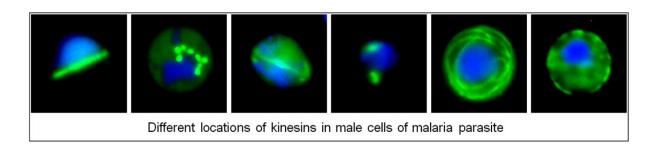


A new study gives an important understanding of how molecular motor proteins are involved in malaria transmission

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Different locations of kinesins in male cells of malaria parasite. Credit: The University of Nottingham

Scientists at the University of Nottingham have made a major breakthrough in understanding how malaria parasites divide and transmit the disease, which could be a major step forwards in helping to prevent one of the biggest killer infections in the world.

Malaria is still the deadliest parasitic disease worldwide, with approximately 241 million cases and over half a million deaths annually. It is caused by a <u>single-celled parasite</u> called Plasmodium, which is transmitted between people by the female Anopheles mosquito when they bite to take blood.



In this new study, published in *PLOS Biology*, scientists have uncovered the crucial roles of a group of motor proteins named kinesins during the parasite life cycle.

The research, led by Rita Tewari, Professor of Parasite Cell Biology in the University's School of Life Sciences, has shown the significance of kinesins in basic cellular processes needed for malaria parasite development, multiplication and invasion, most importantly within the mosquitoes that transmit the parasite.

Kinesins are molecular motor proteins that use energy from the hydrolysis of adenosine triphosphate (ATP—a universal store of energy in all <u>cells</u>), and function in various cellular processes. They are involved in transport, <u>cell division</u>, cell polarity and <u>cell motility</u>.

This latest study showed that of the nine kinesins present in the parasite genome, eight are required for the various functions of cell proliferation to cell movement in the mosquito host which was very surprising.

Researchers at the University of Nottingham have studied the location and function of all kinesins in live parasite cells at various stages of development, both in the mosquitoes which transmit the disease, and in the host where it causes disease. These proteins are important potential drug targets, hence the importance of this study in the search for new intervention targets.

Professor Tewari said: "This is an important genome-wide study and an essential resource for studying the various morphologically distinct parasite cells involved in parasite transmission. It shows how these important motors proteins are involved in forming molecular tracks for movement, multiplication, and transmission."

Dr. Zeeshan, who is the first author of the paper, said: "This is a



comprehensive study on parasite molecular motors. It was very challenging to capture the dynamics of these proteins in live parasite <u>cells</u> within mosquitoes. Most importantly, we could study the formation of the male gamete (sperm), which involves a rapid multiplication process that completes within 10-12 min after the female mosquito has ingested blood from an infected host. Multiple kinesins are involved in efficient production of male gametes and deletion of kinesin genes halts parasite transmission, a discovery that can be explored further for <u>drug discovery</u>.

"In addition, we found one motor protein, <u>kinesin</u>-13, which is essential for parasite multiplication in all stages of the life cycle."

The study was carried out in collaboration with several scientists; Tony Holder at the Francis Crick Institute, London; Prof Carolyn Moores at Birbeck College; Profs Sue Vaughan and David Ferguson at Oxford Brookes; Prof Mathieu Brochet and Ravish Raspa at the University of Geneva; and Prof Karine Le Roch and Steven Abel at the University of California. This study demonstrates the power of multidisciplinary science and how networking and collaboration lead greater global understanding in science. The work was funded by BBSRC, MRC, CRUK, Wellcome Trust, NIH and NIAID.

More information: Genome-wide functional analysis reveals key roles for kinesins in the mammalian and mosquito stages of the malaria parasite life cycle, *PLoS Biology* (2022). DOI: 10.1371/journal.pbio.3001704

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