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John D. Ash
Christian Grimm
Joe G. Hollyfield
Robert E. Anderson
Matthew M. LaVail
Catherine Bowes Rickman Editors

Retinal Degenerative Diseases

Mechanisms and Experimental Therapy



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Elizabeth Jean Ozan Anderson

April 17, 1941-April 11, 2011

Each of the preceding volumes of these Retinal Degeneration Symposia have been dedicated to an individual who has been an important sponsor or contributor to the field of retinal degeneration research. This volume is dedicated to the late Elizabeth Anderson, an avid and enthusiastic supporter of the young scientists who attend these meetings, and wife of Robert E. (Gene) Anderson, one of the original organizers of these meetings. At several RD Symposia, Elizabeth was the principal organizer of the spouses' program, actively planning and supervising excursions for the non-scientists in attendance. She functioned as special "hostess" for

young scientists, making sure that they were introduced to many of the senior investigators in retinal degeneration research. Because of our close friendship with Gene and Elizabeth, the Editors of this volume asked that we contribute some personal remembrances of Elizabeth for this dedication.

Although we have known Gene since 1970, we first met Elizabeth after our move to Houston in 1977 to become a part of the Cullen Eye Institute at Baylor College of Medicine. During our 17 years at Baylor, we were with Elizabeth and Gene on numerous occasions; we traveled together and became close friends.

Elizabeth was in college working on a bachelor's degree in nursing when she and Gene first met. This completed, Elizabeth went on to become an accredited nurse anesthetist and worked in a number of hospitals in Houston. Elizabeth was my anesthetist (JGH) when I required oral surgery in the early 1980s. The surgeon and peridontist that were treating me warned me on how painful these procedures might be and quickly convinced me to have this performed under general anesthesia in a local hospital. I checked into the hospital the night before the surgery scheduled for early the next morning. I remember being quite anxious when wheeled to the operating room, but Elizabeth had already started an IV and was by my side assuring me that she would not let me feel any pain. The next thing I remember is being awakened by a nurse back in my room who was insistent that I stay awake and drink lots of fluid to flush the remaining anesthetics from my system. Quickly the copious fluid volumes consumed required a visit to the toilet, and I called for a nurse to assist me, because I was still quite unsteady. With the nurse's help, I clumsily got out of the bed with my hospital gown in disarray and made my way to the facilities. I noticed that the nurse giggled as I moved off the bed but thought nothing of it until I discovered, as she had already observed, a big red ribbon tied securely around the most intimate part of my anatomy. Immediately I knew that Elizabeth had been up to some mischief while I was under sedation! Later when I confronted her, she assured me that she had not touched me, but that others in the OR were involved. She did finally admit to bringing the red ribbon into the OR that morning. When I questioned her about the choice of color she smiled and

said, "Darlin', I had a blue ribbon, but that color is reserved for my husband!"

Over the years, we traveled with Elizabeth and Gene to many interesting parts of the world, and on each trip, museums were always one of her favorite destinations. She loved paintings and sculpture. Many who frequent museums stroll slowly through the galleries, pausing when a painting catches one's eye, and then move on, but not Elizabeth. She would read every word of every description on every painting in every room. Gene and Joe would quickly look for a gallery with a bench or chair on which to rest while Elizabeth devoured each display. This love of art prompted her to formally enroll in a local college, and she was working toward a degree in art history at the time of her death.

Elizabeth had very strong opinions about a variety of issues, or perhaps we should say, about most issues. She was fearless, with no reservations whatsoever in sharing her views, and rarely softened her position to please others. One example of this occurred in 2002 during the week of the International Conference of Eye Research that convened in Geneva, Switzerland. The four of us, along with a few other couples, were dinner guests in the home of a Swiss vision scientist. As the evening progressed, and the empty wine bottles accumulated, politics became the subject and it quickly became apparent that Elizabeth and our host's husband did not share the same views. Frustrated that her pronouncements were being challenged, she pushed her chair back, stood up at the table and sang "I'm Proud to be an American", in which she was joined by several others. At the end, everyone at the table, including Elizabeth, had a great laugh, and fortunately the discussion moved on to another subject.

Elizabeth loved to travel, and many of her recurring annual trips were as an accompanying spouse when Gene's profession took him to a scientific meeting, usually held at some exotic destination. Early on at these conferences Elizabeth showed her concern for the young scientists in attendance. It was her personal goal to see that each young scientist she interacted with at the meeting's social function would be able to meet their most admired senior researcher. It was this special characteristic that prompted Ann Milam, a retired vision scientist in Seattle and long time friend of Elizabeth's,

to organize an endowment in Elizabeth's name to support travel for young scientists working in the area of retinal degeneration research to attend the annual meeting of the Association for Research in Vision and Ophthalmology. Solicitations were initially made to Elizabeth and Gene's closest friends and family: then to the nearly 1,000 researchers who have attended the biennial Retinal Degeneration Symposia. Jeff Boatright also distributed a solicitation of support to the distribution list of Molecular Vision. Only a few days before Elizabeth's death, donations had reached \$ 50,000, a level sufficient to provide support for one travel fellow each year. Elizabeth was extremely pleased to be honored and recognized with this tribute. Over 300 individuals have contributed to this endowment that now exceeds \$ 120,000, a sum sufficient to fund 2–3 annual travel fellowships. Recipients of these fellowships will be designated as an Elizabeth Anderson Travel Fellow, allowing Elizabeth's name to appear every year in the ARVO program in perpetuity.

