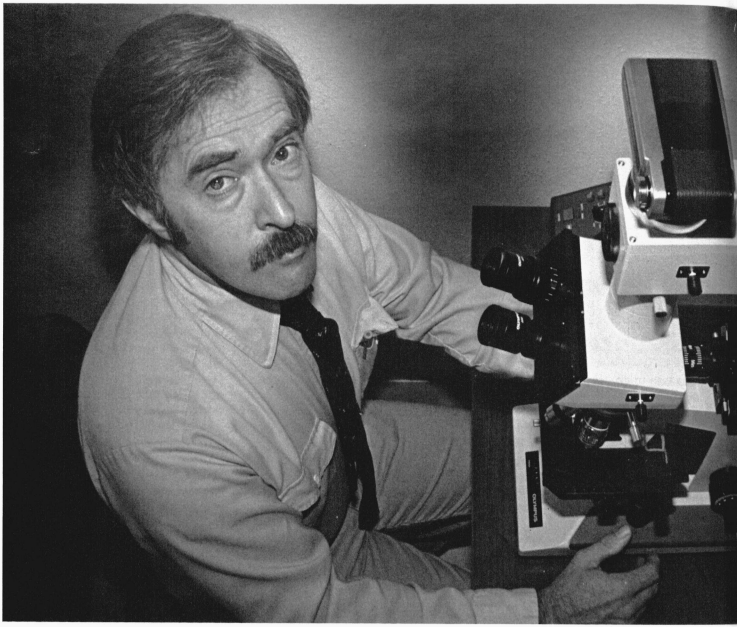


ZEROING IN ON MALARIA

By CAROL AGAIN

BOLSTERED by a $1.9 million contract, Mizzou's internationally acclaimed malaria research team is developing a vaccine for the world's deadliest disease.

The Agency for International Development awarded the three-year contract to support ongoing work of Dr. Ted Green, associate professor of veterinary microbiology, and the 13-member research team he leads. AID's previous support of Green's malaria research totals $1.84 million.

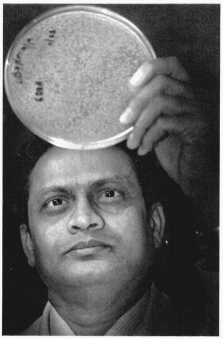
The Mizzou team's task is to produce a vaccine for the merozoite stage of malaria. Already, it's developed a candidate vaccine of purified protein that has withstood all testing thus far.

Malaria is a disease of the past in this country. But worldwide, some one billion people living in the tropics and semitropics are at risk. Transmitted by mosquitoes carrying malaria parasites, the disease strikes 300 million each year.

"There's a resurgence of malaria worldwide," says Green, who attributes this to mosquitoes' developing resistance to insecticides and the banning of some of these substances for environmental reasons. Political and economic unrest in some countries have disrupted efforts to control the insects as well, he says.

At the same time, the parasites have become resistant to some chemotherapeutic agents used to treat the disease. "So we need new drugs, new methods of mosquito control and, of course, a vaccine."

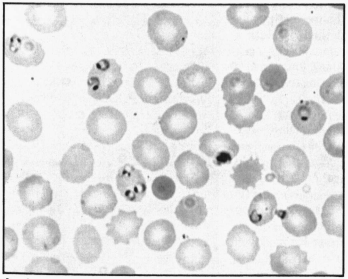
GREEN, who began his vaccine research six years ago at the Parke-Davis Research Laboratories in Detroit, came to Mizzou in 1980. "There was closely related research going on here on Babesia, a malaria-like disease of cattle," he notes. "I also liked the University



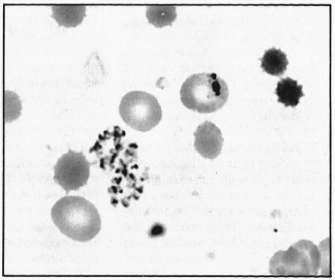
The research of Dr. Ted Green, far left, garnered a $1.9 million contract from the Agency for International Development this fall. Green leads a research team that is part of an international quest to develop a malaria vaccine.

