
This copy is for your personal, non-commercial use only.

If you wish to distribute this article to others, you can order high-quality copies for your colleagues, clients, or customers by [clicking here](#).

Permission to republish or repurpose articles or portions of articles can be obtained by following the guidelines [here](#).

The following resources related to this article are available online at www.sciencemag.org (this information is current as of April 7, 2011):

Updated information and services, including high-resolution figures, can be found in the online version of this article at:

<http://www.sciencemag.org/content/332/6026/185.full.html>

This article **cites 13 articles**, 6 of which can be accessed free:

<http://www.sciencemag.org/content/332/6026/185.full.html#ref-list-1>

This article appears in the following **subject collections**:

Microbiology

<http://www.sciencemag.org/cgi/collection/microbio>

ous genes essential to gene expression processes such as transcription, RNA processing, and translation, as well as DNA replication and repair, cytoskeletal organization, and numerous ion channels (8, 9). Genetic suppression experiments of He *et al.* suggest that U4atac mutations reduce U12-dependent splicing, and presumably the functional gene products, to less than 10%. Yet infants affected by the mutations are carried to term, are born (with multiple developmental defects but without gross malformations), and can live up to 3 years. How is this possible, given that the depletion of proteins specific to the U12-dependent spliceosome leads to cellular growth arrest (10)? One possibility is that the severity of the splicing defects is transcript-specific, as suggested by the data from patient cells in both the He *et al.* and Edery *et al.* studies, and from larvae of the

fly *Drosophila melanogaster*, which contain mutations in the U6atac snRNA (11). Alternatively, the activity and requirements for the U12-dependent spliceosome may vary in different tissues. Indeed, tissue specificity is seen in retinitis pigmentosa and spinal muscular atrophy, which are caused by mutations in ubiquitously expressed spliceosome components or in the snRNP assembly factor SMN (1), respectively.

The findings of He *et al.* and Edery *et al.* raise further questions about the mechanism and effects of the splicing defects. The next steps include biochemical characterization of patient cells and transcriptome analysis from multiple tissues, possibly using animal models, to understand the impact of the mutations and the connection to the disease phenotype. Additionally, cells carrying the mutations may serve as models to understand the mech-

anistic basis of similar diseases. Such investigations will hopefully also clarify the longstanding issue of whether the U12-dependent spliceosome is an outdated molecular relic that is being phased out or whether it has special regulatory functions in metazoan cells.

References and Notes

1. T. A. Cooper, L. Wan, G. Dreyfuss, *Cell* **136**, 777 (2009).
2. H. He *et al.*, *Science* **332**, 238 (2011).
3. P. Edery *et al.*, *Science* **332**, 240 (2011).
4. A. A. Patel, J. A. Steitz, *Nat. Rev. Mol. Cell Biol.* **4**, 960 (2003).
5. S. Nottrott *et al.*, *EMBO J.* **21**, 5527 (2002).
6. O. V. Makarova *et al.*, *EMBO J.* **21**, 1148 (2002).
7. M. K. Doma, R. Parker, *Cell* **131**, 660 (2007).
8. N. Sheth *et al.*, *Nucleic Acids Res.* **34**, 3955 (2006).
9. C. B. Burge *et al.*, *Mol. Cell* **2**, 773 (1998).
10. C. L. Will *et al.*, *RNA* **10**, 929 (2004).
11. H. K. J. Pessa *et al.*, *PLoS ONE* **5**, e13215 (2010).
12. We thank J. J. Turunen, J. Verbeeren, and B. Verma for excellent suggestions on this manuscript.

10.1126/science.1205503

MICROBIOLOGY

Rapid Insect Evolution by Symbiont Transfer

Francis M. Jiggins¹ and Gregory D. D. Hurst²

Microbiologists have long recognized the importance of horizontal gene transfer—the movement of genetic material between organisms—in adaptation. It is common for plasmids (rings of DNA that are separate from chromosomal DNA) and phage (viruses that infect bacteria) to move between bacterial species, and their movement is often accompanied by the transfer of traits, such as antibiotic resistance, that are of great adaptive importance. In contrast, in multicellular organisms, the mutational variation

upon which natural selection acts is generated independently within each species. It has recently become clear, however, that horizontal transfer of traits can play a major role in arthropod evolution. Studies of insects have detailed cases in which traits under selection are encoded by a bacterial symbiont. These microbes are commonly maternally inherited within species and therefore provide variation that is accessible for the process of natural selection. Like plasmids, however, symbiotic bacteria also occasionally move to a different host species. On page 254 of this issue, Himler *et al.* (1) present just such a case study. It documents fast evolution after the introduction of a new symbiont into a population of

A symbiotic bacteria dramatically increases reproduction and survival in a common insect pest.

the whitefly *Bemisia tabaci*. They detail the spread of a *Rickettsia* bacterial symbiont that, in just 6 years, dramatically increased the survival and fecundity of its host in the southwestern United States.

