

## PROTIST WEB ALERT

# Malaria – The Biological Terminator

Malaria, which is caused by the apicomplexan protist, *Plasmodium*, is the major re-emerging disease throughout the world. More than 40% of the world's population suffers from this disease and it is especially lethal for children. To make this topically appreciated, the Malaria Foundation International (<http://www.malaria.org/>) stated that "The malaria epidemic is like loading up seven Boeing 747 airliners each day, then deliberately crashing them into Mt. Kilimanjaro." This disease was thought to be almost eliminated in the 1950's and 1960's by global use of DDT to kill the mosquito vectors and the availability of effective drugs, but then it returned with a vengeance, reminding one of the Schwarzenegger "terminator" robot

(<http://www.cs.virginia.edu/oracle/arnie.html>) that could not be killed! The reasons for this resurgence include the political and economic elimination of spraying programs and development of resistance of mosquitoes to DDT, the development of resistance of the parasites to anti-malarial drugs probably aggravated by misuse, and environmental changes caused by human mobility, human overpopulation and industrialization of the tropical forest regions. In addition, climatic warming looms as an almost certain disaster on the near horizon, threatening the movement of malaria into temperate zones. The seriousness of this problem has been recognized by the World Health Organization which has recently initiated a global campaign against malaria with the ambitious title, "Roll Back Malaria" (<http://www.who.int/health-topics/malaria.htm>), and also by TDR (the Special Programme for Research and Training in Tropical Diseases hosted at WHO) (<http://www.who.int/tdr>) which launched a novel "Medicines for Malaria Venture" as a not-for profit, independent organization under Swiss law, in which researchers and public health organizations can interact closely with drug companies for drug development ([http://www.malaria-medicines.org/pages/page\\_main.htm](http://www.malaria-medicines.org/pages/page_main.htm))

Enough said.

There are many excellent web sites dealing with the disease and the parasite and a few excellent sites on the genomic sequencing projects. Due to its notoriety, *Plasmodium* was early selected as a candidate for genomic sequencing and this has now been almost accomplished by a consortium of laboratories

([http://www.sanger.ac.uk/Projects/P\\_falciparum/who&what.shtml](http://www.sanger.ac.uk/Projects/P_falciparum/who&what.shtml)),

in spite of major technical difficulties such as a very high AT% and an instability of clones in *E. coli*. Chromosomes 2, 3 and 5 of the 14 total chromosomes are finished and the rest are in the closure stage, including the infamous "Blob" (= chromosomes 6–8). The availability of the entire 30 Mbp genomic sequence will put research on this protist on a new level, essentially changing the paradigm so that global questions can be asked. This bodes well for the development of new rational chemotherapies and even vaccines.

### PlasmoDB: The Plasmodium Genome Resource

(<http://plasmodb.org/>)

This is an example of how to construct a site that brings together diverse information and makes it easily accessible to both the bioinformatically challenged and the cognoscenti of the *Plasmodium* research community. The site was created by David Roos, Christen Stoeckert and Ross Coppel and maintained by Roos and talented programmers such as Brian Brunk, Jessica Kissinger and others. The sequence information originates from the three major *Plasmodium* genomic sequencing centers, the *Plasmodium falciparum* Sequencing Group at the Sanger Center

([http://www.sanger.ac.uk/Projects/P\\_falciparum/](http://www.sanger.ac.uk/Projects/P_falciparum/)), the Institute for Genomic Research (TIGR) (<http://www.tigr.org/tdb/edb2/pfa1/htmls/>) and the Stanford University DNA Sequencing and Technology Center (<http://sequence-www.stanford.edu/group/malaria/index.html>), and in addition EST and

GSS sequences from a variety of laboratories are integrated into the genomic information. It also includes Optical Mapping Data from the David Schwartz laboratory (<http://www.cmb.wisc.edu/profiles/SchwartzDavid.html>). Sequence data from five *Plasmodium* species are provided and the data appears to be frequently updated.

There is an obligatory initial registration (cookies on, if you please!) and login at each use. A step by step tutorial allows the user to rapidly learn the details of gene searching. The obligatory *Plasmodium*-specific Blast server is provided as well as an E-PCR server which allows one to search the genome for STS markers. A powerful amino acid motif program using Perl regular expressions is better than the standard Prosite analysis available in most gene analysis packages. Text searching within gene descriptions or using sequence features is also provided. A novel feature is the ability to search for genes by functional expression based on EST or microarray data. This should become more valuable as

more laboratories begin utilizing genomic expression analysis. For those without internet access, a CD has been created with the support of TDR with the entire malaria genome sequence database. (<http://plasmodb.org/WHO-CD/WH OCD3/>)

A variety of well documented tools are available for browsing the genomic data such as gene prediction using GlimmerM and Phat, all Blast hits for any contig, and an interesting "Self-Blast" browser, which searches for contamination of sequences between chromosomes.

*A true service to the research community.*

**Larry Simpson**

HHMI-UCLA, 6780 MacDonald Research Laboratories,  
675 Charles E. Young, Dr. S.,  
Los Angeles, CA 90095-1662, USA

fax 1310 206 8967  
e-mail [simpson@hhmi-ucla.edu](mailto:simpson@hhmi-ucla.edu)