Following this travel fellowship tribute in her honor, the Foundation Fighting Blindness announced the naming of a 5-year grant, the Elizabeth Anderson Career Development Award. A few days later the American Health Assistance Foundation named one of their two-year, \$ 120,000 awards, the Elizabeth Anderson Macular Degeneration Grant. Collectively, these numerous tributes to Elizabeth are a clear indication how she and Gene are respected and admired by the vision research and ophthalmology community. At the end of her struggle, death became Elizabeth's friend, because it alone brought her the peace from her illness that money could not buy, and it removed the suffering that her physicians could not cure. She left a wonderful legacy: that of a devoted wife, loving mother, devoted grandmother and an unforgettable friend to many who work in vision research and ophthalmology.

Mary E. Rayborn and Joe G. Hollyfield Cleveland, Ohio
Death leaves a heartache that no one can heal,
Love leaves a memory that no one can steal.

(from an old Irish tombstone)

Preface

The International Symposia on Retinal Degeneration have been held in conjunction with the biennial International Congress of Eye Research (ICER) since 1984. These RD Symposia have been highly successful and have become one of the most well attended meetings in the field. The RD Symposia are successful because they allow basic and clinician scientists from around the world to convene and present their new research findings in a format that allows sufficient time for discussions and one-on-one interactions in a relaxed atmosphere, where international friendships and collaborations can be fostered.

The XVth International Symposium on Retinal Degeneration (RD2012) was held in Bad Gögging, Bavaria, Germany July 16–21, 2012. The RD2012 meeting ties the RD2010 meeting in size, which was the largest ever. The meeting brought together 230 basic and clinician scientists, retinal specialists in ophthalmology, and trainees in the field from all parts of the world. In the course of the meeting, we had 6 plenary lectures, 43 platform presentations and 117 poster presentations. 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.

For the first time, the RD Symposium was organized around a theme, this time focused on the role of innate and acquired immunity in the initiation and progression of retinal degenerative diseases. The recent discovery that mutations in genes related to regulation of the immune system are responsible for 50% of the familial forms of age-related macular degeneration (AMD) demonstrates the important role the immune system plays in this disease. Based on these findings, it seemed appropriate to focus part of the RD2012 on the role of the immune system in degenerative retinal diseases. To accomplish this goal, six plenary speakers who work in the field of innate and acquired immunity were invited to participate in the RD2012 meeting. The speakers included: *V. Michael Holers*, Professor of Rheumatology, University of Colorado, School of Medicine, Denver, Colorado, USA; *Paul McMenamin*, Professor of Anatomy & Developmental Biology, School of Biomedical Sciences, Faculty of Medicine, Monash University, Melbourne, Australia; *Scott Cousins*, Professor of Ophthalmology, Duke University School of Medicine, Durham, North Carolina, USA; *Frederic Geissmann*, Professor and Chairman, Inflammation

x Preface

Biology, King's College, London, United Kingdom; *Thomas Langmann*, Professor and group leader at the Institute of Human Genetics, Regensburg, Germany; and *Chi-Chao Chan*, Chief of Immunopathology Section, Laboratory of Immunology, National Eye Institute (NEI), National Institutes of Health (NIH), Bethesda, Maryland, USA. These speakers are world leaders in the fields of complement activation and signaling, the role of monocytes and microglia in retinal degeneration, and the role of cytokines in retinal degeneration. The remainder of the program included topics important to retinal degeneration including: gene therapy, neuroprotective therapy, mechanisms of cell death, mechanisms of neuroprotection, novel animal models of inherited retinal degenerations and AMD, macular degeneration, phenotype/genotype correlations, and transplantation and other cell-based approaches. The resulting program was one of the most comprehensive and up-to-date of any meeting dealing with retinal degeneration.

The meeting was organized by a nine-member committee that included the permanent members Joe G. Holyfield, Christian Grimm, Robert E. Anderson, Matthew LaVail, Catherine Bowes Rickman, and John D. Ash; and the local organizing committee members, Bernhard Webber, Ernst Tamm, and Olaf Strauss. The Symposium received international financial support from a number of organizations. We are particularly pleased to thank The Foundation Fighting Blindness, Columbia, Maryland, for its continuing support of this and all previous biennial Symposia, without which we could not have held these important meetings. In addition, for the sixth time, the NEI of the National Institutes of Health contributed in a major way to the meeting. In the past, funds from these two organizations allowed us to provide 25–35 Travel Awards to young investigators and trainees working in the field of retinal degenerations. In addition, we received generous funding from Pro Retina Germany and the Fritz Tobler Foundation Switzerland. In total, we were able to fund 57 Travel Awards, the largest number ever for these Symposia.

