Evolution of Development

Secondary article

Ehab Abouheif, *Duke University, Durham, North Carolina, USA*

Gregory A Wray, *Duke University, Durham, North Carolina, USA*

The field of evolutionary developmental biology provides a framework with which to elucidate the 'black box' that exists between evolution of the genotype and phenotype by focusing the attention of researchers on the way in which genes and developmental processes evolve to give rise to morphological diversity.

Article Contents

Introduction

At the end of the nineteenth and beginning of the twentieth century, the fields of evolutionary and developmental biology were inseparable. Evolutionary biologists used comparative embryology to reconstruct ancestors and phyletic relationships, and embryologists in turn used evolutionary history to explain many of the processes observed during animal development. This close relationship ended after the rise of experimental embryology and Mendelian genetics at the beginning of the twentieth century. Now, after almost 100 years of separation, these two fields have reunited to form a distinct discipline called 'evolutionary developmental biology', whose aim is to understand the relationship between evolution of genotype and evolution of phenotype, as well as how developmental genes and processes evolve.

Embryos and Evolution, Heterochrony

Recapitulation, the idea that ancestral adult forms repeat themselves during the embryonic or juvenile stages of their descendants, has been a deeply influential idea in the history of biological thought. During the nineteenth century, it provided a general framework for reconstructing the ancestors and evolutionary histories for countless organisms. The appearance of gill arches during an early ontogenetic stage of a mammalian embryo, for example, was used as evidence that fish are the ancestors of mammals.

Ernst Haeckel was perhaps the most influential proponent of recapitulation. In 1874, he put forth his famous 'biogenetic law', which states that 'ontogeny recapitulates phylogeny'. Haeckel used his law to postulate the twenty-two ancestors that appear during the development of human embryos. Although Haeckel's primary interest was in the reconstruction of ancestors and evolutionary histories, he wanted to provide a mechanical cause for his biogenetic law. This led him to propose that phylogeny literally causes ontogeny through two processes: terminal addition, which adds new features to the end of ontogeny, and condensation, which deletes earlier ontogenetic stages to make room for new features (Gould, 1977).

As the field of comparative embryology blossomed during the early twentieth century, a considerable body of evidence accumulated that was in conflict with the predictions of the biogenetic law. Because ontogeny could only change by pushing old features backwards in development (condensation) in order to make room for new features (terminal addition), the timing of developmental events could only be accelerated. Walter Garstang showed that this apparent constraint on evolutionary change in development imposed by the biogenetic law was broken by numerous organisms: not only can evolutionary shifts in the timing of developmental events occur in the opposite direction (i.e. retardation), but novel features are not always terminal additions. Garstang wrote a series of influential articles and witty poems highlighting the presence of juvenile features of ancestors in the adult stages of descendants. Perhaps the most famous example occurs in the axolotl, *Ambystoma mexicanum* (**Figure 1**). This salamander does not metamorphose, and aquatic larval features, such as gills and a tail fin, are retained throughout adult life. Conversely, most of the other salamander species within the same genus undergo complete metamorphosis and lose their gills and tail fins.

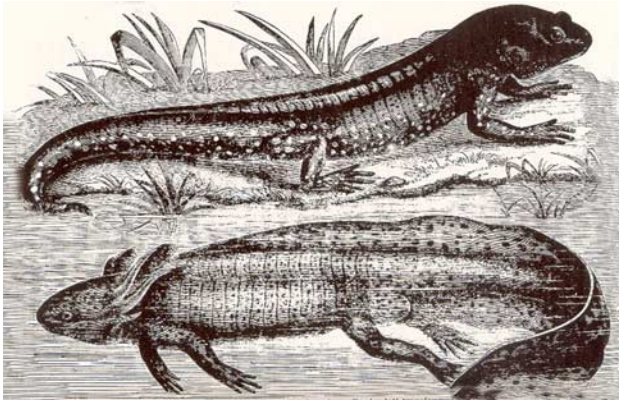

Figure 1 The Mexican Axolotl. From Dumeril A (1867) *Annales Des Sciences Naturelles-Zoologie et Biologie Animale* **7**: 229–254.

Thus, the most parsimonious interpretation of this observation is that the ancestral salamanders of this genus underwent complete metamorphosis and lost their gills and tail fin, whereas the retardation of development observed in *Ambystoma mexicanum* is an evolutionarily derived feature relative to its ancestors (Raff, 1996).

Haeckel was aware of exceptions to his biogenetic law, and coined the term 'heterochrony' to describe them. Heterochrony, the dissociation of the relative timing or onset of developmental events between ancestral and descendent ontogenies, was soon recognized as more the rule than the exception. The biogenetic law, and thus any relationship between evolutionary and developmental biology, began to lose favour. With the contemporaneous rise of Mendelian genetics and experimental embryology, the fields of evolutionary and developmental biology were set on independent trajectories for most of the twentieth century (Gould, 1977; Raff, 1996).

