

Preface

Knowledge of the development and evolution of the neural crest sheds light on many of the oldest questions in developmental and evolutionary biology. What is the role of germ layers in early embryogenesis? How does the nervous system develop? How does the vertebrate head arise developmentally, and how did it arise evolutionarily? How did the vertebrate dorsal nervous system, heart, skeleton, teeth (and the neural crest itself) originate? How do growth factors and *Hox* genes direct cell differentiation and embryonic patterning? What goes wrong if development is misdirected by mutations, or if embryos are exposed to exogenous agents such as drugs, alcohol, or excess vitamin A (retinoic acid)?

Twenty years ago, I was instrumental in organizing the publication of a facsimile reprint of the classic monograph by Sven Hörstadius, *The Neural Crest: Its properties and derivatives in the light of experimental research*, originally published in 1950. Included with the reprint was an analysis of subsequent studies on the neural crest and its derivatives. A decade later, the first edition of this book was published (Hall, 1999a). The explosion of interest in and knowledge of the neural crest over the past decade prompted me to write this second edition.

As in my 1988 overview of the reprinting of ‘Hörstadius’—as his book is known to many—and as in the first edition of this book, I take a broad approach in dealing with the discovery, embryological and evolutionary origins, migration, differentiation and cellular derivatives of the neural crest. Cells from the neural crest are associated with many developmental abnormalities, many of which have their origins in a defective neural crest (NC) or in defective neural crest cells (NCCs). The book would be incomplete without discussing neurocristopathies—those tumors and syndromes involving NCCs or those birth defects in which NCCs play a role.

The book is organized into three parts.

Part I (Discovery and Origins) begins with a chapter devoted to the discovery of the neural crest and the impact of that discovery on entrenched notions of germ-layer specificity and the germ-layer theory, a theory that placed a straitjacket around embryology and evolution for almost a century. Primary and secondary neurulation and the neural crest as the fourth germ layer are introduced in this chapter.

In Chapter 2, I discuss the embryological origins of the neural crest, including the identification of future NCCs in gastrula-stage embryos; molecular and cellular

markers of future NCCs; neural and neural crest induction; and rostrocaudal patterning of the developing neural tube and neural crest.

Chapter 3 takes NCCs out of the neural tube with discussions of:

- the delamination of NCCs from the neural tube as mesenchymal cells (a process requiring the transformation of epithelial to mesenchymal cells, usually written in the text as EMT or epithelial → mesenchymal transformation),
- NCC migration and the nature of the extracellular matrices (ECM) through which or along which they migrate, and
- the differentiative potential of NCCs.

Chapter 4 is devoted to the evolutionary origins of the neural crest through an analysis of fossils and of cell types, genes, and gene networks in extant cephalochordates (amphioxus) and in urochordates (chiefly ascidians) in an effort to answer the question ‘Is there any evidence of precursors of the neural crest in urochordates or in cephalochordates?’ The second aim of Chapter 4 is to examine the origin of neural and skeletal tissues of neural crest origin in the first vertebrates (i.e., chordates with a head), and the origin of the jaws in the transition from jawless to jawed vertebrates.

Part II (Neural-Crest Derivatives) presents an analysis of our knowledge of the cell types into which NCCs differentiate. The organization of this part differs from the first edition in which the chapters were organized by major groups of vertebrates, each of which included a discussion of similar cell types—neural, pigment, and skeletal cells. In this edition, I have organized each of the four chapters around major class of cells and the tissues and organs they form or to which they contribute:

- pigment cells and color patterns (Chapter 5);
- neurons and the nervous system (Chapter 6);
- cartilage, bone, and skeletal systems (Chapter 7); and
- dentine-forming cells and teeth, and the smooth muscle, septa and valves of the heart (Chapter 8).

These chapters cover:

- **trunk neural crest cells** (TNCCs)—Chapter 5;
- the **vagal and sacral neural crest** (VNC, SNC), peripheral nervous system (spinal and cranial ganglia), autonomic and parasympathetic nervous systems (sympathetic and parasympathetic ganglia, enteric ganglia, adrenal chromaffin cells), Schwann and glial cells, and Rohon-Béard neurons—Chapter 6;
- **cranial neural crest cells** (CNCC), chondroblasts and osteoblasts, mesenchyme, the skeletogenic (chondrogenic) neural crest, and epithelial-mesenchymal interactions—Chapter 7;
- the odontogenic neural crest, odontoblasts (dentine-forming cells), tooth formation, and the **cardiac neural crest (CarNC)**, the heart, and development of valves, septa and the aortic arches—Chapter 8.

Part III consists of two chapters, Chapter 9 devoted to tumors of neural-crest origin (neurocristopathies), Chapter 10 to a reconsideration of NCC development in the context of birth defects.

Chapter 9 includes discussions of neuroblastomas, neoplasia, and examples of syndromes based in defective NC or NCCs, the two major examples being APUDomas and DiGeorge syndrome.

Chapter 10 broadens the scope to birth defects (often but not always involving the neural tube to which NCCs contribute) or which are induced by a teratogen—vitamin A and craniofacial defects in this case. Mutations affecting NCCs are discussed as is the ability of NCCs to compensate for lost cells, a developmental property known as regulation and a discussion that brings us full circle to the differing potentials of subpopulations of NCCs and whether any NCCs persist as stem cells in embryos or adults.

To avoid interrupting the flow of the text, I have placed most references and some supporting statements in numbered notes, which are gathered at the end of each chapter, and which serve as an annotated bibliography through which access to the literature may be obtained. I have not included all of the literature published before 1999, much of which is in the first edition (Hall, 1999a*). Otherwise, I have surveyed the literature to early 2008. References marked with an * are significant reviews or analyses. Occasionally, I use footnotes (⊗) for general points that apply throughout. Similarly, boxes are used for items of general interest, biographies, or interesting case studies. †signifies an extinct taxon. Gene names are italicized and capitalized (*Shh*), proteins are in plain text and capitalized (Shh). Human genes and proteins are capitalized (*SHH*, SHH). As a shorthand expression for a transformation or interaction I use the symbol →>. The text is extensively illustrated and there is a detailed index. A list of abbreviations is provided. From that list, the following are abbreviations for regions of the neural crest (NC) or for populations of neural crest cells (NCCs).

NC	NCCs
CarNC — cardiac neural crest	CarNCCs — cardiac neural crest cells
CNC — cranial neural crest	CNCCs — cranial neural crest cells
NC — neural crest	NCCs — neural crest cells
SNC — sacral neural crest	SNCCs — sacral neural crest cells
TNC — trunk neural crest	TNCCs — trunk neural crest cells
VN — vagal neural crest	VNCCs — vagal neural crest cells

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Brian K. Hall

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Hall, B.K.

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