Microorganisms and Biofilms

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Microscopic techniques to investigate malaria pathogenesis

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Malaria is transmitted to vertebrate hosts by the bite of female Anopheles mosquitoes that are infected with the sporozoite form of protozoan parasites of the genus Plasmodium [1]. Sporozoites are deposited in the skin upon transmission into vertebrate hosts and move at high speed (1-2 µm/s) to find and enter into blood vessels [Fig 1]. Once in the blood they are transported to the liver, where they enter hepatocytes to differentiate into blood cell invading forms. These so-called pre-erythrocytic stages of the malaria parasite are clinically silent yet critical for establishing infection in the mammalian host [2].

Sporozoites migrate using a unique locomotion called gliding motility [2], which enables them to penetrate host tissues (skin and liver), entering the blood vessel and to invade hepatocytes. The clinical symptoms of malaria manifest during the erythrocytic cycle of the parasite [3]. A characteristic feature of infection is the accumulation or sequestration of parasite-infected red blood cells (RBCs) in various organs avoiding the spleen-dependent killing mechanism [4]. Sequestration results from adhesive interactions between parasite-derived proteins expressed on the surface of infected RBCs and a number of host molecules on the surface of endothelial cells [Fig 2] [5].

In order to investigate the interaction between the parasite and the host at the different stages of the complex life cycle, we employ in vitro and in vivo imaging approaches, high-resolution microscopy (AFM) and other biophysical instruments (optical tweezers) to study the pathogenesis of the parasite. These will be presented in the talk.

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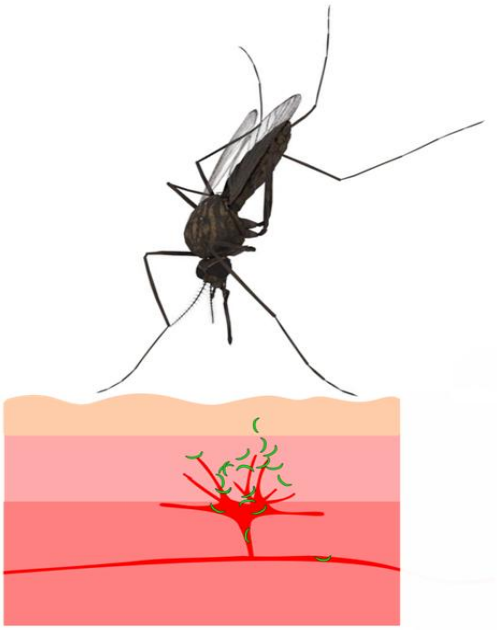

Fig 1. : Female *Anopheles* mosquitoes inject the sporozoite form of the parasite into a human host. To successfully continue the infection, sporozoites must invade blood vessels in the dermis using their gliding motility system.

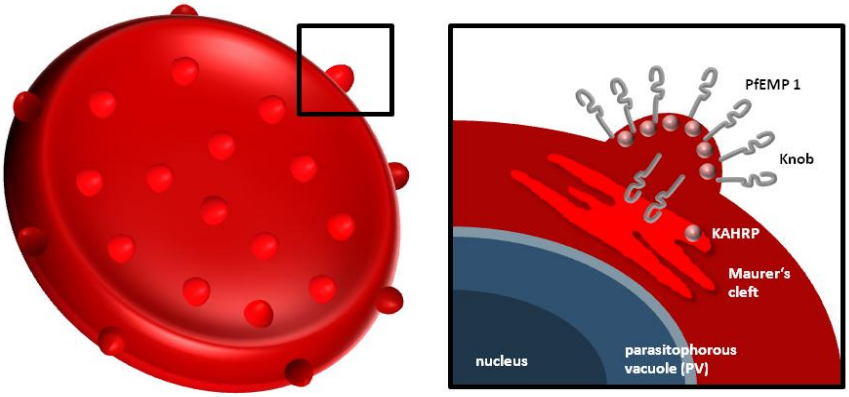

Fig 2. : The virulence of *Plasmodium falciparum* malaria is related to the parasite's ability to evade host immunity through tissue-specific adhesion of infected erythrocytes (IEs). The *P. falciparum* erythrocyte membrane protein 1 (PfEMP1) family expressed on dome-shaped protrusions called knobs on the IE surface is central to both.