Orgel was the first to admit that the idea of directed panspermia lacked any empirical evidence, and he certainly believed that the emergence of life on earth was more likely, but he thought that the idea should be entertained by origin-of-life researchers, at least on sleepless nights. This bold speculation was one indication among many of Orgel's honest assessment of the enormous difficulties faced by the origin-of-life field. He conceded on many occasions that our understanding of the problem is still greatly lacking. At the same time he was convinced that only persistent research could reveal the detailed path from a lifeless planet to the first organized living systems.

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—*I.F.*

Origin of vertebrates

The origin of vertebrates, more than of any other animal group, has been the subject of vigorous historical debate, and this continues to be the case. However, a renaissance in integrative organismic biology has reinvigorated debate, sparked by fundamental new insights into the origin of vertebrate characteristics from within the field of developmental genetics. In turn, this has stimulated anatomists and paleontologists to test the hypotheses that have emerged from within this field. Much of this work has revealed how cherished assumptions are unfounded and has provided new perspectives on the origin of the major animal group to which we ourselves belong.

The starting point of the modern perspective on the origin of vertebrates is the new-head hypothesis. In essence it observes that although the differences between vertebrates and their nearest invertebrate relatives are vast, virtually all these characters owe their origin to just a few embryological novelties and are mainly associated with the head. In the main, these are the neural crest and neurogenic placodes (specialized regions of embryonic ectoderm), both of which form specialized sensory organs, while neural crest cells also differentiate into skeletal, connective, and muscle tissue. The hypothesis was also framed within an evolutionary scenario, drawing upon evidence from comparative anatomy, developmental biology, and paleontology and arguing that the establishment of the vertebrate body plan was associated with a trend of increasingly active food acquisition, from passive filter feeding to predation. The new-head hypothesis has proved extremely influential, to the extent that most of the research during the ensuing decades has been aimed at testing its assumptions and postulates in fields as diverse as molecular developmental genetics, molecular phylogenetics, comparative anatomy, and paleontology.

MOLECULAR DEVELOPMENTAL GENETICS

Molecular developmental genetics is concerned with the role of gene expression and gene interaction in relation to embryology. It did not even exist as a coherent discipline when the new-head hypothesis was formulated, but it is from within developmental genetics that the greatest challenges to the hypothesis have emerged.

First, the hypothesis that vertebrates possessed a literal new head, that essentially they are invertebrates with a head added to the front, was tested. This was achieved by examining in lancelets (presumed the closest invertebrate relative of the vertebrates) the patterns of expression of genes in the head of vertebrates. These genes, known as *Hox* genes, are found in all animals and are expressed very early in development, directing and regulating the expression of other genes. Thus they have a fundamental role in organizing the early embryo, especially its head-tail axis. Although they are present in all animals, vertebrates have the most *Hox* genes of all, and some are expressed within the head-tail axis of the embryo only at the level of the hindbrain. The results of the experiments revealed that a portion of the front end of the lancelet body is equivalent to the vertebrate hindbrain, and thus the new head, though a vertebrate novelty, was a development of an invertebrate chassis rather than a wholly new domain.

The discoveries in this new field are too many to recount here, but before moving on we must make mention of the discovery of a possible nascent neural crest and epidermal placodes in the tunicates, invertebrate chordate relatives of the vertebrates. Although many invertebrate groups possess migratory cell populations, those of tunicates exhibit the same patterns of gene expression and some of the fates of neural crest cells. Tunicates also possess rudimentary sense organs that develop from ectodermal thickenings, like neurogenic placodes, and exhibit a common suite of genes during their development. Thus although the repertoire of embryological derivatives is far smaller, it appears that tunicates possess neural crest cells and epidermal placodes in all but name. The question remains, however, why tunicates should possess these fundamental embryological novelties when lancelets, closer relatives of vertebrates, do not.

COMPARATIVE GENOMICS

Comparisons of vertebrates and invertebrates at the anatomical and embryological levels clearly mark out vertebrates as in some essence more complex than their spineless relatives. This theme has now been extended to the level of the genome, the library of an organism's genetic constitution. It was discovered that vertebrates possess a greater number of *Hox* genes than any other animal, but that quality is not particularly significant because the precise number varies within invertebrates. *Hox* genes are sometimes organized in a cluster, meaning that they are located within the same physical domain on a chromosome, and all animals possess just a single *Hox* cluster except vertebrates, which possess at least two *Hox* clusters, each equivalent to the one found in invertebrates. This simple feature might suggest only that the origin of vertebrates coincided with a duplication of the *Hox* cluster—no mean observation given the fundamental role played by *Hox* genes during embryology. However, further comparative surveys of vertebrate and invertebrate genomes have revealed that the same phenomenon is encountered in countless other genes and gene families. This has led to the conclusion that the origin of vertebrates coincided either with wholesale gene duplication, possibly at the chromosome level, or the prevailing hypothesis, that the entire genome was duplicated. Under either scenario this would have provided a vast number of novel functionally redundant genes that were available for co-option to new functions, possibly explaining the origin of vertebrates. In fact, it has been argued since the early 1970s that only genome-scale gene duplication could provide for so many fundamental novelties evolving in concert, such as at the origin of vertebrates and the origin of jawed vertebrates. We now know that similar events or episodes have punctuated vertebrate evolution, since genome duplication is also implicated in the origin of jawed vertebrates and the origin of teleost fishes—events in which vertebrate anatomy has been adapted at a scale comparable with that of the origin of vertebrates, at least on the evidence of living vertebrates.

