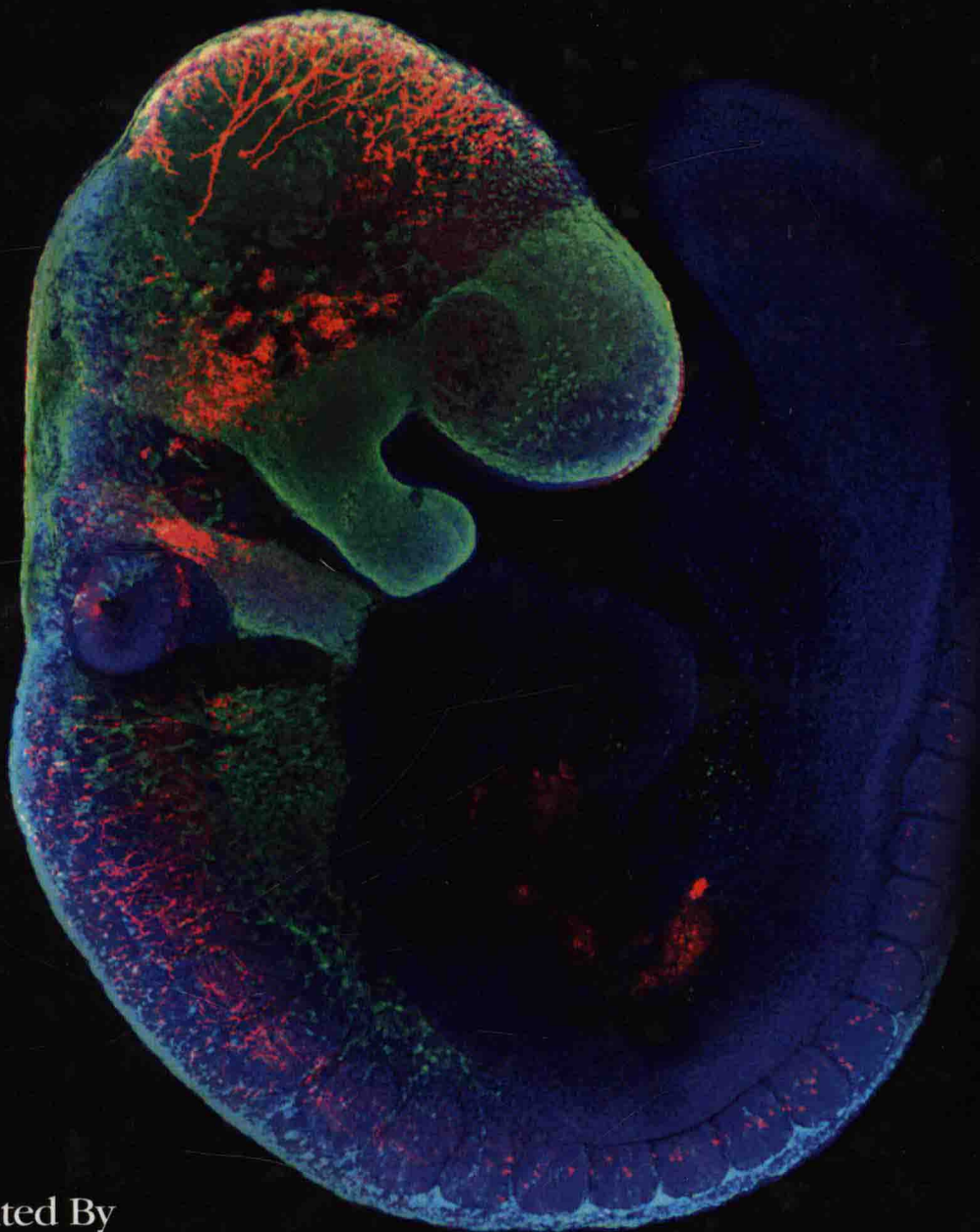


Neural Crest Cells

Evolution, Development and Disease



Edited By
Paul A. Trainor

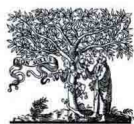
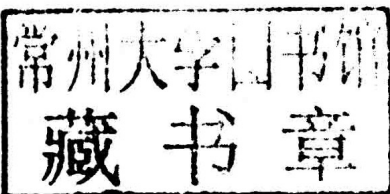


