



Studying insecticide resistance and the physiology of mosquitoes to facilitate the prevention of vector borne diseases.

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ABSTRACT

Over 80% of the world's population is at risk of contracting vector-borne diseases, the majority of which are transmitted by mosquitoes. Mosquito transmitted diseases impose a significant burden on human health and economic development, disproportionately impacting people living in the most vulnerable situations. Malaria for example is the fifth most deadly infectious disease worldwide, killing annually more than 600,000 people, with the majority of deaths (80%) reported in Africa, in children under the age of five. Europe is also not immune to mosquito transmitted diseases. Cases of West Nile virus are annually reported in several countries and new invasive mosquito species, that are vectors of diseases, have spread to Europe.

In the absence of effective vaccines and prophylactic drugs that can be used on a continent-wide scale, preventing the outbreak of vector borne diseases is best achieved by controlling the insect populations. This currently largely relies on the use of insecticides. However, our reliance on a limited number of active ingredients has acted as a strong selection pressure for the emergence of highly insecticide resistant mosquito populations. Our research focuses on elucidating the molecular basis of insecticide resistance, which is a prerequisite for the design of efficient insecticide resistance management strategies. We are also exploring different biological processes in mosquitoes for the identification of novel insecticide targets.

Insecticide resistance is a trait with a complex genetic basis. We use a multidisciplinary approach to identify genes and mutations associated with the phenotype and subsequently validate their role. Examples of our work include the identification and characterization of enzymes that detoxify insecticides, including esterases and cytochrome P450s. Our work has established several genes as markers of resistance. We also apply functional genetics (CRISPR genome editing) to validate the role of nucleotide polymorphisms, present on the insecticide's target proteins. Through functional genetics we also aim to unravel the complex interactions between different resistance mechanisms and understand how resistance levels are being shaped.

We also aim to get better insight into the mosquitoes' physiology. We have explored the biosynthetic pathway of the cuticle, that plays a critical role in mosquitoes' response to environmental stressors, including insecticides. We have isolated oenocytes, the cells that synthesize cuticular hydrocarbons (the main component of the outermost layer of the cuticle) and determined their transcriptome. We identified candidate genes for each step of the hydrocarbon biosynthetic pathway and validated their role using functional genetics. Recently we have also initiated a project aiming to identify genes essential for blood digestion and heme metabolism, which allows mosquitoes to benefit from hematophagy, the main trait that establishes them as disease vectors.