Scientists exploit malaria's Achilles' heel

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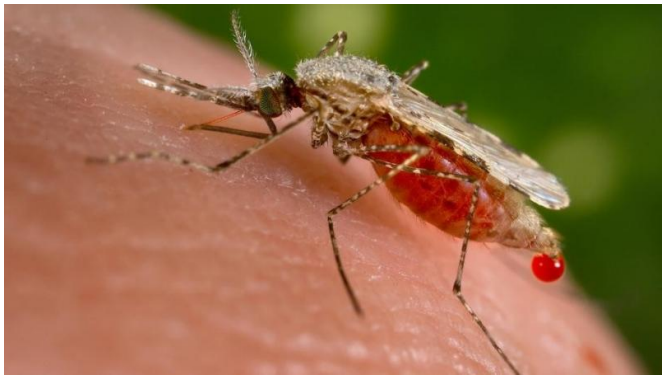

Malaria is transmitted via mosquitoes. Credit: Australian National University

Malaria researchers at The Australian National University (ANU) have found one of the malaria parasite's best weapons against drug treatments turns out to be an Achilles' heel, which could be exploited to cure the deadly disease.

The findings could prolong the use of several anti-malarial drugs, including the former wonder drug chloroquine, to treat the mosquito-borne disease which kills 600,000 people around the world each year.

Lead researchers Dr Rowena Martin and PhD student Sashika Richards, from the ANU Research School of Biology, said changes in the protein that enable the parasite to evade several anti-malarial drugs - including chloroquine - make the parasite super-sensitive to other therapies.

"Malaria is one of the biggest killers in the world, particularly for young children and pregnant women in Africa and the Pacific, and our research could help save countless lives in some of the world's poorest countries," Dr Martin said.

Dr Martin said the interactions of the modified protein with certain drugs were so intense that it was unable to effectively perform its normal role, which was essential to the parasite's survival.

"We also found that the changes that allow the protein to move chloroquine away from its anti-malarial target simultaneously enable the protein to deliver other drugs to their anti-malarial targets," she said.

"The other important phenomenon we found is when the protein adapts itself to fend off one of these drugs, it is no longer able to deal with chloroquine and hence the parasite is re-sensitised to chloroquine.

"Essentially, the parasite can't have its cake and eat it too. So if chloroquine or a related drug is paired with a drug that is super-active against the modified protein, no matter what the parasite tries to do it's checkmate for malaria."

Dr Martin said the super-sensitivity phenomenon also occurred in other drug-resistant pathogens, such as bacteria, and in cancer cells.

Ms Richards said the findings would improve the cure rates for people with malaria, and could help stop the emergence and spread of drug-resistant malaria.

"Health authorities could use our research to find ways to prolong the lifespan of anti-malarial drugs," Ms Richards said.

She said prolonging the use of existing drugs was crucial, as it would give scientists time to find the next anti-malarial drug.

"The current frontline anti-malarial drug, artemisinin, is already failing in Asia and we don't have anything to replace it," she said.

"It will be at least five years before the next new drug makes it to market. The low-hanging fruit is gone, and it's now very costly and time consuming to develop new treatments for malaria."

The study was supported by National Health and Medical Research Council (NHMRC) funding.

More information: Sashika N. Richards et al. Molecular Mechanisms for Drug Hypersensitivity Induced by the Malaria Parasite's Chloroquine Resistance Transporter, *PLOS Pathogens* (2016). DOI: 10.1371/journal.ppat.1005725

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