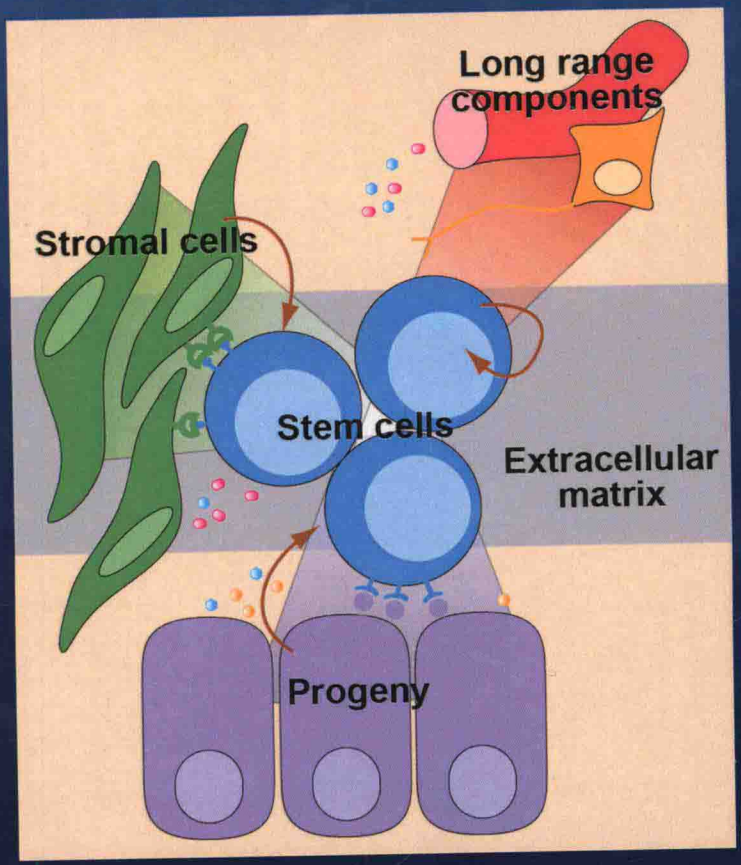
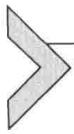
Stem Cells in Development and Disease



Edited by

Michael Rendl



VOLUME ONE HUNDRED AND SEVEN

CURRENT TOPICS IN DEVELOPMENTAL BIOLOGY

Stem Cells in Development and Disease

Edited by

MICHAEL RENDL

Black Family Stem Cell Institute,
Department of Developmental and Regenerative Biology
Icahn School of Medicine at Mount Sinai, NY, USA

ELSEVIER

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

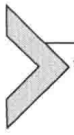
Academic Press is an imprint of Elsevier

Academic Press is an imprint of Elsevier
525 B Street, Suite 1800, San Diego, CA 92101-4495, USA
225 Wyman Street, Waltham, MA 02451, USA
The Boulevard, Langford Lane, Kidlington, Oxford, OX5 1GB, UK
32 Jamestown Road, London NW1 7BY, UK
Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands

First edition 2014

ISBN: 978-0-12-416022-4
ISSN: 0070-2153

Printed and bound by CPI Group (UK) Ltd, Croydon, CR0 4YY



VOLUME ONE HUNDRED AND SEVEN

CURRENT TOPICS IN DEVELOPMENTAL BIOLOGY

Stem Cells in Development and Disease

CURRENT TOPICS IN DEVELOPMENTAL BIOLOGY

"A meeting-ground for critical review and discussion of developmental processes"
A.A. Moscona and Alberto Monroy (Volume 1, 1966)

CONTRIBUTORS

Yaser Atlasi
Department of Pathology, Josephine Nefkens Institute, Erasmus MC, Rotterdam, The Netherlands

Nick Barker
Institute of Medical Biology, Singapore, and MRC Centre for Regenerative Medicine, The University of Edinburgh, Edinburgh, United Kingdom

Andrew S. Brack
Center for Regenerative Medicine, Massachusetts General Hospital; Harvard Medical School, and Harvard Stem Cell Institute, Boston, Massachusetts, USA

Natasha C. Chang
The Sprott Centre for Stem Cell Research, Ottawa Hospital Research Institute, and Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

