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NEWS AND VIEWS

PERSPECTIVE

Genetics of host–parasite interactions: towards a comprehensive dissection of *Drosophila* resistance to viral infection

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One of the major challenges in evolutionary biology is to unravel the genetic basis of adaptation. This issue has been gaining momentum in recent years with the accelerated development of novel genetic and genomic techniques and resources. In this issue of Molecular Ecology, Cogni *et al.* (2016) address the genetic basis of resistance to two viruses in *Drosophila melanogaster* using a panel of recombinant inbred lines with unprecedented resolution allowing detection of rare alleles and/or alleles of small effect. The study confirms the role of previously identified genes of major effect and adds novel regions with minor effect to the genetic basis of *Drosophila* resistance to the *Drosophila* C virus or the sigma virus. Additional analyses reveal the absence of cross-resistance and of epistasis between the various genomic regions. This detailed information on the genetic architecture of host resistance constitutes an important step towards the understanding of both the physiology of antiviral immunity and the evolution of host–parasite interactions.

Keywords: adaptation, genomics/proteomics, host-parasite interactions, insects, quantitative genetics

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It has been argued that identifying the genetic basis of adaptation may add little to the understanding of some evolutionary phenomena (Rausher & Delph 2015). Indeed, even in research areas where the genetic architecture of adaptation is relevant, the identification of the particular genes involved may not be essential. For example, the genetics of host–parasite interactions may be captured by a matching allele model, in which specific parasite and host genotypes can only infect and resist, respectively, antagonists with a particular (matching) allele. Alternatively, it may follow a gene-for-gene model, where some parasites infect a subset of hosts, whilst others infect the whole range of host genotypes. Distinguishing between these alternatives is important because only under the matching allele model is selection for increased recombination expected (Agrawal & Lively 2002). Importantly, it was recently found that the interaction between *Daphnia magna* hosts infected by *Pasteuria ramosa* is consistent with a matching allele model (Luijckx *et al.* 2013). However, the identification of the specific alleles involved in the interaction was not necessary for this compelling result.

Still, some features of the genetics of host–parasite interactions are highly relevant to understand their evolution. For example, the number of genes coding for host resistance impacts on the degree of maladaptation of parasites in a heterogeneous landscape (Ridenhour & Nuismer 2007). One of the systems with more information concerning the genetics of host resistance is that of *Drosophila* and its parasites. Indeed, several studies have identified genes or genome regions responsible for variation in survival upon bacterial (e.g. Sleiman *et al.* 2015) and viral infections (e.g. Magwire *et al.* 2012; Martins *et al.* 2014). In the latter case, alleles of major effect have been recurrently identified to confer resistance to *Drosophila* C virus (DCV) (*Pastrel*; Magwire *et al.* 2012; Martins *et al.* 2014) and to the sigma virus (*ref(2)P* and *CHKov1*; Bangham *et al.* 2007; Magwire *et al.* 2011). However, candidate alleles of minor effect (*CG16998*, *UbcE2H*; Martins *et al.* 2014) and rare alleles of large effect (*Ge-1*; Cao *et al.* 2016) have been identified in some studies, but not in others. These different outcomes may arise because standing genetic variation in these loci is absent from some of the initial populations, different approaches have intrinsically distinct outcomes (association studies *vs* experimental evolution), or studies differ in their degree of resolution.

