To conquer malaria…

Genetically Modified Mosquitoes

By Jay Hardy, CLS, SM (NRCM)

Jay Hardy is the founder and president of Hardy Diagnostics. He began his career in microbiology as a Medical Technologist in Santa Barbara, California.

In 1980, he began manufacturing culture media for the local hospitals. Today, Hardy Diagnostics is the third largest culture media manufacturer in the United States.

To ensure rapid and reliable turn around time, Hardy Diagnostics maintains six distribution centers, and produces over 3,000 products used in clinical and industrial microbiology laboratories throughout the world.

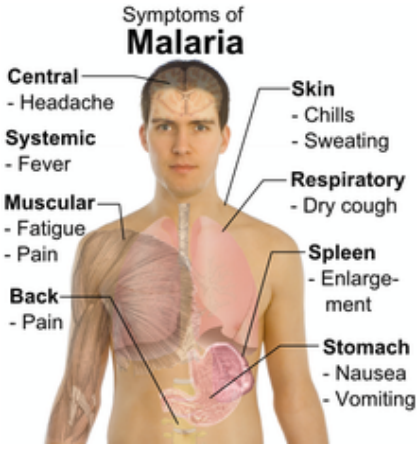
Researchers at the University of Arizona have successfully bioengineered the world's first malaria-proof mosquito. **They claim this new genetically modified mosquito has 100 per cent immunity to the malaria parasite, rendering it incapable of spreading the disease to humans.** The hope is that wild-type mosquitoes will be replaced with the new malaria-proof strains, effectively wiping out the disease.

All research is being conducted in a highly secure lab so the insect has no chance to escape while scientists work on methods to replace wild populations with the lab-bred *Anopheles* mosquitoes. So far, the experimental strain has been 100% successful in blocking the development of the malaria parasite.

Malaria Epidemiology

Malaria infects 250 million people worldwide and kills one million people every year, most of them children; 89% of deaths occur in Africa. About 1,500 cases are diagnosed in the United States every year.

Approximately 25 species of *Anopheles* are significant carriers of several forms of the malaria parasite; *Plasmodium falciparum* being the most significant to humans.



A New Approach

In order to disrupt the formation of sporozoites in the mosquito, researchers used molecular biology techniques to alter a piece of genetic code that controls a biochemical pathway inside the mosquito's cells. They achieved immunity by targeting a gene that controls a

signaling protein known as Akt, which is involved in the development of the parasite inside the mosquito. By genetically engineering this switch permanently to "on," more Akt was produced, enabling the immune system to fight off the *Plasmodium* parasite.

Genetic modifications will give the mosquitoes a competitive edge over the wild strains.

Professor Michael Riehle, an entomologist at the University of Arizona who led the research, said: "We were just hoping to see some effect on the mosquitoes' growth rate, lifespan, or their susceptibility to the parasite, but it was great to see that our construct blocked the infection process completely."

The challenge now, he said, would be to make further genetic modifications to give the mosquitoes a competitive edge over the wild strains.

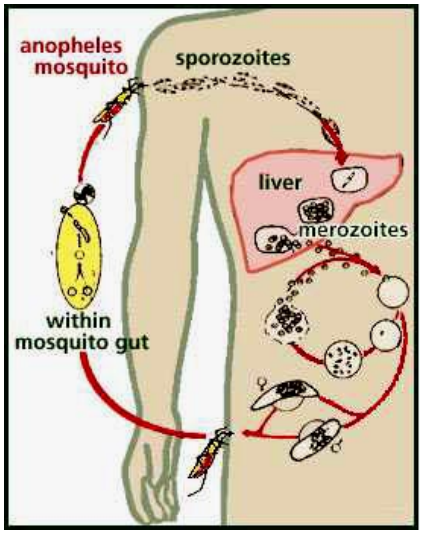
However, the persistent danger of creating a super strain that could become an even greater nuisance to mankind must be considered and feared.

Malaria Life Cycle – Mosquito Portion

Mosquitoes mainly feed on plant nectar; however, the female must ingest a blood meal in order to supply iron and protein to develop her eggs.

The female is attracted to humans by their CO_2 and volatile organic substances. Before ingesting their victim's blood, the female injects her saliva, which contains an anticoagulant.

If the victim is a carrier of malaria, the *Plasmodium* cells from the blood squeeze through the mosquito's midgut lining and begin a complex cycle of development that takes about two weeks to complete.



Most of the parasite cells don't survive and are destroyed by the mosquito's immune cells. However, a small number survive and attach themselves to the outside of the midgut wall and develop brooding cells called oocysts, which 10-12 days later produce thousands of new *Plasmodium* cells or sporozoites.

Malaria Life Cycle – Human Portion

After the sporozoites have fully developed in the female mosquito, she injects her infected saliva into the skin of her next blood meal victim.

Once in the human blood stream, a single sporozoite of *Plasmodium falciparum* invades a liver cell. Here the parasite grows and within six days produces 30,000-40,000 daughter cells called merozoites, which are released into the blood when the liver cell ruptures. In the blood, after a single merozoite invades a red blood cell, the parasite grows in 48 hours and produces 8-24 daughter cells, which are released into the bloodstream when the red blood cell ruptures.

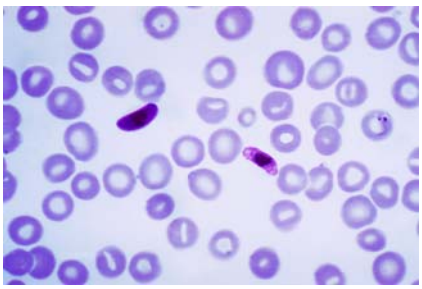
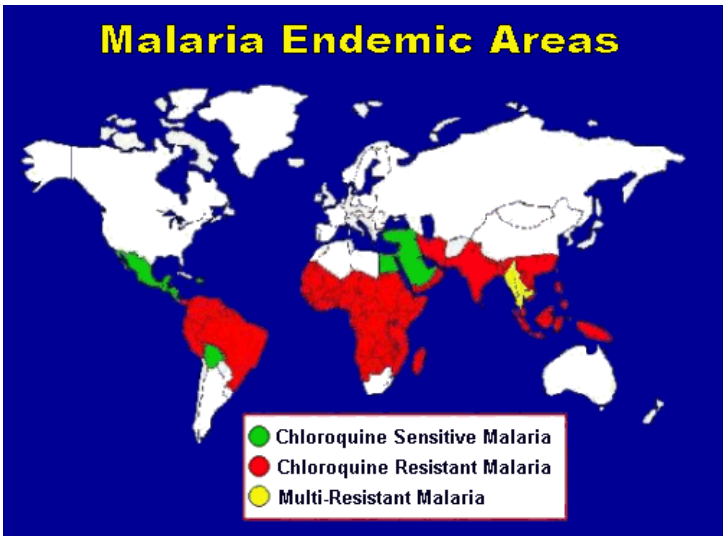


Figure 1: **Plasmodium falciparum** ***micro and macro-gametocytes in human blood.***

Treatment
Currently, two important currently used antimalarial drugs are derived from plants whose medicinal values had been used for centuries: artemisinin from the Qinghao plant (*Artemisia annua*, China, 4th century) and quinine from the cinchona tree (South America, 17th century).



HIV/AIDS, tuberculosis, and malaria kill over six million people every year. There are over 300 million new cases of malaria every year. By looking at new approaches to prevention, such as bioengineering, it is hoped that, just like smallpox, killer infectious diseases like malaria will someday be rendered harmless.

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