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NEWS AND VIEWS

Perspective

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Promiscuity punishes sexual deviants

Leif Engqvist[1] | Steven A. Ramm[2]

[1]Division of Behavioural Ecology, Institute of Ecology and Evolution, University of Bern, Bern, Switzerland

[2]Evolutionary Biology, Bielefeld University, Bielefeld, Germany

Correspondence
Leif Engqvist, Division of Behavioural Ecology, Institute of Ecology and Evolution, University of Bern, Bern, Switzerland.
Email: leif.engqvist@iee.unibe.ch

Sex is good for us, but it is a compromise. For the benefit of being able to produce genetically variable offspring, we must pay the cost of passing on only half our genes to each of them. Whilst evolutionary biologists still puzzle over the precise details of why the benefits of sex so frequently seem to outweigh the costs (Neiman, Lively, & Meirmans, 2017), one major challenge to sexual reproduction is the fact that if we pass on only half our genetic material to each gamete, there is a strong incentive for each individual allele to try to gain an unfair representation during gamete production. Fundamental to stabilizing sex once it evolves is therefore the ability to ensure a fair meiosis. Nevertheless, this system is not perfect, and some selfish genetic elements – so-called meiotic drivers – manage to tip the meiotic scales in their favour and gain a transmission advantage (review in Burt and Trivers, 2006). In this issue of Molecular Ecology, Manser, Lindholm, Simmons, and Firman (2017) demonstrate that in house mice, the effectiveness of one such harmful transmission distorter is reduced by polyandry and hence that population viability can be somewhat restored by female promiscuity.

KEYWORDS
evolution, genetic conflicts, polyandry, sexual selection, sperm competition

Few meiotic drive elements have been studied in any detail, but prime among those that have is the *t* haplotype found in house mice (Figure 1). First discovered in 1927, it is a substantial fragment of mouse chromosome 17 that contains many genes, does not recombine due to the presence of four large inversions and is present at varying levels in natural populations, with an average frequency typically ranging around 5%–25% (Ardlie, 1998; Burt & Trivers, 2006). The *t*'s driving ability is well understood and comes about because the *t* haplotype contains several distorter loci that inhibit the motility of both + and *t* sperm, but also a responder gene that restores the function of the *t*-bearing sperm, leading to an up to 90% transmission ratio. Nevertheless, it has a marked deleterious effect on carriers. First, *t* homozygous individuals do not usually survive. But second – and crucially – it also has a potentially substantial negative impact on heterozygous males: because wild-type sperm are incapacitated, *t*/+ heterozygotes are likely to be inferior sperm competitors should they compete with sperm from wild-type males over the fertilization of ova, making the *t* haplotype costly to males that carry it. Thus, the degree to which female mice mate with multiple males will be a major factor in determining the fertilization success of *t*-carrying males. In this and other drive systems, sperm competition may thus be an effective suppressor of drive (Haig & Bergstrom, 1995) and could potentially explain why selfish genetic elements, such as the *t*-complex, are less frequent in natural populations than expected, thereby resolving the "low-frequency paradox" (Ardlie, 1998).

This effect of sperm competition opens up new avenues for female mating strategies, as the *t* is not only costly to the males carrying it, it is also costly for females to mate with *t*-males. Due to the complete inviability of *t*/*t*-homozygotes, *t*/+-heterozygous females may lose up to 50% of their offspring depending on the strength of drive. One way for females to escape this would be to avoid *t*/+-males as mates and instead mate preferentially with wild-type males (Reinhold, Engqvist, Misof, & Kurtz, 1999). Yet, it may be difficult to

distinguish males carrying meiotic drive alleles. A less effective, yet far simpler, female strategy is to be polyandrous and mate with more than one male. How does this work? Remember that the reason why meiotic drive elements do drive is that they are able to kill sperm not carrying it, which should inevitably lead to reduced sperm competitiveness of *t*-males (Sutter & Lindholm, 2015). Thus, meiotic drive elements should drive less effectively in competition with wild-type males and females can reduce the cost of drive by mating with more males and thereby increase the chance to fertilize her eggs by wild-type sperm. In case of complete drive (all +-sperm are killed), such cryptic female choice would reduce the proportion of offspring sired by the drive carrying male to 33% from the expected 50%. Nevertheless, the element is still driving, as the proportion of offspring fertilized by driving *sperm* is higher than the expected 25%. Thus, it is not only that meiotic drive elements select for polyandry (Wedell, 2013), polyandry is expected to reduce the effectiveness of drive. From this, we can thus deduce two clear predictions: (i) *t*-males should lose out in sperm competition, and (ii) because of this, polyandry should reduce the frequency of the selfish *t* haplotype in the population.

Exactly, these predictions were tested in the study by Manser et al. (2017), yielding fascinating results. The key advance of the study was to take advantage of experimentally evolved lines of house mice to ask how the *t* haplotype behaves in contrasting social environments. These lines were not originally generated for this express purpose, but rather to study the consequences of polyandry and male adaptations to sperm competition, with some lines evolving under enforced monogamy (each female mated to a single male three times) and others under a polyandrous regime (each female mated to three different males). They have already yielded considerable insights, including identifying that monogamous versus polyandrous line males differ in a number of key sperm traits (Firman & Simmons, 2010; Firman et al., 2015), resulting in greater sperm competitiveness of the latter (Firman & Simmons, 2008). Manser et al. realized that experimental evolution under monogamy vs polyandry also provides the perfect test for whether polyandry really can keep the *t* haplotype at bay.

