Scientists find new antimalarial drug targets

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Credit: CDC

Researchers have discovered crucial new processes that allow malaria parasites to escape red blood cells and infect other cells, offering potential new treatment targets. The team are already working with pharmaceutical companies to use this knowledge to develop new antimalarial drugs - a critical step in the battle against drug-resistant malaria.

"Over 400,000 people die of malaria each year, and resistance to

common antimalarial drugs is growing," says Professor Mike Blackman, Group Leader at the Francis Crick Institute, who led the research. "We're studying the deadliest malaria parasite, *Plasmodium falciparum*, to try to find new drug targets that work in a different way to existing treatments."

In the latest study, published in *Nature Microbiology*, the team have identified two key proteins that malaria parasites need to escape red blood cells and infect fresh cells. The research was done in collaboration with the Proteomics Science Technology Platform at the Crick as well as scientists at Birkbeck College, King's College London and the London School of Hygiene & Tropical Medicine.

"We've already started collaborating with GSK to see if designing drugs that target these proteins could form the basis of a new antimalarial drug," says Dr James Thomas, Crick postdoctoral scholar and joint first-author of the paper.

When malaria parasites invade red blood cells, they form an internal compartment where 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 red cell membrane.

The team used genetic knockout experiments to show that a protein called SUB1 is essential for the parasite to break through the internal compartment, while SERA6 - which is activated by SUB1 - is essential for the parasite to break through the red blood cell membrane.

Using analytical tools, the team then figured out how SERA6 breaks through the blood cell membrane. Crick PhD student and joint first-author Michele Tan explains: "There is a strong chicken wire-like meshwork that sits under the red blood cell membrane to provide

strength and support. We found that SERA6 cuts the chicken wire, causing the blood cell membrane to collapse and rip open so that the parasites can escape."

The paper 'A protease cascade regulates release of the human malaria parasite Plasmodium falciparum from host red blood cells' is published in *Nature Microbiology*.

More information: James A. Thomas et al, A protease cascade regulates release of the human malaria parasite Plasmodium falciparum from host red blood cells, *Nature Microbiology* (2018). DOI: 10.1038/s41564-018-0111-0

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