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Evolutionary genetics: Dissecting a sexually antagonistic polymorphism

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Males and females experience divergent selection on many shared traits, which can lead to 'sexual antagonism' — opposing fitness effects of genetic variants in each sex. A new study in the fly *Drosophila serrata* links sexually antagonistic selection on cuticular hydrocarbons to a single major-effect gene.

Sexual dimorphism is one of the most conspicuous forms of adaptation. Famous examples include the peacock's tail or the stag beetle's mandibles. Yet, although males and females often experience divergent selection for sexual dimorphism (e.g. in locomotion in fruit flies[1], height in humans[2] or leaf thickness in the white campion[3]), they also share the same genome, which constrains its evolution. The constraint of a shared genome gives rise to 'sexual antagonism', where alternative variants at a genetic locus have opposing fitness effects in each sex. Consider, for example, a genetic variant that increases body size in both sexes, segregating in a population in which selection favours larger males and smaller females. This variant would be beneficial to males but deleterious to females and would therefore be sexually antagonistic. Although sexually antagonistic genes are predicted to be common[4], identifying them has been difficult[5]. In some cases[6–10], researchers have been able to identify genes with different effects in the two sexes, but it is unclear whether the trait is under sexually antagonistic selection. In other cases[11], researchers have been able to link genes to sexually antagonistic fitness effects, but the traits affected remain unknown. Put simply, a 'textbook example' of sexual antagonism describing genotypic, phenotypic and fitness effects has so far proven elusive. A recent study in *Current Biology* by Bosco Rusuwa, Henry Chung, Stephen Chenoweth and colleagues[12] fills this gap by describing a single major gene affecting a sexually antagonistic trait in the fruit fly *Drosophila serrata*.

Rusuwa, Chung and colleagues[12] focussed on organic compounds known as cuticular hydrocarbons (CHCs), which are secreted by flies onto the surface of their exoskeleton. CHCs act as sealants against water loss and as signalling molecules during social and sexual interactions. Importantly, these two functions impose diverging demands on the chemical properties of the CHCs. Water-proofing the cuticle is best achieved by long-chained hydrocarbon molecules that tightly stick to the surface of the fly, especially in warmer climates where desiccation risk is higher. By contrast, the pheromone function of CHCs requires short-chained molecules that are more volatile.

In their study, Rusuwa, Chung and colleagues[12] centre on these dual demands on CHCs and their potentially conflicting effects on the survival and reproductive success of *D. serrata* (Figure 1). The authors examined CHC profiles from flies sampled along a north–south gradient on the Australian east coast, where the species is native. They made two main observations: first, all populations along the coastal transect were dominated by a 'common' CHC profile comprising a mixture of short- and long-chained molecules; second, in the northernmost populations an appreciable fraction of flies showed a 'northern' profile enriched for long-chained CHCs. The spatially varying distribution of 'northern' and 'common' profiles suggested that the two distinct CHC blends have fitness effects that vary with climatic context. Lab experiments soon confirmed this. On the one hand, Rusuwa, Chung and colleagues[12] found that 'northern' females had better heat-shock and desiccation resistance than 'common' females, fitting with the higher protective effect of long-chain CHCs; on the other hand, 'common' males showed higher mating success than 'northern' males, reflecting their richer bouquet of volatile short-chain CHCs. The experiments thus helped explain the clinal trait distribution in the wild: 'northern' flies are more tolerant to the warmer climate of northern Australia, while 'common' flies are otherwise more reproductively successful. Intriguingly, the experiments also implied that CHC profiles are under sexually antagonistic selection, with the 'northern' profile conferring survival benefits to females, while the 'common' profile confers reproductive benefits to males.

Having established that CHC profiles are under sexually antagonistic selection, Rusuwa, Chung and colleagues[12] looked for the underlying genes. Using different mapping approaches, they found a very strong association between the type of CHC profile and a single genomic region containing several members of the fatty acyl-CoA reductase (FAR) gene family, which has previously been implicated in CHC synthesis[13]. The authors were able to further pinpoint the differences between CHC profiles to one specific member of this gene family — *DsFAR2-B* — that shows a number of coding differences between 'common' and 'northern' flies. *DsFAR2-B* has hallmarks of a credible candidate: it is unique among the *D. serrata* FAR genes in being expressed in the specialised cells that synthesise CHCs, and its paralogue in the related fly model *Drosophila melanogaster* could be shown to affect the relative abundance of

long and short-chained CHCs. In addition, population genetic analyses revealed signatures of balancing selection in several exons of *DsFAR2-B*, compatible with sexually antagonistic selection maintaining variation in populations in which the gene is polymorphic.

Overall, the study of Rusuwa, Chung and colleagues[12] uses a wide range of complementary approaches to paint a comprehensive portrait of a sexually antagonistic gene. Their study demonstrates antagonistic effects of alternative CHC profiles on male and female fitness, delineates how these effects are rooted in the ecological context of the populations and clearly links CHC variation to causal effects of the *DsFAR2-B* gene. The links between *DsFAR2-B* and sexually antagonistic fitness effects are more explicit than in other candidates[6–10] where the mapping between genotype, phenotype and fitness is less well established, and statistical confidence for the genetic association with fitness is higher than for previous sexually antagonistic gene candidates identified through genome-wide scans[11]. While further work will be required to pinpoint the specific causal polymorphism(s) and to quantitatively link lab-estimated fitness effects to wild-derived variant frequencies (as in other cases of adaptive genes[14], such as *Mc1r* in beach mice and *Eda* in sticklebacks), the work of Rusuwa, Chung and colleagues[12] represents the most compelling and complete example of an individual sexually antagonistic gene to date.

