

Two peroxidases mediate refractoriness in *A. gambiae*

Carolina Barillas-Mury and Sanjeev Kumar

Laboratory of Malaria and Vector Research, National Institutes of Health, 12735
Twinbrook Parkway, Rockville, MD 20852

The epithelial responses of the Refractory (R) *A. gambiae* L3-5 strain to *P. berghei* ookinete invasion were evaluated. In contrast to previous reports on the irreversible damage caused by parasite invasion in susceptible (S) mosquitoes, the invaded cells suffered very little damage and only an occasional loss of microvilli was observed in the R strain. There was no induction of Nitric Oxide Synthase (NOS), nor peroxidase activity and no tyrosine nitration could be detected. All other markers of cell damage, such as Serpin-10 translocation and induction, nuclear degeneration, cell detachment, protrusion into the lumen and formation of a basal actin ring were also negative. Four of the peroxidases induced in the midgut by *Plasmodium* infection in S females were not induced not induced in R. However, two peroxidases were expressed at higher levels in R mosquitoes infected with malaria. One of them, induced by infection in the S strain, was constitutively activated in R mosquitoes. The second one, which is strongly suppressed in S, is induced in R. Silencing of either peroxidase resulted in a partial but significant reversion to a refractory phenotype. One of these peroxidases is secreted into the midgut lumen, suggesting that the fate of invading ookinetes in the R strain might be already determined even before they invade the epithelial cell.