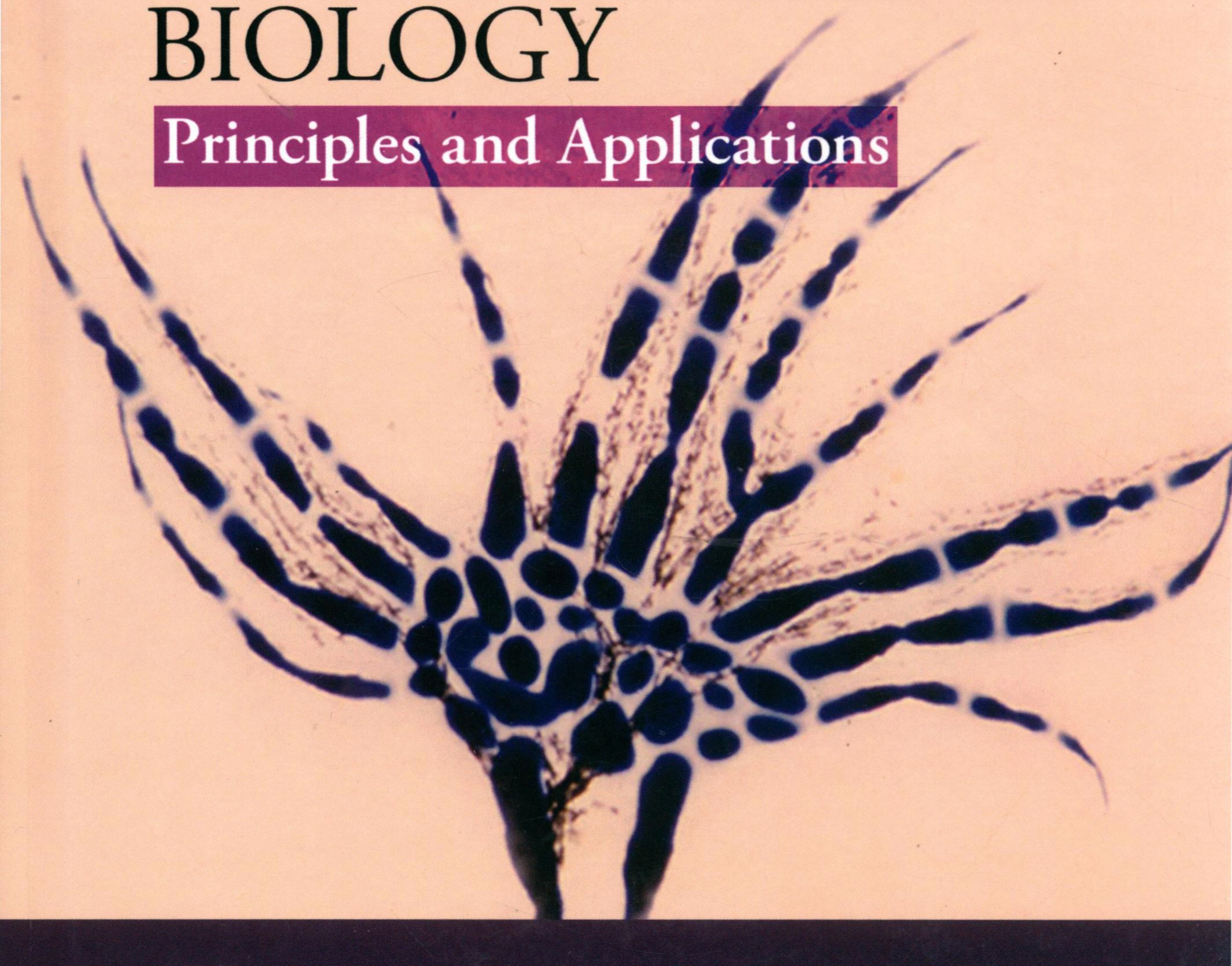
edited by

David M. Gardiner

CRC Press Series in
Regenerative Engineering

REGENERATIVE ENGINEERING AND DEVELOPMENTAL BIOLOGY

Principles and Applications



CRC Press
Taylor & Francis Group

BIOMEDICAL SCIENCE

edited by
David M. Gardiner

CRC Press Series in
Regenerative Engineering

REGENERATIVE ENGINEERING AND DEVELOPMENTAL BIOLOGY

Principles and Applications

Regenerative Engineering and Developmental Biology: Principles and Applications examines cutting-edge developments in the field of regenerative engineering. Specific attention is given to activities that embrace the importance of integrating developmental biology and tissue engineering, and how this can move beyond repairing damage to body parts to instead regenerate tissues and organs. The text furthermore focusses on the five legs of the field of regenerative engineering, including: materials, developmental biology, stem cells, physics, and clinical translation. This book was written by leading developmental biologists; each chapter examines the processes that these biologists study and how they can be advanced by using the tools available in tissue engineering/biomaterials. Individual chapters are complete with concluding remarks and thoughts on the future of regenerative engineering. A list of references is also provided to aid the reader with further research. Ultimately, this book achieves two goals. The first encourages the biomedical community to think about how inducing regeneration is an engineering problem. The second goal highlights the discoveries with animal regeneration and how these processes can be engineered to regenerate body parts. *Regenerative Engineering and Developmental Biology: Principles and Applications* was written with undergraduate and graduate-level biomedical engineering students and biomedical professionals in mind.

- Covers cutting-edge research on engineering regeneration related to the cell information grid
- Contains contributions from world-class researchers in cell regeneration engineering and technologies
- Delves into cell physiology related to proliferation, migration, and differentiation
- Examines tools that have been developed for genomics
- Includes substantive application chapters that examine specific organ/ tissue regeneration

K25679

CRC Press
Taylor & Francis Group
an informa business
www.crcpress.com

6000 Broken Sound Parkway, NW
Suite 300, Boca Raton, FL 33487
711 Third Avenue
New York, NY 10017
2 Park Square, Milton Park
Abingdon, Oxon OX14 4RN, UK

ISBN: 978-1-4987-2331-2
90000
9 781498 723312

Gardiner

REGENERATIVE ENGINEERING AND DEVELOPMENTAL BIOLOGY

CRC

Regenerative Engineering and Developmental Biology

Principles and Applications

Edited by
David M. Gardiner
Department of Developmental and Cell Biology
University of California Irvine
Irvine, California

CRC Press
Taylor & Francis Group
Boca Raton London New York

