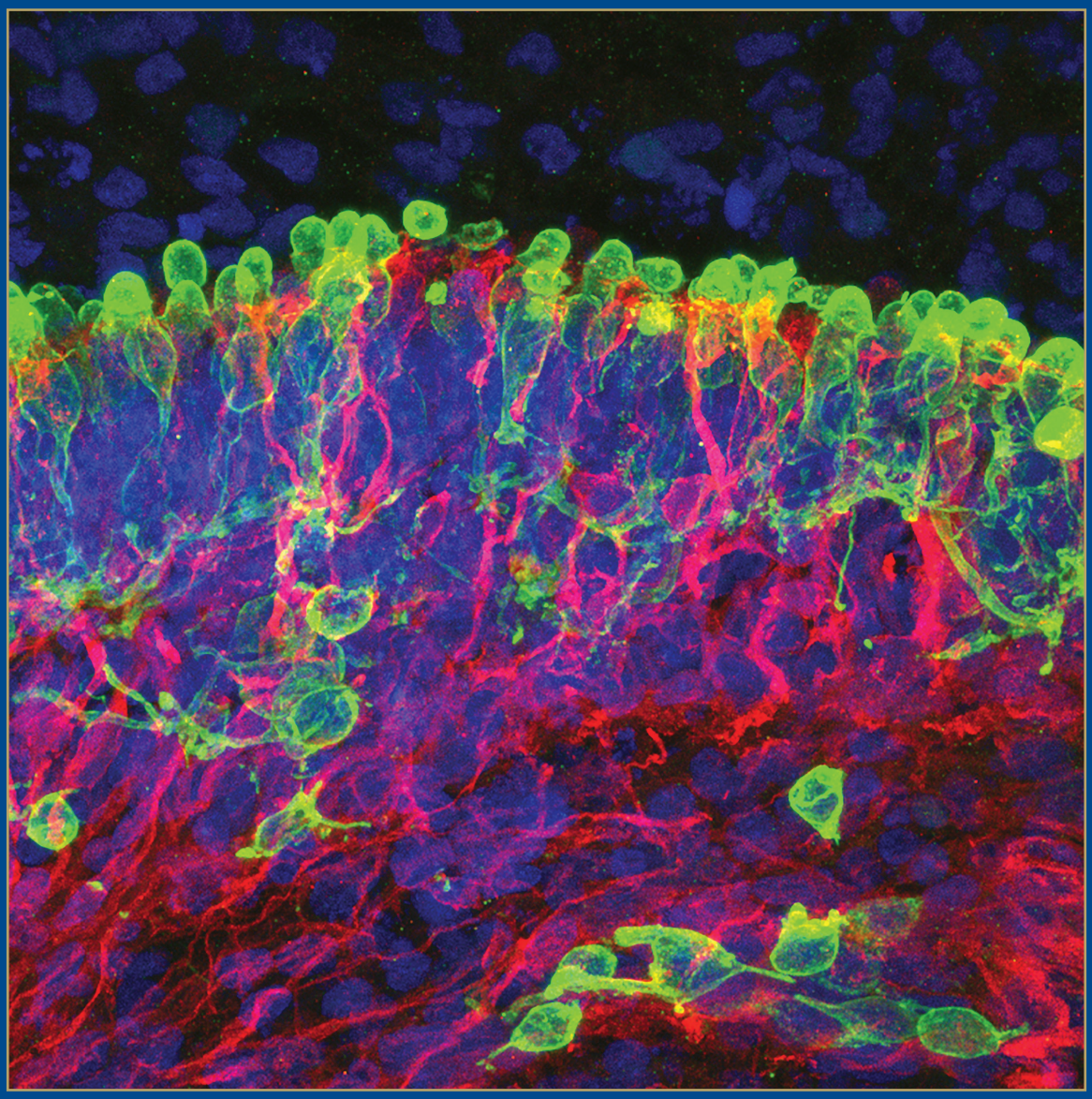
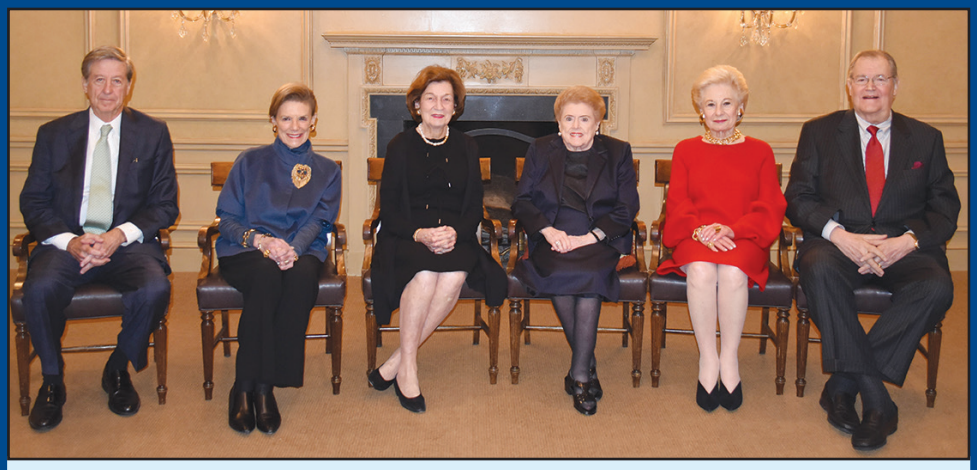


