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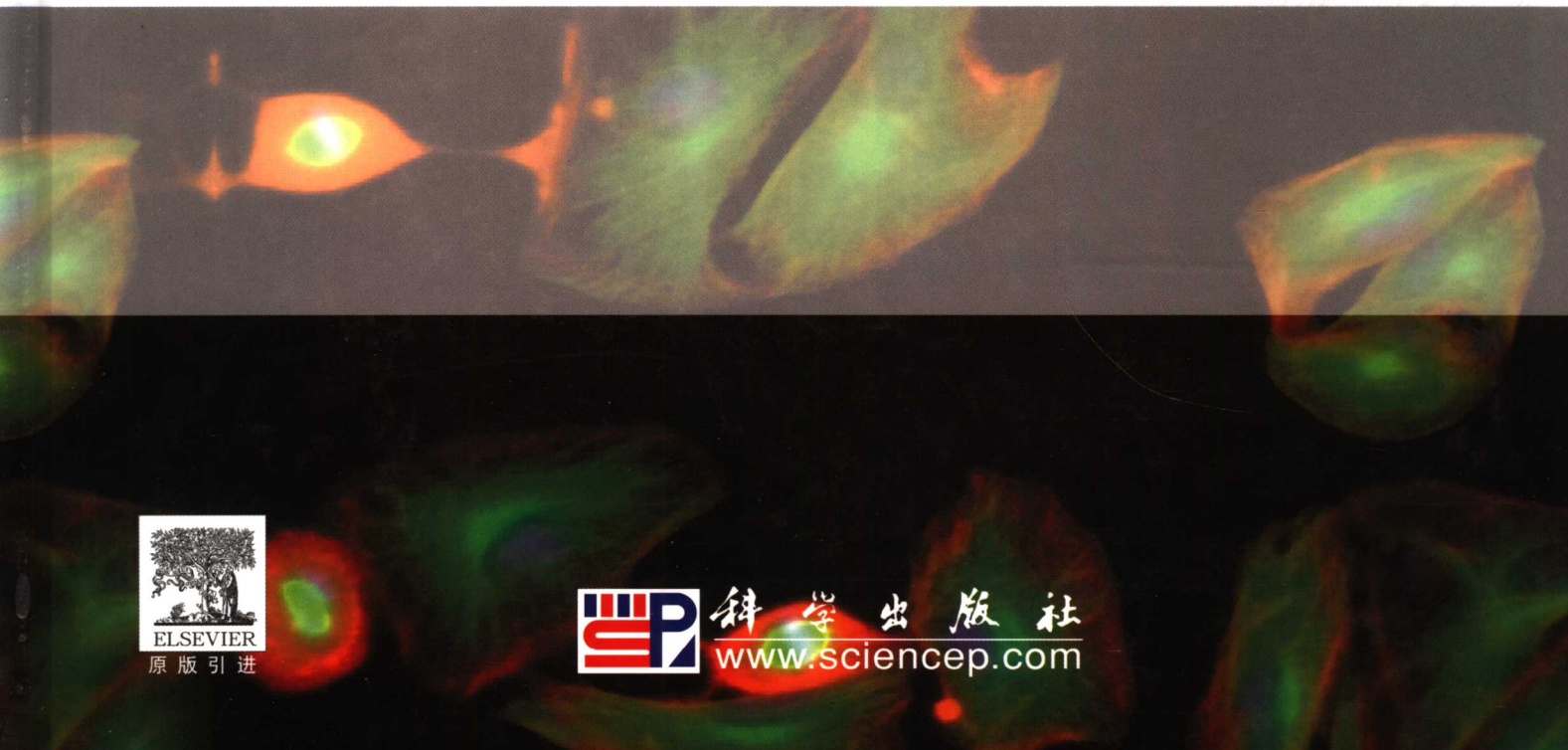
Regenerative Biology and Medicine

