

adulticides. Greater attention should be paid to source reduction and environmental sanitation, to decrease reliance on insecticides and reduce selection pressure on already resistant populations.

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IDENTIFICATION OF METABOLIC INSECTICIDE RESISTANCE GENES IN *Aedes Aegypti* FROM MARTINIQUE (FRENCH WEST INDIES): FROM GENOTYPES TO PHENOTYPES

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Since more than 10 years, *Aedes aegypti* is responsible for severe dengue outbreaks in the Caribbean and particularly in Martinique (French West Indies). Organophosphates and pyrethroids were used for decades for mosquito control which contributed to increase the pressure of selection on resistance genes in field mosquito populations. Larval and adult bioassays carried out on a field-caught mosquito population (Vauclin) showed high levels of resistance to temephos (x175) and deltamethrin (x68). No insensitive acetylcholinesterase was detected in Vauclin strain whereas high Kdr-allelic frequency (0.86) was identified at 106 position (Iso to Leu). Biochemical assays showed higher oxidase, GST and esterase activities in the resistant strain compared to the susceptible strain in both larvae and adults. The use of classical synergists (DMC, DEF and PBO) confirmed the role of detoxification enzymes in insecticide resistance, in addition to the kdr mutation. Analysis of the expression of detoxification genes at both larval and adult stages using the 'Aedes detox Chip' allowed to identify several potential genes responsible for resistance. Fifteen probes were over-expressed in larvae of the resistant strain including 13 P450s (CYP4, CYP6 and CYP9 families), 1 GSTs and 2 CCEs (CCEae2C and CCEunk7o). Eleven probes were over-expressed in adults including 8 P450s (CYP9 and CYP6 families) and 2 CCEs (CCEae3a and CCEae4b). Interestingly, 4 CYP genes were over expressed at both life stages (CYP9J22v1, CYP9J22v2, CYP6Z6 and CYP6M6). A better understanding of metabolic resistance genes underpinning the resistant phenotypes is essential to implement more effective and sustainable dengue vector control strategies.

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UNEXPEXTED NEUROTOXIC EFFECTS OF THE REPELLENT DEET OCCUR THROUGH AN INHIBITION OF ACETYLCHOLINESTERASE ACTIVITY IN INSECT AND MAMMAL NERVOUS SYSTEM

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The repellent N,N-diethyl-m-toluamide or DEET remains the gold standard for insect repellents. Unfortunately, the mode of action and toxicity of this repellent remains largely unknown. Here, we reported the effects of DEET on the insect and mammal nervous system using a complementary approach including toxicology performed on insect *in vivo*, electrophysiology, pharmacology and biochemistry. The results showed that DEET is not simply a behaviour-modifying chemical but also

exert insecticidal effect on *in vivo* insects. External application of DEET on the cercal-afferent giant-interneuron synapses in the terminal abdominal ganglion of the American cockroach showed that DEET (from 0.5 to 1 μ M and in presence of 1 μ M atropine) increased drastically both amplitude and duration of the Excitatory Postsynaptic Potentials (EPSP). Additional electrophysiological recordings performed on isolated mouse phrenic-hemidiaphragm muscles showed that DEET (500 μ M) is able to prolong about 3 fold the decay time constant of both synaptic potentials and currents. The *in vitro* effect of DEET on the activity of two purified AChE, one from an insect (*Drosophila melanogaster*) and the other from humans (AChE and BChE) confirmed that DEET (from 1 to 10 mM) inhibits the hydrolysis of ACh by AChEs and to diminish AChE carbamylation rate by propoxur. These results then indicate that DEET is a competitive inhibitor for AChE. These findings have important implications for DEET usage and provide new material potentially explaining one cause underlying the gulf war sickness syndrome.

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MONITORING THE OPERATIONAL IMPACT OF INSECTICIDE USAGE FOR MALARIA CONTROL ON *ANOPHELES FUNESTUS* FROM MOZAMBIQUE

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Indoor residual spraying (IRS) has again become popular for malaria control in Africa. DDT was re-introduced into Mozambique's IRS programme in 2005 and is increasingly becoming the main insecticide used for malaria vector control in Mozambique. The selection of DDT as the insecticide of choice in Mozambique is evidence-based, taking account of the susceptibility of *Anopheles funestus* and *An. arabiensis* to all available insecticide choices, as well as operational costs of spraying. Sentinel sites were monitored for insecticide resistance using WHO bioassays and biochemical assays. Assays were conducted on 1-3 day old F1 offspring of field collected adult caught females to determine levels of insecticide resistance and gene resistance frequency in the malaria vector population. Previously lambda cyhalothrin had replaced DDT in Mozambique in 1993. However, resistance appeared quickly to this insecticide and, in 2000, the pyrethroid was phased out and the carbamate bendiocarb introduced. Low level resistance was detected by biochemical assay to bendiocarb in 1999 in both *An. funestus* and *Anopheles arabiensis*, although this was not evident in WHO bioassays of the same population. In surveys conducted between 2002 and 2006, the levels of bendiocarb resistance detected in *An. funestus*, populations using WHO bioassays increased. Probably due to elevated levels of Acetylcholinesterase levels found in the same populations. Pyrethroid resistance in populations, linked to elevated levels of monooxygenase activity, decreases with the reduction of pyrethroids for control. This process of monitoring resistance has been incorporated into an integrated malaria decision support aiding malaria control programmes to make informed decisions and policy.

Corbel Vincent, Stankiewicz M., Pennetier Cédric, Fournier D., Molgo J., Stojan J., Hougard Jean-Marc, Lapied B. (2008)

Unexpepected neurotoxic effects of the repellent deet occur through an inhibition of acetylcholinesterase activity in insect and mammal nervous system

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