RETINA RESEARCH FOUNDATION

2018 annual report

Retina Research Foundation Board of Directors



RRF Founding Families
John Dawson, Dede Weil, Nancy Japhet, Dr. Alice McPherson, Suzanne Miller, and Henry Gissel

Cover photo courtesy of Elizabeth Capowski, PhD
Gamm lab, Waisman Center, University of Wisconsin-Madison

Cross section of a maturing three-dimensional retinal organoid generated from human induced pluripotent stem cells. Cone photoreceptors are shown in green and Muller glia are shown in red.

Retina Research Foundation

Annual Report
2018

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RRF Executive Committee
John Dawson, Ames Smith, Dr. Frank Eggleston,
Dr. Alice McPherson, Rich Walton, Bettie Lee

Ladies of the RRF Board
Rose Cullen, Shara Fryer, Suzanne Miller, Bettie Lee *(standing, left to right)*
Dede Weil, Nancy Japhet, Dr. Alice McPherson, Jacque Royce *(seated, left to right)*

President's Message

Dear Friends,

As we approach the 50th anniversary of the founding of Retina Research Foundation, let us take a moment to consider what has remained constant through the years since RRF was originally established. RRF has achieved much success by adhering to sound principles such as working in collaboration with the most outstanding ophthalmological organizations worldwide and offering a carefully designed, balanced program of vision research, international fellowships, young scientist development, and physician career advancement.

Our challenge going forward is enlarging the scope of our thinking to be ready for growth, change, and improvement when opportunities arise. We must continue to search out the most promising new ideas in vision research and to incorporate them into our existing successful programs.

In the next fifty years, what new directions will we explore in our battle to fight blindness? Time will tell, but our plan is to proceed in a way that will encourage creative thinking and promote new research avenues in basic science. Only striking out into the future with vigor, seeking innovative approaches, can give us the confidence to continue working towards a world that is free of blinding conditions and diseases.

Please join me in working towards a better future - it is possible with your continued interest and support.

With gratitude,

Alice McPherson M. D.

Alice McPherson, MD
President

Overview of Research - 2018

Retina Research Foundation supports an exemplary variety of programs in retina research around the world. The following is a brief recap of RRF research supported in 2018, which illustrates the wide scope of RRF activities.

RRF Pilot Study Grants – Investigation of New Research Topics

Baylor College of Medicine, Houston, TX

Samuel Wu, PhD – Kayser Research Project
Yingbin Fu, PhD – Basic Research Grant
Milan Jamrich, PhD – Lawrence Research Project
Rui Chen, PhD – Manning Research Project
Graeme Mardon, PhD – Miller Research Project
Richard Hurwitz, MD – Wilson Research Project

University of Texas MD Anderson Cancer Center, Houston, TX

Louise C. Strong, MD – Humble Research Project

University of Texas Medical Branch-Galveston, Galveston, TX

Wenbo Zhang, PhD – Bovay Research Project

Texas A&M Health Science Center, Temple, TX

Lih Kuo, PhD – Gueymard Research Project

University of Wisconsin, Madison, WI

Curtis Brandt, PhD – Murfee Macular Degeneration Project

Indiana University, Indianapolis, IN

Timothy Corson, PhD – Basic Research Grant

University of Utah, John Moran Eye Center, Salt Lake City, UT

Wolfgang Baehr, PhD – Basic Research Grant

RRF Cox Macula Society Research Grant – administered by The Macula Society

Cagri Besirli, MD, PhD – University of Michigan, Ann Arbor, MI

Research Chairs – Ongoing Proven Research Projects

Baylor College of Medicine, Houston, TX

Ching-Kang Jason Chen, PhD – RRF Research Chair

University of Wisconsin, Madison, WI

Kevin W. Eliceiri, PhD – Helmerich Chair, Assoc. Director, McPherson Eye Research Institute
Nader Sheibani, PhD – RRF Research Chair
David Gamm, MD, PhD – Humble Distinguished Director, McPherson Eye Research Institute
T. Michael Nork, MD – Murfee Chair, McPherson Eye Research Institute
Barbara Blodi, MD – Albert Chair, McPherson Eye Research Institute

