Preface

Regeneration, the homeostatic ability to maintain tissue structure in the face of normal cell turnover or loss of tissue damaged by trauma or disease, is a developmental process that continues throughout life and is essential for life. Investigation of the cellular mechanisms of natural regeneration, including the molecular properties of regeneration-competent cells permissive for regeneration, and the interactions of these cells with surrounding instructive or support cells has become one of the hottest topics in the field of regeneration and developmental biology. It is now understood that widely different regenerative phenomena, from epithelial cell turnover to limb regeneration in amphibians share many common features. The value of comparative molecular analysis of regeneration-competent versus regeneration-deficient tissues, via bioinformatics and systems biology approaches is being recognized as a way to provide insights into why a tissue or appendage regenerates in some species or mutants, but not in others.

Fifty years ago, John Gurdon showed that the nuclei of frog tadpole intestinal cells could be reprogrammed by egg cytoplasm to a zygotic state that would support the development to adulthood of a clone of the donor. Sixteen years ago, Ian Wilmut and Keith Campbell showed the same thing for mammalian nuclei in cloning Dolly, the sheep. And just 6 years ago, Shinya Yamanaka's laboratory identified four transcription factors involved in the pluripotency circuits of embryonic stem cells (ESCs) that, when transfected into skin fibroblasts, reprogrammed them to ESC-like cells called induced pluripotent stem cells (iPSCs) that could be directed to differentiate into a wide variety of adult cell types. Gurdon and Yamanaka were awarded the 2012 Nobel Prize in Medicine for their work, which has opened the door to potential regenerative medical therapies for many types of injuries and degenerative diseases, as well insights into disease etiology and the ability as to screen for therapeutic molecules and compounds. Insights into both the mechanisms of nuclear reprogramming and how to use dedifferentiated cells are growing rapidly.

This book entitled "New Perspectives in Regeneration" is a compendium of current findings in vertebrate and mammalian wound healing and regeneration. In this volume we present 11 reviews that cover a wide range of regenerative topics, from wound repair and its relation to regeneration, through the regeneration of lenticular, neural, and musculoskeletal tissues and limb regeneration, to the epigenetics of regeneration and the role of the cell cycle. Nuclear reprogramming and cellular plasticity are recurring themes throughout the volume.

We begin in the first part with two papers on wound repair. The first by Wietecha, Cerny, and DiPietro describes in-depth the important process of angiogenesis. One of the most novel parts of this chapter is the focus on how vessels are degraded and the molecules involved. This is key during the remodeling phase of the healing response and of course is what is important to block tumor formation. The second is a general and thorough review by Kawasumi, Sagawa, Hayashi, Yokoyama, and Tamura comparing wound repair and regeneration in amphibians and mammals, with a focus on limb regeneration.

In the first paper of the second part, Monaghan and Maden examine the role and importance of biological plasticity in vertebrate appendage regeneration to provide a framework for asking questions about how to look at models of regeneration. This is especially important in the lens regeneration model presented in the next chapter by Henry, Thomas, Hamilton, Moore, and Perry. Only certain larval and adult fish, salamanders, and frogs are known to regenerate their lens and these include newts, salamanders, fish, and Xenopus. A thorough review of the molecular pathways involved in this process in Xenopus is presented.

Part III begins with a paper by Viswanathan and Joshi that explores the role of stem cells in all aspects of regenerative medicine, including cell-based therapies, tissue engineering, and the activation or recruitment of stem cells to organs of interest. Next, reviews by Cameron, Milner, Lee, Cheng, Fang, Jasiuk, and by Milner and Cameron, address musculoskeletal regeneration and compare and contrast amphibian and mammalian systems. Both these papers review the use of stem cells and dedifferentiation and address current important issues of tissue engineering.

In the fourth part are two reviews of CNS regeneration. The first by Steward, Sridhar, and Meyer, compares the successful regeneration of mammalian PNS to the much poorer regeneration of the CNS, and reviews the reprogramming strategies used to convert non-neural cells to neural cells. The second, by Zupanc and Sirbulescu, explores the teleost fish as a model to study the regeneration of CNS tissue. Teleost fish are particularly interesting because their tails are often lost to predator fish and they regenerate not only their tails but also their spinal cord. Thus, learning what they use to regenerate is intriguing and revealing.

Finally, in the last part, we present two papers exploring subcellular events that support a regenerative response. The first paper by Maki and Kimura describes a

study exploring the epigenetic changes occurring during regeneration. Here, besides a review of general epigenetic changes previously reported is a discussion of a highly novel finding, the use of an oocyte-type linker histone protein, B4, that is specifically used in the embryo and then reappears in regenerating newt lens tissue during trans-differentiation. The second paper by Heber-Katz, Zhang, Bedelbaeva, Song, Chen, and Stocum is a comparison between amphibian and mouse regenerative tissue and examines cell-cycle regulation in the axolotl limb and MRL mouse ear tissue and finds striking similarities in terms of G2 arrest and the expression of proteins specific to this process, including Evi-5.

We hope you enjoy it!

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http://www.springer.com/978-3-642-35809-8

New Perspectives in Regeneration
Heber-Katz, E.; Stocum, D.L. (Eds.)
2013, X, 281 p., Hardcover
ISBN: 978-3-642-35809-8