

Novel anti-malarial drug candidate found

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As part of a multicenter study, UT Southwestern Medical Center researchers have identified a series of chemical compounds that might serve as starting points for the identification of new classes of anti-malarial drugs.

"[Malaria](#) remains one of the most globally significant infectious diseases that we face," said Dr. Margaret Phillips, professor of pharmacology at UT Southwestern and one of the senior authors of the study, which appears in the May 20 issue of *Nature*. Malaria affects about 40 percent of the world's population and kills about a million people a year, she said. The parasite that causes the disease is spread by mosquito bites.

Drugs are the mainstay of malaria treatment, yet the [malaria parasite](#) is notorious for developing [drug resistance](#), which compromises current chemotherapy.

"Novel chemical compounds with anti-malarial activity represent a potent tool in the process of developing new drugs to treat this disease," Dr. Phillips said.

The study, done in collaboration with Dr. Kiplin Guy of St. Jude Children's Research Hospital in Memphis and other researchers, started with a "library" of 309,474 chemical compounds.

The researchers used a technique called high throughput screening, which allowed them to test thousands of compounds quickly to identify those with anti-malarial action.

"In addition, publishing the full set of identified compounds will maximize the chances for the most-promising candidates to move into large-scale drug development programs," Dr. Phillips said.

The screen identified 1,152 compounds that killed the parasite. The researchers then followed up with further tests to determine the mechanism of action of the identified compounds, where possible.

Dr. Phillips and her group tested whether any of the identified compounds killed malaria parasites by inhibiting an enzyme necessary to make pyrimidine, an intermediate molecule for creating DNA. She discovered that three of the library's compounds with anti-malarial activity blocked this enzyme. Two of those had similar chemical structures to a class of known compounds that she and her colleagues have been studying for possible drug development. The third compound previously was not known to target the enzyme.

"It looked very different from anything we knew about before," she said.

Having a variety of anti-malarial drugs with different chemical structures and modes of action is important because different types of drugs are given together to slow the parasite from developing resistance, Dr. Phillips said.

In all, the researchers from the various centers found 172 compounds that are "reasonable starting points" for development of new types of drugs.

"We call the identified candidates 'hits,' but if any of them are going to become drugs, they're going to have to undergo chemical modification," Dr. Phillips said. "For instance, they may need to be altered chemically to enter the cell more easily, or to improve their pharmacology so they will be more effective in people."

Provided by UT Southwestern Medical Center

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