Idea to watch

Mitochondria: The Red Queen lies within (Comment on DOI 10.1002/bies.201500057)

Bram Kuijper

From a genetic perspective, sex seems like the worst idea in the world. A sexual parent transmits only half of its genes to its offspring, compared with all of its genes for an asexual parent. Yet despite this considerable cost, the vast majority of eukaryotes engage in sex, which makes the evolution of sexual reproduction an enigma in evolutionary biology [1].

So why might sex be worth its cost? Primarily, sex breaks up associations between alleles at different loci. That is why sex is often considered beneficial in the context of host-parasite coevolution, as it breaks up associations between host alleles that may once have conferred resistance to parasites but no longer do so, while at the same time generating novel resistance combinations. This is called the 'Red Queen' hypothesis and is one of the major explanations (but not the only one) why sex is so common. However, its generality is debated: for one, selection needs to be strong and outcomes are highly sensitive to the genetic architecture of resistance [1].

In this issue, Havird et al. [2] suggest a novel hypothesis, in which mitochondria drive the evolution of sex. Mitochondria are organelles carrying their own DNA (mtDNA), containing genes indispensable for metabolism. Yet, we know from animal taxa that mtDNA mutates much faster than nuclear DNA (nDNA). Consequently, metabolism is in constant jeopardy of being disrupted by deleterious mutations, which is exacerbated by a limited scope for mtDNA recombination, so that mutations continuously accumulate (Muller's ratchet).

DOI 10.1002/bies.201500099

CoMPLEX, University College London, London, UK

Corresponding author:
Bram Kuijper
E-mail: a.kuijper@ucl.ac.uk

Havird and coworkers make the case that rapid mutations and limited recombination are not restricted to specific taxa, but rather ancestral features of mitochondria. Consequently, because all eukaryotes rely (or have once relied) on this crucial organelle, they have been under selection for billions of years to do something about this ongoing mitochondrial erosion.

Havird et al. suggest that the remedy against mitochondrial erosion is sex: when faced with a deleterious mitochondrial mutation, selection favors compensatory mutations in the nucleus that reduce its deleterious effect [3]. However, due to the high rate of mitochondrial mutation accumulation, the ideal combination of compensatory mutations may no longer exist when novel mitochondrial variants arise. Sex can overcome this, by breaking up old combinations between nuclear alleles and creating new associations that are better at reducing the effect of novel mitochondrial dysfunctions. Hence, sex may well have been a central feature of mitonuclear coadaptation.

To assess the generality of this exciting hypothesis, a formal model incorporating mitochondrial natural history would be the ideal next step. One aspect to consider is that mitochondria are exclusively vertically inherited. Extrapolating from existing models on the Red Queen process, we know that vertically transmitted parasites favor the evolution of sex more strongly than horizontally transmitted ones [4], which may be good news for this hypothesis. Next, mitochondria may evolve quickly, but the question is exactly how quickly. Hosts encounter many different parasites, with some of them able to change in the course of days or months due to horizontal transmission, horizontal gene transfer, and large population sizes. In comparison, subsequent generations of hosts experience largely the same mtDNA, as germline mutation rates of $\sim 1 \times 10^{-5}$ per basepair per generation are fast relative to nDNA, but maybe not so fast in comparison to parasites or environmental change. That said, mitochondria have imposed an uninterrupted selection pressure on their hosts ever since the origin of the eukaryotes, something which is unmatched by any parasite. This may well be the most convincing argument why mitochondria are more than innocent bystanders when it comes to the evolution of eukaryote sex.

Acknowledgements
Nick Lane and Arunas Radzvilavicius are thanked for comments on the manuscript. Funded by an EPSRC-funded 2020 Science fellowship (EP/I017909/1).

The author has declared no conflict of interest.

References

1. **Otto SP.** 2009. The evolutionary enigma of sex. *Am Nat* **174**: S1–14.
2. **Havird JC**, **Hall MD**, **Dowling DK.** 2015. The evolution of sex: a new hypothesis based on mitochondrial mutational erosion. *BioEssays* **37**: 951–8.
3. **Lane N.** 2011. Mitonuclear match: optimizing fitness and fertility over generations drives ageing within generations. *BioEssays* **33**: 860–9.
4. **Agrawal AF.** 2006. Similarity selection and the evolution of sex: revisiting the red queen. *PLoS Biol* **4**: e265.

 Bioessays 37: 934,