We thank the outstanding management and staff of the beautiful Monarch Hotel in Bad Gögging, which is located midway between Regensburg and Munich. The hotel was easily accessible, but relatively remote, which created the ideal atmosphere to encourage participation of attendees in all scientific sessions and informal meetings during meals. We would like to thank the hotel staff for all of their assistance in making this an exceptionally smooth-running conference and a truly memorable experience for all of the attendees. We would like to express our appreciation for the musical talent of Franz Badura. During our excursion to the Weltenburg monastery, Franz played several beautiful pieces in a Baroque church. Many attendees mentioned this as a highlight of the excursion. We thank Barbara Gareis and her staff in coordinating with the hotel and assisting with the poster boards and other meeting logistics. Barbara is an assistant to Ernst Tamm at the University of Regensburg. We also acknowledge the diligent and outstanding efforts of Ms. Holly Whiteside, who carried out most of the administrative aspects of the RD2012 Symposium. 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 not available previously, and we Preface xi

are deeply indebted to her. Holly worked with Bo Dong and John D. Ash to develop the RD2012 website that for the first time included electronic submission of abstracts, registrations, and online payments.

Finally, we honor the memory of a most beloved regular attendee and supporter of the RD symposium by dedicating this book to Elizabeth Anderson. Elizabeth was a constant advocate for young scientists, as she often encouraged them to get involved in the meeting and to interact socially and informally with the senior scientists. Elizabeth was a major proponent of such interactions, and her encouragement is one of those intangible acts that influence our careers more than we could know.

John D. Ash Christian Grimm Joe G. Hollyfield Robert E. Anderson Matthew M. LaVail Catherine Bowes Rickman

Travel Awards

We gratefully acknowledge National Eye Institute, NIH, USA; the Foundation Fighting Blindness, USA; Pro Retina Germany; and the Fritz Tobler Foundation, Switzerland for their generous support of 57 Travel Awards to attend the RD2012 meeting. Eligibility was restricted to graduate students, postdoctoral fellows, instructors and assistant professors actively involved in retinal degeneration research. These awards were based on the quality of the abstract submitted by each applicant. Catherine Bowes Rickman chaired the Travel Awards Committee of eleven senior retinal degeneration investigators. The travel awardees are listed below. Each awardee submitted a chapter to this proceedings volume.