CRC Press is an imprint of the
Taylor & Francis Group, an **informa** business

CRC Press
Taylor & Francis Group
6000 Broken Sound Parkway NW, Suite 300
Boca Raton, FL 33487-2742

Printed on acid-free paper

International Standard Book Number-13: 978-1-4987-2331-2 (Hardback)

Visit the Taylor & Francis Web site at
http://www.taylorandfrancis.com

and the CRC Press Web site at
http://www.crcpress.com

Printed and bound in the United States of America by Sheridan

Regenerative Engineering and Developmental Biology

CRC PRESS SERIES IN

REGENERATIVE ENGINEERING

SERIES EDITOR

Cato T. Laurencin

University of Connecticut Health Center, Farmington, USA

PUBLISHED TITLES

Regenerative Engineering and Developmental Biology: Principles and Applications

David M. Gardiner

Preface

This book represents one of the next steps in the development of the field of regenerative engineering. Beginning with the view that we can achieve human regeneration through the convergence of developmental biology and engineering, this new field has moved forward as evidenced in publications, birth of the new journal *Regenerative Engineering and Translational Medicine*, and the establishment of the new Regenerative Engineering Society as part of the American Institute of Chemical Engineers. Collectively, these activities embrace the view of the importance of integrating developmental biology and tissue engineering to be successful moving beyond repairing damage to body parts in order to regenerate tissues and organs.

This new book is envisioned as the next step beyond the seminal textbook *Regenerative Engineering** that was written for an advanced undergraduate audience of biomedical engineering students. Unlike this book that laid out the broad range of topics and scientific disciplines to be integrated into regenerative engineering, *Regenerative Engineering and Developmental Biology: Principles and Applications* focuses on one of the core scientific disciplines, developmental biology. This is part of a series of books in the *Regenerative Engineering Series* with Dr. Cato Laurencin as the series editor. Collectively, these books will focus on one or multiples of the five legs of the field of regenerative engineering: materials, developmental biology, stem cells, physics, and clinical translation. The chapters within this book were written by leading developmental biologists who were challenged to think about how the processes that they study could be controlled by using the tools available through tissue engineering/biomaterials. Rather than discussing a list of genes and developmental pathways, the authors approached their topics more broadly, and provided insights and speculations about how to take the next step toward proregenerative therapies. For each chapter, there is enough detail to support these conclusions and thoughts about what to do next, along with references to guide the reader as to where to go for more details.

