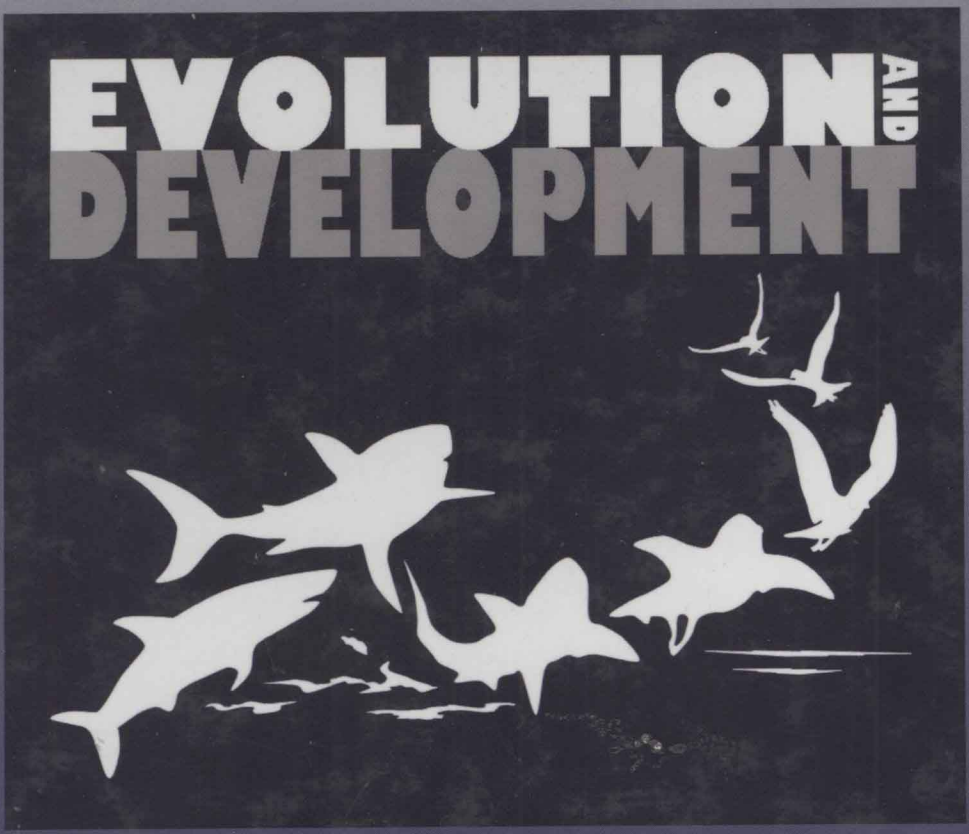
EVOLUTION AND DEVELOPMENT



Edited by

William R. Jeffery

VOLUME EIGHTY SIX

CURRENT TOPICS IN DEVELOPMENTAL BIOLOGY

Evolution and Development

Edited by

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Academic Press is an imprint of Elsevier

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525 B Street, Suite 1900, San Diego, CA 92101-4495, USA
30 Corporate Drive, Suite 400, Burlington, MA 01803, USA
32, Jamestown Road, London NW1 7BY, UK
Linacre House, Jordan Hill, Oxford OX2 8DP, UK

First edition 2009

ISBN: 978-0-12-374455-5
ISSN: 0070-2153

Printed and bound in USA
09 10 11 9 8 7 6 5 4 3 2 1

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PREFACE

This is the 86th volume of *Current Topics in Developmental Biology* (CTDB). Considering that this series began in 1968, one could ask why it has taken so long for a thematic CTDB volume to appear on Evo Devo? An answer might be that Evo Devo is at once an old and a newly emerging discipline. Under the alias of evolutionary morphology or embryology, it was a popular scientific study in the 1800s, predating the surfacing of neo-Darwinism in the next century. As a new breed of experimental embryologists, and ultimately molecular embryologists, rushed to determine the secrets of development, the evolutionary perspective was temporarily left by the wayside. In retrospect, this was probably the right course: one should know the rules of development in some detail before attempting to find out how they are fashioned during evolution.