Shuang Chen
Department of Developmental Biology, Washington University, St. Louis, Missouri, USA

Sean M. Cullen
Stem Cells and Regenerative Medicine Center, and Program in Developmental Biology, Baylor College of Medicine, Houston, Texas, USA

Christine M. Fillmore
Stem Cell Program, Boston Children's Hospital; The Harvard Stem Cell Institute, Cambridge, and Department of Genetics, Harvard Medical School, Boston, Massachusetts, USA

Riccardo Fodde
Department of Pathology, Josephine Nefkens Institute, Erasmus MC, Rotterdam, The Netherlands

Naiyang Fu
Stem Cells and Cancer Division, The Walter and Eliza Hall Institute of Medical Research, and Department of Medical Biology, University of Melbourne, Parkville, Victoria, Australia

Margaret A. Goodell
Stem Cells and Regenerative Medicine Center; Program in Developmental Biology, and Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, USA

Valerie Horsley
Department of Molecular, Cell and Developmental Biology, Yale University, New Haven, Connecticut, USA

Yunjoon Jung
Center for Regenerative Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA

Klaus H. Kaestner
Department of Genetics and Institute for Diabetes, Obesity, and Metabolism, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA

Carla F. Kim
Stem Cell Program, Boston Children's Hospital; The Harvard Stem Cell Institute, Cambridge, and Department of Genetics, Harvard Medical School, Boston, Massachusetts, USA

Raphael Kopan
Department of Developmental Biology, Washington University, St. Louis, Missouri, and Division of Developmental Biology, Department of Pediatrics, Cincinnati Children's Hospital, Cincinnati, Ohio, USA

Kristen T. Leeman
Division of Newborn Medicine, Boston Children's Hospital, Harvard Medical School; Stem Cell Program, Boston Children's Hospital; The Harvard Stem Cell Institute, Cambridge, and Department of Genetics, Harvard Medical School, Boston, Massachusetts, USA

Geoffrey J. Lindeman
Stem Cells and Cancer Division, The Walter and Eliza Hall Institute of Medical Research; Department of Medical Oncology, Royal Melbourne Hospital, and Department of Medicine, University of Melbourne, Parkville, Victoria, Australia

Melissa Little
Department of Developmental Biology, Washington University, St. Louis, Missouri, USA, and Institute for Molecular Bioscience, The University of Queensland, St. Lucia, Queensland, Australia

Leendert Looijenga
Department of Pathology, Josephine Nefkens Institute, Erasmus MC, Rotterdam, The Netherlands

Allison Mayle
Stem Cells and Regenerative Medicine Center, and Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, USA

Jon M. Oatley
Center for Reproductive Biology, School of Molecular Biosciences, College of Veterinary Medicine, Washington State University, Pullman, Washington, USA

Eszter Posfai
Developmental and Stem Cell Biology, The Hospital for Sick Children Research Institute, Toronto, Ontario, Canada

Michael Rendl
Black Family Stem Cell Institute; Department of Developmental and Regenerative Biology; Department of Dermatology, and Graduate School of Biomedical Sciences, Icahn School of Medicine at Mount Sinai, New York, USA

Amélie Rezza
Black Family Stem Cell Institute, and Department of Developmental and Regenerative Biology, Icahn School of Medicine at Mount Sinai, New York, USA

Chiara Rolando
Department of Biomedicine, University of Basel, Basel, Switzerland

Janet Rossant
Developmental and Stem Cell Biology, The Hospital for Sick Children Research Institute, and Department of Molecular Genetics, University of Toronto, Toronto, Ontario, Canada

Lara Rossi
Department of Experimental, Diagnostic, and Specialty Medicine (DIMES), Institute of Hematology "L. and A. Seràgnoli", University of Bologna, Bologna, Italy

Michael A. Rudnicki
The Sprott Centre for Stem Cell Research, Ottawa Hospital Research Institute, and Department of Cellular and Molecular Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada

Rachel Sennett
Black Family Stem Cell Institute, and Department of Developmental and Regenerative Biology, Icahn School of Medicine at Mount Sinai, New York, USA