Daniel Adesse

University of Rio de Janeiro, Rio de Janeiro, Brazil

Martin-Paul Agbaga

University of Oklahoma HSC, Oklahoma, USA

Cavit Agca

University of Zürich, Zürich, Switzerland

Alexander Aslanidis

University of Regensburg, Regensburg, Germany

Travis Bailey

University of Notre Dame, Notre Dame, Indiana, USA

Vera Bonilha

Cole Eye Institute, Cleveland, Ohio, USA

Barbara Maria Braunger

University of Regensburg, Regensburg, Germany

Leah Byrne

University of California, Berkeley, USA

Nora Caberov

University of Miami, Miami, FL, USA

Matthew Campbell

Trinity College Dublin, Dublin, Ireland

Xue Cai

University of Oklahoma HCS, Oklahoma, USA

xiv Travel Awards

Timothy Day

University of California, Berkeley, Berkeley, CA, USA

Astra Dinculescu

University of Florida, Gainesville, Florida USA

Jindong Ding

Duke University Medical Center, Durham, USA

Xi-Oin Ding

University of Oklahoma HSC, Oklahoma, USA

Theodore Drivas

University of Pennsylvania, Philadelphia, Pennsylvania, USA

Frank Dyka

University of Florida, Gainesville, FL, USA

Katavoon Ebrahimi

Johns Hopkins Hospital, University Baltimore, Baltimore, MD, USA

Julian Esteve-Rudd

Jules Stein Eve Institute, Los Angeles, USA

Joseph Fogerty

Medical College of Wisconsin, Milwaukee, USA

Tembei Forkwa

University of Regensburg, Regensburg, Germany

Yingbin Fu

University of Utah, Salt Lake City, USA

John Fuller

Johns Hopkins Hospital, University of Baltimore, Baltimore, MD, USA

Sem Genini

University of Pennsylvania, Philadelphia, Pennsylvania, USA

Marina Gorbatyuk

University of North Texas HSC, Fort Worth, USA

Felix Grassmann

University of Regensburg, Regensburg, Germany

Gregory Grossman

Cole Eye Institute, Cleveland, USA

Michelle Grunin

Hebrew University, Hadassah Ein Kerem Med Ctr., Jerusalem, Israel

Zongchao Han

University of Oklahoma HCS, Oklahoma, USA

Hong Hao

National Institutes of Health, Bethesda, USA

Stefanie Hauck

Helmholtz Zentrum, Munich, Germany

Marcus Karlstetter

University Hospital of Cologne, Cologne, Germany

Saravanan Kolandaivelu

West Virginia University Morgantown, West Virginia, USA

Heike Kroeger

University of California, San Diego San Diego, USA

Travel Awards xv

Toshihide Kurihara

The Scripps Research Institute, La Jolla, USA

Aparna Lakkaraju

University of Wisconsin, Madison, Wisconsin, USA

Jonathan Lin

University of California, La Jolla, California, USA

Sreemathi Logan

University of Oklahoma HCS, Oklahoma, USA

Vanda Lopes

University of Coimbra, Coimbra, Portugal

Ulrich Luhmann

UCL Institute of Ophthalmology, London, UK

Haoyu Mao

University of Florida, Gainesville, USA

Lea Marchette

University of Oklahoma HSC, Oklahoma, USA

Emeline Nandrot

Institut de la Vision, Paris, France

Anh Thi Nguyen

Trinity College Dublin, Dublin, Ireland

Ema Ozaki

Trinity College Dublin, Dublin, Ireland

David Rabin

Albany Medical College, Albany, USA

Alison Revnolds

University College Dublin, Dublin, Ireland

Linda Ruggiero

Fordham University New York, USA

Marijana Samardzija

University of Zürich, Zürich, Switzerland

Gloriane Schnabolk

Medical University of South Carolina, Charleston, South Carolina, USA

Chloe Stanton

University of Edinburgh MRC IGMM, Edinburgh, Scotland

Preeti Subramanian

National Eve Institute, Bethesda, USA

Peter Westenskow

The Scripps Research Institute La Jolla, USA

Kerstin Nagel-Wolfrum

Johannes Gutenberg University, Mainz, Germany

Alex Woodell

Medical University of South Carolina, Charleston, USA

Frank Zach

University of Regensburg, Regensburg, Germany

Houbin Zhang

University of Utah, Salt Lake City, Utah, USA

Contents

Part I Basic Processes: Development, Physiology and Function

1	Cell Type-Specific Epigenetic Signatures Accompany Late Stages of Mouse Retina Development	3
	Evgenya Y. Popova, Colin J. Barnstable and Samuel Shao-Min Zhang	3
2	Programmed Cell Death During Retinal Development of the Mouse Eye	9
	Barbara M. Braunger, Cora Demmer and Ernst R. Tamm	
3	Spatial and Temporal Localization of Caveolin-1 Protein in the Developing Retina	15
	Xiaowu Gu, Alaina Reagan, Allen Yen, Faizah Bhatti, Alex W. Cohen and Michael H. Elliott	
4	Glutathione S-Transferase Pi Isoform (GSTP1) Expression in Murine Retina Increases with Developmental Maturity	23
5	RETINA-Specific Expression of <i>Kenv2</i> Is Controlled by Cone-Rod Homeobox (Crx) and Neural Retina Leucine Zipper (Nrl)	31
	Alexander Aslanidis, Marcus Karlstetter, Yana Walczak, Herbert Jägle and Thomas Langmann	
6	AIPL1 Protein and its Indispensable Role in Cone Photoreceptor Function and Survival Saravanan Kolandaivelu and Visvanathan Ramamurthy	43
7	Primate Short-Wavelength Cones Share Molecular Markers with Rods	49
	Cheryl M. Craft, Jing Huang, Daniel E. Possin and Anita Hendrickson	

xviii Contents

8	Exploration of Cone Cyclic Nucleotide-Gated Channel- Interacting Proteins Using Affinity Purification and Mass Spectrometry	5
	Xi-Qin Ding, Alexander Matveev, Anil Singh, Naoka Komori and Hiroyuki Matsumoto	
9	Electrophysiological Characterization of Rod and Cone Responses in the Baboon Nonhuman Primate Model	6
Pai	rt II Basic Processes: RPE	
10	Animal Models, in "The Quest to Decipher RPE Phagocytosis" Emeline F. Nandrot	7
11	In Vivo and in Vitro Monitoring of Phagosome Maturation	
	in Retinal Pigment Epithelium Cells Julian Esteve-Rudd, Vanda S. Lopes, Mei Jiang and David S. Williams	8
12	Lack of Effect of Microfilament or Microtubule Cytoskeleton-Disrupting Agents on Restriction of Externalized Phosphatidylserine to Rod Photoreceptor Outer Segment Tips Linda Ruggiero and Silvia C. Finnemann	Ģ
13	Vacuolar ATPases and Their Role in Vision Lisa Shine, Claire Kilty, Jeffrey Gross and Breandan Kennedy	Ģ
14	Rescue of Compromised Lysosomes Enhances Degradation of Photoreceptor Outer Segments and Reduces Lipofuscin-Like Autofluorescence in Retinal Pigmented Epithelial Cells	10
15	The Role of Bestrophin-1 in Intracellular Ca ²⁺ Signaling	11
Pai	rt III Basic Processes: Methodology	
16	Application of Next-Generation Sequencing to Identify Genes and Mutations Causing Autosomal Dominant Retinitis Pigmentosa (adRP) Stephen P. Daiger, Sara J. Bowne, Lori S. Sullivan, Susan H. Blanton, George M. Weinstock, Daniel C. Koboldt, Robert S. Fulton, David Larsen, Peter Humphries, Marian M. Humphries, Eric A. Pierce, Rui Chen and Yumei Li	12