再生生物学与再生医学

David L. Stocum



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序　言

我的大部分研究是在 Illinois Urbana-Champaign 大学进行的，主要研究两栖动物再生肢体的芽基如何自我组装成替代肢的机制。后来，在印地安那大学 Indianapolis 分校担任院长这段较长的时间中，由于再生学的广阔前景，我开始对其产生浓厚的兴趣，尤其是当 1992 年“神经元不能再生”这个信条被打破的时候，以及 20 世纪 60 年代研究证实哺乳动物大脑中存有能产生新神经元和神经胶质的干细胞。这一新观点导致了一门研究生课程的产生与发展，而这门课我已经在生物系教授了很多年——再生生物学和再生医学。

再生生物学和再生医学是个快速发展的领域，它旨在探寻再生的机制并应用于疾病损伤后恢复组织结构和功能的治疗策略。再生生物学的研究涵盖了组织、器官、附属器等广泛领域的多种动物模型。再生医学包含了细胞移植、生物化人工组织的构建（即“组织工程”）以及原位残余组织的再生诱导。组织工程方面的教科书已经有很多，但主要都是针对工程师的。关于更广阔的再生生物学和再生医学领域的教科书目前还没有。更重要的是，我们应该从更深的层次去理解它的生物学特性而不局限于目前已知的知识。肢体缺失是关于非哺乳动物再生的一个重要讨论部分，例如两栖类，用来作为再生医学研究的动物模型。这些模型非常重要，因为它们能再生组织及其复杂的结构而哺乳动物则不能，这给我们提供了研究它们不同之处的机会并应用于哺乳动物组织再生的研究。因此，本书的主要目的是将再生生物学和再生医学的各个不同方面集中到一起，使读者全面了解各种已经完成和正在进行的基础及临床研究、两者的相互提示、已经取得的进展和潜在的治疗前景。

本书广泛适用于生物学、化学、生物工程学、医学系的研究生和高年级本科生，也适用于学术或临床型医生以及研究人员。第一章概括介绍了这门学科。第二章介绍纤维化这一创伤或疾病导致的组织损伤后最常见的反应。第三章到第十二章介绍再生生物学和相应的特定组织的再生医学。第十三章详细介绍了有关成体干细胞发育潜能的实验研究。第十四章讨论了附属器再生的生物学特性，以及刺激成年蛙和哺乳动物的附属器再生的研究。第十五章综述了生物学和生物伦理学所面临的问题以及发展完善再生医学所面临的挑战。

本书可以以各种方式阅读。阅读第一章和第十五章，以及各章的小结（也可以不读）能对本书的内容有个大概的了解。我在中间的章节详细讨论了不同组织、器官和附属器的再生生物学和再生医学。这些章节能帮助理解再生学的机制和在如何操控组织再生或通过纤维化使组织更快愈合方面所做的研究。

再生生物学和再生医学领域发展非常快，每周都有很多的新发现和报道，大量的文章发表。大量的著作促成了这本书的完成，然而关于再生生物学和再生医学方面的书籍我最多只参考了百分之五。当本书出版时，书中的数据无疑已经陈旧，但我希望书中提到的观点和指导方向仍然是明确的，并能引出现在和将来的研究者对其的新的诠释。

感谢印地安那大学 Indianapolis 分校让我能在担任院长职务的最后阶段抽身完成这本书，感谢 Eli Lilly 公司和印地安那 21 世纪研究技术基金对再生生物学和再生医学中心提供的支持。我非常感谢我

的朋友兼同事 Karen Crawford，Luisa Ann Di Pietro，E. Brady Hancock，Andrew Hawks，Ellen Heber-Katz，George Malacinski，Anton Neff，Rosamund Smith 等对我的手稿提出了宝贵意见。我尤其感激我在新德里的朋友兼同事 Iqbal Niazi，他阅读了我的整篇手稿，并对书的内容和编排提出了宝贵的建议。最后，我要感谢编辑 Luna Han 对我的鼓励、指导和耐心以及我的项目管理人 Carl M. Soares。如有遗漏或错误实属本人之过。

David L. Stocum

Indianapolis

2006 年 8 月

（曹谊林　译）

Preface

Most of my bench research career was spent at the University of Illinois Urbana-Champaign investigating the mechanisms by which the blastema of the regenerating amphibian limb self-organizes into replacement parts. Subsequently, during a relatively long decanal administrative stint at the "starship" Indianapolis campus of Indiana University (Indiana University-Purdue University Indianapolis), I became interested in regeneration from a much broader perspective, particularly when the dogma of "no new neurons" disintegrated in 1992 with the confirmation of reports from the 1960s that the mammalian brain harbored stem cells that were capable of making new neurons and glia. This new perspective led to the development of a beginning graduate course titled "Regenerative Biology and Medicine", which I have now taught in the Department of Biology for several years.

