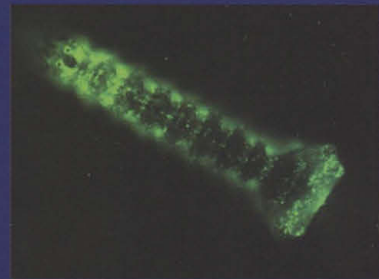


MOS

The mosquito *Anopheles gambiae* is the insect vector that transmits malaria in sub-Saharan Africa, where almost 90% of the world's malaria deaths occur. More than 1 million people, primarily infants and young children, die each year from malaria, principally caused by the parasite *Plasmodium falciparum*. Although much research has focused on understanding the parasite, vector control efforts have historically had the biggest impact. High-density physical and genetic maps of *A. gambiae* have been developed and used to map phenotypes such as insecticide resistance and parasite refractoriness, and transposon-based tools for germ line transformation are now available (green fluorescent protein-transformed larva, above right). Analysis of naturally occurring chromosome inversions (right) and physical map) has shown that *A. gambiae* is a highly polymorphic species composed of a number of chromosomal "forms,"



J. R. Clayton and M. Q. Benedict,



M. Coluzzi, Università degli Studi "La Sapienza," Rome, Italy

each specialized for a different environment associated with human habitation. The genome sequence of *A. gambiae* will enhance our understanding of the biology of this insect, leading to new strategies for control and possibly even eradication of malaria and other mosquito-borne tropical diseases. Beyond its association with disease, the sequence will promote basic research on other arthropods and serve as a window into insect evolution and biology. Further information can be found in the 4 October 2002 issue of *Science*.



SQU Anophe



J. R. Clayton and M. Q. Benedict,
CDC, GA, USA

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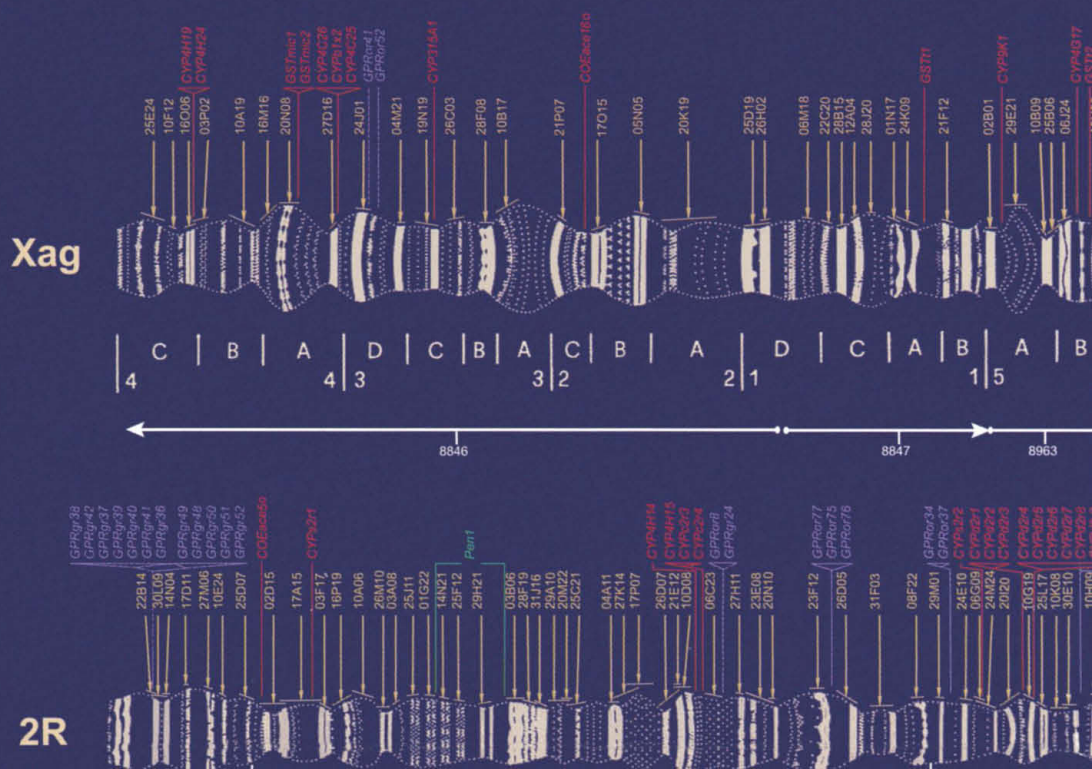
M. Sharakhova, Univ. of Notre
Dame, IN, USA