Contents xix

17	Digital Quantification of Goldmann Visual Fields (GVFs) as a Means for Genotype–Phenotype Comparisons and Detection of Progression in Retinal Degenerations	131
	Sarwar Zahid, Crandall Peeler, Naheed Khan, Joy Davis, Mahdi Mahmood, John R. Heckenlively and Thiran Jayasundera	
18	Simplified System to Investigate Alteration of Retinal Neurons in Diabetes	139
	Shuqian Dong, Yan Liu, Meili Zhu, Xueliang Xu and Yun-Zheng Le	10)
19	What Is the Nature of the RGC-5 Cell Line? C. Sippl and E. R. Tamm	145
Par	t IV Genetics in Retinal Disease	
20	Modeling Retinal Dystrophies Using Patient-Derived	157
	Induced Pluripotent Stem Cells	157
21	Mutation K42E in Dehydrodolichol Diphosphate Synthase (DHDDS) Causes Recessive Retinitis Pigmentosa	165
	Eduardo C. Alfonso, Jeffery M. Vance and Margaret A. Peričak-Vance	
22	IROme, a New High-Throughput Molecular Tool for the Diagnosis of Inherited Retinal Dystrophies—A Price Comparison with Sanger Sequencing	171
	Daniel F. Schorderet, Maude Bernasconi, Leila Tiab, Tatiana Favez and Pascal Escher	
23	Genetic Heterogeneity and Clinical Outcome in a Swedish Family with Retinal Degeneration Caused by Mutations in CRB1 and ABCA4 Genes	177
	Frida Jonsson, Marie S. Burstedt, Ola Sandgren, Anna Norberg and Irina Golovleva	
24	FAM161A, a Novel Centrosomal-Ciliary Protein Implicated in Autosomal Recessive Retinitis Pigmentosa	185
Par	et V AMD: Novel Developments	
25	Molecular Pathology of Macrophages and Interleukin-17 in Age-Related Macular Degeneration Chi-Chao Chan and Daniel Ardeljan	193

xx Contents

26	The Role of Monocytes and Macrophages in Age-Related Macular Degeneration	199
	Michelle Grunin, Shira Hagbi-Levi and Itay Chowers	
27	Microglia in the Aging Retina	207
	Marcus Karlstetter and Thomas Langmann	
28	The Role of Complement Dysregulation in AMD Mouse Models Jin-Dong Ding, Una Kelly, Marybeth Groelle, Joseph G. Christenbury, Wenlan Zhang and Catherine Bowes Rickman	213
29	Prolonged Src Kinase Activation, a Mechanism to	
	Turn Transient, Sublytic Complement Activation into a Sustained Pathological Condition in Retinal Pigment	
	Epithelium Cells	221
	Bärbel Rohrer, Kannan Kunchithapautham, Andreas Genewsky and Olaf Strauß	
30	Inflammation in Age-Related Macular Degeneration	229
	Ema Ozaki, Matthew Campbell, Anna-Sophia Kiang, Marian Humphries, Sarah Doyle and Peter Humphries	
31	Impairment of the Ubiquitin-Proteasome Pathway in RPE	
	Alters the Expression of Inflammation Related Genes	237
32	Inflammatory Biomarkers for AMD	251
	Chloe M. Stanton and Alan F. Wright	
33	Oxidized Low-Density-Lipoprotein-Induced Injury in	
	Retinal Pigment Epithelium Alters Expression of the	
	Membrane Complement Regulatory Factors CD46 and CD59 through Exosomal and Apoptotic Bleb Release	259
	Katayoon B. Ebrahimi, Natalia Fijalkowski, Marisol Cano and James T. Handa	
34	Should I Stay or Should I Go? Trafficking of Sub-Lytic	
	MAC in the Retinal Pigment Epithelium	267
	Aparna Lakkaraju, Kimberly A. Toops and Jin Xu	
35	Hypoxia-Inducible Factor (HIF)/Vascular Endothelial	
	Growth Factor (VEGF) Signaling in the Retina	275
	Toshihide Kurihara, Peter D. Westenskow and Martin Friedlander	

