Imaging New Paths for Malarial Parasites

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In general terms, parasites that cause malaria are injected into the skin by mosquitoes. They then travel into the bloodstream and then to the liver where they invade liver cells and mature into forms called schizonts. Within each schizont, cell division produces thousands of tiny new forms called merozoites, each of which, when released into the bloodstream, is capable of infecting a red blood cell. This "traditional" pathway for malarial parasites may not be the only way these parasites travel through the body. Using some increasingly more powerful immuno-imaging tools, Rogerio Amino, Sabine Thiberge, Béatrice Martin, Susanna Celli, Spencer Shorte, Friedrich Frischknecht, and Robert Ménard have demonstrated an additional route that could have profound implications for developing effective vaccines for this major worldwide disease.[2.]

Plasmodium is the parasite that causes malaria. The infectious form (sporozoite) of *Plasmodium* was engineered with Green Fluorescent Protein (GFP) and mosquitoes injected it into the dermis of rodents (hairless mice, Brown Norway rats, etc.). The path of the parasite could be followed to a certain extent using epifluorescence time-lapse microscopy. The parasites were observed to move in a robust forward-gliding locomotion that was quite distinct from movements *in vitro* or within the salivary ducts of mosquitoes. Whereas some parasites invaded blood vessels and were swept away at speeds expected in blood circulation, others invaded lymphatic vessels. These parasites appeared to be mostly filtered out of the lymph by the first lymph node that they encountered. They were first seen at the location where the lymph vessel enters the node, and in time they relocated toward the vessel leaving the node. During this period, many of the parasites were degraded. Other experiments suggested that dendritic cells of the lymph node were degrading the parasites. Interestingly, if parasites were introduced into the rodent with a syringe, rather that by a mosquito, the number of parasites in the lymph nodes was decreased about 20-fold!

To rule out the possibility that some parasites were getting through the lymph nodes and entering the general vasculature, Amino *et al.* examined lymph nodes further along the drainage route. Less than 1% of the parasites were found further downstream. They also cannulated the thoracic duct, the lymph vessel that carries most of the lymph back to the bloodstream, and no parasites were detected. This convincingly demonstrated that malaria parasites not only enter the bloodstream, as has been known for years, but about 25% of the parasites enter lymph vessels and most are filtered out at the first lymph node they encounter.

This is the first evidence of the *Plasmodium* parasite being processed by the lymphatic system. What may be the most important part of this study is that some parasites are degraded by the dendritic cells of lymph nodes, and thereby present antigens to immunologically active cells. This will be an important factor to consider when developing vaccines for this global scourge.

1. The authors gratefully acknowledge Dr. Rogerio Amino for reviewing this article.

2. Amino, R., S. Thiberge, B. Martin, S. Celli, S. Shorte, R. Frischknecht, and R. Ménard, Quantitative imaging of *Plasmodium* transmission from mosquito to mammal, Nature Medicine 12:220-224, 2006.

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Showing the damage wrought by time and mishandling, the image is a page from the papyrus manuscript known as the Gospel of Judas. This page is one of several found in a leather-bound codex said to date from the third or fourth century C.E., that came to light in the late 1970's. Wrapped in newspaper and stored in shoe boxes, the pages disintegrated into hundreds of fragments as the codex passed through the hands of antiquities dealers and collectors. A five-year effort by a team of preservationists and scholars has led to the recreation and translation of 90 to 95 percent of the manuscript. The results of this undertaking were recently revealed by the Washington, D.C.-based National Geographic Society, which joined forces with the Maecenas Foundation for Ancient Art in Basel, Switzerland, and the Waitt Institute for Historical Discovery in La Jolla, California, to rescue the document. While biblical scholars have focused on translation and interpretation of the Coptic text, an array of microscopes and other analytical instruments have been focused on the papyrus and the ink, to assess the authenticity of this historically significant manuscript. Photograph courtesy of Joseph G. Barabe.

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  reinhilde.stopar@unileoben.ac.at
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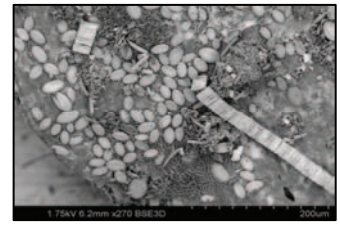

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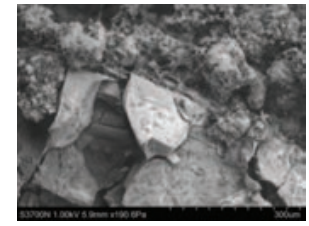

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