Scientists develop novel technique for finding drugs to combat malaria

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Credit: CDC

Each year nearly 600,000 people—mostly children under age five and pregnant women in sub-Saharan Africa—die from malaria, caused by single-celled parasites that grow inside red blood cells. The most deadly malarial species—Plasmodium falciparum—has proven notoriously resistant to treatment efforts. But thanks to a novel approach developed by scientists at Albert Einstein College of Medicine of Yeshiva University and described in the January 20 online edition of *ACS Chemical Biology*, researchers can readily screen thousands of drugs to find those potentially able to kill P. falciparum.

Scientists have known for more than a decade that malaria parasites have an Achilles heel: Like all cells, they require two key building blocks—purines and pyrimidines—to synthesize their DNA and RNA. But malaria parasites can't synthesize purines on their own. Instead, they must import purines from the host red blood cells that they invade. A parasite protein called PfENT1 transports purines from blood cell into the parasites. So drugs that block PfENT1 could conceivably kill the parasites by depriving them of purines they need—but an experimental approach for identifying PfENT1 inhibitors didn't exist, until now.

Einstein's Myles Akabas, M.D., Ph.D., developed a novel yeast-based high-throughput assay for identifying inhibitors of the PfENT1 transporter. Dr. Akabas worked with two MSTP students in his lab (I.J. Frame and Roman Deniskin) as well as colleagues at Einstein (Drs. Ian Willis and Robyn Moir) and Columbia University (Drs. Donald Landry and David Fidock). The researchers used their technique to screen 64,560 different compounds. They identified 171 potential antimalarial drugs. Studies of nine of the most potent drugs showed that they kill P. falciparum parasites in laboratory culture.

"We've shown that the PfENT1 transporter is a potential drug target for developing novel antimalarial drugs," said Dr. Akabas, senior author of the ACS Chemical Biology paper and a professor of physiology & biophysics, of medicine and in the Dominick P. Purpura Department of Neuroscience at Einstein. "By using our rather simple approach, scientists could create similar high-throughput screens to identify inhibitors for killing other parasites that rely on transporters to import essential nutrients."

Provided by Albert Einstein College of Medicine