

Do Convergent Developmental Mechanisms Underlie Convergent Phenotypes?

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Key Words

Convergence · Homology · Evolution of development · Larva · *Hox* complex

Abstract

Convergence is a pervasive evolutionary process, affecting many aspects of phenotype and even genotype. Relatively little is known about convergence in developmental processes, however, nor about the degree to which convergence in development underlies convergence in anatomy. A switch in the ecology of sea urchins from feeding to nonfeeding larvae illustrates how convergence in development can be associated with convergence in anatomy. Comparisons to more distantly related taxa, however, suggest that this association may be limited to relatively close phylogenetic comparisons. Similarities in gene expression during development provide another window into the association between convergence in developmental processes and convergence in anatomy. Several well-studied transcription factors exhibit likely cases of convergent gene expression in distantly related animal phyla. Convergence in regulatory gene expression domains is probably more common than generally acknowledged, and can arise for several different reasons.

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Introduction

Convergence pervades the biological world. From anatomy to protein sequences, it appears at all levels of biological organization; and from fungi to fishes, it permeates the evolutionary history of all groups of organisms [Darwin, 1859; Raff, 1996; Sanderson and Hufford, 1996; Wray, 1996; Moore and Willmer, 1997; Abouheif, 1999; Peintner et al., 2001; Eisthen, 2002; Nishikawa, 2002; Zakon, 2002]. The most celebrated cases of convergence, such as the eyes of cephalopods and vertebrates, are astonishingly similar in detail. Many other spectacular examples of convergence could be cited: bees attempt to mate with orchids, trouts are infected by parasitic clams, and birds vomit distasteful butterflies, all because of convergence.

How does convergence come about? Like many questions in biology, this is really two separate questions. The first issue is evolutionary and ecological: why convergence has evolved. The two classic categories of explanation are natural selection and phylogenetic constraint. By considering a situation in detail, it is often possible to provide more precise answers within each of these broad categories [Eisthen, 2002]. The second issue is genetic and developmental: how convergence has evolved. Here the questions concern the underlying basis for the similarity. The two categories of explanation are that homologous struc-

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tures, developmental processes, or genes were the substrate for the convergent feature, or that they were not. A complete understanding of any particular convergence can only come from answering both the ‘why’ and the ‘how’ questions [Raff, 1996].

This paper examines the relationship between convergence at one level of biological organization (regulatory genes or developmental mechanisms) with that at another (anatomy). Is anatomical convergence the result of conserved, convergent, or independent genetic and developmental bases? Addressing this deceptively simple question necessitates thinking about both the ‘how’ and the ‘why’ of convergence. Perhaps unsurprisingly, the answer is not simple. Convergence in anatomy is sometimes, but by no means always, due to convergent developmental processes; conversely, convergent developmental mechanisms sometimes, but not always, produce convergent structures. The same is true when we probe deeper, into the regulatory genes that control developmental processes.

Convergence and History

Convergence is not an observation – it is a specific hypothesis about evolutionary history [Brooks, 1996; Doyle, 1996; Abouheif, 1999]. What we have available for direct study are features of living species. For some taxa, we can also extract important (but rarely complete) anatomical information from the fossil record. For biochemical, genetic, developmental, physiological, and behavioral features, however, we are largely limited to species alive today.

The features of living organisms are a reflection of evolutionary history, but they are not always an easily interpreted guide to that history. Any similarity or difference that we observe in living organisms could have come about in a variety of ways [Darwin, 1859; Wake, 1999]. If two species differ in some feature of interest, we can confidently conclude that this is the result of divergence since they split from a common ancestor (fig. 1A). We cannot be confident, however, about what that feature was like in the latest common ancestor. It might have resembled the feature as manifest in one or the other living species, it might have been intermediate between them, or it might have been quite different from either.

If the feature of interest is similar among species, the situation is even more difficult to reconstruct – particularly if those species are not closely related. The simplest possibility is conservation: the feature has not changed

