

specimens examined were M molecular forms of *An. gambiae* ss except for one specimen of *An. arabiensis*. Resistance to permethrin, DDT and carbofuran and decreased susceptibility to deltamethrin were detected in all populations of *An. gambiae* sampled. Cross-resistance to both DDT and permethrin was consistent with the high frequency (77-82%) of the Leu-Phe *kdr* mutation. Because the *ace-1R* mutation was found at low frequency (3-12%), carbamate resistance was due primarily to increased metabolism through enzymatic activity. A significant increase in the amount of oxidases and activity of glutathione-S-transferases was observed in comparison to the susceptible reference strain. These results have identified multiple insecticide resistance involving several mechanisms in the M molecular form of *An. gambiae* ss, the main malaria vector in Cotonou. The expansion of vegetable growing within urban areas probably contributed to selection pressure on mosquitoes.

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### THE POTENTIAL FOR MALARIA CONTROL USING FUNGAL BIOPESTICIDES

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There is an urgent need for alternative tools to reduce reliance on chemical insecticides in contemporary malaria control programs. Here we present an overview of recent research demonstrating the potential for using biopesticides based on insect pathogenic fungi, in novel integrated strategies for sustainable control of malaria (and also other diseases such as dengue). Numerous fungal isolates have been shown to infect *Anopheles* mosquitoes via exposure to biopesticide-treated surfaces. Depending on fungal isolate, malaria transmission potential can be reduced through direct mortality (i.e. virulent isolates killing mosquitoes before they can transmit), conditional mortality (i.e. enhanced impact of fungal infection in mosquitoes carrying malaria) and/or transmission blocking (i.e. development of malaria parasites blocked in mosquitoes following fungal infection). In addition, spores have been shown to persist on treated surfaces up to 6 months and to pose minimal risk to human health. Exploration of these effects using models reveals that fungal biopesticides have the potential to cause considerable reductions in the density of malaria-transmitting mosquitoes. Together, these results point to the practical use of insect fungal pathogens within novel strategies of integrated vector management, with potential to both augment existing control measures and enhance long-term sustainability.

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### INSENSITIVE ACETYLCHOLINESTERASE (ACE.1<sup>R</sup>): EVENTS OF INTROGRESSION AND DUPLICATION BETWEEN THE MOLECULAR M AND S FORMS OF ANOPHELES GAMBIAE S.S.

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Characterization of insecticide resistance provides data on the evolutionary processes involved in the adaptation of insects to environmental changes. Understanding the dynamics and the evolution of genes associated with insecticide resistance between closely related taxa represents a great interest, in terms of understanding resistance evolution in the field. This is a key component in establishing effective long-term resistance management strategies to eventually adapt vector control. In an upstream study, the mutation G119S (generating *ace.1<sup>R</sup>* allele) was found in both molecular forms of *An. gambiae* s.s. To establish whether the G119S mutation has arisen independently in each form or by genetic introgression, we analysed coding and non-coding sequences of *ace-1* alleles in M and S mosquitoes from representative field populations from

West Africa. Our data revealed many polymorphic sites shared by S and M forms, but no diversity was associated with the G119S mutation. This indicates that the G119S mutation was a unique event and that genetic introgression explains the observed distribution of the G119S mutation within the two forms. Unexpectedly, sequence analysis of some resistant individuals revealed a duplication of the *ace-1* gene that was observed in both *An. gambiae* s.s. M and S forms. Again, the distribution of this duplication in the two forms most likely occurred through introgression. These results impacts on the question of actual levels of gene flow between the two molecular forms in tropical savannah areas. We can conclude that the G119S mutation could spread rapidly in the field and then compromise the use of organophosphate and carbamate compounds in public health while resurgence of interest in using Indoor Residual Spraying based on these molecules to control malaria vectors. This study underlines the necessity to monitor the G119S mutation in natural populations before planning and implementing malaria control programs based on the use of organophosphate and carbamate.

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### CHANGES IN THE TRANSCRIPTION OF DETOXIFICATION GENES IN RESPONSE TO SELECTION WITH TEMEPHOS AND PERMETHRIN IN AEADES AEGYPTI

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*Aedes aegypti* control campaigns have relied on the use of insecticides for larvae and adult control since 1950. Unfortunately, these insecticides target one of two sites: acetyl-cholinesterase or the voltage dependent sodium channel. This target redundancy and other operational factors have allowed for the selection of insecticide resistance. Resistance mechanisms include primarily structural changes in target sites or increased metabolism by detoxification enzymes. Five *Ae. aegypti* strains from Mexico and one from Iquitos, Peru were selected with temephos and permethrin for five generations. Selection was replicated three times. Resistance ratios (LC50) for temephos selected strains increased 37 - 110 times when compare with the susceptible New Orleans reference strain. Although the Iquitos strain showed an initial LC50 lower than New Orleans, the LC50 increased 75 times after five generations of selection. Initially strains did not show altered acetyl cholinesterase in biochemical activity assays nor mutations in the *Ace1* gene. Using the *Ae. aegypti* microarray detoxification chip we identified genes upregulated in the Iquitos-selected strain that belong to the carboxyl esterase (CCae5C, CCae1C, CCae2C, CCae6C, AaeCOE-1, CCae3o) and mono-oxygenase families (SOD4 and CYP4H31). Permethrin selection resulted in a 12 - 33 fold increase in LC50. Bioassays indicate that knockdown resistance (*kdr*) and post-exposure recovery were the major mechanisms for permethrin resistance in the Mexican strains. *Kdr* allele frequency (Ile1,016) increased almost to fixation after five generations of selection. We observed that *kdr* is dose-dependent and >25 µg permethrin per bottle will produce complete knockdown in a strain homozygous for the Ile1,016 allele. The Iquitos selected strain lacked the *kdr* mechanism and also the Ile1,016 allele, however we observed recovery after permethrin exposure. We identified genes up regulated in the Iquitos selected strain that might be associated with recovery (GSTs-1, CCae2B, Perox3, CYP6Z9, CCEunk6, catalase, Aldox8 and AaeCOE-17). Further work will indicate if these genes are potential markers for insecticide resistance in order to support vector control campaigns.