Beginning in the 1970s, there was a rebirth of interest in Evo Devo, sparked in large measure by the publication of two books: "Ontogeny and Phylogeny" by Stephen Jay Gould (1970) and "Embryos, Genes, and Evolution" by Rudolf Raff and Thomas Kaufman (1983). The latter volume, in particular, described evolution within the backdrop of new genetic and molecular discoveries showing that the rules and basic molecular tool kits used in development are fundamentally similar in all animals and plants. This launched the first phase of Evo Devo, which was devoted to understanding this deep conservation of developmental mechanisms. Although important, conservation is not the key issue in understanding the role of ontogeny in evolution. Instead, we must strive to understand the more complex issue of diversity, that is when, how, and how frequently different ontogenies arise during evolution. This activity defines the second phase of Evo Devo and is what this CTDB volume is about.

A large part of Evo Devo's second phase is understanding when and how major phenotypes evolved, and the emergence of novel biological entities during crucial evolutionary transitions, such as the transition from invertebrates to vertebrates. Two articles in the current volume are centered on this theme. Nikita, Sauka-Spengler, and Bronner-Fraser (Caltech) trace the fascinating evolution of the neural crest to the most basal vertebrates and perhaps even to invertebrate chordates. Zhang, Eames, and Cohn (University of Florida) take a similar approach to understanding the evolution and relatedness of cartilage, and its role in establishing a skeletal renaissance during vertebrate evolution. Another important part of contemporary Evo Devo depends on the comparative approach. Here emerging model systems

consisting of two or more species are used to investigate complex problems, such as the diversity of body plans, the evolution of sexual reproduction, and the loss and gain of phenotypes in extreme environments. Raff and Smith (Indiana University) describe their pioneering studies on direct and indirect developing sea urchins in which the first molecular discoveries are presented for the rapid evolution of axial development. Likewise, Moczek (Indiana University) describes the evolution of horn diversity in horned beetles, a system that has immense potential for improving our understanding of microevolutionary mechanisms, and especially the role of developmental tradeoffs. When emerging models are coupled with pre-existing models—their "rich cousins" with respect to detailed developmental knowledge and molecular genetic tools—powerful new insights can be forthcoming. Thus, Kramer (Harvard University) describes a host of new land plant models linked in this way to *Arabidopsis*, Haag (University of Maryland) shows how divergence in evolution of sex determination can be studied by comparing *Caenorhabditis briggsae* to *C. elegans*, and Jeffery (University of Maryland) charts the importance of pleiotropy using the blind cavefish *Astyanax mexicanus* and zebrafish as companion species. Another important part of Evo Devo is obtaining a more complete understanding of the development of classic systems that are ripe for in depth evolutionary analysis. One of these systems, the polar lobe forming and spirally cleaving gastropod *Illyanassa*, is described here by Lambert (University of Rochester), who shows the importance of localized mRNAs and spatial signaling cues in determining this novel type of development.

The CTDB volume does not cover every contemporary issue in Evo Devo. Indeed, many important topics are not addressed. In this sampling, however, we merely hope to provide examples of how modern cutting-edge approaches are being used to investigate and generate new understanding of some central issues this field. By doing so, we endeavor to encourage, and perhaps even inaugurate, the next major phase in Evo Devo.

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Contents

CHAPTER ONE

GENE REGULATORY NETWORKS IN NEURAL CREST DEVELOPMENT AND EVOLUTION

Natalya Nikitina, Tatjana Sauka-Spengler,
and Marianne Bronner-Fraser

Contents

Abstract

The neural crest is a multipotent migratory embryonic cell population that is present in all vertebrates, but missing from basal chordates. In this chapter, we discuss recent work in amphioxus, ascidians, lamprey, and gnathostomes that reflects the current state of knowledge of the evolutionary origin of this fascinating cell population. We summarize recent evidence for the ongoing diversification of the neural crest in several vertebrate species, with particular reference to studies in nontraditional vertebrate model organisms.