The study also raises broader questions. For instance, to what extent do ecological differences between habitats affect the prevalence of sexually antagonistic variation? Rusuwa, Chung and colleagues[12] revealed the sexually antagonistic effects of CHC profiles through geographic and climatic differences across *D. serrata*'s distribution range, where genetic polymorphism is maintained by sexually antagonistic selection in some (northern) but not other (southern) populations. What remains to be addressed empirically is whether spatial heterogeneity in itself typically promotes or hinders sexually antagonistic polymorphism. Current theory predicts that spatially varying selection enhances the opportunity for sexually antagonistic polymorphism[15].

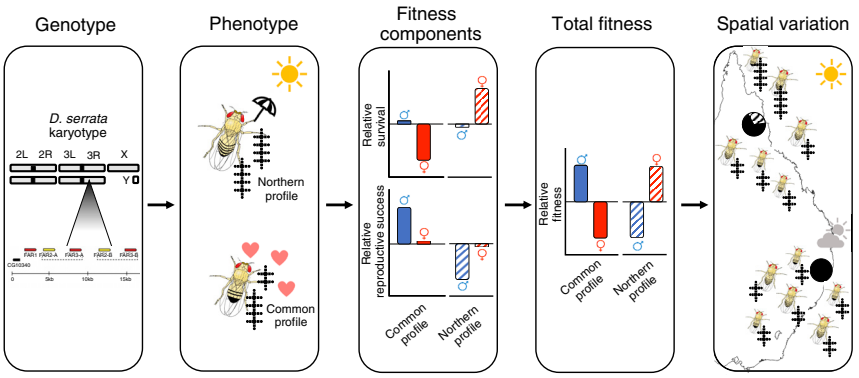

Figure 1. Anatomy of a sexually antagonistic polymorphism in *Drosophila serrata*. Rusuwa, Chung and colleagues[12] link the DsFAR2-B genotype to its effects on phenotype (profile composition of short- and long-chained CHCs), female and male fitness components (survival and reproduction-related traits) and total fitness, and finally its cline on the Australian east coast (where, for simplicity, 'common' and 'northern' profiles are represented by just a short- and a long-chained CHC).

This effect arises because genotypes that are low-quality on a global scale (e.g. the 'northern' CHC profile) can be relatively fit locally (e.g. in northern populations), thereby 'softening' selection and maintaining genetic variation by shifting competition from a global to a local scale.

Another question is how selection pressures on individual fitness components (e.g. survival, mating success) interact to generate sexually antagonistic selection on overall fitness. In the study of Rusuwa, Chung and colleagues[12], the positive effects of the 'common' profile were only visible when considering mating success, while the positive effects of the 'northern' profile were only apparent when measuring survival-related traits. This shows that sexually antagonistic selection on total fitness can emerge even when fitness effects on individual components are not antagonistic[16]. However, it is unknown how widespread such cross-sex antagonistic pleiotropy might be in nature. If it is common, many genuine sexually antagonistic genes are likely to be missed when studies focus on a single fitness component. Further work examining multiple fitness components is therefore much needed, and a recent study of sexually differential genetic variation in the white campion provides an illustrative example[17].

Finally, the polymorphism identified by Rusuwa, Chung and colleagues[12] relates to an old debate in evolutionary genetics: how often does adaptation rely on mutations with small *vs*. large effects? Evolutionary theory based on Fisher's Geometric Model predicts that unconditionally adaptive variants are predominantly of small effect, with large-effect variants being in the minority[18]. The pattern might be different in the case of sexually antagonistic genes, where large-effect mutations are more likely to remain polymorphic under sexually antagonistic selection than mutations with small effects[19]. This would then generate a bias towards detecting large-effect mutations, such as the one reported by Rusuwa, Chung and colleagues[12]. However, genome-wide data currently point to a polygenic basis of sexually antagonistic variation[11]. The intriguing finding of a large-effect sexually antagonistic gene should motivate further theoretical and empirical work on the distribution of phenotypic effect sizes of variants that contribute to the evolution of sexual dimorphism. While Rusuwa, Chung and colleagues[12] certainly provide a textbook example of a sexually antagonistic gene, only such further work will tell us how representative it is of genome-wide sexually antagonistic polymorphism in general.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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Systems neuroscience: Auditory processing at synaptic resolution

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Deeper layers of the auditory system have not been fully mapped in any model system. A new study links comprehensive connectomics of *Drosophila* song perception circuits to physiological response profiles.

Sixty years ago, in his classic book *Nerve Cells and Insect Behavior*, Kenneth Roeder offered the following metaphor for neuroscientific inquiry: "*From many directions, workers are tunnelling hopefully into the mountain, some with steam shovels and others with dental drills. Some travel blindly in a circle and come out close to their point of entrance; some connect, usually in a mismatched fashion, with the burrows of others. Some have chosen to disregard the random activities of their fellows and have worked out in a small region an elegant system of tunnels of their own. Both the attraction and confusion of this multitudinous excavation lie in the fact that none of these workers knows precisely what they are looking for, or what they will find*"[1]. Today, the scene is much the same, though there are of course far more tunnels. And yet among the confusion, a large and cohesive network is under construction in Roeder's main area of research, linking neuronal and animal behaviour in invertebrates. In particular, the advantages of circuit cracking in *Drosophila melanogaster*[2] linked with the emergence of whole-brain connectomes[3–5] indicate that this small animal will have an outsize impact on neuroscience over the next decade.