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A Sampling of the Physical Map

- Bacterial artificial chromosome (BAC) clones
- Insect defense genes
- G protein-coupled receptors for host finding and blood feeding
- Insecticide resistance genes

The diagram of the *A. gambiae* polytene chromosomes was cr
sequence scaffolds that has been mapped and ordered across
being identified by the last four digits of their scaffold ID (e.g.
Oriented scaffolds are marked with arrows at the 3' end. Scaff
The chromosome regions spanned by some of the 2R inversion
are shown (e.g., +1 is the uninverted or wild-type orientation
by C. Blass (1), E. Kokoza (2), A. della Torre (3), A. Cornel (4),
associated with the polytene map was assembled and placed l

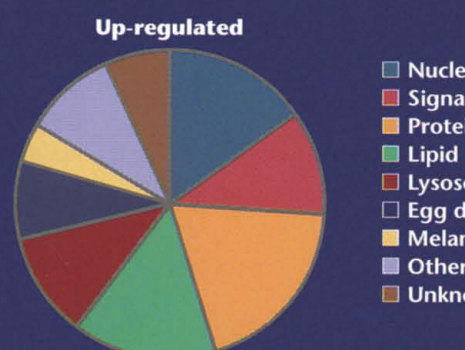
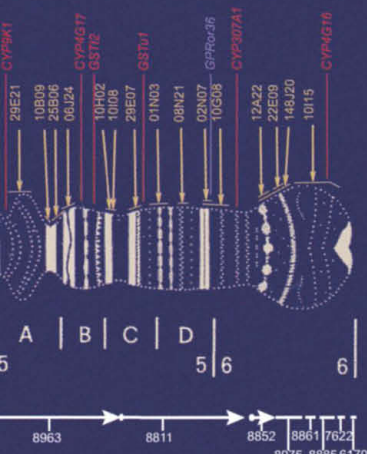


II *meles gambi*

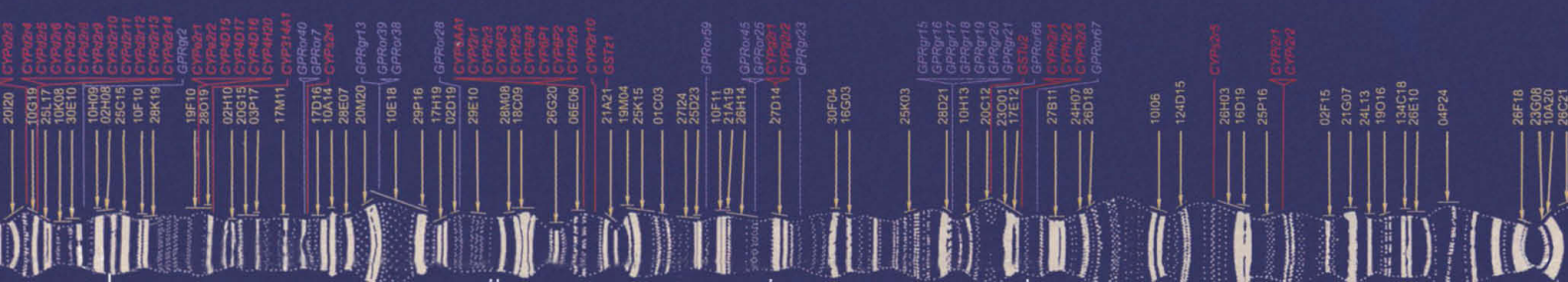
Gene Ex

was created by M. Coluzzi and V. Petrarca (3). The set of
d across the genome is shown with the individual scaffolds
ID (e.g., scaffold AAAB01008880.1 is represented by 8880).
nd. Scaffolds that cannot be oriented do not have arrows.
inversions used to identify chromosomal forms of *A. gambi*
entation of the 2Rj inversion). BAC clone mapping was done
rnel (4), M. Sharakhova (5), and X. Wang (5). All information
placed by M. Unger and F. Collins (5).