Overview of Research - 2018

Research Professorships – Ongoing Proven Research Projects

University of Wisconsin, Madison, WI

Jeremy Rogers, PhD – Gamewell Professor, McPherson Eye Research Institute

Bikash Pattnaik, PhD – Matthews Professor, McPherson Eye Research Institute

Mrinalini Hoon, PhD – Brown Professor, McPherson Eye Research Institute

Established Awards – Awards Recognizing Lifetime Achievement

RRF Award of Merit – presented by The Retina Society – San Francisco, CA – September 13

Paul Sternberg, Jr, MD – Vanderbilt Eye Institute, Nashville, TN

RRF Kayser International Award – presented by International Society for Eye Research (ISER) – Northern Ireland, UK– September 10

Krzysztof Palczewski, PhD – Gavin Herbert Eye Institute – Irvine, CA

RRF Pyron Award – presented by American Society of Retina Specialists (ASRS) – Vancouver, BC – July 22

Joan W. Miller, MD – Mass Eye and Ear and Mass General Hospital, Boston, MA

CL Schepens MD/AAO Award – presented by American Academy of Ophthalmology (AAO) and Schepens International Society (SIS) – Chicago, IL – October 26

Joan W. Miller, MD – Mass Eye and Ear and Mass General Hospital, Boston, MA

RRF Gonin Lecturer – presented by Club Jules Gonin – Jersey, Channel Islands – July 13

Morten Dornonville de la Cour, MD – Glostrup Hospital, Denmark

Gonin Medal – presented by International Council of Ophthalmology (ICO) – Barcelona, Spain – June 16

Jean-Jacques De Laey, MD, PhD – Ghent University Hospital – Belgium

Paul Kayser/RRF Global Award – presented by Pan-American Association of Ophthalmology (PAAO); will be presented again in 2019

International Fellowships – Advanced Subspecialty Training

ICO – RRF Helmerich International Fellowships – administered by International Council of Ophthalmology Foundation (ICOF)

Hassan Mansoor, MD - from Pakistan to Singapore National Eye Center, Singapore

Supalert Prakhunhungsit, MD - from Thailand to Bascom Palmer, Miami, FL

Gillingham Pan-American Fellowships – administered by Pan-American Association of Ophthalmology (PAAO)

Claudio Ignacio Perez Valenzuela, MD - from Chile to University of California (UCSF), San Francisco, CA

Jaime David Martinez Martinez, MD - from Mexico to Bascom Palmer Eye Institute, Miami, FL

