

Robert E. Anderson · Matthew M. LaVail
Joe G. Hollyfield
Editors

Recent Advances in Retinal Degeneration

Dedication



Nicolas G. Bazan, M.D., Ph.D.

Nicolas Bazan is a man of great talent and energy who has overcome many obstacles to achieve the tremendous success he now enjoys in retinal research. We are honored to dedicate this proceedings volume to him.

<https://link.springer.com/content/pdf/bfm%3A978-0-387-74904-4%2F1.pdf>

Robert E. Anderson · Matthew M. LaVail
Joe G. Hollyfield
Editors

Recent Advances in Retinal Degeneration

 Springer

Editors

Robert E. Anderson
Dean A. McGee Eye Institute
University of Oklahoma Health Science Ctr.
608 Stanton L. Young Blvd., DMEI 409
Oklahoma City, OK 73104 USA
robert-anderson@ouhsc.edu

Matthew M. LaVail
Beckman Vision Center
UCSF School of Medicine
10 Kirkham Street
San Francisco, CA 94143 USA
matthew.lavail@ucsf.edu

Joe G. Hollyfield
Cole Eye Institute
The Cleveland Clinic Foundation
9500 Euclid Ave. (i31)
Cleveland, OH 44195
hollyfj@ccf.org

The chapter “Characterization of Gene Expression Profiles of Normal Canine Retina and Brain Using a Retinal cDNA Microarray” has been retracted due to plagiarism. A large portion of its contents were copied from another paper.

ISBN: 978-0-387-74902-0

e-ISBN: 978-0-387-74904-4

Library of Congress Control Number: 2007936186

© 2008 Springer Science+Business Media, LLC

All rights reserved. This work may not be translated or copied in whole or in part without the written permission of the publisher (Springer Science+Business Media, LLC., 233 Spring Street, New York, NY10013, 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.

Printed on acid-free paper

9 8 7 6 5 4 3 2 1

springer.com

Preface

A Symposium on Retinal Degenerations has been held in conjunction with the biennial International Congress of Eye Research (ICER) since 1984. These Retinal Degeneration Symposia have allowed scientists and clinicians from around the world to convene and present their new research findings. The Symposia have been organized to allow sufficient time for discussions and one-on-one interactions in a relaxed atmosphere, where international friendships and collaborations would be fostered.

The XII International Symposium on Retinal Degeneration (also known as RD2006) was held from October 23–28, 2006 in San Carlos de Bariloche, Argentina. The meeting brought together 130 scientists, retinal specialists in ophthalmology and trainees in the field from all parts of the world. In the course of the meeting, 49 platform and 54 poster presentations were given, and a majority of these are presented in this proceedings volume. New discoveries and state of the art findings from most research areas in the field of retinal degenerations were presented. The RD2006 meeting was highlighted by three special lectures. The first was given by Dr. Ruben Adler, Johns Hopkins University Medical School, Baltimore, Maryland, USA. Dr. Adler discussed the hope, reality, and challenges of using stem cells to treat blinding diseases. The second was given by Prof. Pierluige Nicotera. Prof. Nicotera is a leading authority on apoptosis and presented an outstanding lecture on his latest exciting research. The last special lecture was given by Prof. Eliot Berson, Harvard Medical School, Cambridge, MA, who gave an illuminating and informative overview of his work on vitamin A and omega-3 fatty acids in treatment of retinitis pigmentosa.

The Symposium received international financial support from a number of organizations. We are particularly pleased to thank The Foundation Fighting Blindness, Owings Mills, Maryland, for its continuing support of this and the previous biennial Symposia, without which we could not have held these important meetings. In addition, for the third time, the National Eye Institute of the National Institutes of Health contributed to the meeting. We are also grateful to Dr. Konstantin Petrukhin for a travel award from Merck & Co., Inc. – USA. Funds from these organizations allowed us to provide 26 Travel Awards to young investigators and trainees working in the field of retinal degenerations. The response to the Travel Awards program was extraordinary, with 58 applicants competing for the 26 Awards.

