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978-0-521-83798-9 - Retinal Development

Edited by Evelyne Sernagor, Stephen Eglén, Bill Harris and Rachel Wong

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## RETINAL DEVELOPMENT

This advanced text takes a developmental approach to the presentation of our current understanding of how vertebrates construct a retina. The book starts by examining how a patch of ectoderm becomes committed to make the eyes. It proceeds through the generation of the retinal neurons and how they connect up, culminating in the emergence of the first light responses. Written by experts in the field, each of the 17 chapters covers a specific step in this process, focusing on the underlying molecular, cellular and physiological mechanisms. There is also a special section on emerging technologies including genomics, zebrafish genetics and stem cell biology that are starting to yield important new insights into retinal development. Primarily aimed at professionals, both biologists and clinicians working with the retina, this book provides a concise and up-to-date view of what is known about vertebrate retinal development. Since the retina is ‘an approachable part of the brain’, this book is also attractive to all neuroscientists interested in development, as processes required to build this exquisitely organized system are ultimately relevant to all other parts of the central nervous system.

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# RETINAL DEVELOPMENT

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‘This book is dedicated to the prevention of blindness.’

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## Foreword

The editors have assembled an impressive authorship to produce this book on development of the retina. There are several reasons why this is timely. Over the last decade there have been rapid advances in our understanding of the mechanisms involved in formation of the eye and determination of the fate of cells. This has been driven by an explosion of laboratory techniques that have allowed the study of gene expression and characterization of cell and tissue behaviour.

As a consequence there is increasing knowledge of what determines cell function, and of the behavioural relationship between cells. This has resulted in an understanding of genetically determined disease in humans. Many genes' products have been identified during development because they are highly expressed and mutations in these genes have been identified as being responsible for developmental abnormalities in man. Some of these genes express at low levels in adult life fulfilling a house-keeping function, and mutations in these have also been identified as giving rise to progressive retinal degeneration.

Findings from studies of development are of crucial importance to the current attempts to devise biological treatment of retinal diseases. There is ample evidence that growth factors delay cell death due to apoptosis in genetically determined retinal dystrophies in animals, and therapeutic trials in man have been initiated. There is still some doubt as to which agent may be the most appropriate to achieve suppression of apoptosis. Our knowledge of the mechanisms of programmed cell death is derived largely from studies of development and alternative therapeutic approaches may become evident as this work progresses.

There are also efforts to explore the possible role of cell transplantation. This is a major development in medicine in general, and the potential of treating retinal disease has been explored for some years. This was initiated by attempts to replace photoreceptor cells in retinal dystrophies. Many of the early efforts were disappointing but success has been achieved. Cell transplantation may also be applicable to other retinal diseases. Replacement of retinal pigment epithelium would be important in treatment of age-related macular disease, and of endothelial and pericytes would be appropriate in retinal vascular disease such as diabetic retinopathy. Many questions need to be addressed to accomplish success with this approach. What is the most appropriate source of the cells capable of assuming the functional characteristics of retinal cells? What environmental conditions would induce these pluri potential cells to form neurons, retinal pigment epithelium, glial cells and vascular

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cells, and how could these cells be induced to assume appropriate functional relationships with neighbouring cells?

Studies of development are likely to provide answers to these questions. The process of regeneration of the eye in amphibia has been intriguing since it was first observed nearly three centuries ago. With modern techniques it is possible to identify the biology of the phenomenon. The constant enlargement of the retina from its anterior edge in fish throughout life allows investigation of the mechanisms of cell and tissue generation. The relevance of this observation to mammals is illustrated by the observation that pluripotential cells can be retrieved from human donor eyes from the posterior ciliary body.

Thus this book is of great interest both to biologists and to those involved in the study of, and developing treatment for, retinal disease in humans. There are questions that can be addressed only by the study of the embryonic retina, and others that can most easily be answered by the development biologist. This book gives an invaluable account of the biology of the developing retina that demonstrates the value of such studies. Above all it illustrates well the value of research from one discipline to those in another.