Soona Shin
Department of Genetics and Institute for Diabetes, Obesity, and Metabolism, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA

Ana Mafalda Baptista Tadeu
Department of Molecular, Cell and Developmental Biology, Yale University, New Haven, Connecticut, USA

Oliver H. Tam
Developmental and Stem Cell Biology, The Hospital for Sick Children Research Institute, Toronto, Ontario, Canada

David Wei-Min Tan
Institute of Medical Biology, Singapore

Verdon Taylor
Department of Biomedicine, University of Basel, Basel, Switzerland

Jane E. Visvader
Stem Cells and Cancer Division, The Walter and Eliza Hall Institute of Medical Research, and Department of Medical Biology, University of Melbourne, Parkville, Victoria, Australia

Qi-En Yang
Center for Reproductive Biology, School of Molecular Biosciences, College of Veterinary Medicine, Washington State University, Pullman, Washington, USA

PREFACE

Stem cell research is one of the most fascinating and exciting research areas considering the therapeutical potential of stem cells. Manipulation of endogenous stem cells or the application of exogenous stem cells has the great promise to rejuvenate diseased and aged tissues in regenerative therapies. To fulfill this promise, we first need to identify tissue stem cells, define their physiological lineage relationship to differentiated cells, and characterize their functional control by intrinsic regulators and extrinsic factors from the microenvironment. In the past three decades, tremendous progress has been made: from the successful culture of embryonic stem cells and the early discovery of hematopoietic stem cells and stem cells in rapidly renewing skin and intestinal tissues to the more recent identification of neural, mammary, muscle, lung, and germ stem cells as well as hepatic and kidney progenitors. Recent studies have also shed light on the molecular make-up of stem cells and the complexly controlled balance between stem cell self-renewal and differentiation by endogenous transcriptional regulators, microRNAs and their overall epigenetic state, as well as by signaling and cellular communication from and to the microenvironment.

These insights have led to the establishment of stable stem cell cultures and culminated in recent efforts to engineer three-dimensional intestinal, skin, and other tissues. They further guide attempts at differentiation of embryonic and induced pluripotent stem cells and at direct reprogramming of differentiated somatic cells. Finally, our greatly improved understanding of stem cell control and function directly overlaps with studies of cancer biology and aging, as recently discovered cancer stem cells share many regulatory mechanisms with normal tissue stem cells that go awry in cancers and that also become dysregulated in aging tissues.

In this volume of *Current Topics in Developmental Biology* on *Stem Cells in Development and Disease*, 14 contributions from leading stem cell researchers provide a comprehensive overview about our current knowledge of physiological stem cell functions in 11 different mammalian organ systems and of the mechanisms that contribute to aging and cancer. In Chapter 1, Posfai et al. review embryonic and other pluripotent stem cells in the pre- and postimplantation embryo. They comprehensively discuss the latest insights on the sequential lineage specifications in the early developing embryo. Furthermore, they dissect the similarities and differences of *in vivo* pluripotency

development with their stem cell population counterparts propagated *in vitro*. All these developmental aspects are then placed in the context of the major signaling pathways known to play critical roles in the regulation of pluripotency.

Chapters 2–4 are focused on the discussion of well-characterized stem cell systems in the rapidly renewing tissues of the bone marrow, intestine, and skin. In Chapter 2, Goodell and colleagues summarize the main results of many important recent studies on hematopoietic stem cell regulation with a focus on epigenetic control. They thoroughly discuss the latest insights on general principles of epigenetic regulation and the specific epigenetic mechanisms that impact embryonic hematopoietic development and that control the balance between hematopoietic stem cell maintenance and lineage commitment. This review further highlights epigenetic controls in the context of aging and hematopoietic malignancies. In Chapter 3, Tan and Barker review intestinal stem cells and discuss the controversial relationships and hierarchy of different stem cell populations that have been identified within the crypts. They summarize the main competing theories and conflicting results of many important recent studies and offer an integrative discussion of a unifying theory. In Chapter 4, Tadeu and Horsley review the latest insights on epithelial skin stem cells of the epidermis, hair follicles, and sweat glands. They detail the intrinsic and extrinsic controls of adult skin stem cell niches and discuss their relevance for epithelial skin cancer progression and pathology.