NEURAL CREST CELLS

Evolution, Development
and Disease

Edited by

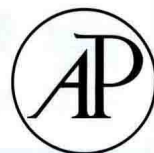
PAUL A. TRAINOR



ELSEVIER

AMSTERDAM • BOSTON • HEIDELBERG • LONDON
NEW YORK • OXFORD • PARIS • SAN DIEGO
SAN FRANCISCO • SINGAPORE • SYDNEY • TOKYO

Academic Press is an imprint of Elsevier



Academic Press is an imprint of Elsevier
32 Jamestown Road, London NW1 7BY, UK
225 Wyman Street, Waltham, MA 02451, USA
525 B Street, Suite 1800, San Diego, CA 92101-4495, USA

Copyright © 2014 Elsevier Inc. All rights reserved

No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means electronic, mechanical, photocopying, recording or otherwise without the prior written permission of the publisher.

Permissions may be sought directly from Elsevier's Science & Technology Rights Department in Oxford, UK: phone (+44) (0) 1865 843830; fax (+44) (0) 1865 853333; email: permissions@elsevier.com. Alternatively, visit the Science and Technology Books website at www.elsevierdirect.com/rights for further information.

Notice

No responsibility is assumed by the publisher for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products, instructions or ideas contained in the material herein. Because of rapid advances in the medical sciences, in particular, independent verification of diagnoses and drug dosages should be made.

British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data

A catalog record for this book is available from the Library of Congress

ISBN: 978-0-12-401730-6

For information on all Academic Press publications visit
our website at www.store.elsevier.com

Cover Figure

The cover figure was kindly provided by Amanda Barlow and is of a late E9.5 DAPI nuclear stained (blue) mouse embryo illustrating the distribution of neural crest cells (green) and the commencement of their differentiation into neurons (red).

Typeset by MPS Limited, Chennai, India
www.adi-mps.com

Printed and bound in United States of America

14 15 16 17 18 10 9 8 7 6 5 4 3 2 1



Working together
to grow libraries in
developing countries

www.elsevier.com • www.bookaid.org

NEURAL CREST
CELLS

Preface

Neural crest cells comprise a migratory, stem and progenitor cell population and are synonymous with vertebrate evolution and development. Although thought to have been first identified by William His in 1868, the term neural crest is attributed to Arthur Milnes Marshall in recognition of the cells anatomical origins. Over the past 145 years, neural crest cells have held the fascination of developmental and evolutionary biologists alike by providing a unique paradigm with which to study various developmental processes such as morphogenetic induction, migratory behaviors, and fate determination.

During the first half of the twentieth century, the majority of neural crest cell research was undertaken in amphibian embryos as reviewed in Horstadius' well-known 1950 monograph. The 1960s saw the introduction of tritiated thymidine cell labeling techniques employed by Weston and Chibon to visualize the migration of neural crest cells throughout the developing amphibian and chick embryos. This was followed shortly thereafter in 1969 through Nicole Le Douarin's seminal introduction of the quail-chick marking system. While similar in principle to the earlier generation of amphibian chimeras by German embryologists such as Andres and Wagner, this now enabled embryologists to distinguish neural crest cells of one species from the surrounding tissue of another species. With this technique, generations of scientists reliably marked and studied the properties of neural crest cells, the principles of which were detailed in Nicole Le Douarin's

1982 book "The Neural Crest." These chimera approaches remain a fundamental staple of neural crest cell research today.

The year 1983 marked another seminal year in the neural crest cell field. Drew Noden illustrated the remarkable properties of cranial neural crest cells and Carl Gans and Glen Northcutt published their "New Head" hypothesis which posited the central importance of neural crest cells in the endless variation of vertebrate craniofacial features throughout evolution. In the late 1980s, new vital dyes cell labeling techniques pioneered by Marianne Bronner and Scott Fraser opened the door to visualizing neural crest cells in any species, but particularly fish and mice. This afforded the opportunity in combination with advances in imaging to follow the dynamics of neural crest cells in real time. Together with advances in molecular techniques, all of these techniques collectively facilitated the study of comparative neural crest cell development, fate, and evolution, highlighting the interplay between patterning and plasticity and spurring the quest to identify the evolutionary origins of neural crest cells. These principles and developments were captured in Brian Hall's 1999 "The Neural Crest in Evolution and Development" and Jean-Pierre Saint Jeannet's 2006 "Neural Crest Induction and Differentiation" books.