1. GENE REGULATORY NETWORK UNDERLIES NEURAL CREST DEVELOPMENT

The neural crest, an embryonic population of migratory and multipotent precursor cells, is traditionally considered a vertebrate innovation. In fact, acquisition of the neural crest and neurogenic placodes is considered to be one of the key events in vertebrate evolution, leading to the appearance of the jaws, cranium, and sensory ganglia, which enabled the transition of

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Current Topics in Developmental Biology, Volume 86
ISSN 0070-2153, DOI: 10.1016/S0070-2153(09)01001-1

early vertebrates from filter feeding to active predation (Gans and Northcutt, 1983; Northcutt and Gans, 1983).

In all vertebrates examined to date, neural crest cells share some common features. These cells arise at the border between neural and non-neural ectoderm. They subsequently undergo an epithelial-to-mesenchymal transition (EMT) to detach from the neural folds or dorsal neural tube, a process that involves alterations in cell shape as well as acquisition of cell surface adhesion molecules and signaling receptors. The latter contribute to the neural crest cells' ability to migrate to diverse sites where they differentiate to form numerous different cell types. Neural crest derivatives include neurons and glia of the peripheral nervous system, bone and cartilage of the facial skeleton, as well as melanocytes and neuroendocrine cells. Interestingly, the neural crest is the only multipotent vertebrate cell type capable of giving rise to many cell types that populate different tissues and organs.

To study neural crest evolution, it is necessary to distinguish between a bona fide neural crest cell and other cell types that might superficially resemble it. Due to the lack of intermediate forms, it is not clear if all neural crest traits were acquired in a single step during the transition from nonvertebrate to vertebrate chordates or if there might have been stepwise acquisition of these properties (Donoghue *et al.*, 2008). For the purpose of this chapter, we define "neural crest" as having the entire repertoire of migratory and differentiative properties and refer to cells with subsets of these properties as "preprototypic crest." In this way, we distinguish between a migrating cell that gives rise to a single derivative that in vertebrates arises from the neural crest (e.g., pigment lineage), from a multipotent precursor that forms multiple neural crest derivatives and has both regulative and regenerative potential.

One convenient way to define the neural crest is via its regulatory state; that is, the network of the signaling molecules and transcription factors that are responsible for its induction, delamination from the neural tube, migration, and differentiation (Sauka-Spengler and Bronner-Fraser, 2006). Such a neural crest gene regulatory network (NC-GRN) confers onto this cell type the classical neural crest characteristics and provides a mechanistic explanation of how these characteristics arise in a developmental context. A framework of basic modules has been proposed to comprise this network (reviewed in Meulemans and Bronner-Fraser, 2004; Nikitina and Bronner-Fraser, 2008; Sauka-Spengler and Bronner-Fraser, 2006, 2008) and provides a solid foundation upon which questions pertaining to the evolution of the neural crest can be addressed.

These regulatory interactions can be divided hypothetically into phases. The first involves *inductive signals* that establish the neural plate border, by upregulation of transcription factors that specify the neural plate border region. These *neural plate border specifiers* in turn regulate *neural crest specifier genes* that activate or repress specific downstream targets that render the neural crest migratory and multipotent.