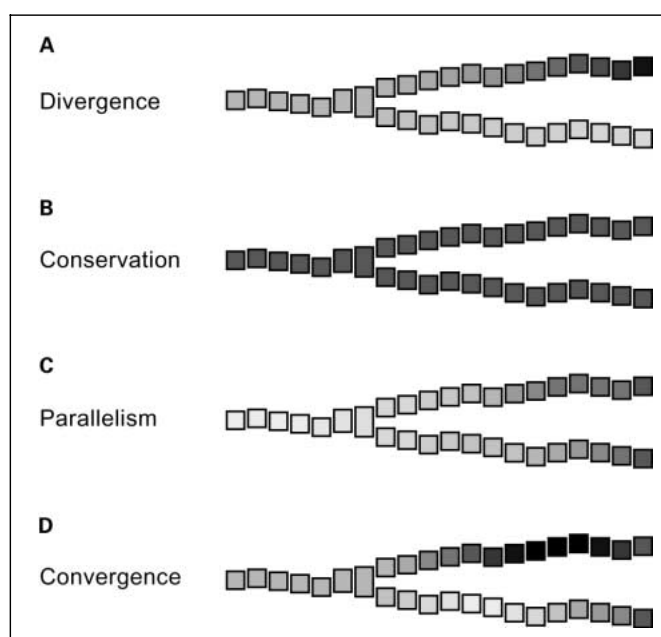


Fig. 1. Divergence (A), conservation (B), parallelism (C), and convergence (D). Similarities and differences in living organisms are observations, but divergence, conservation, parallelism, and convergence are all inferences about evolutionary history. As such, any interpretation of convergence needs to be explicitly tested against other possibilities. The four basic categories of evolutionary history are illustrated here. Time progresses from left to right. When two living organisms differ in some feature (boxes at tips of phylogeny, right-hand end), one or the other or both must differ in that regard from the latest common ancestor, an interpretation of divergence. When two extant species share a common feature, that similarity may have come about through various evolutionary histories. The simplest, and most commonly invoked, hypothesis is conservation. This hypothesis posits that the latest common ancestor possessed the same feature as its descendants. Particularly when the two extant species are distantly related, conservation cannot safely be assumed and other possibilities need to be explicitly tested. A hypothesis of parallelism posits that the feature was different in the latest common ancestor, and that it changed independently in both lineages to the same final state. A hypothesis of convergence is the most complex of the four basic possibilities: it posits that the feature was different in the latest common ancestor, and that it arrived at a common state in the two extant species by different routes.

since the two species last shared a common ancestor (fig. 1B). This is a common conclusion, and one that is often uncritically applied. There are two other basic possibilities, however. Parallelism occurs when a feature changes in the same way independently in two lineages (fig. 1C). The most complicated of the basic cases is convergence. This requires an initial period of divergence, followed by a period when the feature becomes more and

more similar (fig. 1D). The essential feature of convergence is that similar endpoints are reached by different routes.

Distinguishing among conservation, parallelism, and convergence is a process of inference, not of direct observation, because we typically lack direct access to all but the terminal stages of evolutionary change. The obvious exception, mentioned earlier, is anatomy. Even for groups with a relatively good fossil record, however, distinguishing among conservation, parallelism, and convergence is far from straightforward [Sanderson and Hufford, 1996; Wake, 1999]. For features other than anatomy, identifying likely cases of convergence and ruling out other possible explanations for similarity is even more difficult [Wray, 1996; Abouheif, 1999; Bell, 2002; Eisthen, 2002]. Of course, ruling out convergence is equally difficult, as it requires demonstrating stronger support for an alternative interpretation.

The key to recovering biological history and interpreting it is a robust phylogenetic framework [Brooks and McLennan, 1991]. The reason we know that ichthyosaurs and cetaceans represent a spectacular case of convergence is that they are not close relatives within the tetrapod radiation. Conversely, the unobvious similarities that exist in the anatomy of hyraxes and elephants we interpret as conservation rather than convergence, because the two groups are very closely related. Although necessary, this reliance on phylogenetic relationship to recognize convergence introduces a bias: it is much easier to detect convergence when the species being compared are distantly related. Among closely related taxa, almost any similarity is routinely interpreted as conservation, but it would be surprising if some of these similarities did not turn out to be convergence.

Before moving on, a couple of additional points need to be emphasized. First, the basic categories of evolutionary pattern shown in figure 1 apply to any feature of an organism we might be interested in. Convergence is evident in protein sequences, development, physiology, anatomy, and, as mentioned elsewhere in this issue, in the structure and function of the nervous system [Wray, 1996; Messler and Stewart, 1997; Bell, 2002; Eisthen, 2002; Nishikawa, 2002; Zakon, 2002]. Second, the scenarios shown in figure 1 are the simplest possible, idealized cases. In real organisms, the features we are most interested in often have complex evolutionary histories made up of combinations of these processes [Brooks, 1996; Doyle, 1996; Abouheif, 1999; Bell, 2002]. And third, different features can have different evolutionary histories within the same group of organisms. An animal may con-

tain some features that are plesiomorphic (ancestral) and other features that are quite specialized. A platypus is 'primitive' for a mammal in that it lays eggs, but also possesses a sophisticated electrosensory system for detecting prey that is highly specialized.

Convergence in Development and Anatomy

In order to understand how and why a particular case of convergence has evolved, it is useful to examine the relationship between convergent phenotypes and the developmental processes that generate them. The convergent evolution of larval form in sea urchins and other marine invertebrates illustrates the kind of information one can draw from such a comparison when it is made across multiple taxa.

