Malaria mosquitoes defend against contact insecticides by major alterations in their legs

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ABSTRACT

Insecticide resistance is rapidly increasing in spectrum and intensity across Africa. *Anopheles* legs are the key-tissues for insecticide uptake [1]. Here, we show that resistant mosquitoes thicken their leg cuticles via enhanced deposition of cuticular proteins, chitin filaments and, remarkably, cuticular hydrocarbons (CHCs) [2]. The last decarbonylation step of CHCs biosynthesis is catalyzed by CYP4Gs in oenocytes. We characterized the role of both *Anopheles* 4Gs, CYP4G17 and CYP4G16, by functionally expressing them in *D. melanogaster* silenced for the endogenous gene (cyp4g1KD). Heterologous expression of CYP4G16, CYP4G17 and their combination revealed their different abilities to rescue lethal phenotype of cypg1KD flies, while respective CHCs profiles were different, indicating distinct substrate specificities [3]. 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.

REFERENCES

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