

***PLASMODIUM*-MOSQUITO INTERACTIONS**

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The mosquito is an obligatory vector for malaria transmission. Parasite numbers decrease dramatically as development in the mosquito proceeds. Of thousands of gametocytes ingested in a typical infected blood meal, usually less than 10 succeed to reach the oocyst stage. Mosquito defense mechanisms play an important role in parasite attrition. A gene that is dramatically induced in the mosquito midgut in response to ookinete invasion was originally identified from a subtraction library (Abraham et al., J Biol Chem 279:5573-5580, 2004). The gene encodes a serine protease inhibitor (SERPIN6) and is induced only in the invaded cells. Remarkably, silencing SRPN6 expression with dsRNA increased oocyst number by up to four-fold, suggesting that this gene is part of a mosquito defense mechanism against the pathogen. SRPN6 is also induced by exposure of the luminal surface, but not basal surface, of the midgut to bacteria, suggesting that receptors that sense the presence of foreign organisms are polarized on the midgut epithelial cells.

Plasmodium development in the mosquito requires the crossing of two different epithelia: midgut and salivary gland. Circumstantial evidence suggests that crossing requires specific interactions between *Plasmodium* and epithelial surface molecules. Salivary gland invasion by sporozoites is inhibited by the SM1 dodecapeptide (Ghosh et al, Proc Natl Acad Sci USA 98:13278-13281, 2001). Using anti-SM1 antibodies, we have shown that the A-domain of the sporozoite surface protein TRAP is required for salivary gland invasion. SM1 competes with TRAP A-domain for binding to salivary glands. Using UV cross-linking and pull-down with a derivatized SM1 peptide, we have identified the salivary gland surface protein saglin as a receptor for TRAP domain-A attachment. Thus, these experiments have identified a receptor-ligand complex required for *Plasmodium* invasion of the mosquito salivary glands.