Professor Alan Bird  
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## Preface

Vision is undoubtedly our most ‘cherished’ sense, and blindness the most tragic loss in perceiving the world around us. Visual perception begins in the eye, of which the retina is the most important component for interpreting visual signals, including colour, shape and movement. The retina is an ocular extension of the brain specialized in receiving and processing light and images. Although it is merely a few 100 micrometres thick and contains only seven cell types, the retina performs very sophisticated visual processing. Ultimately, it sends ALL information about the outside world to visual centres of the brain via the optic nerve in the form of coded electrical impulses. Understanding how the retina is organized and how it functions is thus of fundamental importance for understanding the entire visual system. It is therefore not surprising that the retina has been the focus of attention of many scientists since the late nineteenth century, when Cajal, in 1893, provided the first account of the anatomical organization of the vertebrate retina.

Although our knowledge of how the retina is organized and functions in adult organisms is absolutely essential, understanding how it is assembled during development is no less important. Indeed, when normal development is impaired, irreversible damage can result, in some cases even blindness. Moreover, understanding how the retina develops is attractive not only to developmental neuroscientists interested in vision, but to all neuroscientists interested in development, because the retina is ‘an approachable part of the brain’, and developmental processes required to build this exquisitely organized system, with well-defined layers and a limited number of cell types, are ultimately relevant to all other parts of the central nervous system.

In the last 10 to 15 years, the advent of powerful new techniques in genetics, molecular biology, imaging and electrophysiology have led to a huge leap forward in our understanding of how the retina develops. The goal of this book is to review all these new advances, while placing them in a chronological context of developmental events, from cell proliferation to the building of neural circuits involved in visual processing. Our intent is to deliver a well-illustrated source of up-to-date information for scientists interested in retinal research, retinal development or development of other parts of the vertebrate brain. We hope that the information gathered will provide deeper insights to all students and researchers aiming to achieve a better understanding of this fascinating part of the brain. We have also deliberately

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*Preface*

highlighted many open questions in every chapter, in the hope that they will inspire other scientists.

### **Reference**

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## Acknowledgements

We wrote this book because it seemed to us there was none available on the development of the vertebrate retina and that such a book would be valuable to both developmental biologists and to those doing translational work, especially in developmental aspects of retinal disease. Our plan was to cover the development of the retina ontogenetically like a developmental story.

We each do research on different aspects of retinal development and were able to write on these aspects but knew that this story would not be complete unless it covered stages and approaches that were the domain of others. Part of the fun of this book for us has been working with these scientists who have tried very hard to oblige us by conforming to a standard chapter style, which we thought was important to the cohesion and uniformity of a book that has been the effort of many. We therefore take this opportunity to thank all the authors for their excellent contributions and for putting up with our prescriptive demands.

Finally just a quick word on why, in spite of our desire for uniformity between chapters, in some chapters the figures show the pigment epithelium at the top while in other chapters the pigment epithelium is shown at the bottom. We tried to get everyone to do it the same way, but this just stirred a large debate that prompted one of us to write this poem in frustration.

The eye is a globe when looked at whole

It has both a dorsal and ventral pole.

Clinical explorers that chart passages North

Claim the PE's on top. "We took photos. We've got 'em"

But Dev Neuro types who to the South sally forth

Take photos that show it's at the bottom.

Finally, we decided that, as long as the authors labelled their figures, we would allow both views.

Besides the authors, we would like to thank Katrina Halliday at Cambridge University Press who helped us put this enterprise together, as well as Clare Georgy and Jo Bottrill who have helped in the final production of the book. We would also like to thank Anne Cowell for her relentless, scrutinizing editing work. We also thank baby Samuel for lending us his beautiful eyes for the cover of the book.

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*Acknowledgements*

Finally, we would like to thank Professor Alan Bird who agreed to write a foreword, and our many colleagues who, since the time of Ramon y Cajal, have contributed to our current understanding of retinal development.