Research Initiatives – Educational and Travel Scholarships

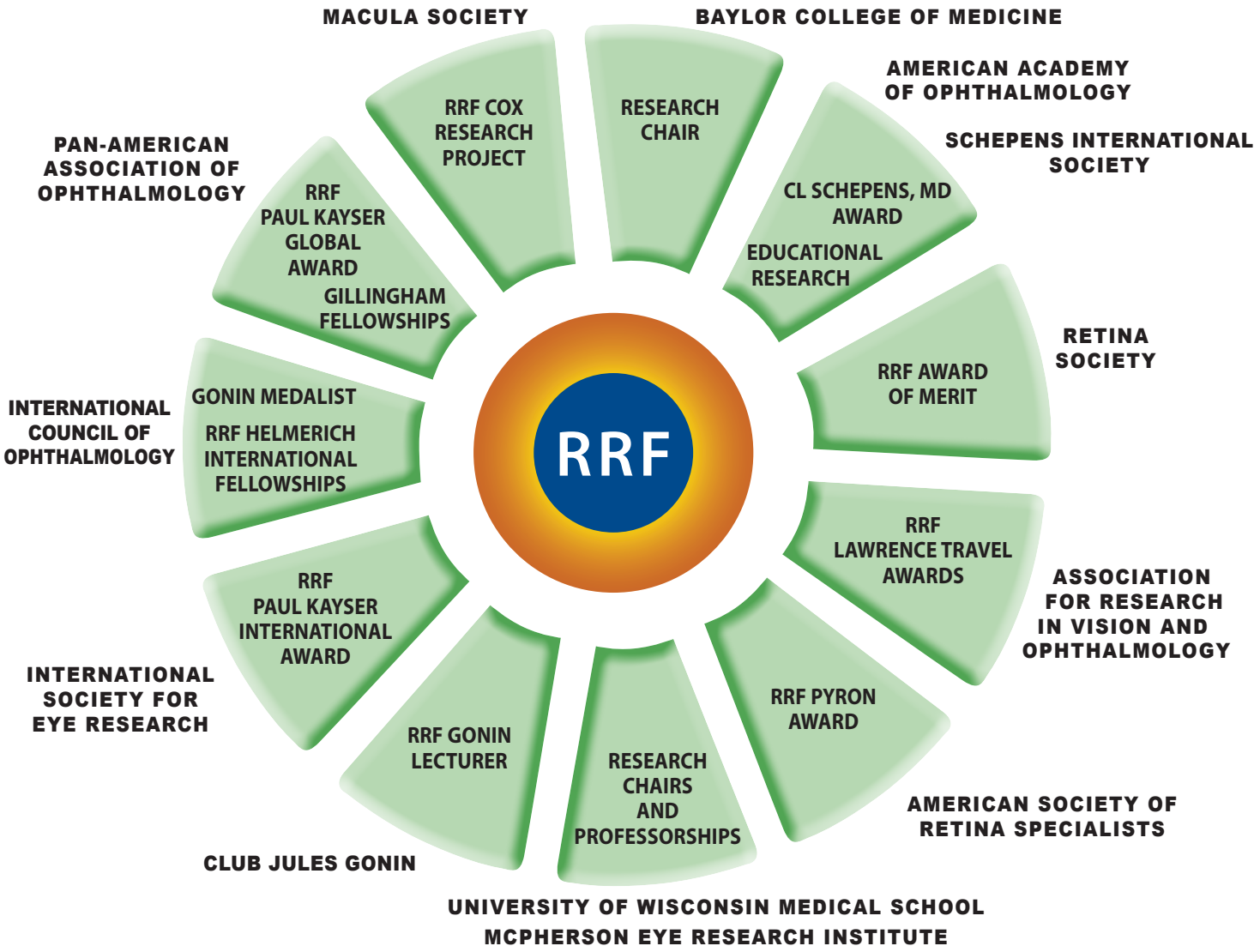
AAO Educational Trust Fund – administered by The Foundation of the American Academy of Ophthalmology (FAAO)

Retina-related educational research programs for clinical and basic science

RRF Lawrence Travel Scholarships – administered by The Association for Research in Vision and Ophthalmology (ARVO)

Twenty-two vitreoretinal scientists representing schools in 13 states and the District of Columbia traveled to the ARVO Annual Meeting to present their scientific research.

COLLABORATING ORGANIZATIONS



COLLABORATING ORGANIZATIONS	AWARD	DATE OF FIRST COLLABORATION WITH RRF
RETINA SOCIETY	RRF Award of Merit in Retina Research	1978
ARVO Assoc. for Research in Vision and Ophthalmology	RRF Lawrence Travel Awards	1984
ISER International Society for Eye Research	RRF Paul Kayser International Award	1986
ASRS American Society of Retina Specialists	RRF Pyron Award	1988
PAAO Pan-American Association of Ophthalmology	Gillingham Pan-American Fellowships Paul Kayser/RRF Global Award	1992 2012
AAO American Academy of Ophthalmology	Educational Trust Fund	1993
MACULA SOCIETY	RRF Cox Research Project	1993
CLUB JULES GONIN	RRF Gonin Lecturer	1996
ICO International Council of Ophthalmology with University of Lausanne and Swiss Ophthalmological Society	Gonin Medalist	1998
BAYLOR Baylor College of Medicine	Research Chair	1998
UW University of Wisconsin School of Medicine and Public Health	Research Chairs and Professorships	1998
MERI McPherson Eye Research Institute	Research Chairs and Professorships	2007
AAO American Academy of Ophthalmology with SIS Schepens International Society	Charles L. Schepens, MD/AAO Award	2008
ICO/ICOF International Council of Ophthalmology	ICO RRF Helmerich International Fellowships	2009

