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Opinion Article

Life Cycle of Female *Anopheles* Mosquito in Human Body

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DESCRIPTION

The malaria parasite develops both in humans and in the female *Anopheles* mosquitoes. The size and genetic complexity of the parasite mean that each infection presents thousands of antigens (proteins) to the human immune system. The parasite also changes through several life stages even while in the human host, presenting different antigens at different stages of its life cycle. Understanding which of these can be a useful target for vaccine development has been complicated. In addition, the parasite has developed a series of strategies that allow it to confuse, hide, and misdirect the human immune system. The natural history of malaria involves cyclical infection of humans and female *Anopheles* mosquitoes. In humans, the parasites grow and multiply first in the liver cells and then in the red cells of the blood. In the blood, successive broods of parasites grow inside the red cells and destroy them, releasing daughter parasites that continue the cycle by invading other red cells.

The blood stage parasites are those that cause the symptoms of malaria. When certain varieties of blood stage parasites (gametocytes, which occur in male and lady forms) are ingested during blood feeding by a female *Anopheles* mosquito, they mate in the intestine of the mosquito and start a cycle of boom and multiplication in the mosquito. After 10-18 days, a form of the parasite called a sporozoite migrates to the mosquito's salivary glands. When the *Anopheles* mosquito takes a blood meal on human, anticoagulant saliva is injected together with the sporozoites, which migrate to the liver, thereby starting a new cycle.

The past decade has seen an unprecedented progress in research on liver stage malaria. This has brought forth the identification of numerous parasite and host factors that are of critical importance to hepatocyte infection and intra-hepatocytic parasite development. Without doubt, research in the coming years will identify additional important factors. However, the study of parasite–hepatocyte interaction must now enter the next phase, by not only identifying critical host–pathogen interactions but also assembling these interactions into a temporal and spatial cascading network that fully delineates parasite infection of and development within hepatocytes at the molecular level, from the point of invasion to the release of merozoites. These studies will be likely performed with rodent malaria models, but the increased maturity of in vitro and in vivo hepatocyte infection models of human malaria parasites gives hope that at least some of this work can be achieved with medically relevant parasite species. This is particularly important for the study of P. vivax hypnozoites in gaining insights into the molecular mechanisms of their latency, their activation, and their interaction with hepatocytes during long periods of persistence.

Female *Anopheles* mosquito causes infection in humans

Infection in humans begins with the bite of an infected female *Anopheles* mosquito. Out of about 460 species of *Anopheles* mosquito, more than 70 species transmit falciparum malaria is one of the best known and most prevalent vectors, particularly in Africa. This infective stage called sporozoites released from the salivary glands through the proboscis of the mosquito enters the bloodstream during feeding. The mosquito saliva contains antihemostatic and anti-inflammatory enzymes that disrupt blood clotting and inhibit the pain reaction. Typically, each infected bite contains 20–200 sporozoites. The immune system clears the sporozoites from the circulation within 30 minutes, but a few escape and quickly invade liver cells (hepatocytes). The sporozoites move in the blood stream by gliding, which is driven by a motor made up of the proteins actin and myosin beneath their plasma membrane. Dengue is a mosquito-borne viral infection causing a severe flu-like illness and, sometimes causing a potentially lethal complication called severe dengue. The incidence of dengue has increased 30-fold over the last 50 years. Up to 50-100 million infections are now estimated to occur annually in over 100 endemic countries, putting almost half of the world's population at risk.

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