During the last three decades, heterochrony has enjoyed renewed interest as an important index of evolutionary change. Although heterochrony provides an adequate description of the dissociations possible in the timing or onset of development events between ancestral and descendent ontogenies, it fails to provide an adequate mechanistic explanation for these developmental events. If heterochrony is to remain an informative means to study the connection between evolution and development, future research must incorporate recent advances from the field of developmental genetics in order to elucidate the genes and mechanisms that underlie heterochronic changes in evolution (Raff, 1996).

Hox Genes

While evolutionary biologists were renewing their interest in heterochrony, developmental geneticists were discovering the existence of sets of genes, specifically transcription factors and signalling molecules, which regulate embryonic development. The initial characterization of these developmental regulatory genes in the fruitfly, *Drosophila melanogaster* (Lewis, 1978; Nüsslein-Volhard and Weischaus, 1980), prompted a search for their counterparts in other animals. It was soon clear that most developmental regulatory genes are evolutionarily conserved across a broad range of animal phyla (McGinnis *et al.*, 1984).

Perhaps no other class or family of developmental regulatory genes has sparked the imagination of biologists as much as the homeotic, or '*Hox*', genes. *Hox* genes encode transcription factors that control the identity or fate of different regions along the anteroposterior axis of the embryo. These genes are generally clustered within the genome, and in many animals are expressed in the same relative order along the main body axis as they are positioned along the chromosome.

Changes in the expression of *Hox* genes along the anteroposterior axis can lead to changes in the identity of body regions. In one of the most famous examples of a homeotic transformation, E. B. Lewis (1978) demonstrated that mutations in the non-protein-coding region in one of the *Hox* genes, *Ultrabithorax*, switch the identity or fate of the third thoracic segment in *Drosophila* into the second. The third thoracic segment possesses a pair of small balancing organs called halteres, whereas the second possesses a pair of fully functional wings. Because the third thoracic segment acquires the identity of the second, the mutant adult fly develops a pair of wings instead of halteres, and the transformed mutant has two pairs of wings instead of one (**Figure 2**).

When *Hox* genes were discovered across a broad range of animal phyla, many biologists began to reconsider the importance of Richard Goldschmidt's theory of saltational evolution (Jacobs, 1990; Gellon and McGinnis, 1998). Goldschmidt's idea was that major evolutionary changes are driven by single large-scale mutations that generate new morphological forms within natural populations. In this context, homeotic mutations, such as the

Figure 2 The ultrabithorax mutation, i.e. wild-type versus four-winged fly. Provided courtesy of Sean Carroll.

mutation in *Ultrabithorax* that produces a four-winged fruitfly, appear to support Goldschimdt's saltational theory of evolution.

However, the notion that dramatic mutations in developmental regulatory genes are the principal cause of the evolutionary transformations between animal body plans is incompatible with our current understanding of neo-Darwinian theory and population genetics. The saltational theory in general fails to explain how such large-scale homeotic mutations are fixed in natural populations. The probability of a large-scale mutation being viable and favourably selected upon by natural selection is very low, and should therefore have little consequence for evolutionary change (Fisher, 1930; Burch and Chao, 1999). It is also critical to distinguish between those mutations that cause dramatic phenotypic transformations in the laboratory, and those that were responsible for the transformations that did in fact appear and persist in natural populations over evolutionary time (Budd, 1999). Furthermore, developmental regulatory genes, including the *Hox* genes, play several different developmental roles, and can drive small-scale evolutionary changes in a manner consistent with a gradual mode of evolutionary change (Akam, 1998).

Stern (1998), for example, demonstrated that the *Ultrabithorax* gene is also responsible for patterning tiny bristles, called trichomes, on the second leg in *D. melanogaster*. He showed that evolutionary changes in the non-protein-coding region of the *Ultrabithorax* gene are in part responsible for the small-scale evolutionary changes and divergence in trichomes between closely related *Drosophila* species. Therefore, this and Ed Lewis's four-winged fruitfly example show that changes in the non-protein-coding regions of *Hox* genes can produce both small-scale and large-scale mutations. For the reasons discussed above, however, only the smaller-scale phenotypic outcomes are likely to be fixed in natural populations and contribute to the generation of morphological diversity.

Hox genes provide an excellent example of how developmental genes and processes can generally evolve. There are, however, many other developmental regulatory genes that play equally important roles in the development and evolution of morphological structures, and which have also been a source of conceptual advance in the field. The role of the *distal-less* gene in the origin of animal appendages (discussed below) serves as a good example.

Embryology, Palaeontology, Genes and Limbs

Evolutionary developmental biology is by nature an interdisciplinary field, whose practitioners routinely draw upon evidence from several disciplines of biology, most importantly genetics, embryology and morphology. Comparing data from these different biological disciplines across taxa can reveal much about the way developmental processes evolve and how they change in relation to the phenotypic features to which they give rise.

