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Editorial overview: Pests and resistance: Resistance to pesticides in arthropod crop pests and disease vectors: mechanisms, models and tools

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Chris Bass received his PhD in Insect Molecular Biology in 2004 from the University of Nottingham and undertook postdoctoral research at Rothamsted Research. Chris moved his lab to the University of Exeter in 2016 to take up a Professorship in Applied Entomology. At Exeter he leads a multi-disciplinary group working on the topic of adaptive evolution in insects. A significant

Arthropod pests are a profound threat to agricultural production and the health of humans and domestic animals. Worldwide, herbivorous insects and mites cause an estimated 18–20% of crop yield loss per annum representing a value of more than US$470 billion [1]. In turn arthropod-vectored diseases account for more than 17% of all infectious diseases, causing more than 700 000 deaths annually [2]. The control of these damaging pests has for many years relied heavily on the use of synthetic pesticides, and the impact of chemistry-based interventions has in many cases been spectacularly successful. For example, between 2000 and 2015 the number of deaths due to malaria halved, 80% of which was attributed to the scale-up of insecticide-based vector control interventions [3]. Unfortunately, the over-reliance on chemical pesticides has led to the emergence of widespread resistance, posing a serious threat to the sustainable control of a large number of insect pests. To effectively address this growing problem, it is necessary to understand the origin, spread and maintenance of resistance, and the underpinning mechanisms involved. The Pests and Resistance section published last year (2017) explored the ecological and evolutionary drivers of pesticide resistance, and how such knowledge can be used to inform Insect Resistance Management (IRM) and Integrated Pest Management Strategies (IPM) [4]. This current section focuses on the *mechanisms* that underpin resistance. An important component of effective IRM/IPM is integrating knowledge on the molecular mechanisms that cause resistance into programmes that prevent, delay, or overcome resistance. For example, once specific resistance-associated genes or mutations are identified and validated, molecular diagnostics can be developed and used to monitor the distribution and frequency of these resistance alleles in the field. Such data can then be used to inform IPM and IRM strategies than aim to slow the further development of resistance mediated by these mechanisms.

Despite the considerable parallels observed in the evolution of resistance in arthropod crop pests and disease vectors, research on each system is often considered (and reviewed) separately. In this section we provide reviews of contemporary work on the evolution of pesticide resistance in both agricultural and medically important pests with the aim of highlighting commonalities and differences for further exploration.

Despite the applied importance of direct research on pest arthropods we wish to acknowledge the profound impact that model species have contributed to our understanding of resistance, and in particular, the fruit fly, *Drosophila melanogaster*. Perry and Batterham outline the enormous

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research focus of the lab is to understand how insects detoxify the natural and synthetic xenobiotics they encounter in the environment. This includes both plant secondary metabolites and man-made insecticides. Chris works closely with industry and other stakeholders to translate the fundamental science into practical tools and strategies that aim to prevent, slow or overcome resistance in crop pests while protecting beneficial insects such as bee pollinators.

Christopher Jones is a Vector Biologist at the Liverpool School of Tropical Medicine (LSTM) and based at the Malawi-Liverpool-Wellcome Trust Clinical Research Programme (MLW) in Blantyre, Malawi. Chris has worked on multiple insects of medical and agricultural importance. Previously, Chris studied insecticide resistance mechanisms as part of his PhD and post-doctoral research. More recently, he has expanded his research portfolio exploring the biology and genomics of insect migration and dispersal in important Lepidopteran pests. He moved to LSTM/MLW in 2017 to set up a vector biology unit in Malawi with the objective of applying his research skills for improved control of vector-borne diseases in the country.

contribution research on this species has provided on our understanding of insecticide targets, metabolism and transport. In many ways, *D. melanogaster* is a perfect model system coming equipped with a sophisticated array of genetic tools and resources. These tools have been of great utility in understanding the interactions between insecticides and the proteins they target. For example, elegant studies using technologies available in *D. melanogaster*, identified the nicotinic acetylcholine receptor subunit, Dα6 as an important target of the insecticide spinosad and characterised mutations that lead to resistance [5–7]. Equally significant advances have been made using this model species on the proteins that metabolise and transport pesticides. These include detoxifying enzymes and membrane transport proteins, often providing a causal link between overexpression of metabolic genes and resistance. Finally, as highlighted in this section last year [8], while insecticide resistance is often thought to come at a cost, identifying and quantifying these can be difficult if confounded by the different genetic backgrounds of resistant and susceptible pest strains. *D. melanogaster* alleviates this issue by allowing the effect of resistance genes or mutations to be readily examined in a defined genetic background. The combination of this with the wide range of behavioural assays that have been developed for this species has provide unprecedented insights into the range of fitness costs associated with a specific resistance mechanism [9,10].

Turning to pest insects, four reviews in this section highlight recent work on the mechanisms and mutations underpinning resistance evolution. The first of these concerns metabolic resistance — the enhanced metabolism/sequestration of insecticides by detoxification enzymes such as glutathione S-transferases (GSTs), cytochrome P450s (P450s) and carboxylcholinesterases (CCEs). Pavlidi *et al.* review recent work on the role of GSTs in the pesticide resistance of crop pests and disease vectors. They find that GSTs in resistant insects and mites confer resistance in two principle ways. Firstly, as for enzymes belonging to other well characterised detoxification enzyme superfamilies, such as P450s and CCEs, GSTs can confer resistance via direct metabolism or sequestration of chemicals. However, in contrast to these other enzyme groups, GSTs may also indirectly mediate resistance by providing protection against oxidative stress induced by insecticide exposure [11]. GST resistance by both mechanisms is primarily mediated by overexpression of the specific enzyme involved, however, recent work on insecticide resistance in the African malaria vector *Anopheles funestus*, has demonstrated that qualitative as well as quantitative alterations to GSTs can lead to resistance [12]. The GST AfGSTe2 is overexpressed in DDT resistant populations of *An. funestus*, however, a single amino acid substitution (L119F) in this enzyme, only found in resistant populations, enlarges the DDT-binding cavity, leading to increased DDT metabolism [12].

While reports of resistance mediated by metabolic or target-site mechanisms are now commonplace a third mechanism — reduced penetration of insecticide through the insect cuticle — has been much less frequently reported, and consequently is comparatively poorly understood. Balabanidou *et al.* highlight contemporary work on this topic and discuss outstanding knowledge gaps. To date, two primary mechanisms of penetration resistance have been described, physical changes in cuticular thickness and alterations in the chemical composition of the cuticle. The challenge for recent studies has been understanding how these alterations arise. New insights on these topics have been provided by recent work on the malaria vector *Anopheles gambiae* [13]. A multi-insecticide resistant strain of *A. gambiae* was found to have a significantly thicker cuticle than susceptible mosquitoes due to enriched deposition of hydrocarbons to the epicuticle (the thin, cuticular

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