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The endosymbiotic box of protective tricks

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This month's Genome Watch highlights how genome and transcriptome sequencing of newly identified endosymbionts helps to connect genetic information to their protective functions.

Predators and pathogens exert strong selective pressures on cellular organisms to evolve and innovate their defence systems. Indeed, diverse cellular systems exist that protect at the chemical level by activating the production of antibiotics and other secondary metabolites, at the physical level through motility and other morphological adaptations and at the genetic level by intercellular trafficking of DNA information. In addition, microbial symbionts may also be acquired as an additional layer of cellular armour. A model of such a protective symbiosis is the interaction between aphids and the intracellular bacterium *Hamiltonella defensa*. In this case, *H. defensa* protects its aphid host from parasitoid wasps by blocking the development of the invading wasp larvae. Genomic analysis showed that *H. defensa* encodes the protection system in its 2.1 Mb genome, including genes encoding toxins, effector proteins and two type III secretion systems[1]. The retention of defence genes in a reduced genome indicates that host defence is essential for endosymbiont fitness and reveals the ecological implications of protective symbioses.

Several recent discoveries revealed intriguing new examples of symbiont-mediated cellular defence systems. The fungus *Mortierella verticillata*, which is frequently found in soils and considered a plant-growth-promoting factor, hosts the endosymbiotic bacterium Candidatus *Mycoavidus necroximicus*. The bacteria protect their fungal hosts against mycophagous nematodes by producing benzolactones that are toxic to nematodes[2]. Genes encoding the factors for the synthesis of benzolactone and other secondary metabolites make up 12% of the 2.2-Mb Ca. *M. necroximicus* genome, which suggests that this species has dedicated some of its metabolic arsenal to protect its host. Another example is the association between the fungus *Rhizopus microsporus*, the cause of mucormycosis, and its endosymbiotic bacterium *Ralstonia pickettii*. *R. pickettii* secretes molecules that suppress growth of amoeba that predate on fungal spores[3]. The 5.2-Mb genome of *R. pickettii* encodes a potentially novel type I polyketide synthase that is expressed during anti-phagocytic activity; in animals, this also facilitates fungal evasion of phagocytic macrophages to overcome the host immune response[3]. A third example is that of the chlamydial endosymbiont *Protochlamydia amoebophila* that protects its amoeba host from the bacterial pathogen *Legionella pneumophila*. It has been proposed that *P. amoebophila* protects its host by competing with *L. pneumophila* for resources in the intracellular niche. The reduced supply of nutrients decreases expression of genes responsible for flagellar assembly in *L. pneumophila*; this blocks the pathogen from transitioning to its transmissive phase and it is then ultimately outcompeted by the chlamydial symbiont[4]. This interaction may also impart a symbiont-derived immunological memory as the amoebal progeny features superior fitness and is protected against infection by *L. pneumophila*[4]. These three examples of protective symbioses are expected to enhance the competitive success of the host populations, which in turn would have important ecosystem implications: amoebae facilitate the turnover of microbial biomass, which releases nutrients and enhances plant growth, and the fungal species are of high relevance in agriculture and animal health.

Endosymbionts also use tricks to protect themselves. A noteworthy example is Candidatus *Bodocaedibacter vickermanii*, an alphaproteobacterium inhabiting the cytoplasm of the kinetoplastid *Bodo saltans*. Its 1.4-Mb genome displayed reduced metabolic capabilities indicating the symbiont's nutritional dependency on its host. Interestingly, it also encoded three different toxin–antitoxin systems. Subsequent transcriptomic analysis showed that these systems were actively expressed and the antibiotic-mediated removal of the symbiont resulted in host death[5]. This finding pointed towards a protective system evolved by Ca. *B. vickermanii* as an 'addictive' toxin–antitoxin trick to make itself essential for host survival.

Together, these recent studies suggest that protective endosymbioses are ubiquitous and may determine microbial community composition and function. Although endosymbiont-mediated protection is often not immediately obvious from genomic data, clues can be provided by, for example, the presence of entire pathways necessary to produce secondary metabolites in highly reduced endosymbiont genomes. In the case of experimentally accessible associations, a combination of omics data and their incorporation into systems biology frameworks will get us closer to recognizing mechanisms that underlie endosymbiont-conferred protection.

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