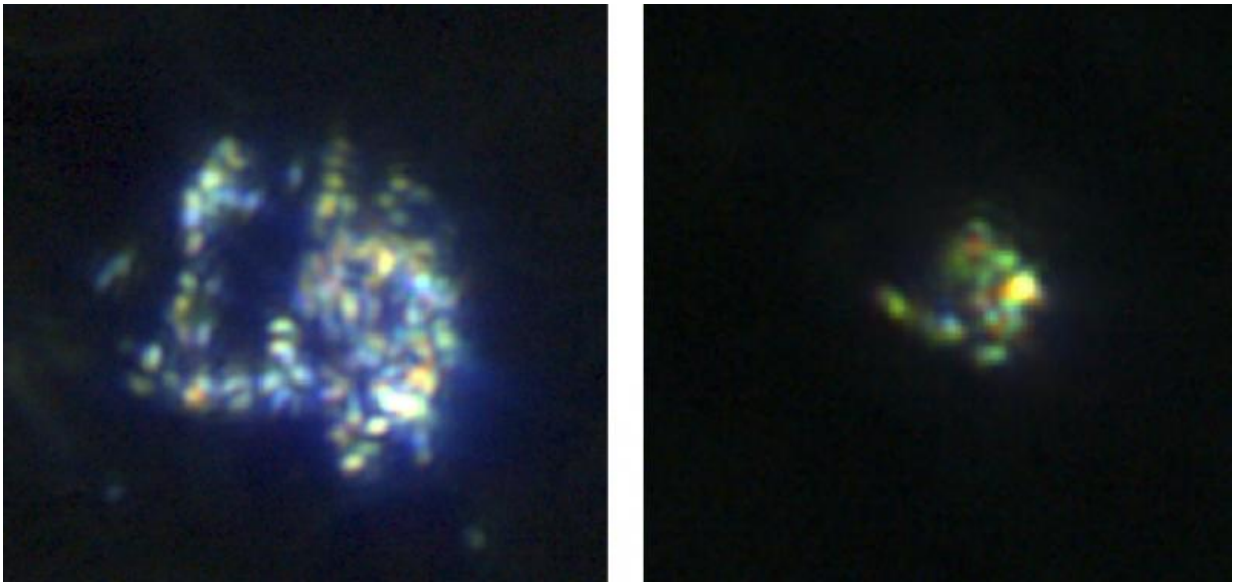
Malarial parasites dodge the kill

May 4 2015



Compared with a healthy malaria parasite (left), a mutant (right) has reduced levels of the protein hemozoin (detected here through light microsocopy), yet survives. Credit: Lin et al., 2015

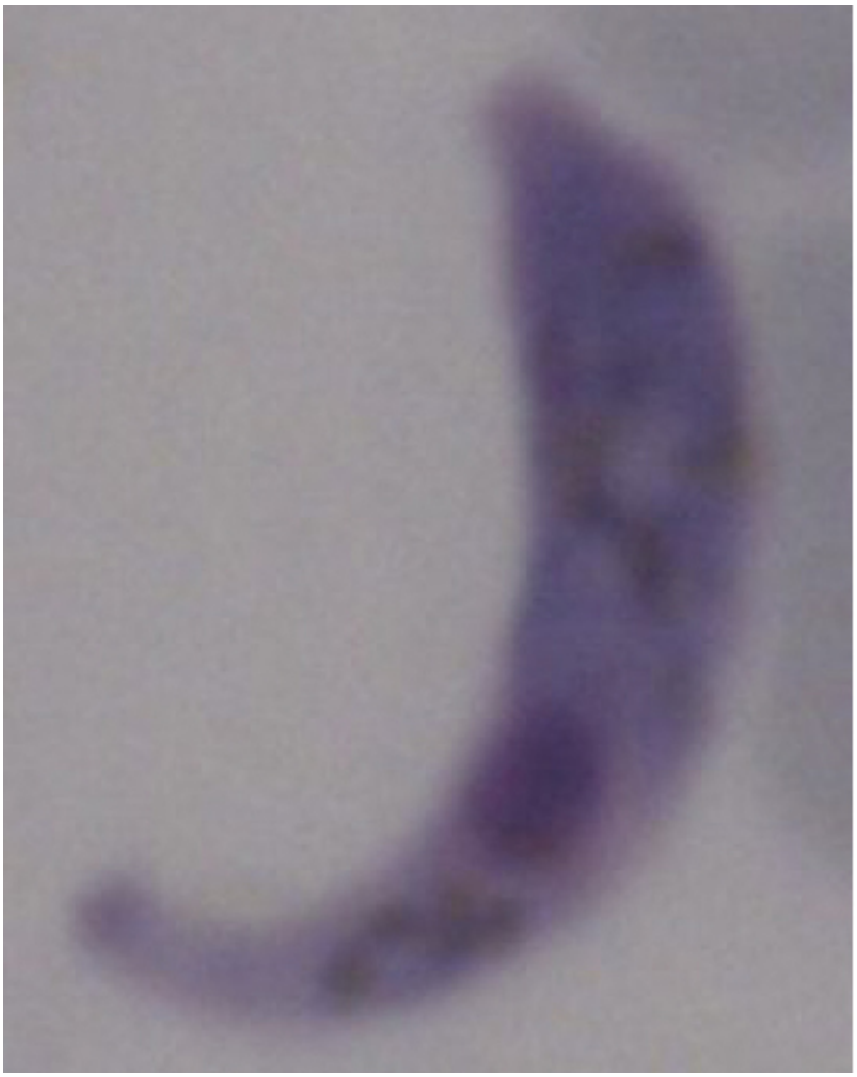
Scientists have uncovered a potential mode of parasite drug resistance in malaria infection, according to a report published in *The Journal of Experimental Medicine*.

Malaria infection includes symptoms such as headaches, fever, fatigue, and vomiting and can be deadly. Transmitted via a mosquito bite, the parasite *Plasmodium* enters the bloodstream and infects red blood cells. The parasite then digests hemoglobin—the oxygen-carrying protein in

the blood—and converts it into hemozoin, a protein indispensable for parasite survival.

While some of the current anti-malarial drugs target this digestion pathway, resistance to these drugs has also been reported. To address this resistance, Leiden University Medical Centre researcher Shahid Khan and colleagues created a mouse parasite lacking critical "Pac-Man" enzymes required to chew up hemoglobin. These mutant parasites are able to survive and multiply inside immature red blood cells called reticulocytes, without making hemozoin. Surprisingly, the mutant parasites cannot be killed by the anti-malarial drug chloroquine, which interferes with hemozoin formation, but yet, remain sensitive to the drug artesunate which targets another pathway of hemoglobin digestion.

The finding that hemozoin formation is not essential for parasite survival in reticulocytes suggests that the parasites can develop different means of survival in the blood affording them certain drug resistance. These discoveries may help guide future research targeting human malaria parasites that can only grow inside reticulocytes and opens up new opportunities for the design of anti-malarial drugs to treat refractory patients.



Lin et al. created a mutant mouse parasite, shown here, that can survive and multiply without making hemozoin. Credit: Lin et al., 2015

More information: Lin, J.-w., et al. 2015. *J. Exp. Med*. DOI: 10.1084/jem.20141731

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