According to the NC-GRN, the formation of the neural crest is initiated by a set of diffusible signaling molecules (Bmp, Wnt, FGF, and Notch) that originate from either the ventral ectoderm or the paraxial mesoderm, and initiate the neural crest transcription program in a strip of cells between the neural plate and the non-neural ectoderm, the neural plate border. The early set of transcription factors, turned on in the prospective neural plate border by the combined activity of the above signaling pathways, are collectively called the neural plate border specifiers and include Pax3, Pax7, Msx1, Zic1, and AP-2 (Meulemans and Bronner-Fraser, 2004; Nikitina *et al.*, 2008). These transcription factors activate another set of genes that are expressed specifically in the prospective neural crest and play important roles in the establishment and maintenance of crucial defining characteristics of the neural crest. These neural crest specifiers include Sox8, Sox9, Sox 10, c-Myc, and Id (important for the survival of the neural crest precursors and maintenance of the pluripotency of the neural crest); Snail1 and Snail2 (play a crucial role in the epithelial–mesenchymal transformation, as well as cell cycle control and the migratory activity of the neural crest cells); and Twist (required for the correct localization of the migrating neural crest cells) (Batlle *et al.*, 2000; Bellmeyer *et al.*, 2003; Cano *et al.*, 2000; Honore *et al.*, 2003; Kim *et al.*, 2003; Soo *et al.*, 2002; Taneyhill *et al.*, 2007; Teng *et al.*, 2008). The neural crest specifiers activate transcription of several possibly interconnected modules that are responsible for the differentiation of the neural crest population into individual derivatives. Simultaneously, they turn on expression of receptors that direct migration of the differentiating neural crest cells to the appropriate destinations in the embryo. Genes belonging to the two latter categories (the neural crest effector genes) include signaling molecules, transcription factors (Mitf, trp2), molecules involved in the cell shape changes essential for the delamination and migration (Rho GTPases and cadherins) as well as cell-type-specific differentiation genes characteristic of neural crest derivatives (collagen) (reviewed in Meulemans and Bronner-Fraser, 2004; Sauka-Spengler and Bronner-Fraser, 2008).

The definition of the neural crest via this NC-GRN has limits, largely due to the fact that the network is not yet complete. Not every single gene involved in the neural crest development has as yet been identified, or can be placed accurately within the network (e.g., Meis, Blimp-1), and the exact architecture and interconnections therein are still in the process of being discovered. However, identification and testing of the core elements of the network allows its application to diverse vertebrates regardless of whether all of the elements and connections are established. This is particularly useful when applied to the formation of vertebrate-specific traits. For this purpose, an in-depth study of network components needs to be conducted exhaustively in a single vertebrate that allows precise spatial and temporal discrimination. The basal lamprey embryo has been extremely

useful due to the large size, slow development, and ease of manipulations of the early embryo. Due to its basal position as an agnathan representative and its close morphological resemblance to 350-million-year-old fossils, the modern lamprey NC-GRN may provide a reasonable approximation of the ancestral vertebrate state.

2. The Evolutionary Origin of the Neural Crest

A hallmark of the vertebrate neural crest is its remarkable plasticity and ability to form many and diverse derivatives. Neural crest cells have stem cell properties, multipotency, and the ability to self-renew, at least for a limited time in their developmental history. The derivatives of a single cell are as diverse as neurons, cranial cartilage, pigment, and glial cells. This incredible versatility gives the neural crest its characteristic traits that classify it as a vertebrate novelty. Its multipotency and migratory ability render this cell type a crucial invention that contributed to the evolutionary success and diversification amongst vertebrates.

All vertebrate species, even the most basal jawless members of this group such as lampreys and hagfishes, have neural crest that is virtually indistinguishable from the neural crest of higher vertebrates in terms of multipotency, migratory behavior, and the gene regulatory network involved in its development. In fact, divergences from the basal NC-GRN appear to occur only at later stages and more distal levels of the network. These steps contribute to formation of derivative structures such as jaw or sympathetic ganglion chain. Although lamprey lack jaws and sympathetic ganglia, they do possess neural crest-derived cranial cartilage and have ganglia-like clusters of neurons scattered along the cardinal veins running in the abdominal cavity (Johnels, 1956), as well as autonomic control of the vasculature by catecholamine-containing nerve fibers, resembling sympathetic/adrenergic control in higher vertebrates. Whether these represent precursors of the homologous structures, or are simply functionally analogous structures has yet to be determined (Horigome *et al.*, 1999; McCauley and Bronner-Fraser, 2003, 2006; Ota *et al.*, 2007; Sauka-Spengler *et al.*, 2007). The evolutionary origins of the neural crest have therefore been sought among our closest chordate relatives, amphioxus and the ascidians.

