New strategy emerges for fighting drug-resistant malaria

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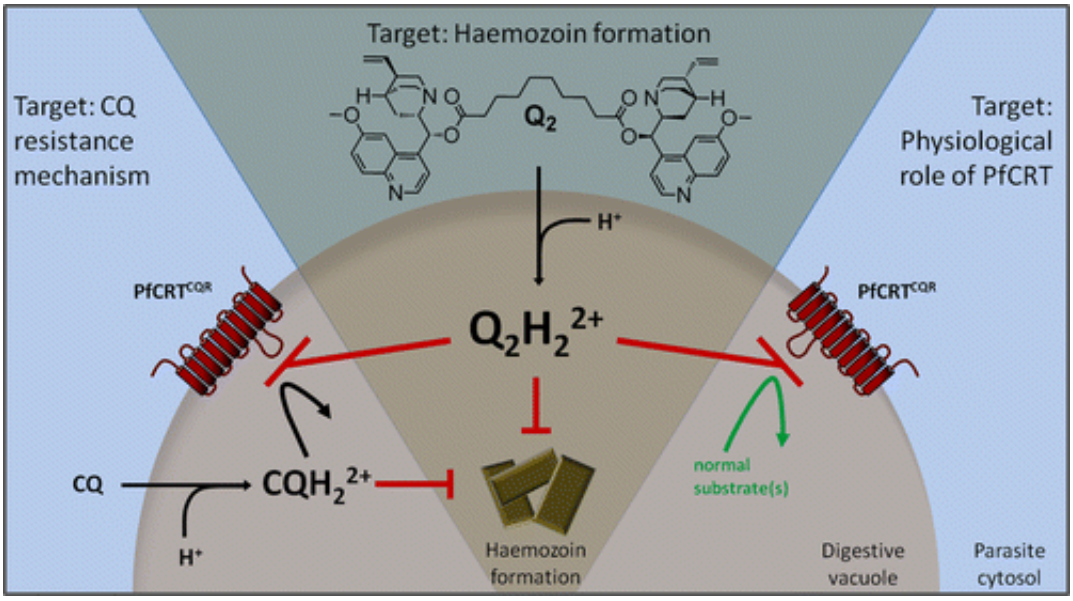

Malaria is one of the most deadly infectious diseases in the world today, claiming the lives of over half a million people every year, and the recent emergence of parasites resistant to current treatments threatens to undermine efforts to control the disease. Researchers are now onto a new strategy to defeat drug-resistant strains of the parasite. Their report appears in the journal *ACS Chemical Biology*.

Christine Hrycyna, Rowena Martin, Jean Chmielewski and colleagues

point out that the parasite *Plasmodium falciparum*, which causes the most severe form of malaria, is found in nearly 100 countries that, all totaled, are home to about half of the world's population. Every day, *P. falciparum* and its relatives hitch rides via mosquitoes to find a human home. An effective vaccine remains elusive and the continuing emergence of drug-resistant parasites is cause for alarm. The good news is that these scientists have designed compounds that work against *P. falciparum* strains that are resistant to drugs such as chloroquine. The team wanted to understand how these compounds worked and to develop new candidate antimalarials.

In the lab, the scientists designed and tested a set of molecules called quinine dimers, which were effective against sensitive parasites, and, surprisingly, even more effective against resistant ones. The compounds have an additional killing effect on the drug-resistant parasites because the compounds bind to and block the resistance-conferring protein. This resensitizes the parasites to chloroquine, and appears to block the normal function of the resistance protein, killing the parasite. "This highlights the potential for devising new antimalarial therapies that exploit inherent weaknesses in a key resistance mechanism of *P. falciparum*," they state.

More information: "Quinine Dimers are Potent Inhibitors of the Plasmodium falciparum Chloroquine Resistance Transporter and are Active against Quinoline-Resistant P. falciparum" *ACS Chem. Biol.*, Article ASAP. DOI: 10.1021/cb4008953

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