Sea urchins have a complex life history, with most species developing by means of a planktotrophic (feeding) larva that bears little resemblance to the adult it develops into (fig. 2). Much of the anatomy of planktotrophic larvae is geared towards grazing efficiently on single-celled algae, including a functional digestive tract and a skeleton that supports arms that increase feeding rates [Strathmann, 1971; Hart, 1991]. These features are widely distributed among the living groups of sea urchins and represent the ancestral state for the group [Strathmann, 1985; Wray, 1992]. Based on the phylogenetic distribution of traits and the fossil record, it is likely that a core set of anatomical features has been conserved for at least 250 million years, just before the major lineages of living sea urchins radiated [Wray, 1992].

Although widespread and ancient, the presence of planktotrophic larvae in the life cycle is not universal among sea urchins. About 20% of living species instead undergo an abbreviated mode of development [Emlet et al., 1987; Raff, 1987; Emlet, 1990]. In most cases, a larva is still present in the life cycle, but it is lecithotrophic (deriving nutrition from yolk). Phylogenetic evidence indicates that lecithotrophic larvae have evolved from planktotrophic larvae on at least a dozen separate occasions [Strathmann, 1985; Raff, 1987; Wray, 1996; Nielsen, 1998]. These independently evolved lecithotrophic larvae are anatomically convergent: their overall form is streamlined, a mouth and functional digestive system are absent, the skeleton is reduced or absent, and the ciliated band is repositioned or lost [Emlet, 1991; Wray and Bely, 1994]. The degree of anatomical convergence is so striking that phylogenetic analysis based on larval anatomy group lecithotrophic species into a well-supported 'clade', even

