Commentary

Symbionts conferring resistance to viruses in insects

Guido Favia

School of Biosciences and Veterinary Medicine,
University of Camerino, Italy

Invited commentary on 'Symbionts commonly provide broad spectrum resistance to viruses in insects: a comparative analysis of Wolbachia strain', Martinez et al.

Recently, *PLoS Pathogens* published an interesting paper of Julien Martinez and collaborators, about the protective role of *Wolbachia* from viral infections in *Drosophila* hosts.¹

This work is part of a wider context of studies aimed to define the mechanisms of *Wolbachia*-mediated protection to a broad spectrum of pathogens in insects infected with specific strains of this bacterium. The exploitation of bacterial symbionts represents a very hot topic in regard to the control of diseases transmitted by insect vectors. In fact, recently the *Wolbachia* infection of mosquito vectors of Dengue virus turned out to be an innovative approach, particularly effective in combating this infection.²

The mechanisms by which *Wolbachia* protects hosts against infection by pathogens remain unclear. They may be due to different modes of action, and may be strongly dependent on the host. In fact it has been shown that *Wolbachia* infection is able to up-regulate the host immune system of *Aedes aegypti* and *Anopheles gambiae* mosquitoes, when transinfected with *Wolbachia* strains from *Drosophila*. While in *Drosophila melanogaster*, neither naturally infected with *Wolbachia* nor transinfected with a non-native strain, this evidence has been reported.

The paper of Martinez and collaborators has elegantly attempted to investigate this issue through a comparative approach aimed to analyse 19 *Wolbachia* strains from different *Drosophila* species transferred into a common *D. simulans* genetic background. These strains have been challenged with *Drosophila C virus* (DVC) and Flock House virus (FHV), both RNA viruses with positive-sense single-stranded genomes. DVC are naturally present in *D. melanogaster* and *D. simulans*, while FHV was originally isolated from

grass grubs *Costelytra zealandica* and it is able to replicate in a wide pattern of insect hosts.³

The assemblage of a large panel of different *Wolbachia* strains into a common host genetic background allowed revealing their diversity in the capacity to increase flies' survival after viral infection. Furthermore, even though FHC and DVC are distantly related, the authors showed scant specificity but remarkable genetic correlations in the protection against both viruses.

Authors attribute the increases in survival as consequence of *Wolbachia* capacity in reducing viral titer, while they assume that the variation in antiviral protection is due to differences in the density of *Wolbachia* in host tissues and, although the mechanisms of protection are still far to be understood, they relate to bacterial density. These results remark that antiviral protection is quite common among *Wolbachia* strains, but the effect is strongly dependent on the host and the strain of *Wolbachia*. This provides important applicative insights not only, as underlined by the authors, because it extends the panel of potential *Wolbachia* strains to be introduced into mosquito populations to limit arboviruses spread, but also because it might explain some apparent contradictions in the protective effect *Wolbachia* may exert in mosquitoes. As a matter of fact, it is reported that *Wolbachia* spread in the recipient mosquitoes might play a dual and conflicting effect on susceptibility to the malaria parasite.

Bian and collaborators reported the establishment of a stable *Wolbachia* strain wAlbB infection in the Asian malaria vector *Anopheles stephensi*.⁴ In the mosquito, wAlbB confers resistance to the human malaria parasite *Plasmodium falciparum*. On the other hand, it has been recently described that the natural *Wolbachia* infection increases the susceptibility of *Culex pipiens* mosquitoes to *P. relictum*.⁵

In conclusion, the paper by Martinez and co-workers is a great step forward to the understanding of the basic mechanisms of protection to viral infections that *Wolbachia* can exercise in different hosts. At the same time, it offers an important contribution to the development of effective strategies for *Wolbachia*-based control of vector borne diseases.

References

- 1 Martinez J, Longdon B, Bauer S, Chan YS, Miller WJ, Bourtzis K, et al. Symbionts commonly provide broad spectrum resistance to viruses in insects: a comparative analysis of *Wolbachia* strains. *PLoS Pathog*. 2014;10(9):e1004369.
- 2 Hoffmann AA, Montgomery BL, Popovici J, Iturbe-Ormaetxe I, Johnson PH, Muzzi F, et al. Successful establishment of

Correspondence to: G. Favia, School of Biosciences and Veterinary Medicine, University of Camerino, Camerino (MC), Italy. Email: guido.favia@unicam.it

- Wolbachia* in *Aedes* populations to suppress dengue transmission. *Nature*. 2011;476:454–7.
- 3 Dasgupta R, Free HM, Zietlow SL, Paskewitz SM, Aksoy S, Shi L, *et al.* Replication of flock house virus in three genera of medically important insects. *J Med Entomol*. 2007;44:102–10.
 - 4 Bian G, Joshi D, Dong Y, Lu P, Zhou G, Pan X, *et al.* *Wolbachia* invades *Anopheles stephensi* populations and induces refractoriness to *Plasmodium* infection. *Science*. 2013;340:748–51.
 - 5 Zélé F, Nicot A, Berthomieu A, Weill M, Duron O, Rivero A. *Wolbachia* increases susceptibility to *Plasmodium* infection in a natural system. *Proc Biol Sci*. 2014;281(1779):20132837.