Contents xxi

36	Is Age-Related Macular Degeneration a Microvascular Disease? Robert F. Mullins, Aditi Khanna, Desi P. Schoo, Budd A. Tucker, Elliott H. Sohn, Arlene V. Drack and Edwin M. Stone	283
37	Genetic Risk Models in Age-Related Macular Degeneration	291
38	A Mechanistic Review of Cigarette Smoke and Age-Related Macular Degeneration Alex Woodell and Bärbel Rohrer	301
39	Measuring Cone Density in a Japanese Macaque (<i>Macaca fuscata</i>) Model of Age-Related Macular Degeneration with Commercially Available Adaptive Optics	309
	Mark E. Pennesi, Anupam K. Garg, Shu Feng, Keith V. Michaels, Travis B. Smith, Jonathan D. Fay, Alison R. Weiss, Laurie M. Renner, Sawan Hurst, Trevor J. McGill, Anda Cornea, Kay D. Rittenhouse, Marvin Sperling, Joachim Fruebis and Martha Neuringer	30)
40	Nuclear Receptors as Potential Therapeutic Targets for Age-Related Macular Degeneration Goldis Malek	317
41	Utilizing Stem Cell-Derived RPE Cells as A Therapeutic Intervention for Age-Related Macular Degeneration Peter D. Westenskow, Toshihide Kurihara and Martin Friedlander	323
Par	t VI Müller Cells, Microglia, and Macrophages	
42	Microglia-Müller Cell Interactions in the Retina	333
43	Isolation and Ex Vivo Characterization of the Immunophenotype and Function of Microglia/Macrophage Populations in Normal Dog Retina Sem Genini, William A. Beltran, Veronika M. Stein and Gustavo D. Aguirre	339
44	Müller Cells and Microglia of the Mouse Eye React Throughout the Entire Retina in Response to the Procedure of an Intravitreal Injection Roswitha Seitz and Ernst R. Tamm	347
45	Subretinal Infiltration of Monocyte Derived Cells and Complement Misregulation in Mice with AMD-Like Pathology Joseph Fogerty and Joseph C. Besharse	355

xxii Contents

46	Ambiguous Role of Glucocorticoids on Survival of Retinal Neurons	
	Tembei K. Forkwa, Ernst R. Tamm and Andreas Ohlmann	
47	Microglia-Müller Glia Crosstalk in the rd10 Mouse Model of Retinitis Pigmentosa	
	Ana I. Arroba, Noemí Álvarez-Lindo, Nico van Rooijen and Enrique J. de la Rosa	
48	The Neuroprotective Potential of Retinal Müller Glial Cells	
49	Leukemia Inhibitory Factor Signaling in Degenerating Retinas Cavit Agea and Christian Grimm	
50	In Vivo Function of the ER-Golgi Transport Protein LMAN1 in Photoreceptor Homeostasis Hong Hao, Janina Gregorski, Haohua Qian, Yichao Li, Chun Y Gao, Sana Idrees and Bin Zhang	
51	Investigating the Role of Retinal Müller Cells with Approaches in Genetics and Cell Biology Suhua Fu, Meili Zhu, John D. Ash, Yunchang Wang and Yun-Zheng Le	
Par	rt VII Degenerative Processes: Immune-Related Mechanisms, Genes and Factors	
52	An Overview of the Involvement of Interleukin-18 in Degenerative Retinopathies	
	Matthew Campbell, Sarah L. Doyle, Ema Ozaki, Paul F. Kenna, Anna-Sophia Kiang, Marian M. Humphries and Peter Humphries	
53	Chronic Intraocular Inflammation and Development of Retinal Degenerative Disease	
54	The Relevance of Chemokine Signalling in Modulating Inherited and Age-Related Retinal Degenerations Ulrich FO Luhmann, Scott J Robbie, James WB Bainbridge and Robin R Ali	
55	The Complement Regulatory Protein CD59: Insights into Attenuation of Choroidal Neovascularization Gloriane Schnabolk, Stephen Tomlinson and Bärbel Rohrer	

