

NEUROMETHODS

Series Editor
Wolfgang Walz
University of Saskatchewan
Saskatoon, SK, Canada

For other titles published in this series, go to
www.springer.com/series/7657

Animal Models for Retinal Diseases

Edited by

Iok-Hou Pang

Glaucoma Research, Alcon Research Ltd, Fort Worth, TX, USA

Abbot F. Clark

*The North Texas Eye Research Institute and Department of Cell Biology and Anatomy,
University of North Texas Health Science Center, Fort Worth, TX, USA*

 **Humana Press**

Editors

Iok-Hou Pang
Glaucoma Research
Alcon Research Ltd
Fort Worth, TX
USA
iok-hou.pang@alconlabs.com

Abbot F. Clark
The North Texas Eye Research Institute
and Department of Cell Biology and Anatomy
University of North Texas Health Science Center
Fort Worth, TX
USA
abclark@hsc.unt.edu

ISSN 0893-2336 e-ISSN 1940-6045
ISBN 978-1-60761-540-8 e-ISBN 978-1-60761-541-5
DOI 10.1007/978-1-60761-541-5
Springer Dordrecht Heidelberg London New York

Library of Congress Control Number: 2009943043

© Springer Science+Business Media, LLC 2010

All rights reserved. This work may not be translated or copied in whole or in part without the written permission of the publisher (Humana Press, c/o Springer Science+Business Media, LLC, 233 Spring Street, New York, NY 10013, USA), except for brief excerpts in connection with reviews or scholarly analysis. Use in connection with any form of information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed is forbidden.

The use in this publication of trade names, trademarks, service marks, and similar terms, even if they are not identified as such, is not to be taken as an expression of opinion as to whether or not they are subject to proprietary rights.

While the advice and information in this book are believed to be true and accurate at the date of going to press, neither the authors nor the editors nor the publisher can accept any legal responsibility for any errors or omissions that may be made. The publisher makes no warranty, express or implied, with respect to the material contained herein.

Cover illustration: Inset: Cross section of the human eye (provided by National Eye Institute, National Institute of Health); Background: Cross section of the mouse retina (provided by Dr. Robert Mullins, University of Iowa).

Printed on acid-free paper

Humana Press is part of Springer Science+Business Media (www.springer.com)

Preface to the Series

Under the guidance of its founders Alan Boulton and Glen Baker, the Neuromethods series by Humana Press has been very successful, since the first volume appeared in 1985. In about 17 years, 37 volumes have been published. In 2006, Springer Science + Business Media made a renewed commitment to this series. The new program will focus on methods that are either unique to the nervous system and excitable cells or which need special consideration to be applied to the neurosciences. The program will strike a balance between recent and exciting developments like those concerning new animal models of disease, imaging, in vivo methods, and more established techniques. These include immunocytochemistry and electrophysiological technologies. New trainees in neurosciences still need a sound footing in these older methods in order to apply a critical approach to their results. The careful application of methods is probably the most important step in the process of scientific inquiry. In the past, new methodologies led the way in developing new disciplines in the biological and medical sciences. For example, Physiology emerged out of Anatomy in the nineteenth century by harnessing new methods based on the newly discovered phenomenon of electricity. Nowadays, the relationships between disciplines and methods are more complex. Methods are now widely shared between disciplines and research areas. New developments in electronic publishing also make it possible for scientists to download chapters or protocols selectively within a very short time of encountering them. This new approach has been taken into account in the design of individual volumes and chapters in this series.

Wolfgang Walz

Preface

Retinal diseases are leading causes of irreversible visual impairment and blindness, affecting over 100 million individuals worldwide. Age-related macular degeneration and glaucoma are the leading causes of blindness in the elderly, while diabetic retinopathy is the leading cause of visual impairment in middle-aged individuals. The prevalence of all three of these retinal diseases will continue to increase as our world's populations continue to age and diabetes becomes endemic. There are a wide variety of additional important retinal diseases, including various acquired retinal degenerations (e.g., retinitis pigmentosa), maculopathies, retinal vascular disorders (e.g., ischemic retinopathies such as central retinal vein occlusion, sickle cell retinopathy, retinopathy of prematurity), and inflammatory retinopathy, each of which has devastating consequences on our most important sense perception.

Appropriate study models, especially animal models, are essential to the understanding of the etiology, pathology, and progression of these diseases. They are also critical to the evaluation, development, and improvement of therapeutic strategies for these diseases. The overall objective of this book is to provide a survey of valuable techniques as well as animal models for the prominent retinal diseases. The book starts with an overview of the morphology of the retina, visual behavior, and genetics and genomics approaches for retinal research, followed by animal models for the research of specific human retinal diseases, e.g., retinal degeneration, age-related macular degeneration, retinopathy of prematurity, diabetic retinopathy, glaucoma, retinal ischemia, and retinal inflammation. Each chapter was written by recognized experts in their respective fields. We hope that this book is valuable to ocular investigators and ophthalmologists currently working in the area of retinal diseases and ophthalmology. Its detailed and practical descriptions of the models should also appeal to those interested in entering this fascinating and important field of research.