In this issue of Molecular Ecology, Cogni *et al.* (2016) add significantly to the understanding of the genetic basis of resistance to viruses in *Drosophila*. The authors use the Drosophila Synthetic Population Resource (DSPR) panel (http://wfitch.bio.uci.edu/~dspr/; Long *et al.* 2014) to identify the genes involved in *Drosophila* differential survival to DCV and sigma virus (Fig. 1). This resource is composed of 1700 recombinant inbred lines that are formed from the interbreeding of two sets of eight fully sequenced inbred founder lines from distinct geographic locations (one of the lines being repeated in the two panels). This panel allows a much finer mapping resolution of quantitative trait loci (QTL), enabling detection of rare alleles present in the original set and of alleles of small effect (Long

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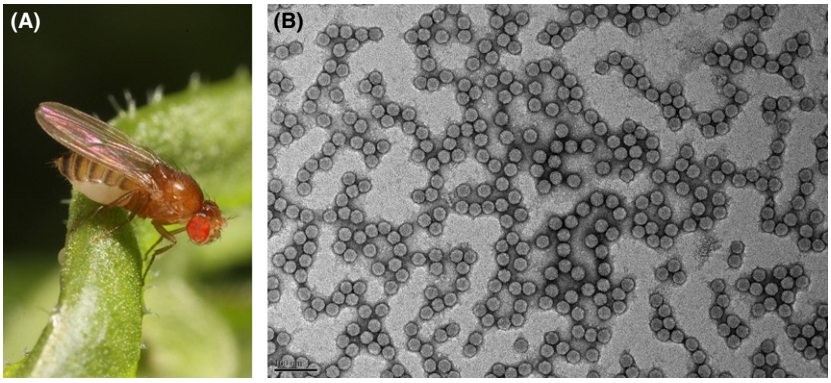

Fig. 1 *Drosophila melanogaster* (A; photograph credit: Darren Obbard) and an electron microscopy image of purified Drosophila C virus (DCV) (B; photograph credit: Estelle Santiago and Jean-Luc Imler).

et al. 2014). The authors confirm the role of *Pastrel* and *ref (2)P* in conferring resistance to DCV and to sigma virus, respectively. These genes had already been identified using the DGRP panel (Bangham *et al.* 2007; Magwire *et al.* 2012) and an evolve-and-resequence methodology (Martins *et al.* 2014). Importantly, they also find additional regions contributing to these responses, namely one new locus involved in resistance to DCV and five extra QTLs involved in fighting sigma virus. This more complete and complex landscape provides a basis for 90% of the response against DCV and 43% for sigma virus. Interestingly, previously-found rare and small-effect alleles were not detected. Given the level of resolution now achieved, it is likely that the lines from which this panel was generated did not contain the relevant allelic variation at those loci. Be it as it may, the finer grain analysis here provided certainly brings to light novel candidates involved in the physiological response deployed against viral infections. Future validation of these candidates will certainly add important new elements to the mechanistic understanding of antiviral immune responses.

Another important conclusion of this study is the absence of cross-resistance and of epistasis among QTLs involved in the response to the same virus, which is an important component of theoretical predictions concerning the evolutionary outcome of host–parasite interactions (*e.g.* Fenton & Brockhurst 2007). Additional analyses, however, point to the existence of yet another QTL that is not directly involved in conferring resistance but that modifies the effect of one of the QTLs affecting resistance to the sigma virus. Further studies will help understanding whether this mild epistasis is a general feature of the host–parasite interaction described here or a result that is specific to the panel of inbred lines used.

We still do not know whether alleles from genes identified through these association studies are those that will increase in frequency during the adaptation process. Indeed, the genetic variance–covariance matrix (the G-matrix) is likely to evolve even within short time frames, especially given that, as shown by this study, more genes are involved in host resistance than previously thought, and this will affect the evolutionary trajectory of hosts and parasites (Gilman *et al.* 2012). Moreover, the genetic architecture of host resistance will interact with that of parasite virulence and generate evolutionary dynamics that cannot be captured by the analysis of one of the players alone. Therefore, the genetic diversity for parasite resistance identified in the host population at a given time may or may not contribute to the evolutionary process. Given the potential importance of the findings presented by Cogni *et al.* (2016) for the evolution of host–parasite interactions, further research on this topic can directly test whether the genes identified participate in the adaptation process, for example via experimental (co)evolution studies, coupled with functional validations.

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SM and ES wrote the paper together.

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