GENOME WATCH

Adaptation: it's a bug's race

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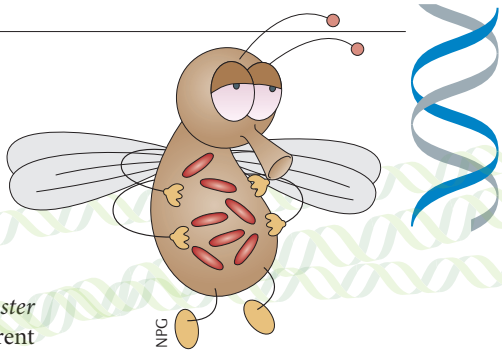

This month's Genome Watch highlights studies that investigate links between *Wolbachia* genotypes and their phenotypes, and explore how *Wolbachia* adapts to new host environments.

Wolbachia is a genus of obligate intracellular bacteria that is found in a diverse range of insects and in some filarial nematodes. Because these bacteria are transmitted vertically, they depend on the survival and reproduction of their hosts to ensure their propagation, but the mechanisms used by *Wolbachia* to control bacterial replication while ensuring host survival are still largely unknown. Furthermore, functional studies on the biology of *Wolbachia* are limited by the inability to maintain *Wolbachia* clones outside their hosts, which means that genetic manipulation of this group of bacteria remains a challenge[1]. However, certain *Wolbachia* strains show characteristic phenotypes and can be used as experimental models in studies investigating genotype–phenotype relationships; for example, in *Drosophila melanogaster*, the *Wolbachia* strain *w*MelPop displays increased virulence that is characterized by increased bacterial replication and reduced lifespan of the flies.

Previously, variation in the copy numbers of Octomom, a ~21-kb genomic region containing 8 genes of unknown function, was identified as one of the possible genetic factors responsible for the phenotypic differences between the virulent *w*MelPop strain and a non-virulent counterpart[2]. Chrostek *et al.*[3] have further characterized how changes in the copy numbers of Octomom affect bacterial virulence. Using a combination of PCR and Sanger sequencing, the authors explored the structure of the Octomom copies in the genome of *w*MelPop and concluded that this region is found in tandem across the genome and amplifies as a unit. The authors then used genetic crosses to establish *D. melanogaster* lines carrying *Wolbachia* with different Octomom copy numbers. Using this strategy, they showed that a high copy number of the Octomom region in the *w*MelPop genome is associated with a more virulent phenotype, which is characterized by high *Wolbachia* titres and shortened fly lifespans. For example, *D. melanogaster* lines carrying two copies of Octomom had their lifespan reduced by 39%, compared with lines carrying a single Octomom copy. However, when flies were maintained at lower temperatures, which makes *w*MelPop non-pathogenic, and were challenged with a natural pathogenic virus (*Drosophila* C virus), a high Octomom copy number became beneficial by providing protection against viral infection and increased the lifespan of infected flies. Therefore, Octomom copy number is a remarkable variable trait that directly influences the phenotype of *w*MelPop and regulates *Wolbachia* proliferation and the susceptibility of its host to viral infection.

However, Octomom copy number is not the only genetic trait associated with an increase in *Wolbachia* replication in flies. Newton *et al.*[4] used a heterogeneous cross of *D. melanogaster* ($chic^{221}$/+) that harbours a reduced titre of *Wolbachia* and found that passaging of the bacteria through three generations of flies resulted in approximately half of the flies displaying *Wolbachia* titres similar to those that are found in wild-type flies. The authors then used high-throughput Illumina sequencing to characterize the *Wolbachia* genomes from four $chic^{221}$/+ lines in order to study how *Wolbachia* adapted to its host. Notably, unique polymorphisms were detected in all of the adapted *Wolbachia* populations that were sequenced, and the majority of polymorphisms were located in non-coding regions of the genome that could potentially have a role in regulating gene expression. As *Wolbachia* is present as a range of genotypically diverse organisms within a host, it is not possible to determine whether these mutations emerged *de novo* or were selected from the original population[4]. Nonetheless, these experiments show how swiftly the *Wolbachia* genome can adapt to changing host genetic backgrounds.

Collectively, these studies have begun to elucidate the mechanisms used by *Wolbachia* to regulate bacterial replication during adaptation to new host environments and could influence the design of control strategies for vector-borne diseases. For example, as virulent *Wolbachia* strains are being used to control the spread of mosquito populations in dengue endemic areas[5], future studies into how changes in the *Wolbachia* genome affect host survival could influence the design of strategies of vector control and disease transmission.

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Competing interests statement
The authors declare no competing interests.