Some of the best examples of this approach come from studies addressing the origin of animal appendages. The developmental regulatory gene, *distal-less*, was one of the first genes to be examined in this context. Distal-less protein is a transcription factor that plays an important role in organizing the growth and patterning of the proximodistal axes of limbs in *D. melanogaster*, and is expressed in the distal regions of the developing limbs (Cohen, 1990). Thus, it came as something of a surprise when *distal-less* expression was detected in the 'appendages' of animals from five additional phyla: (1) chordate fins and limbs, (2) polychaete annelid parapodia, (3) onychophoran lobopodia, (4) ascidian ampullae, and (5) echinoderm tube feet (Panganiban *et al*., 1997).

These results raise an interesting evolutionary question: do these similarities in gene expression indicate that these different appendages are homologous and are therefore derived from an appendage possessed by the most recent common ancestor of these six animal phyla? Although there has been, and continues to be, much debate surrounding this question, most researchers are coming to the conclusion that homology is hierarchical, and that features that may be homologous at one level of biological organization, such as genes and their roles, do not necessarily indicate homology at other levels, such as morphological structures (Abouheif *et al*., 1997). This point becomes clearer when *distal-less* expression is examined in a historical framework, and the homology of different biological levels is defined independently.

The fossil record of vertebrates clearly indicates that the earliest members of this group lack limbs entirely. This kind of historical evidence indicates that the appendages of arthropods, annelids, echinoderms and chordates, as morphological structures, are not homologous. In contrast, comparisons of sequence and expression data indicate that the *distal-less* gene, and possibly its role in patterning proximodistal axes, is homologous in all of these phyla.

Thus, we have an evolutionary scenario in which a nonhomologous structure is being patterned by a homologous developmental gene and by implication, a homologous process. This scenario can be interpreted in at least three ways: (1) *distal-less* was part of a proximodistal patterning system that patterned a limb-like outgrowth in the ancestor of these six phyla, and was then recruited into appendage development independently in several phyla; or (2) *distal-less* was part of a genetic network that patterned axes in a completely unrelated structure in the ancestor of these phyla, and was subsequently recruited independently to pattern the proximodistal axis of nonhomologous appendages; or finally (3) the recruitment of *distal-less*

into appendage development in these phyla was completely coincidental, and the similarities observed in the expression domains of these genes are instances of convergent evolution. It is not possible to distinguish between these interpretations until more comparative data become available. At the very least, however, this example has alerted evolutionary and developmental biologists to the possibility that the evolution of novel structures may involve recruiting existing machinery for generic developmental tasks, such as patterning or cell signalling, rather than inventing them completely *de novo* (Shubin *et al*., 1997). This and other studies highlight the insights to be gained from incorporating evidence from palaeontology, metazoan phylogeny, multiple taxa, and multiple levels of biological organization.

References

Abouheif E, Akam M, Dickinson WJ *et al*. (1997) Homology and developmental genes. *Trends in Genetics* **13**: 432–433.

Akam M (1998) Hox genes, homeosis and the evolution of segmental identity: no need for hopeless monsters. *International Journal of Developmental Biology* **42**: 445–451.

Budd GE (1999) Does evolution in body patterning genes drive morphological change – or vice versa? *BioEssays* **21**: 326–332.

Burch CL and Chao L (1999) Evolution by small steps and rugged landscapes in the RNA virus ϕ6. *Genetics* **151**: 921–927.

Cohen SM (1990) Specification of limb development in *Drosophila* embryo by positional cues from segmentation genes. *Nature* **343**: 173–177.

Fisher RA (1930) *The Genetical Theory of Natural Selection*. New York: Oxford University Press.

Gellon G and McGinnis W (1998) Shaping animal body plans in development and evolution by modulation of *Hox* expression patterns. *BioEssays* **20**: 116–125.

Gould SJ (1977) *Ontogeny and Phylogeny*. Cambridge, MA: Harvard University Press.

Jacobs DK (1990) Selector genes and the Cambrian radiation of Bilateria. *Proceedings of the National Academy of Sciences of the USA* **87**: 4406–4410.

Lewis EB (1978) A gene complex controlling segmentation in *Drosophila*. *Nature* **276**: 565–570.

McGinnis W, Garber RL, Wirz J, Kuroiwa A and Gehring WJ (1984) A homologous protein-coding sequence in *Drosophila* homeotic genes and its conservation in other metazoans. *Cell* 37: 403–408.

Nüsslein-Volhard C and Weischaus E (1980) Mutations affecting segment number and polarity in *Drosophila*. *Nature* 287: 795–803.

Panganiban G, Irvine SM, Sherbon B *et al*. (1997) The origin and evolution of animal appendages. *Proceedings of the National Academy of Sciences of the USA* **94**: 5162–5166.

Raff RA (1996) *The Shape of Life*. Chicago: University of Chicago Press.

Shubin N, Tabin C and Carroll S (1997) Fossils, genes and the evolution of animal limbs. *Nature* **388**: 639–648.

Stern DL (1998) A role of *Ultrabithorax* in morphological differences between *Drosophila* species. *Nature* **396**: 463–466.

Further Reading

Carroll SB (1995) Homeotic genes and the evolution of arthropods and chordates. *Nature* **376**: 479–485.

Shubin N, Tabin C and Carroll S (1997) Fossils, genes and the evolution of animal limbs. *Nature* **388**: 639–648.