Heredity (2004) 93, 239–240
© 2004 Nature Publishing Group All rights reserved 0018-067X/04 $30.00
www.nature.com/hdy

NEWS AND COMMENTARY

Evolutionary developmental biology

Towards a spineless stickleback

W Arthur

Heredity (2004) **93,** 239–240. doi:10.1038/sj.hdy.6800540

Over the last couple of decades, studies on quantitative trait loci (QTLs) have revealed that evolutionary changes in development, and hence in adult morphology, are often underlain not by hundreds of 'polygenes', each with miniscule effects, but by perhaps 10 or 20 genes, of which just a few are responsible for most of the observed phenotypic variation. The mutations in these few important genes can be thought of, in terms of their effects on the phenotype, as 'mesomutations' – that is, they are somewhere between Goldschmidtian macromutations and Fisherian micromutations. This interesting finding, however, raises a difficult issue: why are such mesomutations able to be involved in the evolutionary process? In statistical terms, the bigger the phenotypic effect of a mutation, the more likely it is to render its bearers unfit. The proposal that homeotic mutations could cause major evolutionary changes in insect morphology (Goldschmidt, 1952) was not accepted because the mutants that he discussed, such as *bithorax* and *antennapedia*, were clearly seriously unfit. Would we not expect that mesomutations would be subject to a smaller version of the same problem?

An important part of this problem arises from the broadly pleiotropic nature of genes in general, and of developmental genes in particular. If a developmental gene mutates, it will often lead to multiple changes in the overall ontogenetic trajectory. It might seem reasonable, on an *a priori* basis, to expect that in general, a mutation that produces a large change in one aspect of development will also produce large changes in other aspects of development that are affected by the gene concerned (notwithstanding plenty of exceptions to this 'rule'). If so, then even if one of the changes produces an increase in fitness, this may be outweighed by problems caused elsewhere. However, there is a potential way out of this problem. Many developmental genes have multiple *cis*-acting regulatory regions, with different such regions controlling expression in different tissues, or in different parts of the developing embryo. If a mutation occurs in one of these rather than in the coding region of the gene, it opens up the possibility of there being a significant change in one of the gene's regions of expression but not others. The possible evolutionary significance of this has been clear since the discovery of multiple regulatory regions (see, for example, Carroll *et al*, 2001), but studies illustrating this significance with specific examples have, until recently, been lacking.

The study by Shapiro *et al* (2004) on evolution of pelvic spine reduction in freshwater populations of sticklebacks is thus of enormous importance, because it shows an incredibly clear case of this kind of evolutionary change based on controlling rather than coding regions of a developmental gene (*Pitx1*). Further, it includes many types of information, ranging from molecular, through developmental and morphological, to ecological. It suffers only one major deficiency, which the authors themselves point out, and which I comment on briefly below.

However, first the essence of their story. Sticklebacks, *Gasterosteus aculeatus*, have both marine and freshwater populations in many parts of the world. Typically, fish in marine populations have well-developed pelvic spines that are thought to act as a deterrent to soft-mouthed predators, such as larger marine fish. In contrast, many freshwater populations have much reduced pelvic spines. This is thought to be because of the absence in many freshwater localities of predatory fish and the presence of invertebrate predators that capture the sticklebacks by grabbing hold of their spines.

Shapiro *et al* (2004) performed large-scale crosses between marine and freshwater forms, measured the degree of pelvic reduction in the F2 progeny, and examined the contribution of different linkage groups to the variation. They found that there was a major effect from a QTL at one end of linkage group 7 – the site, it turns out, of the stickleback orthologue of the mouse *Pitx1* gene, mutations of which are known to cause hindlimb reduction. They determined the DNA sequence of the coding region of the gene in marine and freshwater fish, and found it to be identical. However, they also looked at expression patterns of the gene and found that although most regions of expression (eg in the thymus, olfactory pits and neuromasts) were the same, there was an important difference: freshwater fish lacked expression of *Pitx1* in the pelvic region. These findings are all consistent with a mutation in a pelvis-specific regulatory region.

The piece of the jigsaw that is still missing is demonstration of such a mutant region. The problem in coming up with this crucial 'last piece' is that regulatory mutations are much harder to find than their coding-region equivalents. They may be spread over a much longer DNA sequence. Clearly, Shapiro *et al* intend to look for them as the next phase of their work; and if they are successful in their search, they will enhance this already-good evolutionary story.

Broadening out again, this important study can be seen as a contribution to the growing field of microevolutionary evo-devo (Wray and Raff, 1989; Brakefield *et al*, 1996; Beldade *et al*, 2002; Kettle *et al*, 2002). For too long, most microevolutionary studies lacked a developmental component; and most evo-devo studies focused on differences between high-level taxa; the two endeavours did not connect very well. However, as a result of studies like that of Shapiro *et al* (2004), we can increasingly see a holistic picture of the evolution of development, from its microevolutionary beginnings to its long-term interphylum consequences.

Along with several other biologists, I have argued on many occasions (eg Arthur, 2004) that evolutionary theory in the 21st century needs to become more 'inclusive' than the so-called modern synthesis of the 20th century, in which development did not feature nearly enough. It is through studies like that of Shapiro *et al* (2004) that increased inclusivity will be achieved. I hope that there will be many more to follow, based on a wide range of taxa. Fish today, tomorrow the world.

W Arthur is at the Department of Zoology, National University of Ireland, Galway, Galway, Ireland.
e-mail: wallace.arthur@nuigalway.ie

Arthur W (2004). *Biased Embryos and Evolution*, Cambridge University Press: Cambridge, UK.
Beldade P *et al* (2002). *Nature* **416**: 844–847.
Brakefield PM *et al* (1996). *Nature* **384**: 236–242.
Carroll SB *et al* (2001). *From DNA to Diversity*, Blackwell Science: Malden, MA.
Goldschmidt R (1952). *Acta Biotheoret* **10**: 87–104.
Kettle C *et al* (2002). *Evol Dev* **5**: 198–207.
Shapiro MD *et al* (2004). *Nature* **428**: 717–723.
Wray GA, Raff RA (1989). *Dev Biol* **132**: 458–470.