* Laurencin, C. T. and Khan, Y. (2013). *Regenerative Engineering.* CRC Press, Taylor & Francis Group. Boca Raton, FL.

This book is intended to achieve two goals. First, for the developmental biology audience, I encourage everyone to begin thinking about how inducing regeneration is an engineering problem. Historically, developmental biology has been about the discovery of how things work, and it is time to take that knowledge and use it to make something work. This is what engineers do; they build things that work. For the engineering audience, I encourage you to recognize that developmental biologists have discovered a lot about how embryos develop and animals regenerate, and have identified a number of key properties and processes that need to be engineered in order to regenerate body parts. At the end of this book, I have attempted to synthesize the major themes that were addressed repeatedly by the authors. I see this book as an experiment in which leading researchers in developmental biology were asked to write about what is most important from their perspective of how regeneration works. I assume that the important points are those that were written about the most.

Beyond the complexity and diversity of the biology of the many different model organisms discussed, three unifying principles emerged. The first is the recognition that the underlying cellular and molecular mechanisms of embryonic and regenerative development are highly conserved. When thinking about regeneration in a broad sense, it is evident the mechanisms for regeneration (mitosis, migration, and differentiation) evolved very early in the history of life on earth. Thus, it follows that all animals can regenerate to some degree, and that some can do it very well. Historically, developmental genetics has allowed us to discover the signals and pathways that regulate these cellular behaviors. Today, with advances in genomics and tools for genetic manipulation, we can study these mechanisms in an unlimited variety of organisms beyond the traditional, genetically amenable model organisms. We thus are able to revisit the classic models of regeneration in order to tease apart the sequence of events that begin with injury and lead eventually to regeneration of damaged or lost structures.

Equally important is the second principle that the pathways for making an organ in the embryo can be reused for remaking it (regeneration) in the adult. Although there might be differences in the details of controlling these mechanisms in embryos or adults, the developmental pathways worked at least once (during embryonic development), even in animals that do not regenerate well as adults. Therefore, accessing and controlling these developmental pathways are essential, and viable, for engineering regeneration. The conservation of pathways is the remarkable discovery of modern developmental genetics, and the key to regeneration is discovering how to regulate the pathways after injury.

Finally, and most importantly for what actually needs to be engineered, is the principle that we need both the building blocks (the cells) and the instruction manual for how to put the blocks together in order to rebuild a lost or damaged structure. A focus of several of the chapters is on what cells can do (proliferate, migrate, and differentiate/dedifferentiate) leading to the production of a population of regeneration-competent cells. But we know that you need more than just the cells; you also need the information that tells the cells where to go and what to make. This is the regeneration blueprint that we now refer to as the Information Grid. In the end, regeneration is about the replacement of the lost function and not just the structure. Function is an emergent property that is created when different cells become appropriately organized into a functional structure, and it is this information for organizing the cells that is encoded in the Information Grid.

Regenerating the Information Grid by necessity is the goal of regenerative engineering. Advances in how to make regeneration-competent cells (e.g., stem cells, the topic of one of the books in the *Regenerative Engineering Series*) will almost certainly take care of the challenge of getting the building blocks for regeneration in the near future. However, without the information required to orchestrate the behaviors of these cells and their progeny, we will not be able to regenerate structures that restore the lost function. The challenge lies in learning how to provide the necessary information, and I argue that this information has to come from the regeneration engineers. There may come a day in the distant future when it will be possible to induce regeneration of the Information Grid endogenous, but we need to remember the urgency for patients today in need of effective regeneration therapies. The challenge today is twofold; we need to understand what the information is and we need to use the engineering toolbox to provide and to control that information.

Acknowledgments

Many people have put in tremendous effort to think and write about the problem of how to engineer regeneration. They have shared their views about how regeneration works in the context of their particular areas of expertise. They also have shared their best and most creative ideas. In the end, this volume has captured a view of where the field of regeneration biology is in 2017, and we will be able to look back and see how the field has moved forward and built upon these ideas. Most importantly, the goal of this book is to catalyze interactions between developmental biologists and regenerative engineers. On behalf of the many authors, I hope that we have been successful in communicating the views from the side of embryonic and regenerative developmental biology. I therefore thank all the authors for their efforts and their patience. Your contributions are very much appreciated.