We also acknowledge the diligent and outstanding efforts of Ms. Holly Whiteside, who carried out most of the administrative aspects of the RD2006 Symposium, designed and maintained the meeting website, and organized and edited the production of this volume. Holly is the Administrative Manager of Dr. Anderson's laboratory at the University of Oklahoma Health Sciences Center, and she has become the permanent Coordinator for the Retinal Degeneration Symposia. Her dedicated efforts with the Symposia since RD2000 have provided continuity heretofore not available, and we are deeply indebted to her.

We thank Ms. Maria Rosa Adamo of Zafiro Viajes, who provided extraordinary effort in arranging the travel and local program. Thanks also go to Kluwer Academic/Plenum Publishers for its publication.

Finally, we give our heart-felt thanks to our dear friend and colleague, Nicolas Bazan, for his help in every step of the organization and execution of this endeavor. He provided extraordinary input, from the selection of the meeting venue to the procurement of the wine that all of us enjoyed. He also gave an outstanding lecture. We are delighted to dedicate this volume to him.

Robert E. Anderson
Matthew M. LaVail
Joe G. Hollyfield

Contents

Contributors	xvii
---------------------------	------

Part I Keynote Lectures

Curing Blindness with Stem Cells: Hope, Reality, and Challenges	3
Ruben Adler	
Retinal Degenerations: Planning for the Future	21
Eliot L. Berson	

Part II Neuroprotection

Neurotrophins Induce Neuroprotective Signaling in the Retinal Pigment Epithelial Cell by Activating the Synthesis of the Anti-inflammatory and Anti-apoptotic Neuroprotectin D1	39
Nicolas G. Bazan	
On the Role of CNTF as a Potential Therapy for Retinal Degeneration: Dr. Jekyll or Mr. Hyde?	45
William A. Beltran*	
Nanoceria Particles Prevent ROI-Induced Blindness	53
Junping Chen*, Swanand Patil, Sudipta Seal, and James F. McGinnis	
An in-vivo Assay to Identify Compounds Protective Against Light Induced Apoptosis	61
Yogita Kanan*, Anne Kasus-Jacobi, Kjell Sawyer, David S. Mannel, Joyce Tombran Tink, and Muayyad R. Al-Ubaidi	
Role of BCL-XL in Photoreceptor Survival	69
Yun-Zheng Le*, Lixin Zheng, Yuwei Le, Edmund B. Rucker III, and Robert E. Anderson	

The Hypoxic Transcriptome of the Retina: Identification of Factors with Potential Neuroprotective Activity	75
Markus Thiersch*, Wolfgang Raffelsberger, Enrico Frigg, Marijana Samardzija, Patricia Blank, Olivier Poch, and Christian Grimm	

Part III Gene Therapy and Neuroprotection

Lentiviral Gene Transfer-Mediated Cone Vision Restoration in RPE65 Knockout Mice	89
Alexis-Pierre Bemelmans, Corinne Kostic, Maité Cachafeiro, Sylvain V. Crippa, Dana Wanner, Meriem Tekaya, Andreas Wenzel, and Yvan Arsenijevic	

In vitro Analysis of Ribozyme-mediated Knockdown of an ADRP Associated Rhodopsin Mutation	97
Dibyendu Chakraborty*, Patrick Whalen, Alfred S. Lewin, and Muna I. Naash	

Gene Therapy for Mouse Models of ADRP	107
Marina S. Gorbatyuk*, William W. Hauswirth, and Alfred S. Lewin	

Development of Viral Vectors with Optimal Transgene Expression for Ocular Gene Therapies	113
Takao Hashimoto*	

Adeno-Associated Viral Vectors and the Retina	121
John J. Alexander* and William W. Hauswirth	

Genetic Supplementation of RDS Alleviates a Loss-of-function Phenotype in C214S Model of Retinitis Pigmentosa	129
May Nour, Steven J. Fliesler, and Muna I. Naash	