RETINA RESEARCH SITES

PAST AND PRESENT

TEXAS : 11

- Baylor College of Medicine
- Center for Technology
- Houston Advanced Research Center
- UT MD Anderson Cancer Center
- Southwest Research Institute
- Texas A & M Health Science Center
- Texas Children's Hospital
- The Methodist Hospital
- University of Houston
- University of Texas at Galveston
- University of Texas at Houston

PAN AMERICAN : 23

- Buenos Aires, Argentina
- Curitiba, Argentina
- La Paz, Bolivia
- Belo Horizonte, Brazil
- Recife, Brazil
- São Paulo, Brazil
- Porto Alegre, Brazil
- Santiago, Chile
- Bogotá, Colombia
- Cali, Colombia
- San Juan, Costa Rica
- Santo Domingo, Dominican Republic
- San Salvador, El Salvador
- Port-au-Prince, Haiti
- San Lorenzo, Honduras
- Aguascalientes, Mexico
- Mexico City, Mexico
- Nuevo León, Mexico
- Asunción, Paraguay
- Lima, Peru
- San Juan, Puerto Rico
- Montevideo, Uruguay
- Caracas, Venezuela

INTERNATIONAL : 46

- Al Shifa Trust Eye Hospital — Rawalpindi, Pakistan
- Aravind Eye Hospital — Madurai, India
- Asahikawa Medical College — Asahikawa, Japan
- Beijing Institute of Ophthalmology — Beijing, China
- Bern University Hospital — Bern, Switzerland
- Centre for Eye Research — Melbourne, Australia
- Copenhagen University — Copenhagen, Denmark
- Eskisehir Osmangazi University — Eskisehir, Turkey
- Eye & Laser World Center — Giza, Egypt
- Eye Foundation Hospital — Lagos, Nigeria
- Ghent University Hospital — Ghent, Belgium
- Institut de la Vision — Paris, France
- Jimma University — Jimma, Ethiopia
- Jules-Gonin Eye Hospital — Lausanne, Switzerland
- Kasindo Eye Clinic — E. Sarajevo, Bosnia & Herzegovina
- Keio University — Tokyo, Japan
- L V Prasad Eye Institute — Hyderabad, India
- Lariboisiere Hospital — Paris, France
- Lidcombe Hospital — Sydney, Australia
- Lund University — Lund, Sweden
- Magrabi ICO Cameroon Eye Institute — Yaounde, Cameroon
- Mashhad University Medical Services — Mashhad, Iran
- Melles Cornea Clinic — Rotterdam, Netherlands
- McGill University/Montreal General Hospital — Montreal, Canada
- Moorfields Eye Hospital — London, England
- Osaka Medical School/Osaka University — Osaka, Japan
- Research Institute of Ophthalmology — Cairo, Egypt
- Royal College of Ophthalmologists — Edinburgh, Scotland
- Sadguru Netra Chikitsalaya Eye Hospital — Satna, India
- Sankara Nethralaya Eye Hospital — Chennai, India
- Singapore National Eye Center — Singapore
- Siriraj Hospital — Bangkok, Thailand
- St. Thomas Hospital — London, UK
- Sussex Eye Hospital — Brighton, UK
- Tehran University of Medical Sciences — Tehran, Iran
- Toronto Western Hospital — Toronto, Canada
- University of Bonn — Bonn, Germany
- University of Cambridge — Cambridge, England
- University of Iceland — Reykjavik, Iceland
- University of Oxford — Oxford, England
- University of Paris — Paris, France
- University of Erlangen-Nuremberg — Erlangen, Germany
- University of Leipzig — Leipzig, Germany
- University of Regensburg — Regensburg, Germany
- University of Tübingen — Tübingen, Germany
- Western General Hospital — Edinburgh, Scotland