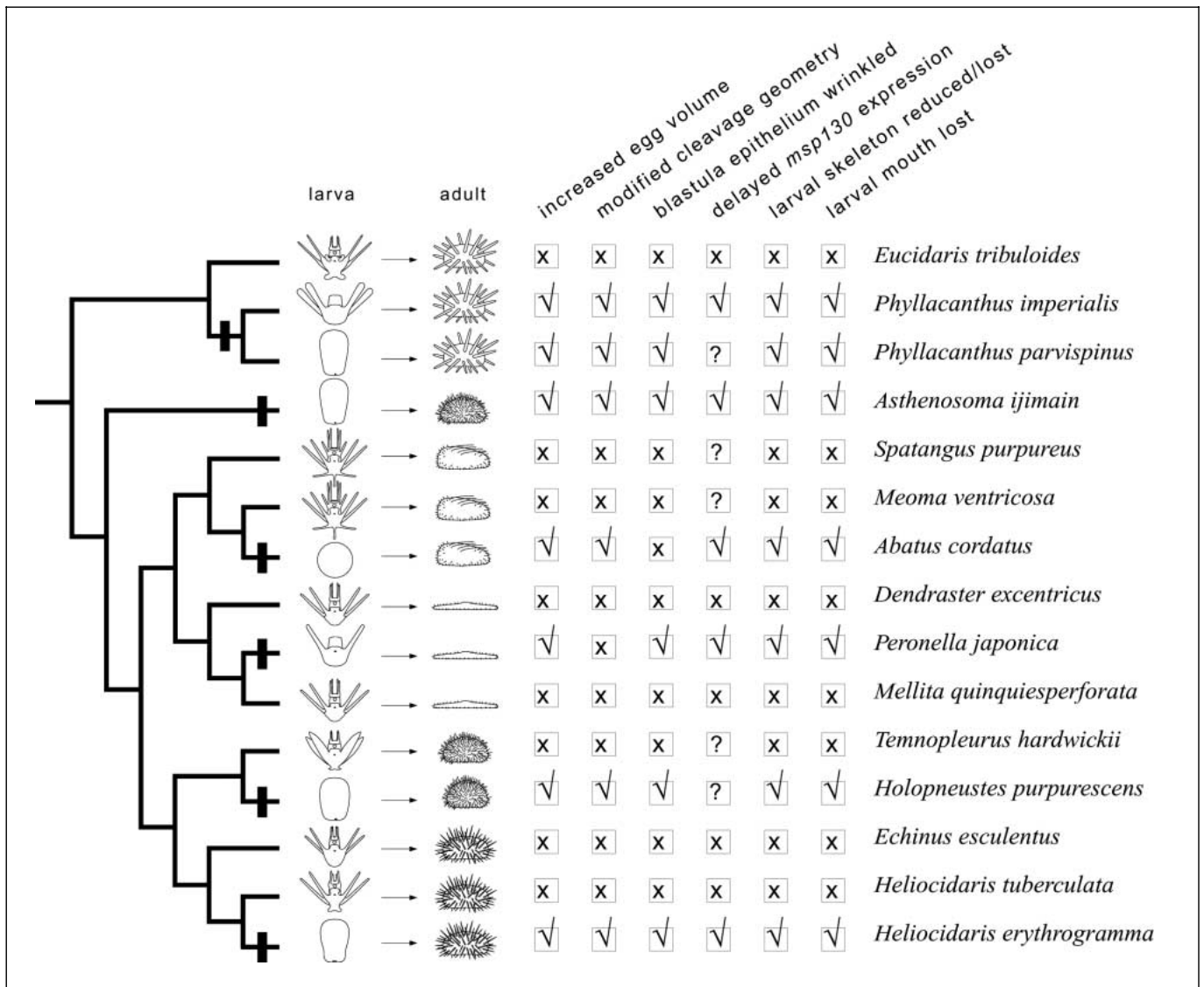


Fig. 2. Convergent evolution of embryonic development in echinoderms. The anatomy of sea urchin larvae shows significant discordance with phylogenetic history. The reconstructed ancestral state is a feeding larva with long arms and a complex internal skeleton [Strathmann, 1988; Wray, 1992]. Although these feeding larvae share many general traits, they have diverged in their detailed anatomy [Wray, 1992], as shown diagrammatically by the small cartoons. On several separate occasions, larval feeding has been lost (black bars on phylogeny) [Raff, 1987; Emlet et al., 1997]. In each case, larval anatomy is both extensively modified and convergently similar [Wray,

1996]. In each of these cases, underlying features of development have also changed in parallel or convergently: egg size [Emlet et al., 1987], egg composition [Byrne et al., 1999; Villinski et al., 2002], geometry of early cell divisions [Wray and Bely, 1994], and timing of gene expression [Wray and Bely, 1994]. Thus, the anatomy of non-feeding larvae in sea urchins provides a relatively well documented case of an association between convergent evolution in anatomy and convergent evolution in development. [Phylogeny from Smith et al., 1995.]

though both adult anatomy and sequence data support many independent origins [Wray, 1996].

Underlying anatomical convergences in lecithotrophic larvae are convergences in several developmental processes. The eggs of these species are invariably much larg-

er, as might be expected, given that the larvae rely on maternal provisions rather than feeding to sustain them until metamorphosis [Emlet et al., 1987; Raff, 1987]. The geometry of early cell divisions in the embryo are modified in almost all cases, with a shift from unequal veg-

etal-most fourth and fifth cleavages to equal cleavages throughout the early embryo [Wray and Bely, 1994]. That this change has evolved repeatedly is rather remarkable, as the micromere daughters of the unequal fourth cleavage operate as the 'organizer' region of the early embryo in species with planktotrophic larvae [Davidson, 2001]. Additional convergently similar changes in early development include a characteristic transient wrinkling of the epithelium during the blastula stage, higher cell numbers during gastrulation, earlier morphogenesis of the coeloms, and reduced time to metamorphosis [Wray and Bely, 1994; Wray, 1996].

Gene expression during oogenesis and in embryos is also convergently similar in species with lecithotrophic larvae. The eggs of lecithotrophs are maternally provisioned with proportionally less vitellogenin and proportionally more wax esters than those of planktotrophs [Byrne et al., 1999; Villinski et al., 2002]. Because wax esters provide a rich source of energy, it makes sense that they would be loaded into the eggs of lecithotrophic larvae, but why this particular compound has been repeatedly utilized and not some other energy-rich molecule is unclear. The parallel proportional reduction in vitellogenin content is also mysterious, as vitellogenin is yolk protein and might be expected to be loaded at higher concentrations in the eggs of lecithotrophs. The fact that vitellogenin is metabolized primarily after metamorphosis might mean that it is functionally tied to larval nutritional mode only indirectly. Zygotic expression of the gene *msp130* is also convergently similar in species with lecithotrophic larvae. This gene encodes a structural glycoprotein that is deposited in and around the biomineral matrix of the larval skeleton [Leaf et al., 1987]. In species with planktotrophic larvae, *msp130* is first expressed during the early phases of gastrulation, which is just before skeletogenesis begins [Wray and McClay, 1989]. Expression is delayed until after gastrulation in lecithotrophs, whose larval skeletons are either lacking or greatly reduced [Parks et al., 1988, 1989; Amemiya and Emler, 1992]. This has presumably freed them from the need to activate early zygotic *msp130* expression, and indeed the onset of expression is more commonly associated with the appearance of adult skeleton during metamorphosis in lecithotrophs [Wray and Bely, 1994].

