

## **Towards blocking malaria transmission in the vector: immune interactions between *Anopheles* and *Plasmodium***

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Approximately one day after *Anopheles* ingests malaria-infected blood, *Plasmodium* ookinetes cross the midgut epithelium and, upon reaching the basal lamina, develop into oocysts. However, large losses in parasite numbers occur during invasion, sometimes resulting in complete elimination of the parasite and terminating the malaria transmission cycle. The mosquito innate immune system is known to be activated during midgut invasion, but to date no direct evidence has been published identifying endogenous mosquito factors that affect parasite development. Our group is using functional genomic analysis and experimentation to understand immune and other molecular interactions between the vector and the parasite, in the perspective of ultimately using this knowledge to reduce malaria transmission in the field, through vector-based interventions.

The major tools in these studies are bioinformatic analysis of the genome sequence of *A. gambiae* (see abstract of E. Zdobnov), gene expression profiling using DNA microarrays (see abstract of G. Christophides), a robust protocol for specific gene inactivation in adult *Anopheles* (S. Blandin *et al.*, 2002, EMBO Reports 3 (9), 852-856), transgenesis, and diverse cell biological methods. We are conducting a genomic RNAi screen for genes modulating parasite transmission. Examples are studies on genes encoding TEP1 (see abstract of E. Levashina) and a leucine-rich repeat protein, LRRP1 plus two C-type lectins, CTL4 and CTLMA2 (present abstract).

I will present evidence that LRRP1 and the two CTLs act as opposing, negative and positive regulators, respectively, of *P. berghei* ookinete development to oocyst. The results demonstrate that mosquito innate immunity can have both antagonistic and protective roles in *Plasmodium* transmission.