I also thank Michael Slaughter, our production assistant at CRC Press, for his patience and support from the beginning to the end, and Dr. Cato Laurence for his vision and efforts leading to the inception and completion of this project. Finally, I express my special thanks to Dr. Susan Bryant for her never-ending support, encouragement, and patience as I worked through the process of bringing this book to completion.

Editor

David M. Gardiner is a professor in the department of developmental and cell biology at the University of California Irvine (UCI), Irvine, California. He received his BA degree in biology from Occidental College, Los Angeles, California; his PhD degree from the Scripps Institution of Oceanography at University of California, San Diego, San Diego, California; and his postdoctoral training at The University of California, Davis, Davis, California. His research has been focused on discovering the mechanisms regulating limb regeneration in salamanders. He pioneered the use of the axolotl (*Ambystoma mexicanum*) as a model system for studies of vertebrate regeneration and developed the accessory limb model as an assay for bioactive compounds that induce dedifferentiation, blastema formation, and limb regeneration. This novel assay is the basis for ongoing studies to identify molecular pathways that regulate regeneration in humans. Professor Gardiner is a fellow of the American Association for the Advancement of Science, a recipient of the Marcus Singer Medal for Excellence in Regeneration Research, and a recipient of the Frontiers in Stem Cell and Regeneration Biology Pioneer Award. He is an author of more than 100 articles and has served on numerous peer review committees, journal editorial boards, and scientific advisory boards. He serves as the associate dean for research and academic affairs in the Francisco J. Ayala School of Biological Sciences at the UCI.

Contributors

Alaa Abdelhamid
Tissue Engineering and Biomaterials Research Unit
College of Dentistry
Qassim University
Al-Mulida, Kingdom of Saudi Arabia

Cristian Aguilar
Department of Biology and Chemistry
Azusa Pacific University
Azusa, California

Md. Ferdous Anower-E-Khuda
Department of Cellular and Molecular Medicine
University of California
La Jolla, California

Joelle Baddour
Department of Chemical and Biomolecular Engineering
Rice University
Houston, Texas

Caroline Beck
Department of Zoology
University of Otago
Dunedin, New Zealand

Susan V. Bryant
Department of Developmental and Cell Biology
University of California Irvine
Irvine, California

Diane Carlisle
Department of Neurological Surgery
and
Department of Medicine
Presbyterian Hospital
University of Pittsburg
Pittsburgh, Pennsylvania

David Chambers
Wolfson Centre for Age-related Diseases
King's College London
London, United Kingdom

Cheng-Ming Chuong
Department of Pathology
Keck School of Medicine
University of Southern California
and
Department of Pathology
Herman Ostrow School of Dentistry
University of Southern California
Los Angeles, California

and

Research Center for Developmental Biology and Regenerative Medicine
Graduate School of Clinical Dentistry
National Taiwan University
Taipei, Taiwan

and

Integrative Stem Cell Center
China Medical University
China Medical University Hospital
Taichung, Taiwan

Peter Currie
Australian Regenerative Medicine Institute
Monash University
Clayton, Victoria, Australia

Carlos Díaz-Castillo
Department of Developmental and Cell Biology
and
Department of Evolution and Ecology
University of California Irvine
Irvine, California

Karen Echeverri
Department of Genetics, Cell Biology and Development
University of Minnesota
Minneapolis, Minnesota

Ophelia Ehrlich
Australian Regenerative Medicine Institute
Monash University
Clayton, Victoria, Australia

José E. García-Arrarás
Department of Biology
University of Puerto Rico
San Juan, Puerto Rico

David M. Gardiner
Department of Developmental and Cell Biology
University of California Irvine
Irvine, California

James Godwin
The Jackson Laboratory
Bar Harbor, Maine

Yona Goldshnmit
Australian Regenerative Medicine Institute
Monash University
Clayton, Victoria, Australia

Hannah Grover
Bioengineering Program
Univeristy of Maine
Orono, Maine

Justin Guay
Department of Biology
Allen Discovery Center
Tufts University
Medford, Massachusetts

Celia Herrera-Rincon
Department of Biology
Allen Discovery Center
Tufts University
Medford, Massachusetts