The majority of insect species host bacterial endosymbionts that live within their cells and are vertically transmitted from parent to offspring (2). Some of these endosymbionts are mutualists that are essential for the survival of the insects, and these can have stable associations with host lineages that last for millions of years (3). Less well understood are the diverse array of “secondary” endosymbionts, which are not essential for the survival of their hosts and often only infect

¹Department of Genetics, Downing Street, Cambridge CB2 3EH, UK. ²Institute of Integrative Biology, University of Liverpool, Liverpool L69 7ZB, UK. E-mail: fmj1001@cam.ac.uk2



Secondary symbiont interactions with insects. (A) In pea aphids, symbionts affect parasitoid resistance, heat tolerance, host plant range, and color. (B) Rove beetles of the genus *Paederus* are defended against spider predation by the toxin pederin, produced by a *Pseudomonas* symbiont. (C) *Drosophila* is protected

against a range of RNA viruses by *Wolbachia* bacteria. (D) Whitefly fitness is enhanced by the presence of *Rickettsia*, which also distort the infected population's sex ratio toward the production of daughters. (E) The butterfly *Eurema hecabe* carries a *Wolbachia* that causes genetically male hosts to develop as females.

certain populations or individuals. There is a growing body of evidence that many of these symbionts represent an “accessory genome” of nonessential genes that can provide benefits, such as resistance to natural enemies (see the figure). Himler *et al.* show that these benefits can be considerable: Whiteflies infected with *Rickettsia* bacteria produced offspring at nearly twice the rate of individuals lacking the infection, and a higher proportion of the offspring survived to adulthood. The inherited *Rickettsia* roughly doubled the fitness of its host in laboratory assays, although the mechanism underlying the increased fitness has yet to be elucidated.

Perhaps the most remarkable observation of Himler *et al.* is the speed with which the *Rickettsia* spread through the population—just 1% of whiteflies were infected in 2000, compared with 97% in 2006. Reports from other species suggest that such rapid invasions may be commonplace in insects. A strain of the bacteria *Wolbachia*, for instance, swept through populations of *Drosophila simulans* in California in just 3 years (4). The rapid spread of this symbiont was predominantly the result of the bacterium causing cytoplasmic incompatibility (the sperm and egg could not form viable offspring), but it also resulted in increased resistance of the host population to viral infection (5). More recently, researchers reported that a *Spiroplasma* bacterium that protects its host against parasitic nematode worms has invaded populations of *Drosophila neotestacea* since the 1980s (6). Beyond these case studies, there are good reasons to believe that adaptation associated with symbiont-encoded traits will commonly be more rapid than adaptation based on mutations in existing insect genes. After lateral transfer, symbionts arrive in a novel host species as a complete genetic package, which has evolved over time to encode complex traits such as natural enemy resistance. Having been selected to encode a trait in their previous host, they will often encode this trait directly in their new host. These symbiont transfers therefore represent “macromutations” that may have a higher selective advantage than “normal” mutations.

Despite the benefits of infection, the relationship between whiteflies and *Rickettsia* is not as benign as it might at first appear. Inherited symbionts have commonly been classified into those that are “nice”—providing benefit to their host—and those that alter host reproduction and spread in the fashion of selfish genetic elements. Being maternally inherited, these microbes have an evolutionary interest only in the production and survival of female hosts; consequently, they have evolved

a variety of traits through which they promote the production and survival of daughters (7). Himler *et al.* found that, in addition to increasing the survival and reproductive success of infected whiteflies, the *Rickettsia* bacteria also caused their hosts to increase the proportion of their offspring that were female. The symbiont is therefore simultaneously acting as a beneficial partner of its female host and as a reproductive parasite, distorting the sex ratio away from that normally produced by the insect. Researchers have found evidence of similar “Jekyll and Hyde” consequences of *Wolbachia* symbiosis in flies; the bacteria both protect their host from a range of RNA viruses and manipulate host reproduction through cytoplasmic incompatibility (5, 8, 9).

