Researchers unlock the secret of multiple insecticide resistance in mosquitoes

March 21 2014

Mosquito. Image: UCLA.

Researchers at LSTM have discovered how unprecedented multiple and extreme-level resistance is generated in mosquitoes found in the rice fields of Tiassalé in southern Côte d'Ivoire. The paper, "CYP6 P450 enzymes and ACE-1 duplication produce extreme and multiple insecticide resistance in the malaria mosquito *Anopheles gambiae*" published in *PLoS Genetics* today, highlights the combination of stringently-replicated whole genome transcription profiling, in vivo transgenic gene expression and in vitro metabolism assays to identify and validate genes from the P450 detoxification enzyme superfamily which are highly expressed in the adult females from the area.

The problem was discovered in 2011 when the *Anopheles gambiae* larvae sampled from the rice paddies of Tiassalé were raised to adults and tested using WHO tube bioassays. They proved to be resistant to all four of the insecticide classes available for mosquito control (Edi et al. Emerging Infectious Diseases 18: 1508-1511, 2012). This is the first wild Anopheles population to display such complete multiple resistance, which is a serious concern when preserving effectiveness of insecticides depends on rotating or combining their use. In addition to many of the mosquitoes surviving a standard one-hour insecticide exposure (used as the WHO standard to monitor the prevalence of resistance), the levels of resistance displayed in Tiassalé were very high, with 50% of mosquitoes tested surviving for longer than four hours exposure to both a carbamate and a pyrethroid.

The new work reveals that two members of the P450 gene superfamily in particular are highly expressed in resistant Tiassalé mosquitoes: CYP6M2 and CYP6P3. When these genes were transplanted into Drosophila, resistance to pyrethroids and carbamates was generated in otherwise susceptible fly strains. These genes are familiar candidates to LSTM researchers who have previously documented their links with pyrethroid and DDT resistance. This new research shows how specific P450 genes can engender resistance across insecticides with entirely different modes of action: DDT and pyrethroids target a voltage-gated sodium channel (a nerve cell membrane channel), whereas carbamates and organophosphates target the neurotransmitter Acetylcholinesterase, encoded by the gene ACE-1. This is where Tiassalé mosquitoes yielded another surprise, contributing to their exceptionally high carbamate resistance,. A well-known single nucleotide resistance mutation at the ACE-1 gene is near ubiquitous in the population, but because almost every female is a heterozygote (possesses a resistant and susceptible allele) it did not seem this could cause any variation in resistance. However, from application of a newly-developed qPCR diagnostic it was found that the ACE-1 gene was duplicated in some individuals, with those resistant to carbamate much more likely to have additional, duplicated copies of the resistant ACE-1 allele.

This combination of distinct mechanisms provides the Anopheles population of Tiassalé with high levels of resistance and resistance across insecticides. Dr David Weetman senior author, said: "The work has given a uniquely detailed insight into the varied mechanisms through which mosquitoes can become resistant to the available arsenal of insecticides. Controlling populations like Tiassalé will be particularly challenging, but understanding of their resistance mechanisms provides tools for monitoring in other west African populations, to help maintain the effectiveness of vector control programmes."

More information: www.plosgenetics.org/doi/pgen.1004236

Provided by Liverpool School of Tropical Medicine

Citation: Researchers unlock the secret of multiple insecticide resistance in mosquitoes (2014, March 21) retrieved 2 May 2024 from https://phys.org/news/2014-03-secret-multiple-insecticide-resistance-mosquitoes.html