Neural Crest Induction and Differentiation

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Neural Crest Induction and Differentiation

Edited by

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DEDICATION

à mes parents

à Victoire, Louis et Fanny

INTRODUCTION

The neural crest was first described in 1868 by Wilhelm His, as “the cord in between” (Zwischenstrang), a group of cells located between the developing neural plate and the future epidermal ectoderm. These cells were seen leaving the dorsal neural tube and aggregating lateral to the neuraxis to give rise to spinal ganglia. Ever since the neural crest has fascinated generations of developmental and evolutionary biologists. My interest in the neural crest does not go back quite as far; it started in April 1986 when as a first year graduate student I attended my first Neuroscience Conference in Bordeaux. The keynote speaker that year was Dr. Nicole Le Douarin, whose lecture sparked my interest in neural crest. A few years later as a postdoctoral research in the laboratory of Dr. Igor Dawid at the NIH, I was able to pursue that interest by initiating studies on neural crest specification in *Xenopus*. This work eventually established the fundamental role of canonical Wnt signaling in the induction of the neural crest. Understanding the molecular basis of neural crest specification and diversification has remained a major research interest of mine since I set up my laboratory in 1998 at the University of Pennsylvania.

In this book I have tried to compile contributions by recognized leaders in the neural crest field who discuss all aspects of modern neural crest biology. From its evolutionary significance, to its specification, migration, plasticity and contribution to multiple lineages of the vertebrate body, to the pathologies associated with abnormal neural crest development and function. Each chapter is intended to be a source of information on the most current advances in the field, highlighting areas of emerging importance as well as some of the challenges that are facing the scientific community working with this cell population.

The first chapter of this book by Noden and Schneider provides an historical overview of some of the debates surrounding the neural crest: from the early days when the neural crest threatened the germ layer theory, to more recent times with the re-evaluation of the concepts underlying the mechanisms of craniofacial patterning. The next two chapters deal with the specification of the neural crest. In Chapter 2, Basch and Bronner-Fraser describe how several signaling pathways, including BMP, Wnt, FGF and Notch signaling, converge at the neural plate border to generate the neural crest and how their concerted action is essential to proper neural crest development. One of the immediate consequences of the induction of the neural crest is the activation of a number of neural crest-specific genes that define the identity of this cell type. In Chapter 3, Sargent describes more specifically the

importance of two sets of transcription factors implicated in the earliest stages of neural crest induction, the *Msx/Dlx* and *TFAP2* families.

One of the key characteristics of the neural crest is its ability to delaminate and migrate away from the dorsal neural tube. In the following chapter (Chapter 4), Duband describes this important step in the ontogeny of the neural crest and summarizes recent advances and trends that have changed the way we look at the delamination and migration of the neural crest. The developmental program that regulates neural crest cell fate as they migrate into the periphery is believed to be both plastic and fixed. In their chapter, Sandell and Trainor (Chapter 5), describe some of the factors and contexts that influence the plasticity and determination of the neural crest, more specifically focusing on the complexity of the tissue interactions that regulate craniofacial morphogenesis. Chapter 6, by Dupin, Creuzet and Le Douarin, reviews a number of *in vivo* cell tracing and *in vitro* single cell culture experiments, which provided important insights into the biology of the neural crest. This chapter also emphasizes the role of *Hox* genes, morphogens and tissues interactions in the development of the skeletogenic neural crest cells.

One of the most remarkable aspects of the neural crest is its amazing multipotency and for this reason five chapters (Chapters 7 to 11) analyze the contribution of the neural crest to several lineages of the vertebrate body. With regard to the neural crest participation to the head skeleton, Knight and Schilling (Chapter 7) discuss recent genetic studies of craniofacial development in zebrafish that have revealed new tissue interactions important to the process of cranial neural crest development. Brown and Baldwin (Chapter 8) focus their review on the derivatives of the cardiac neural crest and discuss the influence of a subset of genes on neural crest-mediated cardiovascular remodeling. Chapter 9 presents an overview of the genetic regulation of pigment cell development. In this chapter, Silver, Hou and Pavan, provide a comparative analysis of studies in different organisms revealing the high level of conservation of this genetic pathway. Other important neural crest derivatives are the sensory neurons residing in the trigeminal and epibranchial ganglia in the head and forming spinal and dorsal root ganglia in the trunk. Raible and Ungos, in Chapter 10, review some of the signals involved in the specification and diversification of the dorsal root ganglia neurons. The enteric nervous system is entirely derived from the vagal and sacral neural crest cells. These cells have to migrate further than any other neural crest cell population in order to colonize the gastrointestinal tract. In Chapter 11, Anderson, Newgreen and Young, describe recent genetic and biological studies that have implicated a variety of signaling pathways in the survival, proliferation, migration and differentiation of the neural crest-derived enteric nervous system.

In the developing embryo, multipotent neural crest progenitors need to integrate cues from the extracellular microenvironment to ensure the generation of appropriate numbers of differentiating progeny. In Chapter 12 Sommer discusses a number of *in vitro* and *in vivo* studies that revealed the importance of growth factor signaling in eliciting diverse biological responses in neural crest cells.

The discovery that a pool of neural crest stem cells persists in several neural crest-derived tissues in the adult has important therapeutic implications. In Chapter 13, Teng and Labosky speculate on future possibilities that will combine our current knowledge of neural crest gene function in the embryo and the manipulation of adult neural crest stem cells in vitro and eventually in vivo. Abnormal survival, proliferation, migration and differentiation of neural crest cells leads to organ and tissue dysplasias with highly diverse clinical and pathological features. The concept of neurocristopathy was introduced three decades ago to unify the diseases arising from aberrant neural crest development. In Chapter 14, Etchevers, Amiel and Lyonnet describe a number of recent advances in basic and clinical research that shed light on some of these pathologies. As a vertebrate innovation the neural crest is considered one of the important steps in the evolution of chordates, and in the last chapter (Chapter 15) Barrallo-Gimeno and Nieto review evidence that have emerged in the last few years that may help explain the steps in the development and appearance of the neural crest during evolution.

In the last several decades a great deal has been learned about the biology of the neural crest. Still a number of important questions remain unresolved. We hope this volume will stimulate activities and efforts to further our understanding of the key processes implicated in the development of this remarkable cell population.

*Jean-Pierre Saint-Jeannet, Ph.D.
Philadelphia, March 2006*

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