Secondary symbionts not only are changing our view of insect evolution but also have important economic and medical implications. Past work has shown that symbionts can alter the species of plants that aphids feed on, potentially changing the number of crops the insects affect (10). Symbionts also alter the rate at which insects can transmit disease. In some cases, they decrease transmission (*Aedes aegypti* mosquitoes infected with *Wolbachia* are less likely to transmit dengue) (11); in others, they increase it (whiteflies infected with *Hamiltonella* bacteria are more likely to

transmit tomato yellow leaf curl virus) (12). The B biotype of *B. tabaci* studied by Himler *et al.* is an important crop pest that spread throughout the world in recent decades (13). The *Rickettsia* may cause *B. tabaci* damage to increase for two reasons. First, the infection directly benefits the *B. tabaci* individual that carries it and thus increases their rate of reproduction. Second, the female-biased sex ratio produced by the *Rickettsia* will increase the intrinsic rate of increase of its host species. It is now clear that symbionts can be both allied to and antagonistic to human interests. Either way, they will be a key feature of agricultural and vector entomology in years to come.

References

1. A. G. Himler *et al.*, *Science* **332**, 254 (2011).
2. K. Hilgenboecker *et al.*, J. H. Werren, *FEMS Microbiol. Lett.* **281**, 215 (2008).
3. N. A. Moran *et al.*, *Proc. Biol. Sci.* **253**, 167 (1993).
4. M. Turelli, A. A. Hoffmann, *Nature* **353**, 440 (1991).
5. S. E. Osborne *et al.*, *PLoS Pathog.* **5**, e1000656 (2009).
6. J. Jaenike *et al.*, *Science* **329**, 212 (2010).
7. J. Engelstädter, G. D. D. Hurst, *Annu. Rev. Ecol. Evol. Syst.* **40**, 127 (2009).
8. L. M. Hedger *et al.*, *Science* **322**, 702 (2008).
9. L. Teixeira *et al.*, *PLoS Biol.* **6**, e1000002 (2008).
10. T. Tsuchida *et al.*, *Science* **303**, 1989 (2004).
11. G. Bian *et al.*, *PLoS Pathog.* **6**, e1000833 (2010).
12. Y. Gottlieb *et al.*, *J. Virol.* **84**, 9310 (2010).
13. J. K. Brown *et al.*, *Annu. Rev. Entomol.* **40**, 511 (1995).

10.1126/science.1205386

IMMUNOLOGY

Eosinophils Forestall Obesity

Rick M. Maizels and Judith E. Allen

Eosinophils in adipose tissue maintain metabolic homeostasis by controlling macrophage activity.

Most human body fat is stored in adipose tissue, and under healthy conditions, it provides a balanced exchange of triglycerides in response to energy demands. But adipose tissue is also the cardinal locus of the metabolic syndrome, whose hallmarks include the accumulation of abdominal fat and insulin resistance, with cardiovascular consequences. Adipose tissue is dynamically linked with the immune system; indeed, the activity of macrophage cells has a key role in progression to obesity (1–4). On page 243 of this issue, Wu *et al.* (5) show that eosinophils, an immune cell typically associated with allergy and worm infection, regulate the macrophage activation state

in mammalian adipose tissue and may have an important role in metabolic homeostasis.

The type of macrophage activated in obese and nonobese individuals differs sharply (3). As a person's body fat increases, the number of macrophages embedded in adipose tissue rises (6). These “classically activated” or “M1” macrophages (CAMs) produce proinflammatory cytokines such as tumor necrosis factor- α (TNF- α) that act systemically and affect metabolism by decreasing the sensitivity of other cells to insulin (7). Adipose tissue itself releases a hormone into the circulation called adiponectin that regulates glucose and fatty acid metabolism. However, in obesity, adiponectin production drops and macrophages produce resistin, which acts systemically to increase insulin resistance and glucose intolerance. This can lead to diabetes.

Centre for Immunity, Infection and Evolution and the Institute for Immunology and Infection Research, University of Edinburgh, Edinburgh EH9 3JT, UK. E-mail: r.maizels@ed.ac.uk