Role of Salivary Gland Secretions in *Anopheles* Mosquito Midgut and *Plasmodium* Development

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ABSTRACT

Mosquito saliva plays a central role in blood meal acquisition plus the development and transmission of the malaria parasite. Functional genomics and proteomics studies have characterized and predicted roles of many proteins in the sialotranscriptome of *An. gambiae* and their predicted roles. Whereas, this approach provides important insights or *a priori* on the role of saliva and its interaction with *Plasmodium* in the midgut, the large amounts of data often presents a problem in determining the best strategy for exploiting the knowledge in malaria control. For this reason, a series of experiments was designed to test and validate several *a priori* in this study: 1) Saliva contains antimicrobial proteins (AMPs) that may modulate bacteria population dynamics in the midgut thus affecting mosquito survival; 2) Saliva contains several catabolic enzymes and protease suppressors thus affecting *Plasmodium* development during blood meal digestion and 3) Saliva contains xanthurenic acid and other molecules whose role remains unknown that may directly or indirectly affect *Plasmodium* development in the midgut.

Surprisingly, mosquito salivary gland homogenate (SGH) of female mosquitoes did not exhibit any antimicrobial activity when tested against 8 bacteria species previously isolated from *An. gambiae* midgets indicating no role for saliva in modulation of endosymbiont bacteria in the midgut. Whereas bacteria was found to be crucial in the larval diet for survival and development in the immature stages, the role of endosymbiont bacteria in the adult mosquito proved ambivalent as it varied from beneficial to harmful under various experimental setups. However, the clear role in larval survival and development indicates the employment of biological controls such

as *Bti* and *Bs* is a winning strategy that should be promoted in integrated vector management. Lastly, SGH was demonstrated to have protease suppression properties that suppressed both the serine proteases and aminopeptidase. Interestingly, *P. falciparum* was also shown to modulate proteases by down-regulating serine proteases and up-regulating aminopeptidase, which was recently discovered as a *Plasmodium* receptor during midgut invasion. SGH suppression of aminopeptidase therefore suggests a possible role for SGH molecules in transmission blocking, however oocsyt counts in mosquitoes fed on infective blood meal + SGH did not differ significantly when compared to control group fed on infective blood meal only.