NATIONAL : 58

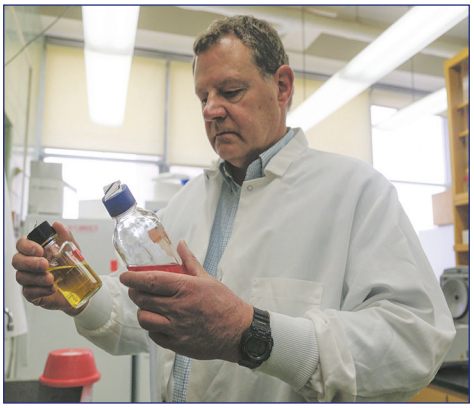
- Bascom Palmer Eye Institute — Miami, FL
- Beaumont Eye Institute/Hospital — Royal Oak, MI
- Byers Eye Institute/Stanford University — Palo Alto, CA
- California Institute of Technology — Pasadena, CA
- Case Western Reserve University — Cleveland, OH
- Casey Eye Institute — Portland, OR
- Charles Retina Institute — Germantown, TN
- City College of New York — New York, NY
- Cleveland Eye Clinic/Cole Eye Institute — Cleveland, OH
- Columbia University — New York, NY
- Cornell University Medical College — Ithaca, NY
- Dean McGee Eye Institute — Oklahoma City, OK
- Duke Eye Center/University Medical School — Durham, NC
- Emory University Eye Center — Atlanta, GA
- Eye Tech Pharmaceuticals — Worchester, MA
- Georgia Regents University — Augusta, GA
- Greater Baltimore Medical Center — Baltimore, MD
- Harvard Medical School — Boston, MA
- Indiana University — Indianapolis, IN
- Johns Hopkins University Medical School — Baltimore, MD
- Joslin Diabetes Center — Baltimore, MD
- Jules Stein Eye Institute — Los Angeles, CA
- Kellogg Eye Center/University of Michigan — Ann Arbor, MI
- Kresge Eye Institute — Detroit, MI
- Massachusetts Eye & Ear Infirmary — Boston, MA
- Massachusetts Institute of Technology — Boston, MA
- McPherson Eye Research Institute — Madison, WI
- Medical University of South Carolina — Charleston, SC
- National Eye Institute — Bethesda, MD
- Northwestern University — Evanston, IL
- Rockefeller University — New York, NY
- Schepens Eye Research Institute — Boston, MA
- Sheie Eye Institute — Philadelphia, PA
- Shiley Eye Center, UC San Diego — La Jolla, CA
- St. Joseph's Hospital — Baltimore, MD
- Tulane University Medical School — New Orleans, LA
- Thomas Jefferson University — Philadelphia, PA
- University of Alabama at Birmingham — Birmingham, AL
- University of California — Berkeley, CA
- University of California — Irvine, CA
- University of California — Los Angeles, CA
- University of California — San Francisco, CA
- University of Colorado — Aurora, CO
- University of Florida — Gainesville, FL
- University of Kansas Medical College — Kansas City, KS
- University of Miami Medical School — Miami, FL
- University of Nebraska HSC — Omaha, NE
- University of Pennsylvania — Pittsburgh, PA
- University of Rochester — Rochester, NY
- University of Southern California — Los Angeles, CA
- University of Utah, John A. Moran Eye Center — Salt Lake City, UT
- University of Washington — Seattle, WA
- University of Wisconsin Medical School — Madison, WI
- Vanderbilt University — Nashville, TN
- Washington University — St. Louis, MO
- Weill Cornell Medicine — New York, NY
- Wills Eye Hospital — Philadelphia, PA
- Wilmer Eye Institute — Baltimore, MD

Research

RRF provided funding for 12 pilot study research projects conducted at leading research institutions. Nine of the projects were named in recognition of generous support through gifts and years of exceptional service to the Foundation. Pilot studies are experimental studies designed "to test the waters" or break new ground. Findings may lead to larger ongoing studies in the future.

Named Basic Research Projects

The Kathryn and Latimer Murfee Macular Degeneration Project

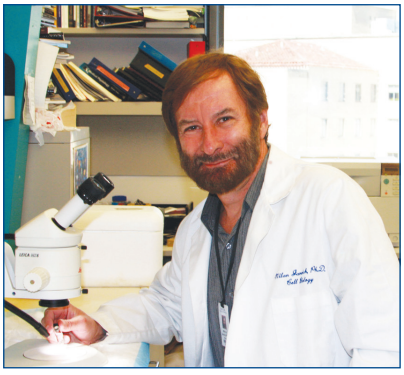


Curtis R. Brandt, PhD
Dept. of Ophthalmology and Visual Sciences
McPherson Eye Research Institute
University of Wisconsin, Madison, WI

Gene therapy for retinal degenerative diseases

The purpose of this project is to determine the mechanism of inflammation triggered by viral gene delivery vector injection in the non-human primate eye. In 2018, Dr. Brandt determined that non-human primate retina tissue expresses components of the inflammasome pathway in a variety of retinal cell types. His lab also discovered that a decrease in host restriction factors increased the transduction efficiency of a viral gene delivery vector in a human Muller cell line.