Lecithotrophic larvae have also evolved from planktotrophic larvae in other groups of marine invertebrates. Examples include other echinoderm classes, enteropneust hemichordates, nemerteans, sipunculids, and polychaete annelids [Jägersten, 1972; Strathmann, 1985; Nielsen, 1998]. The planktotrophic larvae of these different phyla

and classes are anatomically distinctive, with characteristic features that reflect different mechanisms of feeding, locomotion, and defense [Emler, 1991; Nielsen, 1998]. The lecithotrophic larvae that have evolved in each of these clades do not resemble closely related planktotrophic larvae; instead, they are convergently similar to lecithotrophic larvae in other classes and phyla [Emler, 1991].

The reasons why lecithotrophic larvae look similar are probably tied to the parallel ecological situations that they experience [Emler, 1991; Wray, 1996]. Planktotrophic larvae are not competent to metamorphose initially, and must feed for days or weeks before they have put on enough weight to complete metamorphosis. Few individuals survive this planktonic phase of the life cycle, in which mortality rates are probably on the order of 10–20% per day [Morgan, 1995]. Thus, planktotrophic larvae experience strong selection for efficient feeding and resistance to predation [Havenhand, 1995]. Lecithotrophic larvae, in contrast, do not need to feed and are probably under strong selection to shorten this hazardous phase of the life cycle [Hart, 1996]. Structures that are primarily involved in feeding, such as larval skeletons and functional guts, are reduced or lost [Wray, 1996]. Ciliated bands, which are used for both feeding and propulsion in planktotrophs, are repositioned to body edges and perpendicular to the anteroposterior axis so as to maximize propulsion in lecithotrophs [Emler, 1991]. The result is typically a larva with an ovoid body shape, no mouth, and parallel ciliated bands. These phylogenetically unrelated but ecologically and anatomically similar larvae are called schmoos [Wray, 1996].

Whereas early development and gene expression are convergently similar in sea urchins with lecithotrophic larvae, this is not the case when comparisons are extended to more distantly related taxa. The reasons are probably tied to phylogenetic constraints. Although lecithotrophy has evolved independently in several different families and orders of sea urchins [Emler et al., 1987; Raff, 1987], these clades all share many similarities in embryonic and larval development; in contrast, comparisons across phyla involve cases where lecithotrophy evolved in species with far fewer similarities in mechanisms of early development [Strathmann, 1985; Nielsen, 1998]. Given parallel ecological conditions favoring similar changes in larval anatomy, the odds of producing a particular anatomical change in the same way are likely to be higher in more closely related species that share a greater proportion of their developmental mechanisms. Conversely, for species that share few features of development of planktotrophic lar-

vae, the evolution of lecithotrophy is more likely to involve different genetic and developmental bases; yet the similar ecological conditions will favor convergently similar overall phenotypes.

This extended example illustrates two general points about development and convergence. First, similar ecological conditions can produce remarkably convergent developmental modes. This should not be surprising, given the many remarkable cases of convergence in anatomy and physiology that have been documented. Few cases of convergence in development have been studied in detail, but they may not be as unusual as the small number of published examples would suggest. Second, convergence in development is probably inversely related to phylogenetic distance. In relatively closely related species, convergent anatomies may be produced by convergent developmental and molecular processes. In more distantly related species, the likelihood increases that different developmental and molecular mechanisms will contribute to a convergently similar anatomy. This is simply because the number of differences in developmental mechanisms will increase with phylogenetic distance. Thus, convergence at one level of biological organization (anatomy) is not always associated with convergence at another (development), but we can sometimes predict when they will and will not be associated.

Convergence in Developmental Gene Expression

A particularly interesting issue emerging from the field of 'evo-devo' is convergent evolution of gene expression and function during development [Abouheif et al., 1998; Tabin et al., 1999; Wray and Lowe, 2000]. How common is convergence in developmental regulatory gene expression? How similar do such cases appear? There is a widespread, although generally tacit, assumption that convergent gene expression is highly unlikely. This assumption is implicit, for example, when using comparisons of developmental gene expression to make inferences about the homology of structures [e.g., Finkelstein and Boncinelli, 1994; DeRobertis and Sasai, 1996; Holland and Holland, 1999; Lee and Jacobs, 1999]. Yet no serious attempt has been made to examine this issue directly; nor is there any obvious theoretical basis to support the assumption that convergence in gene expression should be rare. Indeed, several likely cases of convergence in regulatory gene expression have now been documented. The implications are quite interesting, both for the exercise of identifying homologous structures in distantly related organisms, and

for understanding how modifications in gene expression lead to the evolution of phenotype.

A few cases of convergently similar gene expression were discussed in the previous section. The delay in *msp130* expression that has accompanied the evolution of lecithotrophy in echinoids on several occasions is perhaps the clearest. Convergent changes in gene expression are also implied by what we know of egg composition in lecithotrophs. In particular, the switch to wax esters probably required convergent changes in the expression of the enzymes that produce these compounds. Nor should we expect such cases to be particularly rare. Natural populations may harbor considerable genetic variation for differences in the expression of genes encoding enzymes and other structural proteins [Segal et al., 1999; Rockman and Wray, in press]. If this is the case, then natural selection should be able to sort this variation in similar ways in similar environments, leading to convergent gene expression.