In the twenty-first century, much of our focus now revolves around the contributions of neural crest cells to congenital disorders and diseases which are collectively termed neurocristopathies. Understanding the true

genetic and cellular etiology and pathogenesis of individual neurocristopathies offers the potential for developing therapeutic avenues for their clinical prevention. Furthermore, continuing advances have uncovered and characterized the pluripotent stem cell-like characteristics of neural crest cells during embryogenesis and their persistence into adulthood. Thus, there is tremendous excitement in the potential for neural crest cells to be used in tissue engineering and regenerative medicine. This book "Neural Crest Cells: Evolution, Development and Disease" ambitiously tries to capture the classic principles and recent advances in our comprehension of the roles of neural crest cells in vertebrate evolution and development. Much of this has come from the application of new genetic, imaging and

systems biology approaches exploring the gene regulatory control of neural crest cell formation, migration, and differentiation. This book also illustrates how this foundational knowledge influences our understanding of the central roles neural crest cells play in the pathogenesis of congenital disorders and diseases and the potential for neural crest cells to be used in tissue engineering and regenerative medicine to treat disorders and disease.

I am extremely grateful to all of the authors for sharing their time, knowledge, and expertise in contributing chapters to this book. I also want to thank all the past and present members of my laboratory as well as colleagues and friends in the neural crest cell field for continually making science and life stimulating and fun.

Acknowledgment

I am indebted to Patrick Tam and Robb Krumlauf for introducing me to neural crest cells and for their scientific training and continual support, mentorship, and friendship.

"Learn from yesterday, live for today, hope for tomorrow. The important thing is to not stop questioning."
Albert Einstein

Contributors

- Sinu Jasrapuria-Agrawal** Department of Biochemistry and Cell Biology, Rice University, Houston, TX, USA
- Kristin Bruk Artinger** Department of Craniofacial Biology, School of Dental Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, USA
- John Avery** Department of Biochemistry and Molecular Biology, University of Georgia, USA
- Chang-Joon Bae** Department of Basic Science and Craniofacial Biology, College of Dentistry, New York University, New York, USA
- Amanda J. Barlow** Department of Surgery, University of Wisconsin, USA
- Jo Begbie** Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, UK
- Erin Betters** Yale University, New Haven, CT, USA
- Marianne E. Bronner** Division of Biology, California Institute of Technology, Pasadena, CA, USA
- Yang Chai** Center for Craniofacial Molecular Biology, Herman Ostrow School of Dentistry, University of Southern California, Los Angeles, CA, USA
- Michael L. Cunningham** Department of Pediatrics, University of Washington, Seattle, USA; Seattle Children's Research Institute, Seattle, USA
- Stephen Dalton** Department of Biochemistry and Molecular Biology, University of Georgia, USA
- Elisabeth Dupin** Institut de la Vision Research Center, Department of Developmental Biology, Paris, France
- Anthony B. Firulli** Riley Heart Research Center, Herman B Wells Center for Pediatric Research Division of Pediatrics Cardiology, Departments of Anatomy, Biochemistry, and Medical and Molecular Genetics, Indiana University Medical School, IN, USA
- Jennifer L. Fish** Department of Orthopaedic Surgery, University of California at San Francisco, San Francisco, CA, USA
- Stephen J. Fleenor** Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, UK
- Heide L. Ford** Department of Pharmacology, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, USA
- Martín I. Garcia-Castro** Department of Molecular Cell & Developmental Biology, Yale University, New Haven, CT, USA
- Robert N. Kelsh** Department of Biology and Biochemistry and Centre for Regenerative Medicine, University of Bath, Bath, UK
- Alberto Lapedriza** Department of Biology and Biochemistry and Centre for Regenerative Medicine, University of Bath, Bath, UK
- Nicole M. Le Douarin** Institut de la Vision Research Center, Department of Developmental Biology, Paris, France
- Pierre Le Pabic** Department of Developmental and Cell Biology, University of California, Irvine, Irvine, CA, USA
- Alan W. Leung** Yale University, New Haven, CT, USA
- Harold N. Lovvorn III** Department of Pediatric Surgery, Vanderbilt University Medical Center, USA
- Peter Y. Lwigale** Department of Biochemistry and Cell Biology, Rice University, Houston, TX, USA
- Roberto Mayor** Department of Cell and Developmental Biology, University College London, UK

