

Malaria research bites back

21 October 2010, By Lindsay Brooke



Scientists at The University of Nottingham and the Wellcome Trust Sanger Institute near Cambridge have pin-pointed the 72 molecular switches that control the three key stages in the life cycle of the malaria parasite and have discovered that over a third of these switches can be disrupted in some way.

Their research which has been funded by Wellcome Trust and the Medical Research Council (MRC) is a significant breakthrough in the search for cheap and effective vaccines and drugs to stop the transmission of a disease which kills up to a million children a year.

Until now little has been known about the cellular processes involved in the development of this deadly disease. The research, published in the journal *Cell Host & Microbe*, involved the very first comprehensive functional analysis of protein kinases in any [malaria](#) parasite. It is also the largest gene knock-out study in *Plasmodium berghei* - a malaria parasite infecting rodents.

Dr. Rita Tewari, in the School of Biology at The University of Nottingham, led the research. Dr. Tewari said: "Blocking parasite transmission is recognised as an important element in the global fight to control malaria. Kinases are a family of proteins which contribute to the control of nearly all [cellular processes](#) and have already become major drug targets in the fight against cancer and other diseases. Now we have identified some key regulators that control the transmission of the malaria parasite. Work to develop drugs to

eradicate this terrible disease can now focus on the best targets. This study shows how systematic functional studies not only increase our knowledge in understanding complexity of malaria parasite development but also gives us the rational approach towards drug development."

The life cycle of the malaria parasite is complex. Once the mosquito has feasted off infected blood fertilisation takes place within the mosquito. The deadly parasites are then injected back into another host in large numbers when the mosquito bites again. Once inside its mammalian host the parasite first infects the liver where it replicates again. After 48 hours millions of parasites are released into the red blood cells of its host where they attack in vast numbers overwhelming their host producing high fever and sickness.

Dr. Oliver Billker, an expert in pathogen genetics at the Wellcome Trust Sanger Institute, said: "This is a major leap forward - we can now set aside these 23 functionally redundant genes. This act of prioritisation alone has narrowed the set of targets for drug searches by a third.

"Our study demonstrates how a large scale gene knockout study can guide drug development efforts towards the right targets. We must now develop the technology to ask across the genome which pathways are important for parasite development and transmission."

As the malaria parasite becomes increasingly resistant to existing drugs and vaccines the race to find ways of blocking the transmission of malaria is becoming increasingly important. Last month the journal *PLoS ONE* published Dr. Tewari's research which identified a protein, PF16, which is critical in the development of the malaria parasite - specifically the male sex cells (gametes) - which are essential in the spread by mosquitoes of this lethal parasite. The study, led by The University of Nottingham, found a way of disabling the PF16 protein.

In future studies, Dr. Tewari's group is concentrating on the role of other signalling molecules like phosphatases, kinases and armadillo repeat proteins and their interaction in understanding [malaria parasite](#) development. The aim is to identify the best drug or vaccine target along the way.

The University of Nottingham has broad research portfolio but has also identified and badged 13 research priority groups, in which a concentration of expertise, collaboration and resources create significant critical mass. Key research areas at Nottingham include energy, drug discovery, global food security, biomedical imaging, advanced manufacturing, integrating global society, operations in a digital world, and science, technology & society.

Through these groups, Nottingham researchers will continue to make a major impact on global challenges.

Provided by University of Nottingham

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