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**MOLECULAR AND ULTRASTRUCTURAL
CHARACTERIZATION OF DEVELOPMENT OF MALARIA
PARASITE IN THE MOSQUITO**

By

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Abstract

The malarial ookinete and sporozoite are critical stages for parasite development and transmission. They must invade potential barriers in the mosquito midgut and salivary glands. They are highly motile and possess well-developed cytoskeleton and elaborate secretory organelles. The cytoskeleton supported by surface and secreted proteins plays important roles in parasite development, motility and invasion of target host cells.

Using the rodent malaria model *Plasmodium berghei* (Pb), the expression of eight proteins was studied by immuno-fluorescence and immuno-electron microscopy. The genes of three proteins were characterized.

Four sexual stage proteins, Pbs42, Pbs70, Pbs155a and Pbs155b are expressed in the ookinete. Pbs42, Pbs155a, Pbs155b are localized to the apical region, but no specific organelle for their localization was determined. Pbs70 is localized to the ookinete pellicular inner membrane complex (IMC), and may be a cytoskeletal protein.

A secreted ookinete adhesive protein, PbSOAP (Dessens *et al.*, 2003), was localized to the micronemes using antiserum raised to its recombinant form.

The genes of three putative cytoskeletal proteins, PbIMC1a, PbIMC1b and PbIMC1c were cloned, of which PbIMC1a was further studied by gene knockout.

PbIMC1a has three regions that are highly conserved in its orthologues, and may contain the structural/functional domains. The protein also has considerable homology with the cytoskeletal articulins. PbIMC1a is expressed in the sporozoite, with peripheral staining indicating its association with the IMC. PbIMC1a-null sporozoites are deformed, impaired in gliding motility, failed to invade the salivary glands and to infect mice, indicating the protein's importance in parasite development and infectivity.

PbIMC1b and PbIMC1c have similar structure to PbIMC1a, and represent paralogues in other invasive stages. The proteins together with their orthologues therefore constitute a new class of cytoskeletal proteins unique to *Plasmodium* and related apicomplexan parasites, and would represent potential intervention targets against these parasites of great public health and veterinary importance.

Key words: Apicomplexa, cytoskeleton, infectivity, IMC1, malaria, mosquito, motility, ookinete, *Plasmodium*, sporozoite.