Fort Worth, TX
Fort Worth, TX

Iok-Hou Pang, Ph.D.
Abbot F. Clark, Ph.D.

Contents

| | |
|---|------------|
| <i>Preface</i> | <i>vii</i> |
| <i>Contributors</i> | <i>xi</i> |
| 1 Essentials of Retinal Morphology <i>Robert F. Mullins and Jessica M. Skeie</i> | 1 |
| 2 Visual Behavior <i>Robert M. Douglas, Trevor J. McGill, and Glen T. Prusky</i> | 13 |
| 3 Genetic and Genomic Approaches for Understanding Retinal Diseases <i>Gareth R. Howell and Simon W.M. John</i> | 25 |
| 4 Animal Models for Retinal Degeneration <i>Marijana Samardzija, Stephan C.F. Neubauss, Sandrine Joly, Malaika Kurz-Levin, and Christian Grimm</i> | 51 |
| 5 Animal Models for Age-Related Macular Degeneration <i>Joe G. Hollyfield and Lisa Kuttner-Kondo</i> | 81 |
| 6 Animal Models of Retinopathy of Prematurity <i>Susan E. Yanni and John S. Penn</i> | 99 |
| 7 Animal Models of Diabetic Retinopathy <i>Adrian M. Timmers, Casey M. Miller, and Li Zhu</i> | 113 |
| 8 Nonprimate Models for Glaucoma Retinopathy and Optic Neuropathy <i>Iok-Hou Pang and Abbot F. Clark</i> | 139 |
| 9 Primate Glaucoma Models <i>Ronald S. Harwerth</i> | 165 |
| 10 Animal Models of Retinal Ischemia <i>Jacky Man Kwong Kwong and Joseph Caprioli</i> | 191 |
| 11 Retinal Inflammation: Uveitis/Uveoretinitis <i>Reiko Horai and Rachel R. Caspi</i> | 207 |
| Index | 227 |

Contributors

JOSEPH CAPRIOLI • *Department of Ophthalmology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA*

RACHEL R. CASPI • *Laboratory of Immunology, National Eye Institute, National Institutes of Health, Bethesda, MD, USA*

ABBOT F. CLARK • *The North Texas Eye Research Institute and Department of Cell Biology and Anatomy, University of North Texas Health Science Center, Fort Worth, TX, USA*

ROBERT M. DOUGLAS • *Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, BC, Canada*

CHRISTIAN GRIMM • *Lab for Retinal Cell Biology, Department of Ophthalmology and Center for Integrative Human Physiology, University of Zurich, Zurich, Switzerland*

RONALD S. HARWERTH • *College of Optometry, University of Houston, Houston, TX, USA*

JOE G. HOLLYFIELD • *Department of Ophthalmology, Cole Eye Institute, Cleveland Clinic Lerner College of Medicine, Cleveland Clinic, Cleveland, OH, USA*

REIKO HORAI • *Laboratory of Immunology, National Eye Institute, National Institutes of Health, Bethesda, MD, USA*

GARETH R. HOWELL • *The Jackson Laboratory, The Howard Hughes Medical Institute, Bar Harbor, ME, USA*

SIMON W.M. JOHN • *The Jackson Laboratory, The Howard Hughes Medical Institute, Bar Harbor, ME, USA*
Department of Ophthalmology, Tufts University of Medicine, Boston, MA, USA

SANDRINE JOLY • *Lab for Retinal Cell Biology, Department of Ophthalmology, University of Zurich, Zurich, Switzerland*

MALAIKA KURZ-LEVIN • *Department of Ophthalmology, University Eye Hospital, Zurich, Switzerland*

LISA KUTTNER-KONDO • *Department of Ophthalmology, Cole Eye Institute, Cleveland Clinic Lerner College of Medicine, Cleveland Clinic, Cleveland, OH, USA*

JACKY MAN KWONG KWONG • *Department of Ophthalmology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA*

TREVOR J. MCGILL • *Casey Eye Institute, Oregon Health and Science University, Portland, OR, USA*

CASEY M. MILLER • *Alcon Research Ltd, Fort Worth, TX, USA*

ROBERT F. MULLINS • *Department of Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, IA, USA*

STEPHAN C.F. NEUHAUSS • *Institute of Zoology, University of Zurich, Zurich, Switzerland*

IOK-HOU PANG • *Glaucoma Research, Alcon Research Ltd, Fort Worth, TX, USA*

JOHN S. PENN • *Vanderbilt University School of Medicine, Nashville, TN, USA*

GLEN T. PRUSKY • *Department of Physiology and Biophysics, Weill Cornell Medical College, New York, NY, USA*

Burke Medical Research Institute, White Plains, NY, USA

MARIJANA SAMARDZIJA • *Lab for Retinal Cell Biology, Department of Ophthalmology, University of Zurich, Zurich, Switzerland*

JESSICA M. SKEIE • *Department of Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, IA, USA*

ADRIAN M. TIMMERS • *Alcon Research Ltd, Fort Worth, TX, USA*

SUSAN E. YANNI • *Vanderbilt University School of Medicine, Nashville, TN, USA*

LI ZHU • *Alcon Research Ltd, Fort Worth, TX, USA*