Scientists find new method to fight malaria

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Credit: CDC

Scientists have discovered a new way to slow down malaria infections, providing a possible new target for antimalarial drugs. The team are already working with pharmaceutical companies to use this knowledge to develop new antimalarials - an important step in the battle against drug resistant malaria.

When malaria parasites invade red blood cells, they form an internal compartment in which they replicate many times before bursting out of

the cell and infecting more cells. In order to escape red blood cells, the parasites have to break through both the internal compartment and the cell membrane using various proteins and enzymes.

Scientists at the Francis Crick Institute and The London School of Hygiene & Tropical Medicine have identified a key protein involved in this process. Disrupting this protein reduces the efficiency of parasite escape, slowing down the rate of infection. The research, published in *PLOS Pathogens* was funded by Cancer Research UK, the Medical Research Council and Wellcome.

"The parasite sits in its internal compartment inside the cell, surrounded by lots of proteins, a bit like a baby surrounded by amniotic fluid," says Mike Blackman, Group Leader at the Francis Crick Institute. "We focused on the most common protein, known as SERA5, assuming that it probably has an important role since there is so much of it."

The team used genetic tools to knock out the gene responsible for producing SERA5 in malaria parasites and then took time-lapse video of the cells under a microscope. They found that the parasites broke through the membranes faster than normal but many got stuck on their way out, meaning that they were less likely to invade other red blood cells.

"Malaria parasites don't survive for long outside red blood cells, so if they get stuck on their way out, they might die before they have a chance to infect another cell," says Christine Collins, researcher at the Francis Crick Institute and first-named author of the paper. "We found that parasites lacking SERA5 were about half as efficient as normal parasites at escaping and infecting new cells."

The team are now working with GSK to see if SERA5 or one of the enzymes that it controls could be a potential drug target.

"Drug resistant malaria is a huge problem, so there is a real push to develop new drugs that work in a different way," says Mike. "None of the current antimalarials work by preventing the parasites from escaping red blood cells, so we think that the proteins and enzymes that help the parasites break free could be valuable new targets that we can design drugs for."

The paper 'The Plasmodium falciparum pseudoprotease SERA5 regulates the kinetics and efficiency of malaria parasite egress from host erythrocytes' is published in *PLOS Pathogens*.

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