Regulatory genes are of even more interest, because changes in their expression and function are widely considered to be involved in the evolution of morphology [Wilson, 1975; Raff and Kaufman, 1983; Raff 1996; Carroll et al., 2001]. These are also the genes most commonly used to make inferences about homology of structures among distantly related animals [Abouheif et al., 1997; Holland and Holland, 1999]. The premiere example of regulatory genes are members of the *Hox* complex that encode homeodomain transcription factors. The *Hox* genes famously specify position along the anteroposterior axis in *Drosophila melanogaster*, *Tribolium castaneum*, *Mus musculus*, and *Caenorhabditis elegans*, the only species for which strong functional data exist [Gerhart and Kirschner, 1997; Carroll et al., 2001; Davidson, 2001; Wilkins, 2002]. These genes are expressed in nested domains along the anteroposterior axes of many more animals, and are generally assumed to play the same anteroposterior patterning role throughout at least the Bilateria [DeRobertis and Sasai, 1996; Carroll et al., 2001].

An equally remarkable point, but one that has received far less comment, is that the *Hox* complex is expressed in many non-homologous structures in different phyla. For example, in insects its first expression domain encompasses almost all cells within the early embryo, and later it is expressed in the gut; in mice it is first expressed within the hindbrain, and later within the somites, limb buds, and reproductive tract; and in sea urchins, it is expressed in the coeloms [reviewed in: Duboule, 1995; Carroll et al., 2001; Davidson, 2001]. Few of these sites of expression are homologous. Some expression domains encompass

