

NEWS AND VIEWS**Perspective**

Transgenerational and developmental plasticity at the molecular level: Lessons from *Daphnia*

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Listen to the news and you are bound to hear that researchers are increasingly interested in the biological manifestations of trauma that reverberate through the generations. Research in this area can be controversial in the public realm, provoking societal issues about personal responsibility (are we really born free or are we born with the burden of our ancestors' experience?). It is also a touchy subject within evolutionary biology because it provokes concerns about Lamarckianism and general scepticism about the importance of extra-genetic inheritance (Laland et al., 2014). Part of why the research in this area has been controversial is because it is difficult to study. For one, there is the problem of how long it takes to track changes across generations, making long-term, multi-generational studies especially tricky in long-lived species. Moreover, there are presently very few (if any) known molecular mechanisms by which environmental effects can be incorporated into the genome and persist for multiple successive generations, casting doubt on their evolutionary repercussions. Fortunately, you only have to look in your local pond to find the creatures that are teaching us a great deal about how and why the experiences of parents are passed down to their offspring. In this issue of *Molecular Ecology*, Hales et al. (Hales et al., 2017) illustrate the power of *Daphnia* ("water fleas") for making headway in this field.

KEYWORDS

genomics/transcriptomics, life history evolution, phenotypic plasticity, maternal effects

Daphnia are freshwater macro-invertebrates that are a favoured prey item for the fish with whom they often share a lake or pond (Figure 1). But *Daphnia* are not passive victims of their enemies—they produce defences such as a protective "helmet" and altered life histories and behaviour when danger lurks (Agrawal et al. 1999). What is fascinating about these antipredator defences is that *Daphnia* mount them in response to their own direct experience of predatory cues (within-generation (developmental) plasticity), in response to their parents' experience of predatory cues (transgenerational plasticity) and over evolutionary time—via genetic variation that is favoured by natural selection.

In addition to the fact that their phenotypic responses to cues about predation risk are well documented, *Daphnia* are also great

subjects because they are amenable to long-term, carefully controlled studies. Their rapid generation time—approximately 10 days—makes it relatively easy to track environmental effects across multiple generations. Further, *Daphnia* can reproduce asexually, which means researchers can readily generate clones of different genotypes and then expose those clones to different environments, a powerful tactic for disentangling genetic and environmental influences.

Some clones of *Daphnia* are more plastic in response to predator cues than others, making them great subjects for investigating the evolution of phenotypic plasticity. Even more intriguing is that there is a variation among clones in whether they exhibit stronger within-generation or transgenerational plasticity. For example, clones that



FIGURE 1 *Daphnia* depicted with predator lurking in the background. *Daphnia* photo credit: Hajime Watanabe. Fish photo credit: U.S. Fish and Wildlife. Photos licensed for use under public domain with credit to authors in Schield et al. (2016)

are common in lakes under consistently intense predation pressure by fishes respond with strong transgenerational plasticity to develop faster. Clones that live in lakes with variable predation risk respond by accelerating their own development, but do not exhibit strong transgenerational plasticity (Walsh, Cooley, Biles, & Munch, 2015). These results are broadly consistent with some evolutionary theory about how the rate and predictability of environmental change favours different types of phenotypic plasticity (Dall, McNamara, & Leimar, 2015). What's more surprising is that individual clones seem

to specialize on either within-generation or transgenerational plasticity, but not both (Walsh et al., 2015). For example, when directly exposed to cues of predation risk, one clone of *Daphnia* slows down the development time by a little. However, their resulting offspring develop considerably *faster*. In other words, this clone exhibits strong transgenerational plasticity and relatively weak within-generation plasticity, and the two forms of plasticity operate in opposite directions.

In this issue of *Molecular Ecology*, Hales et al. (Hales et al., 2017) show that this same pattern—strong transgenerational plasticity coupled with weak within-generation plasticity—is mirrored at the molecular level. Hales et al. used RNA-Seq to compare gene expression between *Daphnia* that had been exposed to cues linked to predation risk (the smell of fish and dead *Daphnia*) relative to a control (unexposed) group (generation 1). The authors interpret the resulting differentially expressed genes as within-generation plasticity genes. They then reared the offspring of those two treatments for two subsequent generations *in the absence of predator cues* and compared the gene expression profiles of the two lineages at generation 2 and generation 3 (Figure 2). The resulting transgenerational plasticity genes differ in expression as a function of parents' (generation 2) or grandparents' (generation 3) experience with predation risk.

