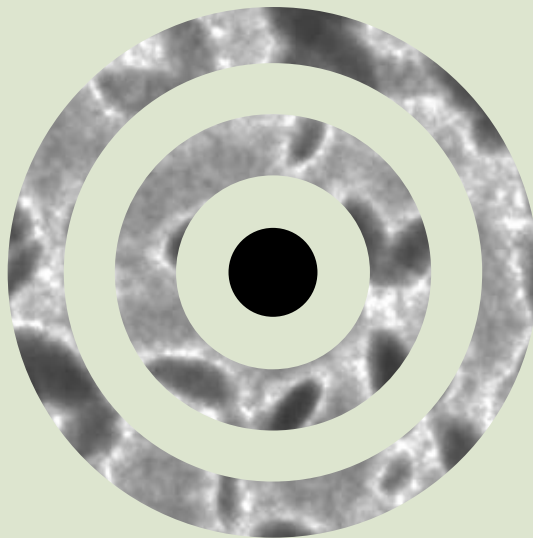


# Taking the bite out of **MALARIA**



**RESEARCH TARGETS  
DEFENSES OF RAPIDLY  
MUTATING PARASITE**



# Humankind and malaria have been locked in an evolutionary arms race for thousands of years.

The past century has seen major advances on our side, in the form of anti-malaria drugs and improved public health. But because the parasite has a generational lifespan of weeks or months and exists in vast populations within each infected host, it's often able to stay many steps ahead of us, developing mutations to evade our medications.

Meanwhile, this war exacts a terrible toll: Every year, more than 500 million people become severely ill with malaria. More than a million of them die.

J. Koji Lum and his colleagues at Binghamton University want to take a closer look at how the malaria parasite *Plasmodium falciparum* evolved resistance to chloroquine, the best weapon humans have ever had in the fight.

Lum, associate professor of anthropology and biological sciences, and Ralph Garruto, professor of biomedical anthropology, have about 11,000 archived human blood samples from malarious regions of the Pacific collected from the 1950s to the present.

A \$1.5 million grant from the National Institutes of Health will allow them to analyze these samples and document the accumulation of genetic changes that resulted in chloroquine's treatment failure in the Pacific.

"We're on this treadmill running as fast as we can to create these medicines just to keep up with the relatively rapid mutation rate of the parasites," Lum said. "Our project is trying to say, 'Look, the most successful anti-malarial drug in history was chloroquine. It lasted for decades in some regions of the world. It's still effective in some areas like South America.

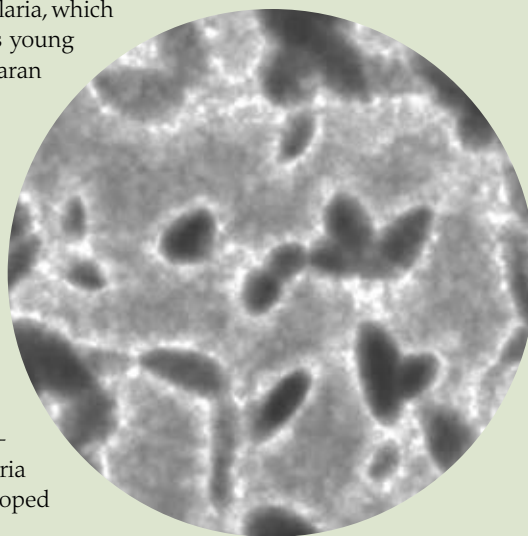
"Can we, by examining how the *falciparum* parasite evaded this medicine, gain insights into slowing down the treadmill a little bit, trying to figure out ways that we can use medicines more intelligently? Are there insights we can gain from the failure of chloroquine to allow us to get the most bang for the buck from the new anti-malarials?"

Other researchers have speculated about the parasite's genetic mutations, but no one has ever been able to document the path it actually took to its current status.

The World Health Organization estimates that malaria causes an average loss of 1.3 percent annual economic growth in countries with intense transmission. Some 40 percent of the world's population is at risk of malaria, which disproportionately affects young children in sub-Saharan Africa.

Lum argues that global warming, which is expanding the tropical regions of the globe, and a global economy, in which parasites and mosquitoes can move across borders with goods, money and people, should spark renewed interest in malaria among people in developed countries.

"All vector-borne diseases, everything that relies on a mosquito, are going to become bigger problems as our temperatures increase and the variance in our weather patterns increases," Lum said. "And the time it takes to move around the planet is a small fraction of the incubation time for our diseases."





**“Arguably, malaria has killed more people in human history than anything else.”**

— J. Koji Lum

Symptoms of malaria include fever, headache and vomiting, usually within 10 to 15 days of being bitten by an infected mosquito. Left untreated, malaria interrupts the blood supply to vital organs, in severe cases resulting in coma and death.

There's cyclical interest in eradicating malaria, which has effectively been eliminated from temperate regions of the globe. But the last full-scale push to wipe out the disease was a World Health Organization campaign following World War II. Experts theorized that DDT spray could kill the mosquitoes that carry the parasite while chloroquine tablets could treat those already affected by the disease. After 15 years of concerted effort, it was clear the plan was a failure.

"Since then," Lum said, "it's been the ugly stepchild of public health because this massive effort had been tried and it had failed."

Small-scale initiatives have since met with some success. For instance, malaria was recently eliminated from an island in Vanuatu with a population of about 600 using nothing more than existing tools

and about \$10 per person. The whole population — not just the symptomatic children, who are usually the most likely to be treated — had to be given medication once a week for 2.5 mosquito life cycles, or about nine weeks.

What stands in the way of repeating this achievement in the South Pacific across the globe?

From Lum's perspective, it's largely an issue of health-care infrastructure. "On paper, it's easy," he said. "There are no 'black boxes' in the technology, but there are a lot of logistical hurdles. There's a big gap between knowing how to do it and actually implementing it."

It's as easy — and as hard — as answering this question: How do you find everyone every week and ensure they take the medicine?

"It's kind of a Catch-22," Lum said. "If you knew how to find everybody, and you knew how to talk to everybody, it wouldn't be a problem because you would have the basic health-care infrastructure. When you don't have that, it remains a problem."

Lum doesn't hold out much hope for a new super-drug, either. "One of the problems with designing drugs for malaria is that there's not much profit in it," he said. "The people who need these medicines don't have any money. If they could afford \$2 a week to save their child, then they could afford to have basic health-care infrastructure. There's not a big purse to entice these pharmaceutical companies into pushing the envelope of drug development."

That brings us back to chloroquine, which costs pennies per dose and was once incredibly effective. Lum wonders if a higher dose of chloroquine could be the answer, or perhaps periodically removing the drug from use and allowing susceptibility to recover. In any event, he hopes finding out more about the malaria parasite's basic biology as it pertains to drug resistance will offer some insights.

"Arguably, malaria has killed more people in human history than anything else," he said. He still believes we can win the war. ■

— Rachel Coker