IMAGING AND VISUALIZATION

Fluorescent parasite reveals trade secrets

Fluorescent parasites allow researchers to achieve real-time visualization of the process of liver infection by *Plasmodium*, the pathogen responsible for malaria.

Malaria still threatens large segments of the world's population, even though the general pathology of the disease is relatively well understood. The devil is in the details, however, and there are questions that would best be answered if one could directly observe *Plasmodium* going about its dirty work. Intravital microscopy—the imaging of tissues in a living animal—has been a useful research tool for many decades. But according to Ute Frevert, a researcher at New York University, this technology has only recently been applied to *Plasmodium*.

An important breakthrough came with the recent development of a fluorescent strain *P. berghei* (Natarajan *et al.*, 2001). This powerful tool has now helped Frevert and her colleagues to tackle an important mystery —the process by which *Plasmodium* parasites obtain access to liver hepatocytes from the bloodstream. Earlier studies indirectly support a model in which the organisms use Kupffer cells, specialized macrophages lining the liver vasculature, as a gateway to the spaces in which the hepatocytes reside. The Frevert group confirmed this model, using mosquitoes to infect mice with the parasite, and then intravitally imaging the liver to generate movies that reveal the fluorescent parasites gliding along the liver sinusoids, and eventually binding and forcing their way through the Kupffer cells (Frevert *et al.*, 2005). Frevert's team also learned that the parasites spend extended periods in the capillary prior to hepatocyte infection, time which they may be using to trigger broad deactivation of local Kupffer cells—eliminating a key line of defense against infection.

This approach could also prove highly effective for studying the pathology of other parasites. "People assume a lot about what happens *in vivo*," says Frevert, "but they don't really know unless they see it. I think that other parasites like, for example, *Toxoplasma* or *Leishmania*, develop in sites of the body that are accessible for this technique. I think that if people adapt this technology to other microbial infections, they could get a lot of insight into dynamic events... not only the spreading of the infection itself, but also the defense mechanisms of the host."

Michael Eisenstein

RESEARCH PAPERS

Frevert, U. *et al.* Intravital observation of *Plasmodium berghei* sporozoite infection of the liver. *PLoS Biol.* **3**, e192 (2005).

Natarajan, R. *et al.* Fluorescent *Plasmodium berghei* sporozoites and pre-erythrocytic stages: a new tool to study mosquito and mammalian host interactions with malaria parasites. *Cell Microbiol.* **3**, 371–379 (2001).