Through genetic engineering, Dr. Ram Guntaka, left, is translating research into a vaccine. Guntaka manipulates genes to produce malarial protein to be used in creating the vaccine.

Patricia De la Vega, below, feeds the cultures used in the malaria research. She arrived at Mizzou this fall from the Instituto Nacional de Salud-Bogota, another major laboratory site in the research network.



A microscope reveals malaria parasites in red cells.



The parasites later multiply and invade more cells.

Research specialist Jamie Wibbenmeyer operates a fraction collector in a column chromatographer to purify merozoites. The surface proteins of these parasites are a key to creating a malaria vaccine.

structure and the potential for interaction," evident in the disciplines represented on the UMC research team.

Faculty, research staff and graduate students from veterinary microbiology, veterinary pathology, microbiology, health-related professions, laboratory animal medicine, Dalton Research Center and the Instituto Nacional de Salud-Bogota serve on Mizzou's team. "The idea is to use everything at our disposal to make the vaccine the best possible," Green says.

But even with an interdisciplinary effort, the problem is bigger than any one laboratory, he says. Vaccines must be developed for each of malaria's three stages, which are characterized by different forms of the malaria parasite, because none has been found to be 100 percent effective. "Once all of these are combined into one vaccine, malaria could be better controlled."

THE DISEASE'S complexity prompted AID to form an international research network whose major lab sites include the University, The Rockefeller University, Scripps Institution, New York University, Michigan State University, Uniformed Services University, the University of Illinois, the Instituto Nacional de Salud-Bogota in Colombia and the Center for Disease Control in Atlanta.

Each lab researches different phases of the disease. In the first stage, malaria parasites, in a form called sporozoites, invade the liver. Symptoms occur in the second stage, when the sporozoites evolve into merozoites and invade red blood cells. Every 48 hours, a merozoite can multiply 20 times, attacking more red cells and resulting in anemia, chills, fever or death. In the third stage, mosquitoes that bite the malaria victim become reinfected and are able to transmit the disease.

The Mizzou team's research begins with parasites obtained from malaria patients in Africa and Central Asia. These are grown in cultures of human red blood cells and then put into a gelatin solution. The normal cells stack up like checkers and sink, but parasite-invaded cells float, allowing researchers to isolate them.

These cells are then put into a culture where they release merozoites. Because the culture contains no new cells to invade, the merozoites remain unchanged and are collected for research.

Green estimates that one billion merozoites—all of which could fit on the head of a pin—are grown weekly in Mizzou labs.

The parasites are a key to creating the vaccine. "Researchers feel that the action of antibodies in a malaria victim's body is directed against the surface proteins of merozoites," Green says. A surface-protein vaccine, then, should stimulate the body to produce enough antibodies to establish immunity. Should a vaccinated person be bitten by an infected mosquito, the antibodies would attach to the merozoites, forming a glob. Trapped, the merozoites would die within minutes.

A FEAT in developing the vaccine is separating the surface proteins from the rest of the microscopic merozoites. "Obviously, you can't peel them," Green says.

So researchers expose the merozoites to radioactive iodine and put them in gels that separate the proteins into layers by molecular weight. X-ray films then identify those layers labeled with radioactive iodine. "Ideally, only those proteins exposed were on the outside of the merozoites," Green explains. While the gel method is not the only way to separate the proteins, it is one of the most effective, he adds.

The next hurdle is translating the research into a vaccine. The amount of protein obtained each month from merozoites in the lab probably couldn't vaccinate more than 10 people, Green says, "so we could never make it available to the one billion people at risk unless we go to other techniques."

The answer, Green says, is a genetically engineered vaccine. "We could have a 'factory' growing the surface proteins, not parasites. We could get a million times more protein."

Research team member Dr. Ram Guntaka, associate professor of microbiology, is leading the quest to produce the proteins. After extracting merozoites' genetic material, he isolates single genes and manipulates them to produce protein in bacterial colonies.

"We're hoping one colony will produce the malarial protein," Green says.

THE MALARIA expert hopes a purified protein vaccine can be tested on animals in a year. Researchers will first inject rabbits and then South American Aotus monkeys.

"An educated guess is that it will be five years before we actually vaccinate humans," he says. "We want to be very careful." □