- Laura Menendez** Department of Biochemistry and Molecular Biology, University of Georgia, USA
- Barbara Murdoch** Department of Biology, Eastern Connecticut State University, CT, USA
- Jenean H. O'Brien** Department of Pharmacology, School of Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, USA
- Rangarajan Padmanabhan** Department of Animal and Avian Sciences, University of Maryland, College Park, MD, USA
- Carolina Parada** Center for Craniofacial Molecular Biology, Herman Ostrow School of Dentistry, University of Southern California, Los Angeles, CA, USA
- Kleio Petrattou** Department of Biology and Biochemistry and Centre for Regenerative Medicine, University of Bath, Bath, UK
- Davalyn R. Powell** Department of Craniofacial Biology, School of Dental Medicine, University of Colorado Anschutz Medical Campus, Aurora, CO, USA
- Andrew Prendergast** Department of Biological Structure, University of Washington, USA
- David W. Raible** Department of Biological Structure, University of Washington, USA
- Jean-Pierre Saint-Jeannet** Department of Basic Science and Craniofacial Biology, College of Dentistry, New York University, New York, USA
- Pedro A. Sanchez-Lara** Children's Hospital Los Angeles, Department of Pediatrics & Pathology and Laboratory Medicine, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA; Center for Craniofacial Molecular Biology, Ostrow School of Dentistry, University of Southern California, Los Angeles, CA, USA
- Lisa Sandell** Birth Defects Center—MCCB, School of Dentistry, University of Louisville, Louisville KY, USA
- Thomas F. Schilling** Department of Developmental and Cell Biology, University of California, Irvine, CA, USA
- Richard A. Schneider** Department of Orthopaedic Surgery, University of California at San Francisco, San Francisco, CA, USA
- Quenten P. Schwarz** Centre for Cancer Biology, SA Pathology, Frome Road, Adelaide, Australia
- Paul Sharpe** Department of Craniofacial Development and Stem Cell Biology, Dental Institute, Kings College London, Guy's Hospital, London, UK
- Pablo H. Strobl-Mazzulla** Laboratory of Developmental Biology, Instituto de Investigaciones Biotecnológicas-Instituto Tecnológico de Chascomús (CONICET-UNSAM), Chascomús, Argentina
- Lisa A. Taneyhill** Department of Animal and Avian Sciences, University of Maryland, College Park, MD, USA
- Eric Theveneau** Department of Cell and Developmental Biology, University College London, UK
- Paul A. Trainor** Stowers Institute for Medical Research, Kansas City, MO, USA; Department of Anatomy and Cell Biology, University of Kansas School of Medicine, Kansas City, KS, USA
- Joshua W. Vincentz** Riley Heart Research Center, Herman B Wells Center for Pediatric Research Division of Pediatrics Cardiology, Departments of Anatomy, Biochemistry, and Medical and Molecular Genetics, Indiana University Medical School, Indianapolis, IN, USA
- Kristin E. Noack Watt** Stowers Institute for Medical Research, Kansas City, MO; Department of Anatomy and Cell Biology, University of Kansas School of Medicine, Kansas City, KS, USA
- Sophie E. Wiszniak** Centre for Cancer Biology, SA Pathology, Frome Road, Adelaide, Australia
- Hu Zhao** Center for Craniofacial Molecular Biology, Ostrow School of Dentistry, University of Southern California, Los Angeles, CA, USA

Contents

Preface	xiii
Acknowledgment	xv
Contributors	xvii

I

NEURAL CREST CELL EVOLUTION AND DEVELOPMENT

1. The Neural Crest, a Fourth Germ Layer of the Vertebrate Embryo: Significance in Chordate Evolution

NICOLE M. LE DOUARIN AND ELISABETH DUPIN

General Characteristics of the Neural Crest	4
Transition from Invertebrates Chordates to Vertebrates	5
The Molecular Control of EMT Studied in NCC Development	6
Role of the NC in the Development of the Vertebrate Head	7
The Evolutionary Origin of the Vertebrate Nervous System	9
The Genetic Identity of Vertebrate Secondary Brain Organizers as Landmarks for CNS Evolution in Deuterostomes	12
Are Precursors of the NC Present in Non-Vertebrate Chordates?	13
The Multiple Roles of the NC in the Construction of the Vertebrate Head and Brain	14
<i>Hox</i> Gene Expression in the Cephalic NC	15
Malformations of the Brain Induced by FSNC Removal	17
Effect of Forced Expression of <i>Hox</i> Genes in the FSNC on Face and Brain Development	18
Role of the Cephalic NC in the Regulation of <i>Fgf8</i> Production by the ANR and Isthmus	19