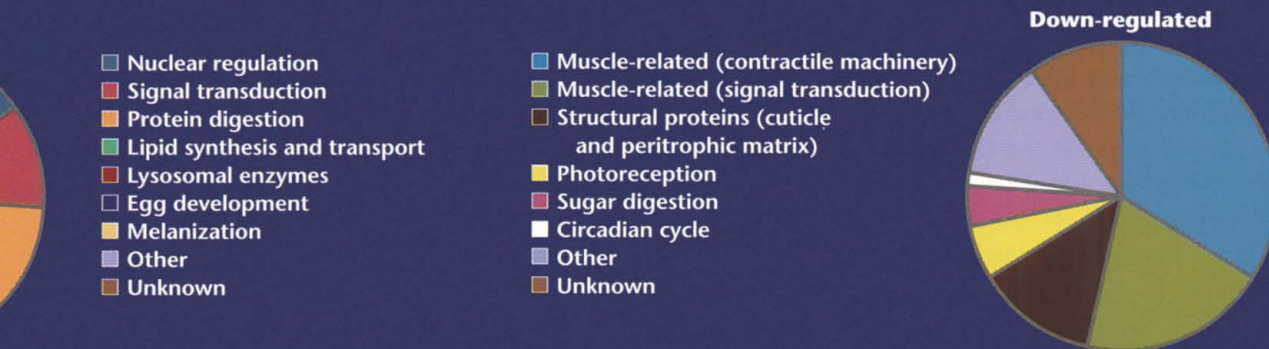
- (1) European Molecular Biology
Laboratory, Heidelberg, Germany
- (2) Institute of Cytology and Genetics, N
Russia
- (3) University degli Studi "La Sapienza,
- (4) University of California, Davis, CA,
- (5) University of Notre Dame, Notre I



To survive and produce eggs, the female
quito ingests up to four times its own w
blood. Interfering with that process coul
powerful means of insect control. To ide
genes differentially expressed in respon
to a blood meal, Holt *et al.* (above and
Science, 4 October 2002) compared app
imately 40,000 expressed sequence tags
(ESTs) from blood-fed female *A. gambi*
with an equal number of ESTs from fem
mosquitoes fed only a sugar solution.

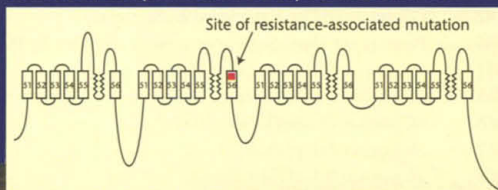


Gene Expression in Blood-Fed Mosquitoes

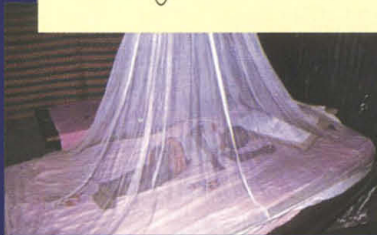


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H. Ranson, Liverpool School of Tropical Medicine, UK



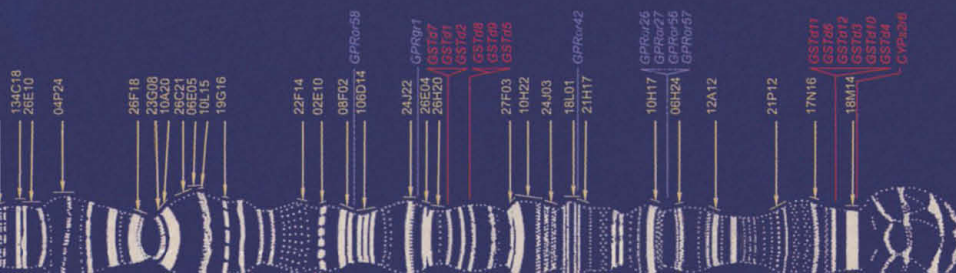
J. Hemingway/WHO



Insecticides continue to be important components of most malaria control strategies, and insecticide-treated bed nets are now widely used. Unfortunately, resistance to permethrin and other pyrethroid insecticides has already appeared in *A. gambiae* populations in several African countries.

Mutations have been identified in the gene encoding the sodium channel protein that is the target of action of pyrethroid insecticides (above, left; *VSC1* on map), and up-regulation of metabolic enzymes in the

glutathione-S-transferase and cytochrome P450 gene families, which help degrade and detoxify insecticides, also contributes to resistance (GSTs and CYPs on map). Also shown on the map are two acetylcholinesterase genes (*COEac16a* and *COEac5a*) and



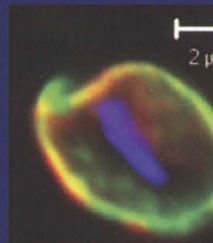
Malaria parasites must evade a complex array of mosquito defenses to successfully complete their long and complex life cycle in the mosquito host. In one strain of *A. gambiae*, the mosquito blocks parasite development by encapsulating and killing the ookinete stage as it completes its transit of the midgut cells (left). Different mechanisms of *Plasmodium* inhibition have been identified and mapped in other strains, and candidate genes are now being identified.

