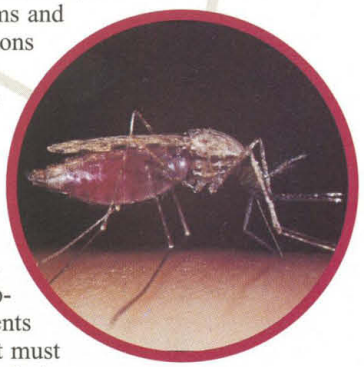


The genome sequence of *Anopheles gambiae*, the major mosquito vector of the malaria parasite *Plasmodium falciparum*, as well as analyses of its gene content and organization, are reported by several teams of investigators in this issue.* In addition, the sequence of the *P. falciparum* genome appears in this week's issue of *Nature*. The genomes of these two organisms, along with that of the human, provide a triad of critical genetic information relevant to all stages of the malaria transmission cycle and offer unprecedented opportunities to the scientific and public health communities engaged in the fight against malaria, a disease that takes a huge toll on humanity.

Hundreds of millions of malaria cases and nearly three million malaria-related deaths are estimated to occur each year, predominantly in sub-Saharan Africa; however, more than 40% of the global population lives in countries where the disease is endemic. *P. falciparum*, the most lethal malaria parasite, is transmitted from one human to another by *A. gambiae* and other anopheline mosquito vectors. These insects are both efficient vehicles of malaria transmission and the Achilles' heel of the transmission cycle. It was primarily through vector control efforts that malaria was nearly eradicated in the middle of the 20th century in the Americas, India, and Asia. Even in Africa, where transmission is most intense, vector control remarkably reduced the burden of malaria. The formal World Health Organization eradication effort was stopped just short of its goal for many reasons, including problems with insecticides. An immediate goal for using the genomic sequence data for *A. gambiae* will be to identify targets for new and environmentally sound approaches to vector control.

The availability of the genomic sequence data for each of the three organisms involved in malaria transmission will clarify the pathophysiologic relationships among human host, parasite, and vector. Among the many issues that can now be better addressed are the mechanisms of the range of refractoriness of the *Anopheles* species to *Plasmodium*, evasion of host immunity by the parasite, resistance to insecticides and antimalarial drugs, and identification of potential vaccine antigens. This research may allow targeting of control efforts or manipulation of genomes to reduce transmission or disease.

The *A. gambiae* genome contains significant levels of genetic polymorphism that present a challenge for assembly as well as an unprecedented opportunity to address questions of population biology. Existing assembly paradigms have difficulty distinguishing repeated sequences from diverged haplotypes (see Holt *et al.* in this issue, p. 129). The haplotype pattern provides insight into the ecological and evolutionary history of the organism, especially with regard to the various cytotypes that are considered to be incipient species. Single nucleotide polymorphisms and other markers offer the opportunity to study gene flow through mosquito populations and predict the likely spread of traits such as resistance and refractoriness.



The bulk of the sequencing work for *A. gambiae* was completed in a public-private partnership that, although not the first of its kind, is another shining example of the possibilities of such programs. The high degree of cooperation and collaboration among all of the many researchers involved made this extraordinary achievement possible. Many additional partners, especially in malaria-endemic countries, will be required if we are to take full advantage of the potential fruits of this project.

The genomic advances reported this week promise to foster new collaborations and a concordance of resources in malaria research. The challenge and opportunity for scientists is to use the freshness and excitement of these developments to forge new relationships, develop new tools, and ask the critical questions that must be answered if we are to reduce the enormous and unrelenting global burden of malaria.

**Kathryn S. Aultman, Michael Gottlieb, Maria Y. Giovanni, Anthony S. Fauci**

Kathryn S. Aultman is Vector Biology and Ecology Program Officer at the National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health, Bethesda, MD. Michael Gottlieb is chief of the Parasitology and International Programs Branch, NIAID. Maria Y. Giovanni is assistant director for Microbial Genomics and Advanced Technologies, NIAID. Anthony S. Fauci is the director of NIAID.

*The *A. gambiae* sequence data are all available in publicly accessible online databases at the European Bioinformatics Institute (www.ebi.ac.uk), the National Center for Biotechnology Information (www.ncbi.nlm.nih.gov), and elsewhere.

CREDITS: (CLOCKWISE FROM TOP RIGHT) MECKES/OTTAWA/PHOTO RESEARCHERS INC.; JIM GATHANY/CDC; DIGITAL STOCK CORP.