

Transcriptional analysis of insecticide resistance in *Anopheles stephensi*, using cross species microarray hybridization

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Abstract

A large scale microarray containing 11,760 unique EST clusters and a small scale ‘Detoxification chip’ containing 231 genes putatively involved in insecticide detoxification, both from the malaria vector *Anopheles gambiae*, were used in cross species microarray hybridizations, to monitor gene expression in insecticide resistant and susceptible *An. stephensi* laboratory strains. Approximately 7,000 and 180 unique ESTs (for the large and small scale array respectively) gave a positive signal with the *An stephensi* probes. Around 60 of these unique ESTs were strongly up-regulated in the highly insecticide resistant strain *Dubs*. These included glutathione S-transferases, carboxylesterases and cytochrome P450 oxidative metabolic complex genes. In addition, several genes, belonging to families not previously associated with insecticide resistance, such as members of the NADH-ubiquinone oxidoreductase complex, genes implicated in muscle development and a Nitric-oxide Synthase, were expressed at statistically higher levels in the resistant strain. Interestingly, genes possibly involved in thickening of the adult cuticle showed the most striking up-regulation, which might indicate the presence of a physiological mechanism which reduces insecticide uptake in the resistant insects. In contrast, two peroxidases were up-regulated in the susceptible strain *Beech*. Microarray data were verified by extensive real time PCR, on cloned *Anopheles stephensi* genes. The possible use of the microarray technology in cross mosquito species applications and its contribution to insecticide resistance management in malaria control programs are discussed.