The Evolution of Skeletal Structures in the Vertebrate Phylum	19
Conclusions and Perspectives	20
Abbreviations	22
Acknowledgments	22
References	22

2. Induction and Specification of Neural Crest Cells: Extracellular Signals and Transcriptional Switches

CHANG-JOON BAE AND JEAN-PIERRE SAINT-JEANNET

Introduction	27
NC Induction at the NPB	29
Timing and Tissues	30
Signaling Factors	32
Gene Regulatory Network Involved in NC Specification	38
NPB Specifier Genes	38
NC Specifier Genes	39
Conclusions and Perspectives	41
Acknowledgments	42
References	42

3. The Cell Biology of Neural Crest Cell Delamination and EMT

LISA A. TANEYHILL AND RANGARAJAN PADMANABHAN

Introduction	51
Loss of Intercellular Adhesion	52
Adherens Junctions	52
Tight Junctions	58
Acquisition of Migratory Capacity	60
Rho GTPases and the Cytoskeleton	60
Appropriate Substrate for Migration	62
Breakdown of Basal Lamina	62
ECM	63
Integrins	64
Conclusions and Perspectives	66
References	66

4. Neural Crest Cell Migration: Guidance, Pathways, and Cell–Cell Interactions

ERIC THEVENEAU AND ROBERTO MAYOR

Pathways of Neural Crest Cell Migration: An

Overview 73

Cephalic Neural Crest Cell Migration 75

Inhibitors 75

Positive Regulators of Cephalic Neural Crest Cell Migration 76

Trunk Neural Crest Cell Migration 77

The Ventromedial Pathway 77

The Dorsolateral Pathway 78

Cell–Cell Interactions During Neural Crest Cell Migration 78

Neural Crest–Neural Crest Interactions and Cell Polarity 78

Neural Crest–Neural Crest Interactions Promote Collective Guidance 80

CIL-Based Dispersion Is Counterbalanced by Mutual Attraction to Promote Collective Cell Migration 80

Dialogue Between Neural Crest Cells and Their Local Environment 81

Conclusion and Perspectives 82

Acknowledgments 83

References 83

5. Epigenetic Regulation of Neural Crest Cells

PABLO H. STROBL-MAZZULLA AND
MARIANNE E. BRONNER

Introduction 89

Histone Modifications 90

Methylation 92

Acetylation 93

Histone Variants 94

Chromatin Modifiers 95

DNA Methylation 96

Conclusions and Perspectives 96

Acknowledgments 97

References 97

6. Neural Crest-Mediated Tissue Interactions During Craniofacial Development: The Origins of Species-Specific Pattern

JENNIFER L. FISH AND RICHARD A. SCHNEIDER

Introduction 102

From Where Does Craniofacial Pattern Come? 102

Origins and Functions of Craniofacial Tissues 102

Tissue Interactions and the Evolution of Species-Specific Pattern 105

Origins of Species-Specific Pattern 106

Comparative Early Development of Neural Crest 106

Tissue Interactions that Program the Neural Crest 107

Neural Crest and the Origins of Species-Specific Pattern 108

Mechanisms of Species-Specific Pattern in the Neural Crest-Derived Skeleton 111

Mechanisms of Species-Specific Pattern in the Craniofacial Musculature 113

Mechanisms of Species-Specific Pattern in the Craniofacial Integument 113

Conclusions and Perspectives 114

References 115

II

NEURAL CREST CELL DIFFERENTIATION AND DISEASE

7. Neural Crest Cells in Craniofacial Skeletal Development

THOMAS F. SCHILLING AND PIERRE LE PABIC

Introduction 127

Skeletogenic NC Specification and Anterior–Posterior Patterning 128

The Ectomesenchymal Lineage and its NC

Origins 128

Anterior–Posterior Identities of Cranial NCC 130

Defining the Spatial Extent of the EM and its Derivatives 130

Patterning Within Craniofacial Skeletal Primordia 131

A GRN of D–V Pharyngeal Patterning	131
Midfacial Integration	134
Modular Patterning of Tongue and Teeth	136
Gene Regulatory Interactions in the Developing Skull Vault	137
Translating Patterning into Growth and Survival	138
Environmental Factors in Craniofacial Development	140
Cranial NC Development and Evolution	141
Conclusions and Perspectives	143
References	144