In subsequent chapters, other well-established and more recently discovered stem cells and progenitors of several organ systems are discussed. In Chapter 5, Fu et al. review the lineage relationship of different stem and progenitor cell populations of the mammary gland. With an insightful discussion, they provide reconciliatory explanations to new competing theories regarding lineage relationships within the epithelial mammary gland. It continues with a thorough overview of the molecular control of mammary stem and progenitor cell regulation by steroid hormones and other molecular players and finally ties together the latest insights regarding implications for breast cancer. In Chapter 6, several established and novel features of satellite stem cells are reviewed by Chang and Rudnicki in a comprehensive discussion of many recent insights, including: the emerging concept of satellite stem and progenitor cell heterogeneity, novel findings regarding the embryonic origin of muscle stem cells, and the requirement of Pax7 in satellite cells. Finally, this chapter discusses age- and disease-related decline of muscle stem cell function and provides an outlook on potential stem cell

transplantation therapies. In Chapter 7, Rolando and Taylor summarize the latest insights on the developmental origin of adult hippocampal neuronal stem cells with a focus on controlling signaling pathways and transcription factors. Then, they dissect the heterogeneous nature and function of adult neurogenic stem cells and niches and, in this context, the role of important signaling pathways. Finally, this chapter discusses recent insights into the role of adult hippocampal neuronal stem cells in epilepsy, aging, and depression. In Chapter 8, Leeman et al. review recently discovered lung stem and progenitor cells. They summarize the identification of several different lung epithelial stem cells, the role of lung stromal and endothelial cells, and their relevance for lung cancers. Discussed are further recent advances toward cell-based therapies by applying bone marrow-derived mesenchymal stem cells and directed differentiation of induced pluripotent stem cells. In Chapter 9, Yang and Oatley review spermatogonial stem cells in physiological and pathological conditions. They first discuss the origin of spermatogonial stem cells, then the molecular mechanisms regulating their maintenance, and the latest insights into germ cell tumor formation. In Chapter 10, Shin and Kaestner describe recently discovered hepatic progenitor cells. They discuss competing and controversial theories regarding the cellular origin and precise identity of these stem cell-like cells. In Chapter 11, Kopan et al. review the role of nephrogenic progenitors in kidney morphogenesis and dissect extrinsic regulatory influences by stromal signals, in addition to intrinsic transcriptional controls. They then discuss the impact of these latest insights on renal hypoplasia and the general control of cessation of nephrogenesis.

In Chapter 12, Rezza et al. provide a niche-centric view on the general intrinsic regulation of stem cells and their extrinsic control by the microenvironment. A dissection of the cellular organization of adult stem cell niches is followed by an extensive discussion of established and novel molecular regulators in adult stem cell niches. It closes with a brief discussion of stem cell niche dysfunction in aging and cancer. The final Chapters 13 and 14 establish in greater detail the stem cell and niche-related processes and molecular mechanisms that are dysregulated in cancers and during aging, respectively. Atlasi et al. in Chapter 13 first provide a general discussion of the historical perspective, the definitions, and the emerging concept of cancer stem cells. In addition, they analyze the control of cancer stem cells by signaling pathways with a focus on Wnt/β-catenin signaling, and discuss the similarities of germ cell tumors with embryonic pluripotent stem cells. Finally, Jung and Brack review in Chapter 14 the dynamic changes in stem

cells during aging that are only recently beginning to be uncovered. They discuss the molecular players in cellular aging and the extrinsic regulation mediating aged cellular and tissue homeostasis. They finally provide important examples of aging mechanisms in major well-known stem cell systems.

This volume of *Stem Cells in Development and Disease* is a collection of 14 timely and comprehensive reviews on the current knowledge and recent insights of stem cell functions in several different organ systems. New biotechnological breakthroughs in the past decade have brought tremendous advances that have greatly increased our understanding of stem cell functions, which ultimately brings us closer to the prospect of applying stem cell therapies to human disease. It is my hope that reading the diverse chapters in this volume will provide the different stem cell fields with new ideas and fresh perspectives.

MICHAEL RENDL

CONTENTS