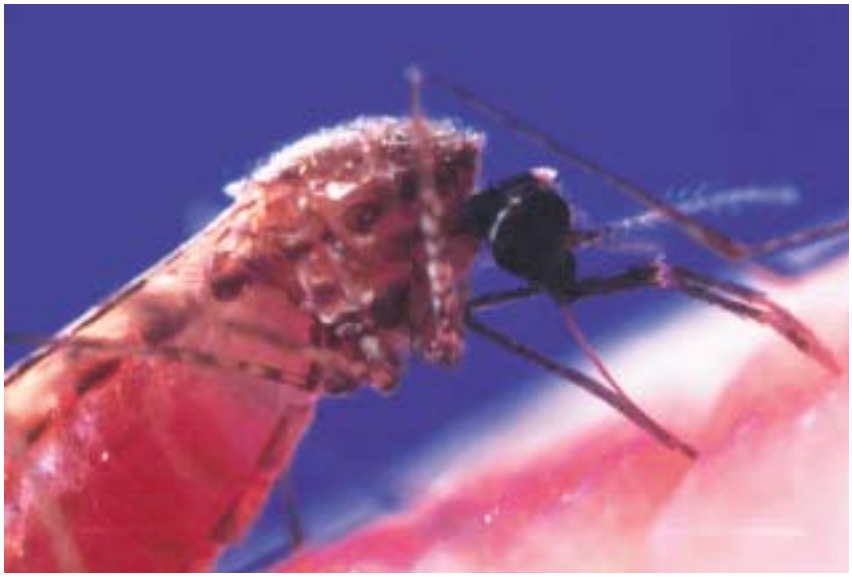
News

Malaria and mosquito genomes sequenced, but funding falls short



WHO/TDR/Stammers

Anopheles gambiae: adult female feeding on human blood.

The genetic code of the complete genomes of *Plasmodium falciparum*, the most lethal of the several malaria parasites, and its major African carrier, the mosquito *Anopheles gambiae*, were published in *Nature* and *Science* this October, bringing these tiny organisms into the same exalted domain as the human genome itself.

Already it turns out that 550 of *P. falciparum*'s 5300 genes are closely related to plant genes — opening the way to research on new drugs based on insecticides. The genes code for — or create — a recently discovered organelle in the body of the parasite called an apicoplast. The apicoplast in turn is very similar to the chloroplast in plant cells, the body that allows plants to photosynthesize, or grow in sunlight.

This doesn't mean that malaria parasites, which are animals, can grow in sunlight. It just means that during their evolution one of them must have absorbed the chloroplast, probably from an alga, found it useful for other purposes, and grew faster and outcompeted their colleagues, creating the *P. falciparum* we know today. The modern organism uses the apicoplast to make fatty acids, similar to cholesterol in humans, that are essential to its survival.

From the early genome data three years ago, a German group identified a particular mechanism in the apicoplast that looked ripe for attack (*Science* 1999; 285:1573-6), and recommended trying an existing drug called fosmidomycin, which had been developed for urinary infections; the group showed it cured mice of malaria, and is now in late clinical trial.

This was one of the first fruits of genome mapping, and represents just one kind of knowledge it can give us: comparative genomics, which entails comparing the letters and organization of the genome of one species with those of another. It may prove useful in accelerating research towards new treatments.

Similar stories are already emerging from *Anopheles gambiae*, the key mosquito vector of malaria. Its gene sequences are being compared with those of the famous laboratory fruitfly, *Drosophila melanogaster,* which itself has been exhaustively researched for several decades. Now it seems we can identify, by comparison and contrast with *Drosophila*, the genes in the mosquito which are responsible for the malaria parasite's survival in the mosquito gut, as well as genes for moulting, reproduction, and successful blood feeding. All these could form new points of attack on the mosquito.

Knowledge of these genomes and the human genome — the parasite, the vector, and its victim — gives us "the opportunity to take a holistic approach in understanding how the parasite interacts with the human host", Alan Cowman, a molecular parasitologist at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, told *Science*.

Nevertheless the function of two-thirds of the parasite's genes are still mysterious, and perhaps peculiar to the parasite itself. No amount of comparison may determine the function of the proteins they create, and lengthy and difficult research may be required to follow exactly what they do.

It is rather as if, like Galileo, we had turned a telescope for the first time on the Moon, and seen the wonder and detail of its craters and mountains, casting shadows in the sunlight. Suddenly Galileo could compare the Moon with the Earth, yet it was 300 years before anyone landed on Earth's partner in space. So with the genomes of malaria and its vector; we can wonder immediately at the detail of our vision, but it may take a long time and much funding before any of this knowledge turns into a tangible product in the village or the local hospital.

