Study identifies new way to kill the malaria parasite

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Credit: CDC

Scientists have discovered new ways in which the malaria parasite survives in the blood stream of its victims, a discovery that could pave the way to new treatments for the disease.

The researchers at the Medical Research Council's (MRC) Toxicology Unit based at the University of Leicester and the London School of

Hygiene & Tropical Medicine identified a key protein, called a protein kinase, that if targeted stops the disease. The study is published today in *Nature Communications*.

Malaria is caused by a parasite that lives inside an infected mosquito and is transferred into the human through a bite. Once inside the body, parasites use a complex process to enter red blood cells and survive within them. By identifying one of the key proteins needed for the parasite to survive in the red blood cells, the team have prevented the protein from working, thus killing the parasite. The discovery could be the first step in developing a new drug to treat malaria.

The scientists - funded by the Medical Research Council (MRC) and the Wellcome Trust - used state-of-the-art methods to dissect the biochemical pathways involved in keeping the malaria parasite alive. This included an approach called chemical genetics where synthetic chemicals are used in combination with introducing genetic changes to the DNA of the parasite.

The researchers found that one protein kinase, (PfPKG) plays a central role in various pathways that allow the parasite to survive in the blood. Understanding the pathways the parasite uses means that future drugs could be precisely designed to kill the parasite but with limited toxicity, making them safe enough to be used by children and pregnant women.

Co-lead author of the study Professor Andrew Tobin from the MRC Toxicology Unit which is located at the University of Leicester, said: "This is a real breakthrough in our understanding of how malaria survives in the blood stream and invades red blood cells. We've revealed a process that allows this to happen and if it can be targeted by drugs we could see something that stops malaria in its tracks without causing toxic side-effects."

Professor David Baker, co-lead author from the London School of Hygiene & Tropical Medicine, said: "It is a great advantage in drug discovery research if you know the identity of the molecular target of a particular drug and the consequences of blocking its function. It helps in designing the most effective combination treatments and also helps to avoid drug resistance which is a major problem in the control of malaria worldwide."

According to the World Health Organization malaria currently infects more than 200 million people world wide and accounts for more than 500,000 deaths per year. Most deaths occur among children living in Africa where a child dies every minute of malaria and the disease accounts for approximately 20% of all childhood deaths.

Professor Patrick Maxwell, chair of the MRC's Molecular and Cellular Medicine Board, said: "Tackling malaria is a global challenge, with the parasite continually working to find ways to survive our drug treatments. By combining a number of techniques to piece together how the malaria parasite survives, this study opens the door on potential new treatments that could find and exploit the disease's weak spots but with limited side-effects for patients."

More information: Phosphoproteomics reveals malaria parasite Protein Kinase G as a signalling hub regulating egress and invasion, *Nature Communications*: DOI: 10.1038/ncomms8285

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