8. Neural Crest Cell and Placode Interactions in Cranial PNS Development

STEPHEN J. FLEENOR AND JO BEGBIE

The Cranial Peripheral Nervous System	153
Ectodermal Placodes	155
The Pre-Placodal Region	157
Interactions	158
NCC Interactions with the Pre-Placodal Region	158
NCC Interactions with Placodal Derivatives	158
Evolutionary Significance	162
Conclusions and Perspectives	162
Acknowledgments	163
References	163

9. Neural Crest Cells in Ear Development

LISA SANDELL

The Ear	167
Timing and Position of Otic NCC Emigration	169
NCC Derivatives in the Inner Ear	170
NCC in Middle Ear and Outer Ear Development	173
Neurocristopathies of the Middle and Outer Ear	176
Genetic Regulation of NCC Middle and Outer Ear Development	177
NCC and Evolution of the Ear	178
Concluding Remarks	180
References	181

10. Neural Crest Cells in Ocular Development

SINU JASRAPURIA-AGRAWAL AND PETER Y. LWIGALE

Introduction	189
Neural Crest and Early Eye Development	191
Signaling Between NCC and the Optic Cup	192
Signaling Between NCC and the Lens	193
Signaling Between NCC and Ectoderm	194
Other Contribution of NCC to Ocular Tissues	194
Indirect Neural Crest Contribution to the Eye via Trigeminal and Ciliary Nerves	195
Neural Crest Related Ocular Defects	196
Conclusions and Perspectives	198
References	199

11. The Cardiac Neural Crest and Their Role in Development and Disease

JOSHUA W. VINCENTZ AND ANTHONY B. FIRULLI

Introduction	206
NCC Specification	207
Migration and Morphogenesis of the cNCC	207
Invasion of the cNCC into the Pharyngeal Arches and OFT Cushions	212
Remodeling of the Pharyngeal Arch Arteries	212
Septation of the OFT	214
Valvulogenesis in the OFT	214
NCC Differentiation	214
Evolution of Neural Crest Cell Contribution to the Heart	216
Molecular Regulators of cNCC Development and Links to Congenital Heart Disease	218
22q11 Deletion Syndrome	218
Alagille Syndrome	218
Noonan Syndrome	219
4q Deletion Syndrome	219
Dietary Factors Influencing Cardiac Neural Crest Cell Development	220
Fetal Alcohol Syndrome	220
Retinoic Acid	221
Conclusions and Perspectives	222
Acknowledgments	222
References	222

12. Neural Crest Cells in Enteric Nervous System Development and Disease

AMANDA J. BARLOW

Introduction	231
GDNF, GFR α 1, and RET Signaling	234
Neurturin, GFR α 2, and RET Signaling	235
Endothelin 3 (EDN3)/Endothelin Receptor B (EDNRB) Signaling	235
Transcription Factors	235
KIAA1279	236
L1CAM	236
TCF4	236
Neuregulins	236
Signaling Pathway Interactions in ENS Development and HSCR	237
Genes Involved in ENS Development, not Currently Associated With Human Disease	237
Regulation of the NCC Population That Migrates Toward and Then into the Foregut	238
Regulation of ENCC Survival, Migration, Proliferation, and Differentiation Within the Gut Wall	239
ENCC Survival Within the Gut Wall	239
ENCC Migration Along the Gut Wall	240
ENCC Proliferation Within the Gut Wall	241
ENCC Differentiation Within the Gut Wall	243
HSCR and Cell Transplantation Therapies	244
HSCR: Beyond Colonic Aganglionosis	245
Conclusions and Perspectives	246
Acknowledgments	246
References	246

13. Neural Crest Cells and Peripheral Nervous System Development

ANDREW PRENDERGAST AND DAVID W. RAIBLE

Overview	256
Definition of Trunk Neural Crest	256
Divergent Neural Crest Migratory Pathways Reflect Fate Restriction of the Trunk Neural Crest	257
Neural Crest Fate Restriction Begins Long Before the Observation of Overt Differentiation Markers	258
Factors that Specify the Neural Crest Continue to Modify Neural Crest Fate Proliferation, Survival, and Fate Choice	260