Morphological Aspects Related to Long-term Functional Improvement of the Retina in the 4 Years Following rAAV-mediated Gene Transfer in the RPE65 Null Mutation Dog	139
Kristina Narfström, Mathias Seeliger, Chooi-May Lai, Vaegan, Martin Katz, Elizabeth P. Rakoczy, and Charlotte Remé	

Virus-mediated Gene Delivery to Neuronal Progenitors	147
Tonia S. Rex*	

Part IV Animal Models of Retinal Degeneration

Loss of Visual and Retinal Function in Light-stressed Mice	157
Drew Everhart, Ana Stachowiak, Yumiko Umino*, and Robert Barlow	

ERG Responses and Microarray Analysis of Gene Expression in a Multifactorial Murine Model of Age-Related Retinal Degeneration 165
 Goldis Malek, Jeffery A. Jamison, Brian Mace, Patrick Sullivan, and Catherine Bowes Rickman

Oxygen Supply and Retinal Function: Insights from a Transgenic Animal Model 171
 Edda Fahl, Max Gassmann, Christian Grimm, and Mathias W. Seeliger

Characterization of Gene Expression Profiles of Normal Canine Retina and Brain Using a Retinal cDNA Microarray 179
 Gerardo L. Paez*, Barbara Zangerl, Kimberly Sellers, Gregory M. Acland, and Gustavo D. Aguirre

Toward a Higher Fidelity Model of AMD 185
 Brian J. Raisler*, Miho Nozaki, Judit Baffi, William W. Hauswirth, and Jayakrishna Ambati

The Potential of Ambient Light Restriction to Restore Function to the Degenerating P23H-3 Rat Retina 193
 Krisztina Valter, Diana K. Kirk, and Jonathan Stone

Part V Molecular Genetics and Candidate Genes

Mutations in Known Genes Account for 58% of Autosomal Dominant Retinitis Pigmentosa (adRP) 203
 Stephen P. Daiger, Lori S. Sullivan, Anisa I. Gire, David G. Birch, John R. Heckenlively, and Sara J. Bowne

Genetics of Age-related Macular Degeneration 211
 Albert O. Edwards

Retinal Phenotype of an X-Linked Pseudo-usher Syndrome in Association with the G173R Mutation in the *RPGR* Gene 221
 Alessandro Iannaccone, Mohammad I. Othman, April D. Cantrell, Barbara J. Jennings, Kari Branham, and Anand Swaroop

Mutation in the PYK2-Binding Domain of PITPNM3 Causes Autosomal Dominant Cone Dystrophy (CORD5) in Two Swedish Families 229
 Linda Köhn*, Konstantin Kadzhaev, Marie S. I. Burstedt, Susann Haraldsson, Ola Sandgren, and Irina Golovleva

Identification and Characterization of Genes Expressed in Cone Photoreceptors 235
 Mehrnoosh Saghizadeh*, Novrouz B. Akhmedov, and Debora B. Farber

Clinical and Genetic Characterization of a Chinese Family with CSNB1 . . 245
 Ruifang Sui*, Fengrong Li, Jialiang Zhao, and Ruxin Jiang

10q26 Is Associated with Increased Risk of Age-Related Macular Degeneration in the Utah Population 253
 D. Joshua Cameron*, Zhenglin Yang, Zhongzhong Tong, Yu Zhao, Alissa Praggastis, Eric Brinton, Jennifer Harmon, Yali Chen, Erik Pearson, Paul S. Bernstein, Gregory Brinton, Xi Li, Adam Jorgensen, Sara Schneider, Daniel Gibbs, Haoyu Chen, Changguan Wang, Kimberly Howes, Nicola J. Camp, and Kang Zhang

Part VI Diagnostic, Clinical, Cytopathological and Physiologic Aspects of Retinal Degeneration