S. M. Paskewitz, Univ. of Wisconsin, Madison, WI, USA

K. Sutliff/*Science*

One of the important biological traits that make *A. gambiae* such an efficient vector of malaria parasites is its strong preference for blood feeding on humans. Analysis of the mosquito genome has revealed two large multigene families encoding odorant and gustatory receptors (*GPRors* and *GPRgrs* on map), some of which should be important in this host specificity.

Understanding the complex organization of the mosquito immune system will likely lead to innovative strategies for malaria control. Thioester-containing proteins (TEPs) are involved in pathogen recognition and thus may activate parasite-specific immune responses in the mosquito, in the same way that their functional homologs, the complement factors, do in mammals. This confocal microscope image (right) shows a *Plasmodium* ookinete on the basal side of the mosquito midgut. Antibody staining: TEP1 (green); a parasite surface protein, Pbs21 (red); nucleus (blue), colocalization of TEP1 and Pbs21 (yellow).



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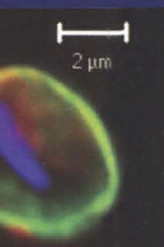
Proofreading: Harry Jach

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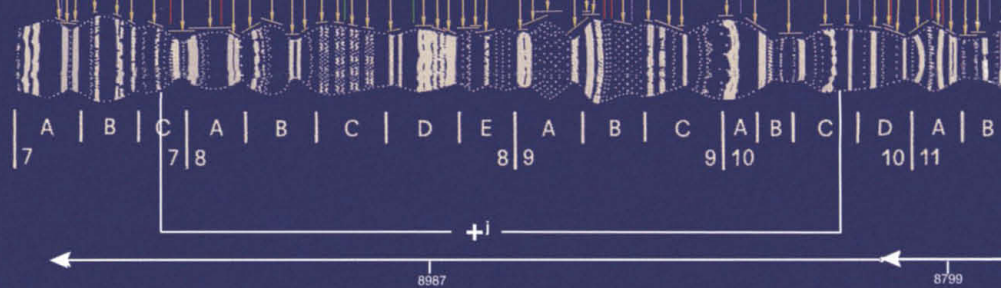
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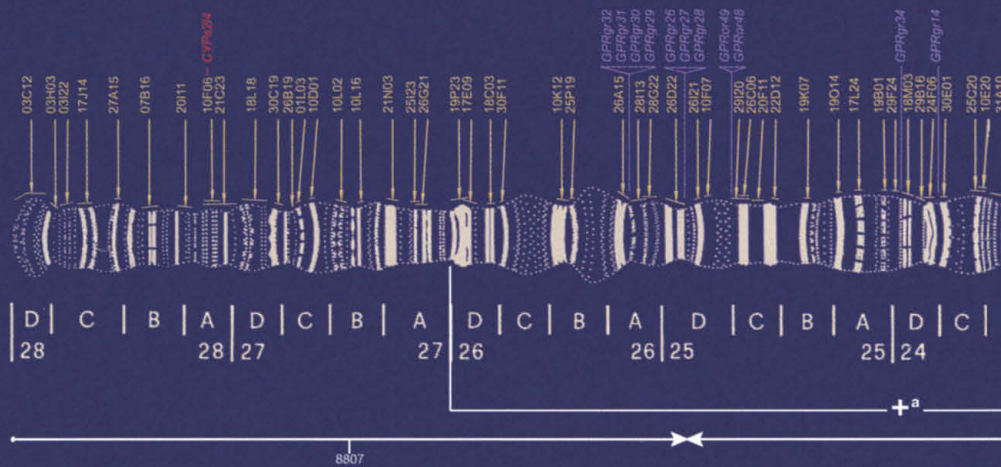
, Fort Collins, CO,