The Survival and Multipotency of Trunk Neural Crest Is Maintained by Several Transcription Factors Expressed During Migration	260
Sox10 Promotes Neural Crest Survival, Supports Glial Development, and Maintains Neural Crest Multipotency	260
ErbB/Neuregulin Signaling Supports Neural Crest Migration and Glial Development	261
Neural Crest Are Instructed to Develop as Autonomic Neurons by BMP Signals Emanating from the Dorsal Aorta	264
BMPs Directly Promote Neuronal Fates	264
BMPs Trigger Changes in Trophic Factor Dependence	266
The Transcriptional Cascade Leading to Autonomic Nervous System Differentiation Is Extensively Cross-Regulatory	267
Autonomic Differentiation Begins with the Expression of Ascl1	267
Expression of the Phox2 Transcription Factors Is Essential for the Continued Development of the Sympathetic Ganglia	267
Insm1 Is Activated Downstream of Phox2b and Promotes Proliferation in Nascent Sympathetic Ganglia	268
HAND1 and 2 Mediate Specific Aspects of Noradrenergic Differentiation	268
GATA Transcription Factors Are Situated Near the End of the Sympathogenic Transcriptional Cascade	269
Lessons Learned from the Autonomic Transcription Factor Cascade	270
DRG Formation Occurs in Overlapping Waves of Neurogenesis That Can Be Followed Using the Trk Receptor Family as Markers of Cell Fate	270
DRG Neurogenesis is Traditionally Understood to Occur in Distinct Waves	270
Ablation of TrkC Signaling Causes the Loss of Large-Diameter Neurons	271
Loss of TrkB Function Causes Loss of a Subset of DRG Neurons	271
Removal of TrkA and its Ligand Cause Loss of Most Small-Diameter Neurons	272
Trk Receptor Studies Are Complicated by the Fact That Trk Receptor Expression Is Not Exclusive	272

The DRG Transcriptional Cascade Is Hierarchical and Sorts Cells into Subtypes 273

The Neurogenins are the Top-Tier Transcription Factors in the DRG Transcriptional Cascade 273

The Subsequent Expression of Other Transcription Factors Is Essential to DRG Development and Maintenance 274

Brn3a and Islet1 Are Initiated After the Neurog Factors and Cooperate to Regulate Many Targets 274

Runx Transcription Factors Further Refine the Dorsal Root Ganglion Sensory Neuron Population 275

Conclusions and Perspectives: Common Features in Autonomic and Sensory Neuronal Development 275

References 276

14. Neural Crest Cells and Pigmentation

ALBERTO LAPEDRIZA, KLEIO PETRATOU AND
ROBERT N. KELSH

Introduction 287

Timing of Pigment Cell Development 290

Pigment Cell Progenitors 290

Fate Choice/Specification 292

Melanocytes 292

Specification of Other Pigment Cell Types 295

Commitment 296

Migration and Patterning 297

Xanthophores 298

Proliferation and Survival 298

Differentiation 299

Morphology 299

Melanin Synthesis 300

Pigment-Type Switching 301

Iridophore Pigmentation 302

Xanthophore Pigmentation: The Pteridine Pathway 303

Conclusions and Perspectives 303

References 304

15. Neural Crest Cells in Vascular Development

SOPHIE E. WISZNAK AND QUENTEN P. SCHWARZ

Introduction 314

Blood Vessel Development and Structure 314

The Cardiovascular System 314

Blood Vessel Development 315

Blood Vessel Maturation 315

Neural Crest Contribution to Blood Vessels 317

Neural Crest Contribution to Pharyngeal Arch Artery Development and Patterning 317

Neural Crest Cell Contribution to the Cardiac Outflow Tract 319

Neural Crest Cell Contribution to Cranial Vessel Smooth Muscle Coating 321

Innervation of the Vasculature by the ANS 324
The ANS 324

Function of Innervation in Blood Vessel Homeostasis 325

Function of Innervation in Cardiac Conduction 326

Mechanisms of Blood Vessel Innervation 327

Neural Crest Involvement in Neurovascular Patterning 329

Neurovascular Congruence 329

Blood Vessel Patterning by Peripheral Nerves 330

Conclusions and Perspectives 330

References 331

16. Neural Crest Cells and Cancer: Insights into Tumor Progression

DAVALYN R. POWELL, JENEAN H. O'BRIEN,
HEIDE L. FORD AND KRISTIN BRUK ARTINGER

Introduction 335

Similarities Between Neural Crest Delamination/ Migration and Tumor Progression 336

