

## Scientists find new way to fight Malaria drug resistance

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An anti-malarial treatment that lost its status as the leading weapon against the deadly disease could be given a new lease of life, with new research indicating it simply needs to be administered differently.

The findings could revive the use of the cheap anti-malarial drug <u>chloroquine</u> in treating and preventing the mosquito-bourne disease,



which claims the lives of more than half a million people each year around the world.

The parasite that causes <u>malaria</u> has developed resistance to chloroquine, but research carried out at the Australian National University (ANU) and Germany's University of Heidelberg has shown that the parasite <u>protein</u> that causes resistance has an Achilles' heel.

"We studied diverse versions of this protein and in all cases found that it is limited in its capacity to remove the drug from the parasite," said malaria researcher Dr Rowena Martin, from the ANU Research School of Biology.

"This means malaria could once again be treated with chloroquine if it is administered twice-daily, rather than just once a day".

Once hailed as a wonder drug, chloroquine is still used in developing nations in the South Pacific, Africa, Asia and South America, but has been withdrawn from use in many developed countries.

Dr Martin and her colleagues also revealed how the protein may have developed resistance to chloroquine.

"We found that the protein gains the ability to move chloroquine out of the parasite through one of two evolutionary pathways, but that this process is rigid – one wrong turn and the protein is rendered useless," she said.

"This indicates that the protein is under conflicting pressures, which is a weakness that could be exploited in future antimalarial strategies."

Dr Martin said the findings, published in the latest *Proceedings of the National Academy of Sciences* of the United States of America, could be



used to help millions of people in developing nations who are at risk of catching malaria.

She said that there is also potential to apply the findings to several chloroquine-like drugs that are also becoming less effective as the <u>malaria parasite</u> builds up resistance.

Dr Martin, however, does not recommend taking large doses of chloroquine.

"The key is to increase the frequency of chloroquine administration, for example by taking a standard dose in the morning and another at night. If you take too much all at once it can kill you," she cautions.

More information: Robert L. Summers, Anurag Dave, Tegan J. Dolstra, Sebastiano Bellanca, Rosa V. Marchetti, Megan N. Nash, Sashika N. Richards, Valerie Goh, Robyn L. Schenk, Wilfred D. Stein, Kiaran Kirk, Cecilia P. Sanchez, Michael Lanzer, and Rowena E. Martin. "Diverse mutational pathways converge on saturable chloroquine transport via the malaria parasite's chloroquine resistance transporter." *PNAS* 2014; published ahead of print April 11, 2014, DOI: 10.1073/pnas.1322965111

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