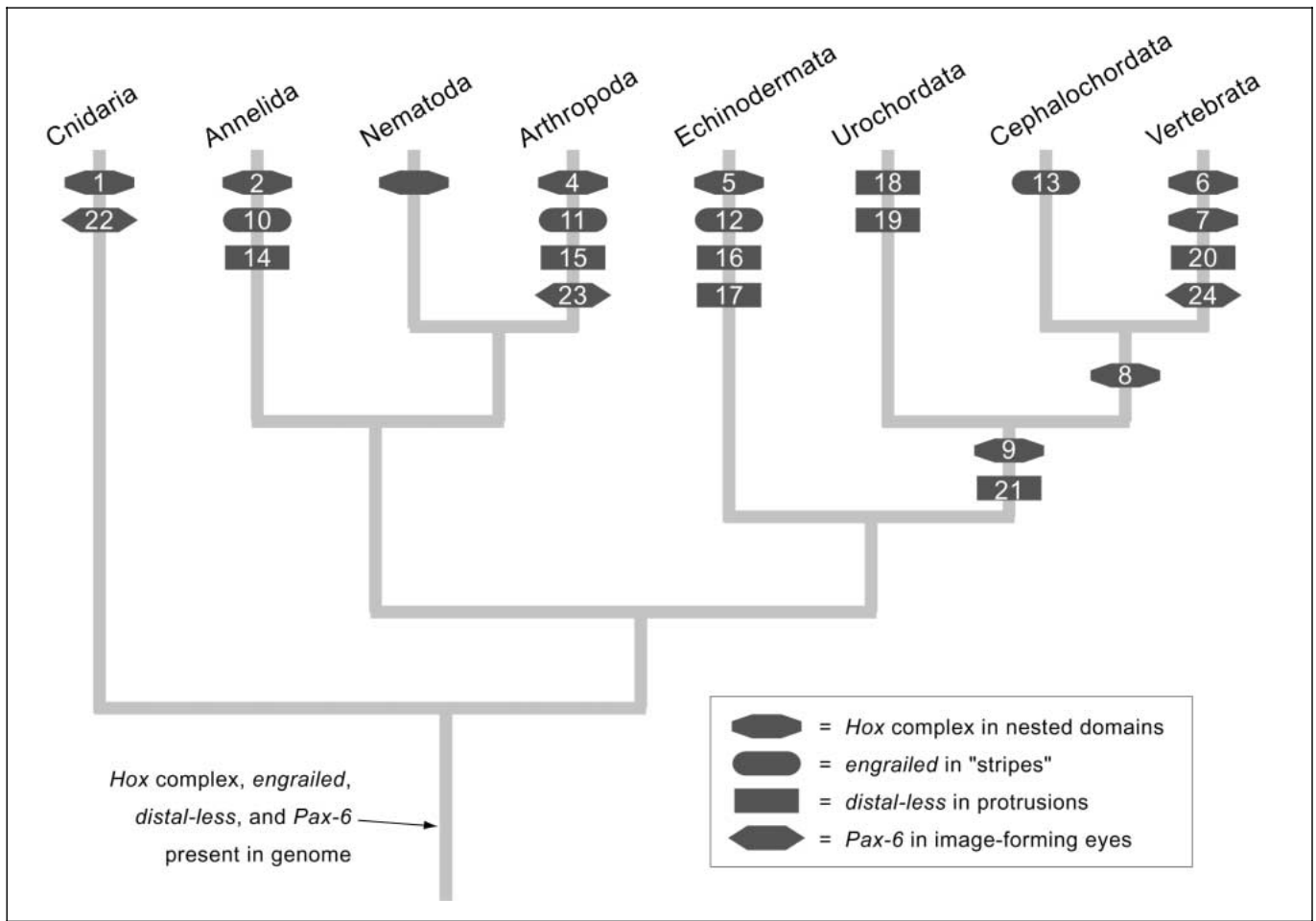


Fig. 3. Convergent evolution of regulatory gene expression domains. Similarities in gene expression are almost always interpreted as conserved, but it has become clear that some similarities in gene expression are more plausibly interpreted as cases of convergence. Some likely cases of convergence in the expression of four gene families are illustrated here for metazoans. *Hox* complex: 1 planula/polyp ectoderm, 2 central nervous system, 3 various scattered cells, 4 embryonic blastoderm, 5 larval coeloms, 6 fin/limb buds, 7 reproductive

tract, 8 hindbrain, 9 somites. *Engrailed*: 10 ectoderm in leeches (but not more basal polychaetes), 11 embryonic blastoderm, 12 ectoderm of adult arm in ophiuroids (but not other echinoderms), 13 somites. *Distal-less*: 14 ectoderm of parapodia, 15 gills/appendages, 16 podia (tube feet), 17 brachiolar arms of asteroid larvae (but not in other echinoderm larvae), 18 ampullae of larvae, 19 siphons of adults, 20 fin/limb buds, 21 gill bars. *Pax-6*: 22 rhopalia of medusae, 23 compound eyes, 24 eyes. See text for discussion and references.

almost all of the body and others only a small fraction of it, whereas various sites of expression are distributed across all three germ layers and a surprising variety of organs. Homology is particularly implausible among different expression domains within the same species (e.g., hindbrain and leg). The inevitable conclusion is that the expression of the *Hox* complex has evolved into new locations and times during development on several separate occasions (fig. 3) [Duboule and Wilkins, 1998; Wray and Lowe, 2000; Davidson, 2001; Wilkins, 2002].

Furthermore, many of these *Hox* redeployments are convergently similar. Although clearly independently

evolved, each of these cases exhibits colinearity, a striking and detailed similarity in gene expression. Colinearity means that the spatial order of each *Hox* paralogue's expression within the embryo corresponds to its location along the chromosome. This detailed similarity of expression is not surprising at one level. Transcriptional regulation within the *Hox* complex is thought to involve a molecular 'bucket brigade', such that the most 5' ('anterior') paralogue can activate the paralogue 3' to it, which in turn can activate the next paralogue, and so forth [Gerhart and Kirschner, 1997; Davidson, 2001]. Thus, any mutation that activates transcription of a *Hox* gene in a new

location might also indirectly activate all the genes 3' to it within the complex.

The *Hox* complex is a spectacular case of molecular convergence, but hardly the only example. The *engrailed* gene, which also encodes a homeodomain transcription factor, is required to establish segment boundaries in *Drosophila*. It is expressed in segmentally-repeated stripes along the anteroposterior axis. In at least three other phyla, engrailed is also expressed in 'stripes', although in one case these stripes are mesodermal rather than ectodermal (fig. 3) [Wedeen and Wiseblat, 1991; Holland et al., 1996; Lowe and Wray, 1997]. Here the similarities are probably superficial rather than indicative of homology among the structures where the gene is expressed, because other genes involved in insect segmentation do not show similar stripes of expression in these phyla. In addition, in all three cases besides arthropods, other species within the same phylum lack engrailed 'stripes'. Of course, any gene that is expressed in an iterative structure such as ganglia or somites will itself display an iterative expression domain, potentially leading to convergent similarity that is superficial rather than indicative of common ancestry. This is probably one of the most common ways in which superficially similar patterns of gene expression arise.

A more complicated situation involves the *distal-less* gene (*dll* in insects, *Dlx* elsewhere), which also encodes a homeodomain transcription factor, but is not part of a gene complex. It is required for correct limb outgrowth in *Drosophila* [reviewed in Tabin et al., 1999]. Remarkably, *distal-less* is also expressed in the developing limbs and fins of vertebrates, the podia of sea urchins, the siphons and ampullae of ascidians, and parapodia of annelids (fig. 3) [Lowe and Wray, 1997; Panganiban et al., 1997]. *Distal-less* is thus expressed in several appendages that are almost certainly not homologous. Yet the spatial and temporal similarities in gene expression are surprisingly close: in nearly all cases, the gene is only expressed in the most distal portion of the appendage and primarily during appendage outgrowth.

