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Sarah Gardner Dominican University of California, sarah.gardner@dominican.edu

Dave Albee Dominican University of California, david.albee@dominican.edu

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Researcher, students study malaria drug resistance

A manuscript by researchers from the University of California San Francisco (UCSF), Makerere University in Uganda, and Dominican University of California biologist Dr. Roland Cooper, which examines the sensitivity of malaria parasites to anti-malarial treatment, has been accepted for publication in the journal Antimicrobial Agents and Chemotherapy. The report is a culmination of a five-year study of drug-resistant malaria parasites from African children, who are the most at risk of dying from malaria.

The manuscript is titled "Impact of anti-malarial treatment and chemoprevention on the drug sensitivity of malaria parasites isolated from Ugandan children."

Cooper, an associate professor of biology in <u>Dominican's Department of Natural Sciences and</u> <u>Mathematics</u>, is involved with two new federally funded research projects focused on controlling the spread of drug-resistant malaria and establishing new drug treatments to combat anti-malarial drug resistance.

"The goal is to develop a safe, effective, and affordable anti-malarial drug that can be added to the very limited number of drugs currently in use," Cooper said. "With recent reports of resistance to the new class of anti-malarial drugs occurring in Southeast Asia, there is dire need for new drugs to augment the current worldwide anti-malarial campaign."

Malaria remains one of the world's deadliest diseases. Each year, malaria causes up to 660 million clinical cases and claims around one million lives, mostly children under the age of five and pregnant women of sub-Saharan Africa. The situation is largely attributed to the spread of multi-drug resistant strains of *Plasmodium falciparum* that are completely resistant to former front-line drugs such as chloroquine. With no vaccine available, there is a dire need for low cost, effective, safe, and sustainable malaria treatments.

The work involving UCSF and Makerere University is funded by a new grant from the National Institutes of Health (NIH). Cooper spends his summers in Uganda working alongside clinical trials involving malaria patients at Tororo District Hospital in eastern Uganda. In recent years he has involved <u>Dominican</u> <u>undergraduate and graduate students in this work</u>. Last summer, Stephanie Rasmussen '15, who is pursuing her MS Biology degree in Cooper's lab, and Dominican alum Jordan Rode '14 studied the evolution of drug resistance in malaria from infant children in Uganda. They were joined by a UC Berkeley student, Christine Lam.

Cooper and the students also attended a malaria research conference in Kampala where he gave two presentations.

During the academic year Cooper is continuing his research in his lab at Dominican in order to characterize drug resistance genes from parasites collected from the Tororo lab. Preliminary findings showed that sensitivity is slightly decreasing toward some new artemisinin combination therapies (ACTs) now being used as the standard treatment for malaria. However, the kind of resistance currently seen in Southeast Asia to ACTs has not yet been seen anywhere in Africa.

"We hypothesize that anti-malarial drug resistance will increase over time in Uganda and therefore much of Africa. Preemptive analysis of parasites will be critical to characterizing resistance mechanisms before resistance is widespread."

To test the hypotheses, the researchers monitor the drug sensitivities of malaria parasites isolated from Ugandan patients under varied levels of drug pressure; characterize the genetic profiles of these parasites; assess the fitness, virulence, and transmissibility costs of resistance in both clinical and laboratory settings; and characterize high level resistance selected either clinically or in the laboratory.

"We believe that focused evaluations of fresh isolates from the clinic will best equip us to characterize the emergence of high level resistance in Africa, where the malaria problem is greatest, and where timely

characterization of resistance mechanisms can be most valuable," Cooper said.

In another project funded by the U.S. Department of Defense, Cooper is working with colleagues from Portland State University and Walter Reed Army Institute of Research to study the use of acridones, a group of organic compounds that show great potential as anti-malarial drugs. The goal is to determine the potential of malaria parasites to become resistant to these newly developed compounds.

"When we go to Africa in summer, we also test these compounds in parasites freshly isolated from malaria patients, to be certain the drugs have good potency against parasites with a wide range of genetic variation," Cooper said.