The key result of their study is that there were relatively few within-generation plasticity genes, but a large number of transgenerational plasticity genes. These findings suggest that this clone responds more strongly at the molecular level to the environment experienced by their mother or grandmother than their own personal experience. Interestingly, many of the genes that were associated with transgenerational plasticity in generation 2 were also associated with transgenerational plasticity in generation 3, but there was a smaller set of genes in generation 3. Together, these results imply that the molecular signature of intergenerational risk is mostly conserved across generations, but the effect of historical experience with risk decays overtime. Finally, very few genes were common to both within-generation plasticity and transgenerational plasticity,

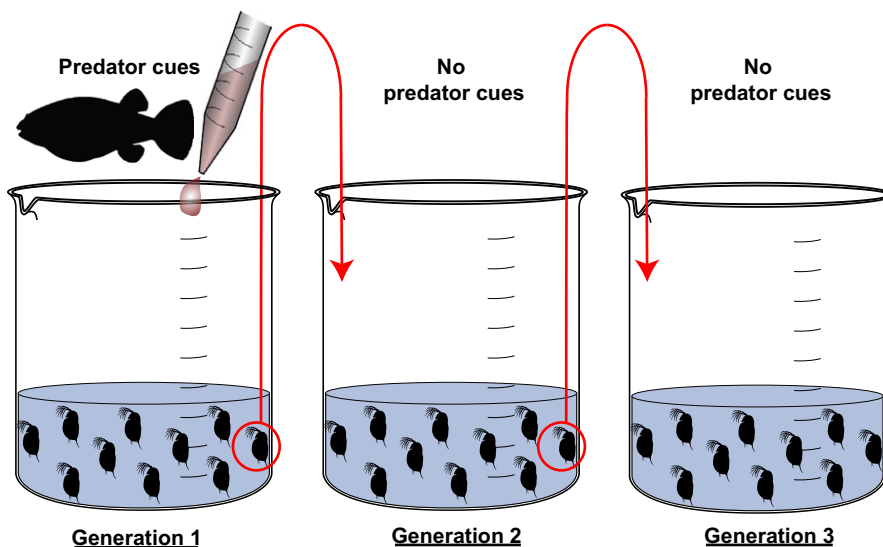


FIGURE 2 Experimental design used in Hales et al. (2017). A clonal generation representing the third common-garden generation of *Daphnia ambigua* was exposed to predator cues in generation 1. A single neonate from the second clutch was transferred in a new jar (generation 2). Generations 2 and 3 were not exposed to any additional predator cues, so any differentially expressed genes in these generations are a product of transgenerational plasticity stemming from the initial predator cues in generation 1. Image credit: Todd Castoe

which suggests that the two forms of plasticity are distinct at the molecular level and potentially free to evolve independently of one another. If this is the case, then this could explain how selection on the underlying gene regulatory mechanisms favoured different forms of plasticity in different environments, that is, transgenerational plasticity in temporally variable environments and within-generation plasticity in more stable environments.

What is remarkable about these RNA-Seq results is the extent to which they agree with the phenotypic patterns documented earlier (Walsh et al., 2015): relatively weak within-generation plasticity, relatively strong transgenerational plasticity, which is maintained for at least two generations but dampens over time, and different phenotypes associated with the two. These results are also consistent with epigenetic work from the same research group, which recently showed that exposure to predator cues in one generation leads to consistent patterns of genomewide methylation in the following generation in this clone (Schield et al., 2016).

The results raise a number of intriguing questions. *Why*, for example, does this clone exhibit opposite patterns of within-generation vs. transgenerational plasticity, a pattern now supported at both the phenotypic and molecular level? The clone appears incapable of being plastic both within and between generations – does this reflect a necessary trade-off between them, or are there other explanations, for example, compensation or parent-offspring conflict (Auge, Leverett, Edwards, & Donohue, 2017)? Another perspective is that insofar as the specific cue that triggers within-generation plasticity (smell of fish and smell of dead conspecifics) is presumably different from the specific cue that triggers transgenerational plasticity, those cues might convey different information and hence generate different responses. Independent selective events could have shaped these responses, resulting in different regulatory mechanisms. In this vein, it would be interesting to know whether the maternal cue from F1 to F2 is the same as the signal from F2 to F3, and how this signal does or does not differ from the smell of fish. If the cue is the same across generations, how is it retained? One possibility is via small RNAs, which are an increasingly common culprit implicated in transgenerational plasticity (Grentzinger et al., 2012).

Perhaps more than any other animal system, *Daphnia* are at the leading edge of our understanding of transgenerational plasticity from an evolutionary perspective. The system offers many more opportunities to make serious headway in this area. Obvious next steps include examining transgenerational and within-generation plasticity at the molecular level in different clones: do clones that specialize on within-generation plasticity exhibit a trade-off with transgenerational plasticity at the molecular level, for example? Are there common features of the molecular signatures of plasticity across clones? More generally, the system offers unparalleled opportunities to learn how animals integrate information from their ancestors, parents and personal experience at both the phenotypic and molecular level (Stamps & Krishnan, 2014). Key parameters to explore in this area include the reliability of the cue and the costs of failing to respond to information about risk. Finally, while Hales et al. found that within- and transgenerational plasticity are distinct at the molecular level, further study on other

systems are warranted in order to assess the generality of these findings. Recent studies on *Daphnia* (Lind, Yarlett, Reger, Carter, & Beckerman, 2015) and guppies (Ghalambor et al., 2015), for example, came to opposite conclusions about whether adaptive vs. nonadaptive plasticity can accelerate adaptation. Further studies comparing the fascinating *Daphnia* to other systems (vertebrate, invertebrate, sexual and asexual) can help us refine our understanding of the conditions under which different forms of plasticity are expected to be equivalent or distinct at the molecular level.

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