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The effects of pyrethroid resistance on transcription of metabolic enzymes in a major African Malaria vector, Anopheles funestus

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2012-01-11
http://hdl.handle.net/10539/10961

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ABSTRACT

Anopheles funestus is a major vector of malaria in the southern African region. Insecticide resistance to pyrethroid and carbamate insecticides has been recorded in populations of this species in South Africa and Mozambique. This study aimed to determine the relationship between pyrethroid resistance and gene expression of two closely related genes, *CYP6P9* and *CYP6P13*, by age and sex in a resistant strain *An. funestus* from southern Africa, FUMOZ-R. The insecticide susceptibility assays showed that percentage survival in both FUMOZ-R sexes significantly decreased as age increased. The mRNA expressions of *CYP6P9* and *CYP6P13* were higher in FUMOZ-R relative to the insecticide susceptible strain (FANG). The expression of permethrin resistance varies with age in *An. funestus* FUMOZ-R. The results indicate that other genes may also be involved in insecticide resistance. In addition to this, the expression profile of other metabolic genes involved in insecticide resistance was also investigated. A microarray based approach was used to identify genes differentially expressed in FUMOZ-R and FANG. As the full set of detoxification genes in *An. funestus* are unknown, this study investigated the utility of the *An. gambiae* detox chip to screen for differentially expressed detoxification genes in *An. funestus*. After optimization of the hybridisation conditions, over 90% of the probes showed a positive signal. Only three genes were significantly ($P<0.001$) differentially expressed in the females, *CYP6P9*, *COI* and *CYP6M7*. The same genes were also significantly differentially expressed in the adult males, together with an additional 21 transcripts. The third part of this study investigated the gene expression in the first instar, fourth instar and 3-day old adults in FUMOZ-R using the *An. gambiae* detox chip. The variation in metabolic enzyme gene transcription at the different developmental stages

in *An. funestus* are not known. The identification of differentially transcribed genes at the different life stages provides some insight into the role and function of these genes. A large number of cytochrome P450s (monooxygenases), esterases, glutathione *S*-transferases (GSTs) and other additional genes were differentially expressed in all life stages. This study provided vital information regarding genes potentially involved in pyrethroid resistant and is the first to provide metabolic or detoxifying transcription gene information in *An. funestus*.