Protein critical in malaria parasite development identified

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Research led by The University of Nottingham has opened up a new area of malaria parasite biology which could lead to new methods of controlling the transmission of this deadly disease.

Malaria threatens 40 per cent of the world's human population. It causes disease in 300 million people and kills up to a million children every year.

Research published today in the journal *PLoS ONE* has 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, has found a way of disabling the PF16 protein that contains a structure called an Armadillo repeat.

Dr. Rita Tewari, from the Institute of Genetics at The University of Nottingham said: “Male gametes move using flagella, which are ancient

structures that are formed in a unique way in the malaria parasite. This is the first report describing the role of the Armadillo repeat protein PF16 in the flagellar biology of male sex cells in malaria. Blocking formation of these cells is an important strategy to prevent malaria transmission and this study represents a significant breakthrough in understanding this process."

Transmission of malaria between human and mosquito depends on the sexual stages of the parasite's life cycle. When a mosquito feeds on humanblood containing parasites, it activates the parasite's sexual development, a process essential for transmission of malaria between people. Within the mosquito gut Plasmodium, the malaria parasite develops into male and female gametes (sex cells), which then fertilise. By blocking the formation of these sex cells researchers have found a route to preventing malaria transmission.

Researchers have discovered that the male sex cells — the male gamete — are the only developmental stage of the parasite that possess a flagellum — a tail like projection that protrudes from the cell body and important for the male gamete motility. Until now very little has been know about the identity or function of the proteins which control this part of the parasite biology.

Proteins containing Armadillo repeats have widely diverse functions in biology, including important roles in cell signalling and cancer. PF16 regulates flagellar structure and motility in organisms as diverse as green algae and humans. Researchers in Nottingham and their colleagues have also found some new Armadillo proteins specific to malaria.

The team of researchers from the Institute of Genetics at The University of Nottingham, Imperial College London, the University of Oxford, the MRC National Institute for Medical Research, University of Birmingham,UK and the Dartmouth College,USA, funded by MRC,

Wellcome Trust , Leverhulme Trust have discovered that this flagellum plays a crucial role in the fertilisation of the malaria parasite and have identified the PF16 protein that regulates the movement of the flagellum and how to deactivate it.

The group at Nottingham say they have opened up a new model for the analysis of Plasmodium flagellar biology. This will provide unique insights into an ancient organelle thereby opening up new intervention strategies to control the malaria parasite.

More information: The paper can be found online at: dx.plos.org/10.1371/journal.pone.0012901

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