Joe M. and Eula C. Lawrence Research Project

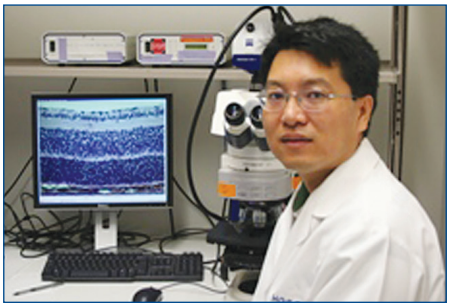


Milan Jamrich, PhD
Dept. of Molecular and Cellular Biology
Baylor College of Medicine, Houston, TX

Function of Rax in the specification, differentiation and survival of vertebrate retinal cells

The goal of this project is to identify genes and processes that are responsible for normal and abnormal vertebrate retinal development, which will lead to a better understanding of eye diseases, and as a result, new diagnostic procedures and treatments will be developed. Rax is a gene that plays a key role in vertebrate eye formation. In 2018 Dr. Jamrich identified the direct target genes of mouse Rax during retinal development by large-scale chromatin immunoprecipitation combined with sequencing (ChIP-seq).

The W.O. Manning Research Project



Rui Chen, PhD
Dept. of Molecular and Human Genetics
Baylor College of Medicine, Houston, TX

Identification and functional analysis of genes involved in retina diseases and development

Dr. Chen's long-term goal is to identify and conduct functional characterization of novel disease genes underlying inherited human retinal disorders. Results obtained from these studies can be directly translated into improving molecular diagnosis and form the basis of developing optimal treatment of human eye diseases, including gene therapy. Dr. Chen has identified multiple LCA and RP disease genes, such as IFT81, REEP6, and CWC27. In addition, several novel candidate genes associated with LCA and RP have been found and are currently under investigation, including FAM57B, a gene that is involved in ceremide biosynthesis. Finally, animal models have been generated for some of these newly discovered disease genes, for which functional studies and developing novel therapeutic approaches are currently underway.

Research

The Paul Kayser Research Project

Samuel Wu, PhD
Cullen Eye Institute, Neurosensory Center
Baylor College of Medicine, Houston, TX

Pharmacological and genetic mechanisms underlying retinal cell death in glaucoma and age-related macular degeneration (AMD)

The objective of Dr. Wu's research is to understand mechanisms underlying retinal synaptic dysfunction and cell death in glaucoma and age-related macular degeneration (AMD). Dr. Wu's lab published three papers and submitted three manuscripts in top international journals. These publications report their new discoveries on how rod and cone signaling pathways mediate light responses in retinal bipolar cells, and how dysfunction of photoreceptors, bipolar cell and amacrine cell synapses affect retinal degeneration in various forms of retinal and brain diseases. Dr. Wu and his lab members gave three presentations at the Association for Research in Vision and Ophthalmology (ARVO) annual meeting in May, 2018 in Honolulu, Hawaii, and one presentation at the FASEB meeting in July, 2018, in Buffalo, New York.

Bertha and I.L. Miller Research Project

Graeme Mardon, PhD
Depts. of Pathology, Molecular and Human Genetics
Baylor College of Medicine, Houston, TX

Genetic and molecular analysis of retinal development

The long-term goal of this project is to improve our ability to prevent, diagnose, and treat human retinal diseases. Dr. Mardon recently developed animal models for a gene associated with congenital blindness, named Kcnj13, which encodes a highly conserved potassium channel protein. In 2018 he found that conditional loss of Kcnj13 function, specifically in the retinal pigmented epithelium (RPE) in his mouse model, causes very early loss of photoreceptors and vision, first detectable by 15 days of age. By three months of age there is complete loss of the photoreceptor layer. He also developed a new system to detect loss of Kcnj13 in the RPE with which living animals with potential retinal degeneration can be identified within minutes instead of weeks, based on the expression of a genetic biosensor.