Meanwhile there is competition for limited funding between those who focus on amplifying control with existing tools, such as insecticide-impregnated bednets and education, and those who point to increasing resistance to cheap drugs and insecticides and advocate research for new weapons against the disease and its mosquito vector. For example, on the one hand we have the Roll Back Malaria initiative (RBM), founded in 1998 by WHO, the UN Development Programme (UNDP), the UN Children's Fund (UNICEF) and the World Bank with the goal of halving the world's malaria burden by 2010, which hardly gives time to wait for research. On the other there are bodies like the UNDP, World Bank and WHO Special Programme

WHO/TDR/Mark Edwards

A Yanomami mother with her child who has cerebral malaria. They are at the Centro Amazonico para Investigación y Control de Enfermedades Tropicales clinic, near Puerto Ayacucho, Venezuela.

Malaria takes its constant toll – a postcard from Kenya

In a congested ward in Kisii in the western highlands of Kenya, 50-year-old Nelly Kwamboka wails, curses and collapses in anguish at the foot of the bed. Her young son has just died.

Two months ago, Kisii bore the brunt of an epidemic of highland malaria, which resulted in hundreds of deaths. Nelly is too shocked to walk. She looks pale and exhausted, after trekking many kilometres with her child to reach the hospital.

Nearby, a mother of two, Elizabeth Momanyi from the village of Bomorenda, Suneka, has already lost one son — and her husband — to the epidemic. She rarely seeks medical services for herself, but when her own fever worsened, neighbours intervened, urging her to go to the hospital. But she is not impressed with the treatment she received: ''Attendants at this hospital are cruel,'' she said. ''During the few occasions I have been here, I have had my prescription written before I even described my condition or had any medical examination.''

In a bed close by, Elizabeth Kemunto had been ailing for two months but could not get to the hospital. Instead, she lay waiting for divine intervention. ''We took her to the local pastor for prayers after which she felt better, but then her condition worsened'' says her mother, Eunice Nyamato. But even then, she did not see the doctor, opting to buy over-the-counter drugs.

Kisii residents told the *Bulletin* that they normally use chloroquine as the first line of treatment because it is cheap. But the malaria parasite here is resistant to chloroquine, and to next-line drugs like Fansidar. By the time some neighbours took Elizabeth to hospital, her condition had deteriorated seriously. She may not live.

Even in the capital, Nairobi, malaria takes its toll. In the city's Kibera slums, Stella Wangui, a casual worker at the Nairobi City Council, recalls how she lost her daughter, Angela Muthini, four years ago to the disease. Stella had travelled to her rural home in Embu with her daughter and remembers Angela playing with other children by a nearby stream.

''She probably died because she was playing there — hundreds of mosquitoes were buzzing around the water,'' she said. ''My beautiful little girl died so quickly. Some days later, I became ill too.'' Back in Nairobi she had bouts of fever at regular intervals, but her temperature always returned to normal without medication. She thought that her body was merely reacting to the death of her daughter. But she decided to take medical tests, which revealed that hers was mild form of malaria ''I thought it would kill me the way it did to Angela,'' she said.

According to Kenya's National Malaria Strategy Paper 2001-2010, malaria kills 26 000 children per year in the country and accounts for 30% of all outpatient attendance. ■

James Njoroge, *Nairobi*

for Research on Tropical Diseases (TDR) and public–private partnerships such as the Medicines for Malaria Venture (MMV) and the Malaria Vaccine Initiative (MVI) whose task is to find new tools.

With over a million children and pregnant women dying from malaria in Africa alone each year (see Box), clearly both approaches are necessary. But while the WHO Commission on Macroeconomics and Health estimated that US$ 2.7 billion a year was needed just to control the disease, only about US$ 200 million a year is being spent on it. Roll Back Malaria, which helps countries develop their own programmes and funding sources, has recently been advised by an external commission to focus its efforts on just a handful of African countries. In research MMV has several products in line but just US$ 15 million a year to spend on them, MVI also, with several candidates, has some US$ 50 million, and TDR around US$ 25 million for malaria. Meanwhile pharmaceutical companies estimate that it costs US$ 500 million to discover, develop and market a new product. In total, investment in control and research is about a tenth of the real need.

The malaria and mosquito genomes bring welcome new hope, but having only a tenth of the resources needed weighs heavily. This seems to be the extent of the world's concern for tropical diseases: it is the same ratio by which the Global Fund to Fight AIDS, Tuberculosis and Malaria falls short of the estimated global needs for HIV/AIDS treatment and control (*Bulletin of the World Health Organization* 2002;80:338). ■

Robert Walgate, Bulletin

Argentina's health system devastated but health workers rally

The financial crisis of the past year has had a devastating impact on health care in Argentina.

With an unemployment rate of about 20% and an estimated 19 million of the population of 37 million living below the national poverty line, public clinics and hospitals have been swamped with patients who can no longer participate in private insurance systems sponsored by unions and employers.