The phylogenetic relationships of different chordate groups have undergone drastic reassessment in the past few years, largely due to the availability of sequenced genomes. For over a hundred years, amphioxus with its very vertebrate-like body organization was considered a sister group to vertebrates, while mostly sessile urochordates were thought of as a more distantly related side group (Wada, 2001). Early phylogenetic analyses of 18S ribosomal RNA sequences in a limited number of species confirmed amphioxus

as the closest vertebrate relative (Turbeville *et al.*, 1994; Wada and Satoh, 1994), while analysis of the complete small and large ribosomal subunit DNA provided ambiguous conclusions (Winchell *et al.*, 2002). A different story began to emerge after a large data set of nuclear genes from a range of deuterostome species was examined, and the long-branch attraction artifact that results in the fast-evolving ascidian species being attracted toward the echinoderm/hemichordate outgroup was taken into account (Blair and Hedges, 2005; Breau *et al.*, 2008; Delsuc *et al.*, 2006). The new view of the chordate phylogeny that emerged demonstrated that ascidians and not cephalochordates are the true sister group of vertebrates. This conclusion received further independent support from the genome-wide analysis of the intron–exon structures in amphioxus and several vertebrate and ascidian species (Putnam *et al.*, 2008).

Consistent with the latest understanding of chordate phylogeny is the fact that amphioxus does not have anything resembling the neural crest (Holland and Holland, 2001), while migratory preprototypic neural crest cells have been discovered in several ascidian species (Jeffery, 2006; Jeffery *et al.*, 2004). Based on the experimental data currently available, two opinions as to the time of the neural crest origin have emerged in the recent years (Fig. 1.1). According to one hypothesis, the neural crest first appeared in the common ancestor of the ascidians and vertebrates, after the separation of the ancestral cephalochordate lineage (Donoghue *et al.*, 2008). Proponents of this view consider the migratory preprototypic neural crest-like cells (NCLCs) found in some of the modern ascidian species as true neural crest cells. Alternatively, these cells may represent an evolutionary experiment or an intermediate step,

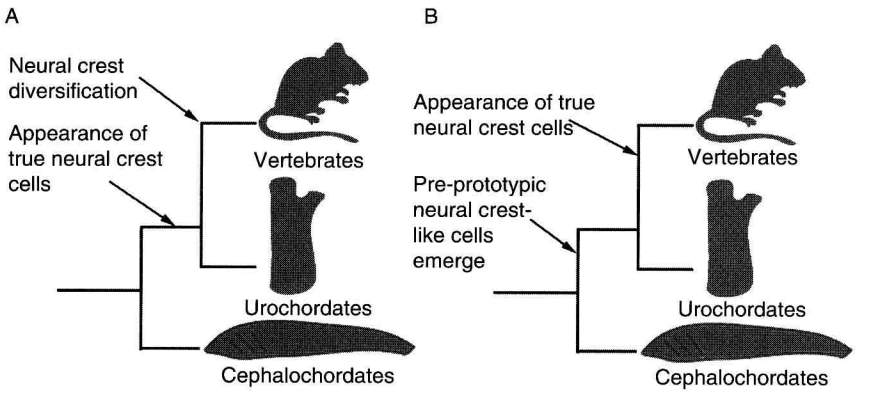

Figure 1.1 Current hypotheses of the time of neural crest origin. According to the first one (A), the neural crest first appeared in the common ancestor of the ascidians and vertebrates, and underwent diversification to form a wider range of derivatives in the vertebrate lineage. Alternatively, the true neural crest may have originated at the base of the vertebrate lineage, after the urochordate–vertebrate split (B).