Training in Tropical Diseases

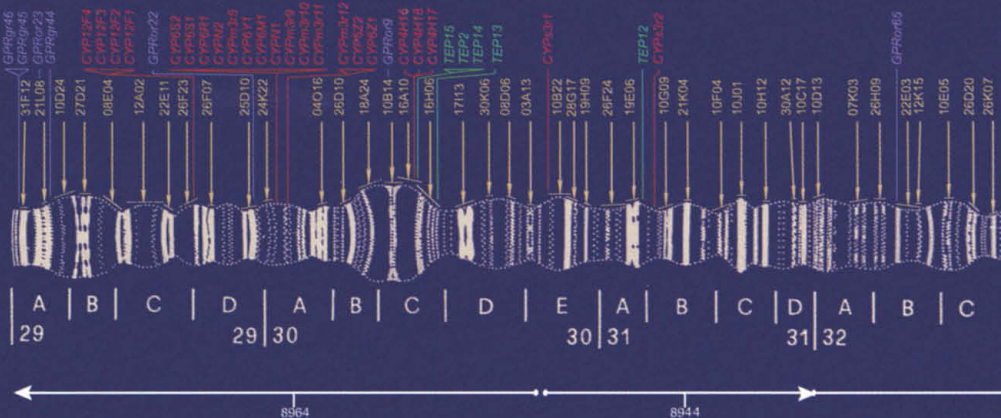
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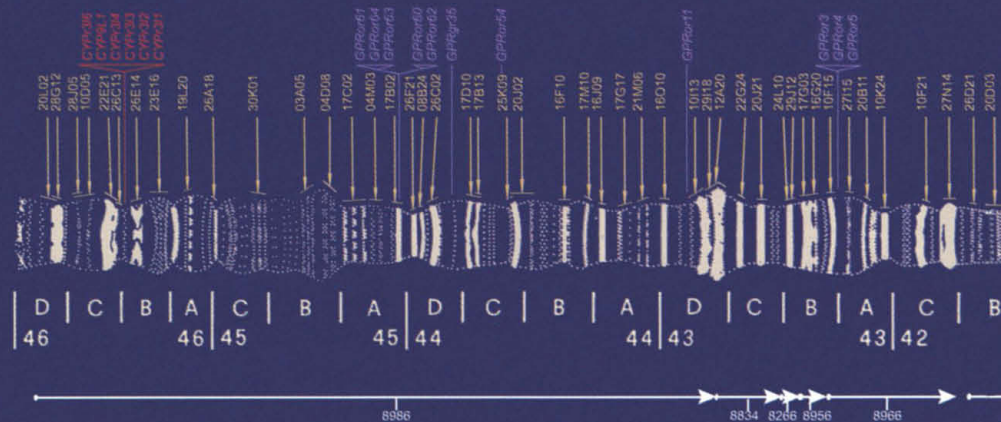
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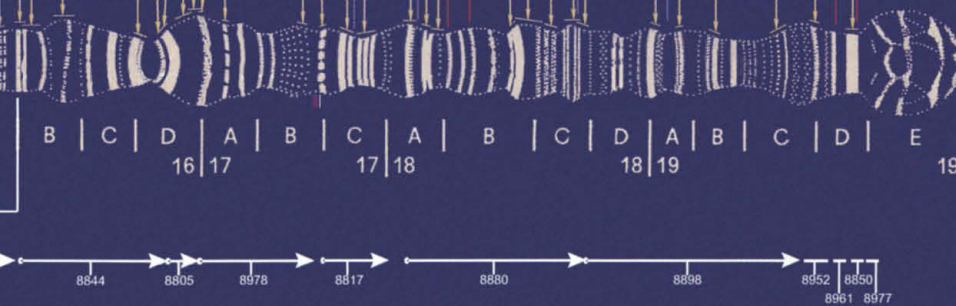


3L



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Sequence data and other information about *Anopheles gambiae*:

A. gambiae genomic and cDNA clones: <http://www.malaria.mr4.org>
 EBI Ensembl Mosquito Map: http://www.ensembl.org/Anopheles_gambiae/
 GenBank: http://www.ncbi.nlm.nih.gov/cgi-bin/Entrez/map_search?chr=agambiae.inf
 Flybase: <http://www.flybase.org>
 Genoscope: <http://www.cns.fr/externe/English/Projets/Resultats/rapport.html>
 AnoDB: <http://konops.imbb.forth.gr/AnoDB>
 Mosquito Genomics: <http://mosquito.colostate.edu>
 Plasmodium Genomics: <http://www.PlasmoDB.org>

the map are two acetylcholinesterase genes (*COEace160* and *COEace50*) and the gene encoding a GABA receptor (*GGCC1*); these three genes encode proteins targeted by other classes of insecticides. Genomic information is expected to facilitate the development of better tools for tracking insecticide resistance and to guide the rational design and selection of alternative insecticides.