PALEONTOLOGY

The excitement created by developmental genetics has led directly to renewed interest in other disciplines, both in testing new hypotheses on the origin of vertebrates and in exploring their implications. This has been especially true of paleontology, where attempts have been made to chase the origin of vertebrates and vertebrate-specific characters ever deeper into geological history. This has been achieved on a number of fronts, for example, the reassignment of long-known but problematic fossil groups, such as the conodonts, as well as new discoveries resulting from systematic and serendipitous searching of the rock record. There is now compelling evidence for vertebrates extending to the Lower Cambrian (520 million years ago) on the basis of a well-preserved soft-bodied vertebrate, *Myllokunmingia,* from the Chengjiang fossil deposit of South China. Skeletonizing vertebrates were present by the Late Cambrian (501 million years ago) at the very latest, as evidenced by the presence of conodonts. What is more, all these early fossils are from rocks deposited under marine conditions, providing compelling evidence for the marine origin of vertebrates.

Paleontology provides not only a timescale for vertebrate origin but also insight into the sequence in which vertebrate-specific characters were acquired, constraining whether or not vertebrate characters evolved in concert or in a staggered fashion over a protracted episode. Unfortunately, there are precious few remains of unequivocal primitive vertebrates in the fossil record, an artifact of their lack of mineralized tissues. Nevertheless, the fossil record of vertebrates more advanced than the most primitive living vertebrates is sufficient to reveal that many characters generally deemed vertebrate specific were actually acquired much later, among now-extinct lineages intermediate between the living lampreys and living jawed vertebrates. In fact, our knowledge of these extinct intermediates is sufficient to exclude the possibility of a major anatomical event to coincide with the genome duplication that can be inferred to have occurred.

Knowledge of the evolutionary relationships of both fossil and living primitive vertebrates has also provided a test of the new-head scenario that food acquisition drove early vertebrate evolution. Undoubtedly the living groups lancelets (filter-feeding invertebrates), lampreys (parasitic jawless vertebrates), and jawed vertebrates (primitively predators) bear this out, but rigorous functional analyses of extinct jawless vertebrates have demonstrated that this progressive pattern is a gross oversimplification of actual events. Some extinct jawless vertebrate groups like the conodonts were undoubtedly sophisticated feeders (scavengers/predators), but most other groups appear to have been deposit feeders, making their living by slurping mud.

Although the fossil record of the most primitive vertebrates has been downplayed here, there has been no shortage of potential candidates identified, including additional fossils from the Lower Cambrian Chengjiang deposit *(Haikouella, Yunnanozoon)* and the Middle Cambrian Burgess Shale *(Pikaia, Nektocaris)*. Note should also be made of the spectrum of bizarre echinoderm-like organisms referred to as the calcichordates, carpoids, or stylophorans. The interpretation of these remains has long been extremely controversial, but some specialists have perceived that among these organisms lie almost every possible kind of intermediate between the deuterostome phyla and the chordate subphyla: tunicates, lancelets, and vertebrates. Changed understanding in interpretation of the interrelationships of the deuterostome phyla (echinoderms, hemichordates, chordates) has, however, shown many of the most important characters to be primitive features of deuterostomes, not derived characteristics of tunicates, lancelets, and vertebrates.

MOLECULAR PHYLOGENETICS

Traditional perceptions of the interrelationships of the deuterostome phyla recognize hemichordates as the closest relatives of the chordates. However, phylogenetic analysis of molecular data has demonstrated that echinoderms and hemichordates are each others' closest relatives, constituting the group Ambulacraria, to the exclusion of chordates.

Historically the relationships of the chordate subphyla have fluctuated, and either tunicates or lancelets have been considered the closest relatives of vertebrates. The modern view is that lancelets are more closely allied to the vertebrates, but this has begun to be questioned with the discovery that tunicates appear to possess evolutionary equivalents of the neurogenic placodes of vertebrates, as well as cells with migratory properties and even some of the fates seen in neural crest cells.

Have these characteristics evolved in parallel among vertebrates and tunicates, or were they lost in amphioxus? This has been partly resolved by analyses of large molecular data sets that have unequivocally identified tunicates as the closest living relatives of vertebrates. More germane are the implications of these discoveries for the view that the origins of the neural crest and neurogenic placodes were the key innovations that underpinned vertebrate evolution. Clearly they were present and had evolved some of their embryological fates among invertebrate chordates well before the origin of vertebrates. Nevertheless, the divergence of vertebrates clearly coincides with an unfolding explosion in the embryological potential of the neural crest and neurogenic placodes.

CONCLUSIONS

Our understanding of the origin of vertebrates has been reinvigorated in recent years, largely as a result of a more holistic approach to understanding the developmental and evolutionary establishment of the major animal body plans. Together these data provide for a more protracted episode of embryological evolution underpinning the vertebrate origin of vertebrates rather than an explosive radiation resulting from one or two key innovations. Many of the features deemed characteristically vertebrate are now recognized to have a prehistory among invertebrates, including the neural crest and neurogenic placodes. Thus in many of its details the new-head hypothesis was wrong, but these are just details. Despite discoveries of events of genome duplication, discoveries of fossil vertebrates tens of millions of years older than the oldest previously known, and a fundamental overhaul in our understanding of the invertebrate relatives of the vertebrates, our perceptions on the origin of vertebrates remain rooted in the neural crest, neurogenic placodes, and the development of a new head.

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