Regenerative biology and medicine is a rapidly developing field that seeks to understand the mechanisms of regeneration and apply that understanding to the development of therapeutic strategies to restore tissue structure and function compromised by injury or disease. The study of regenerative biology covers a wide range of tissues, organs and appendages in several animal models. Regenerative medicine encompasses cell transplantation, construction of bioartificial tissues ("tissue engineering") and the chemical induction of regeneration from residual tissues *in situ*. Several texts on tissue engineering are available, but these are geared primarily to engineers. No texts exist on the broader field of regenerative biology and medicine. Furthermore, in the literature on regenerative medicine, I have seen virtually no overt recognition of the fact that to realize its immense potential, we must gain a much deeper understanding of the biology of regeneration than we currently possess. Also missing is any discussion of strong non-mammalian regenerators, such as the amphibians, as model systems that are relevant to regenerative medicine. These models are important, since they regenerate tissues and complex structures that mammals do not, thus offering an opportunity to learn what is different about them and apply it to mammalian regeneration. Thus, the primary objective of the present book was to bring the many different facets of regenerative biology and medicine together in one place to give the reader an overall view of the kinds of fascinating basic and clinically-oriented research that have been, and are being done, how each informs the other, what progress has been made, and the therapeutic potential that exists.

This book is directed to a broad audience of graduate and advanced undergraduate students in biology, chemistry and bioengineering, medical students, academic and clinical physicians, and research investigators. Chapter 2 deals with fibrosis, the most common response to tissue damage caused by injury or disease. Chapters 3–12 deal with the regenerative biology and the corresponding regenerative medicine of specific clusters of tissues. Chapter 13 details experiments on the developmental potency of adult stem cells and Chapter 14 discusses the biology of appendage regeneration and attempts to stimulate the regeneration of appendages in adult frogs and mammals. The book can be read in several ways. Reading Chapters 1 and 15, and/or all the chapter summaries will provide an abridged content. I have provided the details of regeneration and regenerative medicine for different tissues, organs and appendages between these two chapters. These details are important for understanding mechanisms of regeneration and the kinds of efforts that are being made to manipulate tissues toward regenerative pathways or faster healing by fibrosis.

The field of regenerative biology and medicine is moving incredibly fast, with many new discoveries reported each week, creating torrents of published papers. A massive amount of literature went into the synthesis of this book, yet I have sampled probably no more than 5% of the work on regenerative biology and medicine that exists. The data described here will undoubtedly already be obsolete when the book is published, but the ideas and directions of the field set forth here will, I hope, remain clear and inviting of new interpretations by current and upcoming investigators.

I am grateful to IUPUI for granting me a leave at the end of my deanship to write this book and to Eli Lilly and Company and the Indiana 21st Century Research and Technology Fund for their support of the research of the Center for Regenerative Biology and Medicine, some of which is included here. I very much appreciate the helpful critiques of the manuscript by friends and

colleagues: Karen Crawford, Luisa Ann Di Pietro, E. Brady Hancock, Andrew Hawks, Ellen Heber-Katz, George Malacinski, Anton Neff, and Rosamund Smith. I am particularly indebted to my friend and colleague in New Delhi, Iqbal Niazi, who read the whole manuscript and whose insights on content and organization were invaluable. Finally, I am grateful to my editor, Luna Han, for her encouragement, guidance and patience in this endeavor, and to my project manager, Carl M. Soares. Any sins of omission or commission are mine and mine alone.

David L. Stocum
Indianapolis
August, 2006

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