First adhere, then detach and glide forward

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This is a malaria parasite (green) on an elastic gel with marker beads in two colors. The marker beads are deflected during the parasite's movement. Shown here with red arrows are the calculated force vectors (middle) and traction forces (right). The greatest force occurs at the center of the parasite and is indicated in red. Credit: Department of Infectious Diseases, Heidelberg University Hospital

How do one-celled parasites move from the salivary gland of a mosquito through a person's skin into red blood cells? What molecular mechanisms form the basis for this very important movement of the protozoa? A team of researchers headed by Dr. Friedrich Frischknecht, head of a research group at the Department of Infectious Diseases at Heidelberg University Hospital, observed the initial stage of the malaria parasite that is transmitted by mosquitoes with new microscope techniques.

They discovered that the parasite continually alternates between phases of rapid gliding and phases of firm adhesion to the surface. The interaction of these two processes probably enables the parasite to move rapidly over a long time, which is necessary for successful transmission of the disease. The research was a colaboration within the CellNetworks cluster of excellence and published in the journal *Cell Host & Microbe*.

The CellNetworks cluster of excellence

Researchers from three different disciplines at the CellNetworks cluster of excellence were involved in the study. This is one of the first studies ever in which modern biophysical methods were used to examine parasites. Leading this study were, in addition to Dr. Friedrich Frischknecht of the Parasitology Department, Professor Dr. Ulrich Schwarz from the Institute of Theoretical Physics and Professor Dr. Joachim Spatz from the Institute of Biophysical Chemistry at the University of Heidelberg.

The goal of the CellNetworks cluster of excellence is to describe and understand complex biological networks. It consists of numerous scientific institutions in the Mannheim/Heidelberg region and was founded at the University of Heidelberg in 2006 as part of the excellence initiative of the Deutsche Forschungsgemeinschaft (German Research Foundation) as one of the first excellence institutions in Germany.

How does the motility mechanism of the malaria parasite function?

Malaria is caused by plasmodia, tiny parasites that enter the human body through the saliva of a mosquito when it bites. They use active movements to enter into the bloodstream and from there to cells of the liver and finally into blood cells. A Plasmodium parasite consists of a single cell that has small motors (myosin) in its inner cell wall that are connected to the outer cell wall by movable elements (actin). Certain protein structures (TRAP, thrombospondin-related anonymous protein) are located there, with which the protozoa can adhere to the surface. The components of this motility mechanism that is essential for the parasite are known to a great extent, but the spatial and temporal dynamics of the individual components are still unclear.

The "stick-slip" method

Under special microscopes, the researchers observed how the sporozoites adhere to several sites on the surface via the TRAP protein and then use the short actin filaments to push their body past these adhesion points. "The parasite can stretch forward while still attaching with its rear end - thus building up elastic energy. At the moment when the rear adhesion is detached, energy is released and the sporozoite glides forward rapidly," explains Dr. Friedrich Frischknecht. The researchers call this mechanism the "stick-slip" method. The speed of movement is regulated by the formation and turnover of adhesion sites, the existence and dynamics of which have been described for the first time.

More information: Plasmodium sporozoite motility is modulated by the turnover of discrete adhesion sites. Sylvia Münter, Benedikt Sabass, Christine Selhuber-Unkel, Mikhail Kudryashev, Stephan Hegge, Ulrike Engel, Joachim P. Spatz, Kai Matuschewski, Ulrich S. Schwarz, Friedrich Frischknecht. Cell Host & Microbe, 2009.

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