Cell–Cell Junctions 337

Cell Polarity 338

Rho GTPases 339

ECM, Proteases, and Integrins 340

Migration 341

Signaling and Transcription Factors 342

Neural Crest-Derived Cancers 342

Melanoma 342

Neuroblastoma 345

Glioma and Glioblastoma 346

Other Cancers of Neural Crest Origin 347

Conclusions and Perspectives 348

References 349

III

TISSUE ENGINEERING AND REPAIR

17. Neurocristopathies: The Etiology and Pathogenesis of Disorders Arising from Defects in Neural Crest Cell Development

KRISTIN E. NOACK WATT AND PAUL A. TRAINOR

Introduction	362
Neural Crest Cell Formation	362
Treacher Collins Syndrome (Mandibulofacial Dystosis)	362
Diamond Blackfan Anemia	367
Miller Syndrome (Genee–Weidemann; Wildervanck–Smith; Postaxial Acrofacial Dystosis)	368
Neural Crest Cell Migration	369
Branchio-Oculo-Facial Syndrome	370
Piebaldism	371
Hirschsprung Disease	372
Mowat–Wilson Syndrome	374
Waardenburg Syndrome	374
Metastatic Cancer	376
Melanoma	377
Neuroblastoma	377
22q11.2 Deletion Syndrome	378
Neural Crest Cell Differentiation	379
Congenital Central Hypoventilation Syndrome	380
Oculocutaneous Albinism	381
Craniosynostosis	381
Conclusions and Perspectives	384
Acknowledgments	385
References	385

18. Human Neural Crest Cells and Stem Cell-Based Models

ERIN BETTERS, BARBARA MURDOCH, ALAN W. LEUNG
AND MARTÍN I. GARCÍA-CASTRO

Introduction	395
Embryonic Development of the Human Neural Crest	398

Neural Crest Marker Expression in Human Embryos	398
Neural Crest Markers in Human Cell Lines and Embryonic Fragments	399
Neural Crest Marker Expression: Insights into Neural Crest-Associated Human Diseases	403
Surrogate Models of Human Neural Crest Development	403
Generating Neural Crest Precursors from Human Embryonic Stem Cells	403
hESC Derived Neural Crest Precursors as a Model for Development	404
Neural Crest Derivatives from Neural Crest Precursors	405
Transplantation of hESC Derivatives of the Neural Crest: Advances and Limitations	406
iPSC Contributions to Our Understanding of Human NC Development	406
Using Stem Cells to Model and Treat Neural Crest-Associated Diseases	407
The Relevance of Embryonic Marker Expression Studies to hESC/iPSC-Based Research	408
Conclusions and Perspectives	409
References	409

19. Neural Crest Stem Cell: Tissue Regeneration and Repair

PEDRO A. SANCHEZ-LARA AND HU ZHAO

Introduction	413
Gingival MSC	414
Dental MSC	415
PDL MSC	416
TMJ Stem Cells	417
Bone Marrow Mesenchymal Stem Cells (BMMSCs)	417
Adipose MSC	418
Conclusions and Perspectives	418
References	419

20. Functional Significance of Cranial Neural Crest Cells During Tooth Development and Regeneration

CAROLINA PARADA, YANG CHAI AND PAUL SHARPE

Introduction	423
Tooth Development	424

Origin of Tooth Cells	424
Patterning the Dentition and Instructive Signals for Patterning	425
CNCC and Dental Stem Cells	432
CNCC-Derived Stem Cells in Tooth and Alveolar Bone Regeneration	434
Conclusions and Perspectives	435
Acknowledgments	436
References	436

21. Using Induced Pluripotent Stem Cells as a Tool to Understand Neurocristopathies

JOHN AVERY, LAURA MENENDEZ, MICHAEL L. CUNNINGHAM, HAROLD N. LOVVORN III AND STEPHEN DALTON

Introduction	441
Neural Crest Cells and Neurocristopathies	442
Methods for NCC Differentiation from Pluripotent Stem Cells	443

Neurocristopathies	445
Familial Dysautonomia	445
Hirschsprung's Disease	446
Treacher Collins Syndrome	450
CHARGE Syndrome	452
Noonan and LEOPARD Syndromes	453
22q11.2 Deletion Syndromes	453
Waardenburg Syndrome	454
Piebaldism	455
Conclusions and Perspectives	455
References	455

Index 461



PART I

NEURAL CREST CELL EVOLUTION AND DEVELOPMENT