There are two basic interpretations of these data: either the appendages really are homologous or *distal-less* shows a tendency towards convergent expression in appendages [Tabin et al., 1999; Wray and Lowe, 2000]. The first hypothesis is not as parsimonious as it first appears, as it requires dozens of losses of limbs (early vertebrates clearly lacked limbs, as did early ecdysozoans) and an extraordinary anatomical diversification of the putative ancestral limb (there are virtually no anatomical similarities between echinoderm podia and arthropod legs, for example). On the other hand, the second hypothesis seems to

require a fantastic degree of coincidence. A possible solution is that *distal-less* is part of a regulatory pathway that, once activated by a key regulator, deploys itself in the same topological arrangement irrespective of where that activation takes place [Tabin et al., 1999; Wray and Lowe, 2000]. According to this view, the only difference from the *Hox* complex is that we don't know what the other members of the coordinately-deployed pathway are.

A final example involves *Pax-6/eyeless*, which encodes a paired-box transcription factor. This gene is famously expressed in the eyes of insects, vertebrates, mollusks, and nemerteans [Quiring et al., 1994; reviewed by Gehring and Ikeo, 1999]. Eyes, at least as image-forming organs, are clearly not homologous on anatomical grounds among these phyla; yet in the case of both insects and vertebrates, *Pax-6* is required for eye development. Once again, the similarities in gene expression are interpreted as convergently similar (fig. 3). The probable cause in this case is that these eyes, despite their disparate anatomical designs, all function using homologous photoreceptor cells. In other words, a component cell type is homologous, but the organs within which it is housed in different phyla are not. The situation is more complicated than this, however, because *Pax-6* does more than just specify the photoreceptor cell type, at least in *Drosophila* and *Mus*. In these animals it clearly plays a more fundamental role in regulating other aspects of eye development. Another complication is that *Pax-6* is expressed in many places other than eyes [Quiring et al., 1994; Wilkins, 2002]. Several specific hypotheses have been proposed to explain how the association with eyes could have evolved from an initial role in photoreceptor cell fate specification [Gehring and Ikeo, 1999; Davidson, 2001; Wilkins, 2002]. These hypotheses differ in detail, but they all present scenarios in which *Pax-6* has taken on additional roles in eye development from a starting point restricted to photoreceptor cell specification.

To summarize, several cases are known where the expression domains of key developmental regulatory proteins are convergently similar. Some cases of convergent similarity are probably the result of similar ecological circumstances. The structural genes discussed near the beginning of this section provide likely examples. However, many other cases of convergent similarity involve homologous genes that are expressed in a similar manner in structures that are almost certainly not homologous. Such cases are probably not particularly rare. The examples discussed above are among the most thoroughly studied, but by no means the only examples that could be cited. Superficial similarity in gene expression can probably arise in

several ways: linked transcriptional regulation (genes of the *Hox* complex and *distal-less*), expression in meristic structure (*engrailed*), and expression within a homologous cell type that is later incorporated in non-homologous organs (*Pax-6*). This is probably not an exhaustive list of the possible causes of convergently similar gene expression.

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Subject Index Vol. 59, No. 5–6, 2002

- | | | |
|--------------------------------|------------------------------|--------------------------|
| Adaptation 273 | Gap junctions 250 | Phylogeny 240 |
| Animal behavior 240 | Glomerulus 273 | Prey capture 240 |
| Birds 294 | Glutamate receptors 250 | Primates 262 |
| Cerebellum 312 | Homology 312, 327 | Pufferfish (Fugu) 250 |
| Cerebellum-like structures 312 | <i>Hox</i> complex 327 | Sensory transduction 273 |
| Cerebral cortex 262 | K ⁺ channels 250 | Sound localization 240 |
| Constraint 273 | Larva 327 | Squirrels 262 |
| Convergence 250, 273, 312, 327 | Mammals 294 | Superior colliculus 262 |
| Cortex 262 | Molecular evolution 250 | Syngeny 312 |
| Electric communication 240 | Na ⁺ channels 250 | Thalamus 262 |
| – fish 240 | Neuroethology 240 | Time coding 294 |
| Evolution 262, 294, 312 | Odorant binding protein 273 | Tree shrews 262 |
| – of development 327 | Ontogeny 294 | Visual system 262 |
| Frogs 240 | Opsins 250 | |
| G Protein-coupled receptor 273 | Owls 240 | |

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