Contents xxiii

56	Regeneration-Associated Genes on Optic Nerve Regeneration in Fish Retina	441
57	Dominant Stargardt Macular Dystrophy (STGD3) and ELOVL4 S. Logan and R. E. Anderson	447
58	Modulation of the Rate of Retinal Degeneration in T17M RHO Mice by Reprogramming the Unfolded Protein Response Shreyasi Choudhury, Sonali Nashine, Yogesh Bhootada, Mansi Motiwale Kunte, Oleg Gorbatyuk, Alfred S. Lewin and Marina Gorbatyuk	455
59	Expression of Poly(ADP-Ribose) Glycohydrolase in Wild- Type and PARG-110 Knock-Out Retina	463
60	Current Therapeutic Strategies for P23H RHO-Linked RP	471
61	Pathogenesis of X-linked RP3: Insights from Animal Models	477
62	Unc119 Gene Deletion Partially Rescues the GRK1 Transport Defect of <i>Pde6d</i> Cones Houbin Zhang, Jeanne M. Frederick and Wolfgang Baehr	487
63	Retinal Function in Aging Homozygous <i>Cln3</i> ^{dex7/8} Knock-In Mice Cornelia Volz, Myriam Mirza, Thomas Langmann and Herbert Jägle	495
64	Synergistic Interaction of Tubby and Tubby-Like Protein 1 (Tulp1) Nora Blanca Caberoy	503
65	Interaction of Tubby-Like Protein-1 (Tulp1) and Microtubule-Associated Protein (MAP) 1A and MAP1B in the Mouse Retina Gregory H. Grossman, Craig D. Beight, Lindsey A. Ebke, Gayle J.T. Pauer and Stephanie A. Hagstrom	511
66	CEP290 and the Primary Cilium Theodore G. Drivas and Jean Bennett	519

xxiv Contents

67	Usher Syndrome Protein Network Functions in the Retina and their Relation to Other Retinal Ciliopathies	527
68	The Phenotype of the <i>Good Effort</i> Mutant Zebrafish is Retinal Degeneration by Cell Death and is Linked to the Chromosome Assembly Factor 1b Gene Travis J. Bailey and David R. Hyde	535
69	Knock-Down DHDDS Expression Induces Photoreceptor Degeneration in Zebrafish	543
	Rong Wen, Julia E. Dallman, Yiwen Li, Stephan L. Züchner, Jeffery M. Vance, Margaret A. Peričak-Vance and Byron L. Lam	343
70	Spectral Domain Optical Coherence Tomography Findings in CNGB3-Associated Achromatopsia and Therapeutic Implications	551
	Michael McClintock, Marc C. Peden and Christine N. Kay	
71	Photoreceptor Pathology in the X-Linked Retinoschisis (XLRS) Mouse Results in Delayed Rod Maturation and Impaired Light Driven Transducin Translocation	559
72	Mouse Models for Cone Degeneration	567
73	How Long Does a Photoreceptor Cell Take to Die? Implications for the Causative Cell Death Mechanisms F. Paquet-Durand, A. Sahaboglu, J. Dietter, O. Paquet-Durand, B. Hitzmann, M. Ueffing and P. A. R. Ekström	575
Par	t VIII Degenerative Processes: RPE and Fatty Acids	
74	Endoplasmic Reticulum Stress in Vertebrate Mutant Rhodopsin Models of Retinal Degeneration Heike Kroeger, Matthew M. LaVail and Jonathan H. Lin	585
75	Bisretinoid Degradation and the Ubiquitin-Proteasome System Janet R. Sparrow, Jilin Zhou, Shanti Kaligotla Ghosh and Zhao Liu	593

Contents xxv

76	Analysis of Mouse RPE Sheet Morphology Gives Discriminatory Categories	601
	Yi Jiang, X Qi, Micah A. Chrenek, Christopher Gardner, Nupur Dalal, Jeffrey H. Boatright, Hans E. Grossniklaus and John M. Nickerson	
77	High Glucose Activates ChREBP-Mediated HIF-1α and VEGF Expression in Human RPE Cells Under Normoxia	609
78	Sphingolipids in Ocular Inflammation Annie Y. Chan, Shivani N. Mann, Hui Chen, Donald U. Stone, Daniel J. J. Carr and Nawajes A. Mandal	623
79	Biosynthesis of Very Long-Chain Polyunsaturated Fatty Acids in Hepatocytes Expressing ELOVL4 Martin-Paul Agbaga, Sreemathi Logan, Richard S. Brush and Robert E. Anderson	631
80	Very Long Chain Polyunsaturated Fatty Acids and Rod Cell Structure and Function L. D. Marchette, D. M Sherry, R. S Brush, M. Chan, Y. Wen, J. Wang, John D. Ash, R. E. Anderson and N. A. Mandal	637
Par	rt IX Degenerative Processes: Immune-Related Mechanisms, Genes and Factors	
81	Oxidative Stress Regulation by DJ-1 in the Retinal Pigment Epithelium Vera L. Bonilha, Mary E. Rayborn, Xiaoping Yang, Chengsong Xie and Huaibin Cai	649
82	The Role of Reactive Oxygen Species in Ocular Malignancy	655
83	The Effects of IRE1, ATF6, and PERK Signaling on adRP- Linked Rhodopsins	661
	Wei-Chieh Jerry Chiang and Jonathan H. Lin	
84	Role of Endothelial Cell and Pericyte Dysfunction in Diabetic Retinopathy: Review of Techniques in Rodent Models Jonathan Chou, Stuart Rollins and Amani A Fawzi	669

