Anopheles gambiae immune responses that determine susceptibility to *Plasmodium* infection

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http://www3.niaid.nih.gov/labs/aboutlabs/lmvr/mosquitoImmunityVectorCompetenceUnit/

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We will first examine two mechanisms that mediate mosquito immune responses against Plasmodium: 1) The STAT pathway plays a central role in vertebrate immunity and is conserved in insects, including the mosquito An. gambiae. Gene silencing experiments revealed that the STAT pathway regulates the expression of several genes in response to bacteria and malaria. Activation of this pathway limits Plasmodium infection by mediating a late phase immune response that results in oocyst lysis. 2) Blood feeding triggers the expression of an immuno-modulatory peroxidase, (IMPer) in the midgut on *A. gambiae*. This enzyme prevents the activation of antibacterial immune responses in midgut cells and allows proliferation of bacterial flora. IMPer silencing triggers a strong induction of nitric oxide synthase expression (NOS) and a dramatic decrease in Plasmodium infectivity. NOS is the main mediator of parasite death, as double silencing of IMPer and NOS rescues Plasmodium infection to control levels. We conclude that the physiological induction of IMPer after blood feeding provides a permissive environment for Plasmodium development, as it prevents activation of both antibacterial and NOS-mediated anti-malarial responses. During the final part of the presentation we will explore how *Plasmodium falciparum* evades the mosquito immune system. A selected *An. gambiae* strain (L35) is refractory to new world strains of *P. falciparum* but allows development of Africa strains. The *P. falciparum* gene(s) mediating this difference between strains is being mapped using a genetic cross. The differences in the way mosquitoes respond to these two strains is also under investigation.