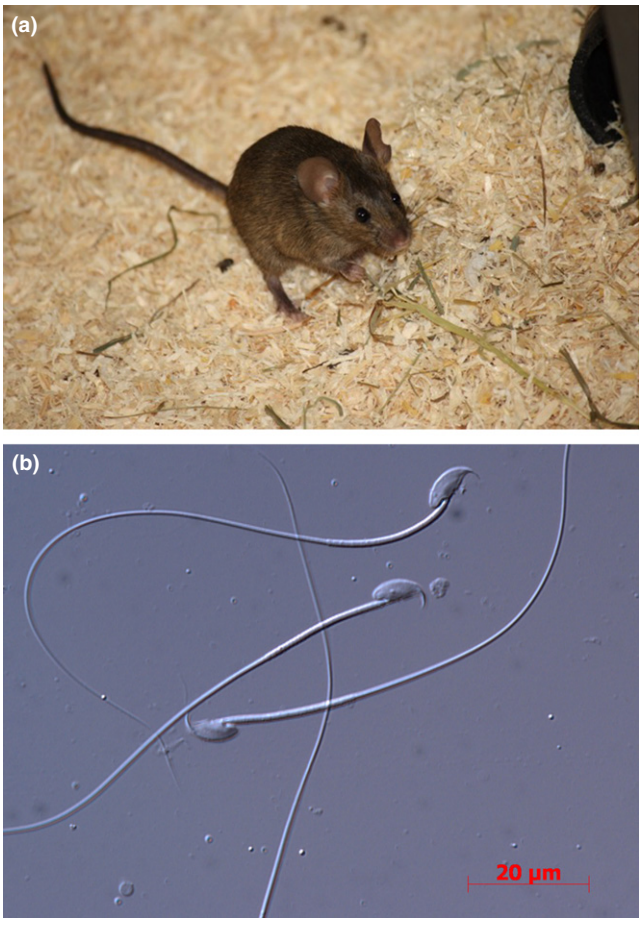

FIGURE 1 An adult house mouse (*Mus musculus*) (a) and mouse sperm (b) (photograph credit: Manuela Ferrari and Renee Firman)

And it seems that it can: exactly as predicted if polyandry provides protection against drive, over the course of 20 generations of experimental evolution there was significant divergence in *t* haplotype frequency according to the mating regime. The frequency of *t*-carrying males remained relatively constant in the four replicate monogamy lines at around 70%, but declined significantly in the four replicate polyandry lines from an initially similar frequency to on average around 40%. Moreover, Manser et al. show that *t*-carrying males are inferior sperm competitors, providing a likely causal explanation for these patterns, and supporting the sperm competition hypothesis for drive suppression.

In our view, the study by Manser et al. (2017) is an elegant and very illustrating example on how molecular methods, hand-in-hand with experimental evolution studies, can effectively reveal substantial changes on the population level. In this example, (experimentally manipulated) behavioural changes leading to a shift in mating system lead to strong changes in the selection on and resulting equilibrium frequency of a selfish genetic element. These changes are cryptic and barely visible on the phenotypic level, but conspicuous and demonstrable on the molecular level. Yet, however illuminating these results are, there are still a few intriguing open questions. First, as expected, *t*-carrying males clearly show a reduced fertility. Surprisingly, though, *t*-males have even lower sperm competitiveness than can be explained from drive alone. Manser et al. (2017) offer two intriguing alternative explanations for this. First, as the drive allele functions by killing sperm that do not carry it, yet protects itself by producing an antidote, it may be that own sperm are harmed as well. Incomplete restoration of sperm function is selectively rather neutral in monandry – if all rival sperm are killed, it does not matter too much if some own sperm are killed as well, all offspring will anyway be *t*-offspring. Yet, in polyandry, it will severely reduce the effectiveness of drive. The second alternative is that *t*-males may strategically reduce their investment in ejaculates. The reasoning behind this idea is that intrinsically less fertile males may benefit by reducing sperm competitiveness even more as they will lose out in sperm competition anyway (Engqvist, 2012).

A second open question is whether polyandry really can quantitatively resolve the low-frequency paradox and not merely provide a

qualitative explanation for lower *t*-frequencies than expected in natural populations. One should test this by explicitly incorporating the newly acquired parameters into existing models (e.g., Manser, Lindholm, König, & Bagheri, 2011). Nevertheless, some details in the study are already quite illuminating. The selection lines originating from monogamous laboratory populations started out with a very high frequency (70%) of *t*-carrying males. Intriguingly, this is almost exactly the frequency expected without sperm competition (Ardlie, 1998). Furthermore, following a few generations of polyandry, the *t*-frequency drops rapidly to levels similar to natural populations, where polyandry is frequent (Dean, Ardlie, & Nachman, 2006). Thus, sperm competition indeed seems an important factor dictating the frequency of the *t* haplotype, preventing it from being able to profit from its driving ability, and strengthening the case that polyandry could more generally provide protection against this class of selfish genetic elements.

AUTHOR CONTRIBUTIONS

L.E. and S.A.R. wrote the manuscript together.

ORCID

Leif Engqvist http://orcid.org/0000-0002-9434-7130
Steven A. Ramm http://orcid.org/0000-0001-7786-7364

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