xxvi Contents

85	Autophagy Induction Does Not Protect Retina Against Apoptosis in Ischemia/Reperfusion Model Nathalie Produit-Zengaffinen, Constantin J. Pournaras and Daniel F. Schorderet	67
Par	rt X Therapy: Gene Therapy	
86	Advances in AAV Vector Development for Gene Therapy in	60
	the Retina	68
87	Cone Specific Promoter for Use in Gene Therapy of Retinal Degenerative Diseases	69
	Frank M. Dyka, Sanford L. Boye, Renee C. Ryals, Vince A. Chiodo, Shannon E. Boye and William W. Hauswirth	
88	Episomal Maintenance of S/MAR-Containing Non-Viral Vectors for RPE-Based Diseases	70
	Adarsha Koirala, Shannon M Conley and Muna I. Naash	
89	Gene Therapy in the Rd6 Mouse Model of Retinal Degeneration Astra Dinculescu, Seok-Hong Min, Wen-Tao Deng, Qiuhong Li and William W. Hauswirth	71
90	Gene Therapy for Stargardt Disease Associated	
	with ABCA4 Gene Zongchao Han, Shannon M. Conley and Muna I. Naash	71
91	Assessment of Different Virus-Mediated Approaches for Retinal Gene Therapy of Usher 1B	72
	Vanda S. Lopes, Tanja Diemer and David S. Williams	
92	Gene Therapy Restores Vision and Delays Degeneration in the CNGB1 ^{-/-} Mouse Model of Retinitis Pigmentosa	73
	Stylianos Michalakis, Susanne Koch, Vithiyanjali Sothilingam,	
	Marina Garcia Garrido, Naoyuki Tanimoto, Elisabeth Schulze,	
	Elvir Becirovic, Fred Koch, Christina Seide, Susanne C. Beck, Mathias W. Seeliger, Regine Mühlfriedel and Martin Biel	
93	Therapy Strategies for Usher Syndrome Type 1C in the Retina Kerstin Nagel-Wolfrum, Timor Baasov and Uwe Wolfrum	74

Contents xxvii

Part	XI Therapy: Protection	
94	Nipradilol Promotes Axon Regeneration Through S-Nitrosylation of PTEN in Retinal Ganglion Cells Yoshiki Koriyama, Marie Kamiya, Kunizo Arai, Kayo Sugitani, Kazuhiro Ogai and Satoru Kato	751
95	Reciprocal Changes in Factor XIII and Retinal Transglutaminase Expressions in the Fish Retina During Optic Nerve Regeneration Kayo Sugitani, Kazuhiro Ogai, Yoshiki Koriyama and Satoru Kato	759
96	N-Acetylserotonin: Circadian Activation of the BDNF Receptor and Neuroprotection in the Retina and Brain P. Michael Iuvone, Jeffrey H. Boatright, Gianluca Tosini and Keqiang Ye	765
97	A High Content Screening Approach to Identify Molecules Neuroprotective for Photoreceptor Cells John A. Fuller, Gillian C. Shaw, Delphine Bonnet-Wersinger, Baranda S. Hansen, Cynthia A. Berlinicke, James Inglese and Donald J. Zack	773
98	Antioxidant Therapy for Retinal Disease	783
99	Pathophysilogical Mechanism and Treatment Strategies for Leber Congenital Amaurosis Yingbin Fu and Tao Zhang	791
100	Current and Emerging Therapies for Ocular Neovascularisation Alison L. Reynolds, David Kent and Breandán N. Kennedy	797
101	Targeting the PI3K/Akt/mTOR Pathway in Ocular Neovascularization Temitope Sasore, Alison L. Reynolds and Breandán N. Kennedy	805
102	Pigment Epithelium-Derived Factor Protects Cone Photoreceptor-Derived 661W Cells from Light Damage Through Akt Activation Matthew Rapp, Grace Woo, Muayyad R. Al-Ubaidi, S. Patricia Becerra and Preeti Subramanian	813
103	Nanoceria as Bona Fide Catalytic Antioxidants in Medicine: What We Know and What We Want to Know	821

Lily L. Wong and James F. McGinnis

xxviii Contents

104	Nanoceria and Thioredoxin Regulate a Common Antioxidative Gene Network in tubby Mice	829
	Xue Cai, Junji Yodoi, Sudipta Seal and James F. McGinnis	
105	Intrascleral Transplantation of a Collagen Sheet with	
	Cultured Brain-Derived Neurotrophic Factor Expressing	
	Cells Partially Rescues the Retina from Damage due to	
	Acute High Intraocular Pressure	837
	Toshiaki Abe, Yumi Tokita-Ishikawa, Hideyuki Onami,	
	Yuki Katsukura, Hirokazu Kaji, Matsuhiko Nishizawa	
	and Nobuhiro Nagai	
106	Neuroprotective Effects of Low Level Electrical	
	Stimulation Therapy on Retinal Degeneration	845
	Machelle T. Pardue, Vincent T. Ciavatta and John R. Hetling	
Inde	x	853

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