ABSTRACT

"Mosquito malaria vectors cloak their legs to resist insecticides"

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ABSTRACT

While malaria continues to claim more than 400,000 lives each year (WHO, 2019), insecticide resistance is rapidly increasing in spectrum and intensity across Africa [1]. *Anopheles* legs are the key-tissues for insecticide uptake, as they comprise the first barrier the insecticide has to bypass to reach its neuronal targets [2]. In this context we use high-throughput methods to shed light to resistant mechanisms present in the first defense line of malaria vectors.

Our data on *An. coluzzii* leg-specific transcriptome provides valuable insights into the legs of pyrethroid resistant and short-term deltamethrin-exposed mosquitoes. The results suggest that xenobiotic detoxification is likely occurring in legs, while the enrichment of sensory proteins, ABCG transporters and cuticular genes is also evident. Constitutive resistance is primarily associated with elevated levels of detoxification and cuticular genes, while short-term insecticide-induced tolerance is linked with overexpression of transporters, GPCRs and GPCR-related genes, sensory/binding and salivary gland proteins [3].

Additionally, comparative proteomic analysis of the legs from resistant and susceptible mosquitoes revealed that resistant mosquitoes thicken their leg cuticles via enhanced

deposition of cuticular proteins, chitin filaments and, remarkably, cuticular hydrocarbons (CHCs) [4].

The last decarbonylation step of CHCs biosynthesis is catalyzed by CYP4Gs in oenocytes. We then focused on these enzymes and using *Drosophila melanogaster* as a tool we indicated the distinct contribution of each enzymes to CHC biosynthesis [5].

Structural and functional alterations in *Anopheles* legs are associated with reduced insecticide penetration that intensifies and potentially broadens resistance phenotype, and might affect other major physiological functions as well.

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