Carboxyethylpyrrole Adducts, Age-related Macular Degeneration and Neovascularization 261
 Kutralanathan Renganathan, Quteba Ebrahim, Amit VasANJI, Xiaorong Gu, Liang Lu, Jonathan Sears, Robert G. Salomon, Bela Anand-Apte, and John W. Crabb

A Possible Impaired Signaling Mechanism in Human Retinal Pigment Epithelial Cells from Patients with Macular Degeneration 269
 Piyush C. Kothary and Monte A. Del Monte

Expression and Cell Compartmentalization of EFEMP1, a Protein Associated with *Malattia Leventinese* 277
 Adam Kundzewicz*, Francis Munier, and Jean-Marc Matter

Role of ELOVL4 in Fatty Acid Metabolism 283
 Vidyullatha Vasireddy*, Majchrzak Sharon, Norman Salem, Jr, and Radha Ayyagari

Organization and Molecular Interactions of Retinoschisin in Photoreceptors 291
 Camasamudram Vijayarathy, Yuichiro Takada, Yong Zeng, Ronald A. Bush, and Paul A. Sieving

Part VII Basic Science Underlying Retinal Degeneration

Proteomics Profiling of the Cone Photoreceptor Cell Line, 661W 301
 Muayyad R. Al-Ubaidi, Hiroyuki Matsumoto, Sadamu Kurono, and Anil Singh

γ -Secretase Regulates VEGFR-1 Signalling in Vascular Endothelium and RPE 313
 Michael E. Boulton, Jun Cai, Maria B. Grant, and Yadan Zhang

Analysis of the Rate of Disk Membrane Digestion by Cultured RPE Cells 321
 Tanja Diemer*, Daniel Gibbs, and David S. Williams

Functional Expression of Cone Cyclic Nucleotide-Gated Channel in Cone Photoreceptor-Derived 661W Cells 327
 J. Browning Fitzgerald, Anna P. Malykhina, Muayyad R. Al-Ubaidi, and Xi-Qin Ding

Phosphorylation of Caveolin-1 in Bovine Rod Outer Segments in vitro by an Endogenous Tyrosine Kinase 335
 Michael H. Elliott* and Abboud J. Ghalayini

Regulation of Neurotrophin Expression and Activity in the Retina 343
 Abigail S. Hackam*

Involvement of Guanylate Cyclases in Transport of Photoreceptor Peripheral Membrane Proteins 351
 Sukanya Karan*, Jeanne M. Frederick and Wolfgang Baehr

Rod Progenitor Cells in the Mature Zebrafish Retina 361
 Ann C. Morris*, Tamera Scholz, and James M. Fadool

α v β 5 Integrin Receptors at the Apical Surface of the RPE: One Receptor, Two Functions 369
 Emeline F. Nandrot, Yongen Chang, and Silvia C. Finnemann

Implantation of Mouse Eyes with a Subretinal Microphotodiode Array ... 377
 Mabelle T. Pardue, Tiffany A. Walker, Amanda E. Faulkner, Moon K. Kim, Christopher M. Bonner, and George Y. McLean

Variation in the Electroretinogram of C57BL/6 Substrains of Mouse 383
 Alison L. Reynolds*, G. Jane Farrar, Pete Humphries, and Paul F. Kenna

A2E, A Pigment of RPE Lipofuscin, is Generated from the Precursor, A2PE by a Lysosomal Enzyme Activity 393
 Janet R. Sparrow, So Ra Kim, Ana M. Cuervo and Urmi Bandhyopadhyayand

Endothelin Receptors: Do They Have a Role in Retinal Degeneration? ... 399
 Vanesa Torbidoni*, María Iribarne, and Angela M. Suburo

**CNTF Negatively Regulates the Phototransduction Machinery
in Rod Photoreceptors: Implication for Light-Induced Photostasis
Plasticity** 407
Rong Wen, Ying Song, Yun Liu, Yiwen Li, Lian Zhao, and Alan M. Laties

About the Editors 415

Index 419