Emmett A. Humble Research Project

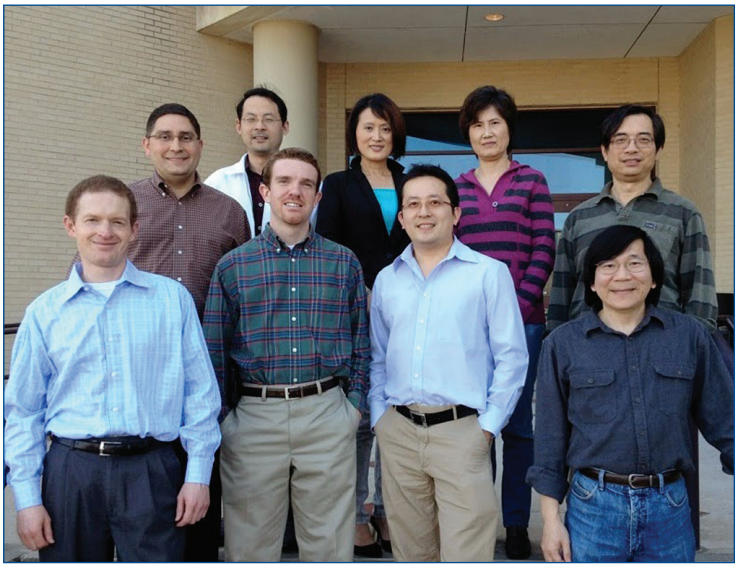
Louise C. Strong, MD
Dept. of Genetics
University of Texas MD Anderson Cancer Center
Houston, TX

Genetic etiology of retinoblastoma

Dr. Strong's goal is to provide a unique early cancer detection program for individuals with a hereditary cancer predisposition, specifically retinoblastoma and Li Fraumeni syndrome individuals. These tumors are a significant health problem as the most frequent cause of death in hereditary retinoblastoma patients is a second malignant neoplasm. It has been an ongoing aim of this project to provide sufficient education and guidelines for patients and family members seeking counseling and/or screening. Increased awareness of the risk of new cancer has been well received.

Research

Adolphe G. and Josephine Roberts Gueymard Research Project



Kuo's retinal research team (Dr. Kuo, front row, far right)

Lih Kuo, PhD
Depts. of Medical Physiology, Surgery, and Ophthalmology
Texas A&M Health Science Center, Temple, TX

Activation of endothelin-dependent RhoA/ROCK pathway elicits retinal arteriolar dysfunction in diabetic retinopathy

This project seeks to identify the mechanisms responsible for the initiation and development of diabetic retinopathy and to develop strategies for the prevention and treatment of this disease. Proper function of the retina depends on a sufficient supply of blood to the retina, and the dysfunction of retinal circulation can lead to disease development. Dr. Kuo demonstrated that acute hyperglycemia and diabetes impair retinal circulation related to activation of endothelin system and RhoA kinase signaling in the vasculature. Moreover, retinal structure and function are susceptible to the alteration of ocular hemodynamics, suggesting that the reduction of blood flow to the eye, as seen in the diabetic subjects, can have additional adverse impact on the retinal function. These findings were published in peer-review journals in 2018.

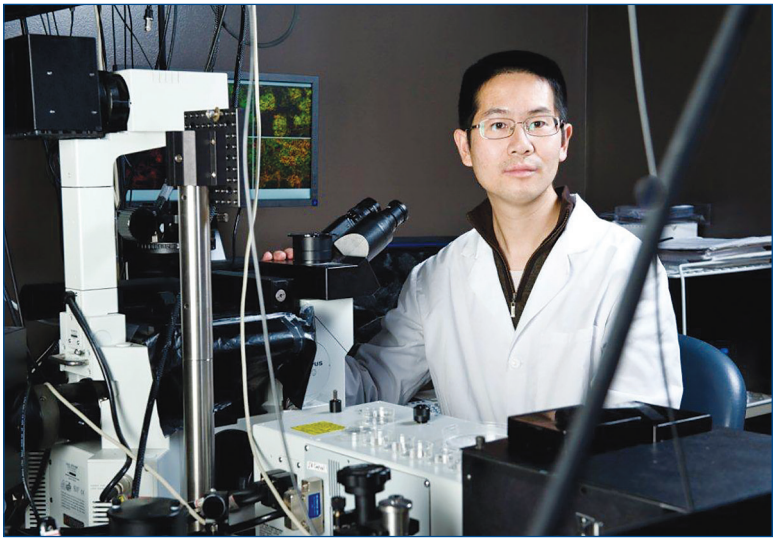
Mary Ellen Wilson Research Project

Richard L. Hurwitz, MD
Dept. of Pediatrics, Ophthalmology, Molecular and Cellular Biology
Co-Director, Retinoblastoma Center
Texas Children's Cancer Center
Center for Cell and Gene Therapy
Baylor College of Medicine, Houston, TX

Immune consequences of gene therapy for ocular disorders

Dr. Hurwitz's hypothesis is that gene therapy protocols for ocular disorders can be optimized by understanding how the unique ocular environment influences the efficacy of gene therapy. He has previously published an association of the vitreous component hyaluronan with the enhanced expression of potentially therapeutic genes transferred by adenoviral vectors. Hyaluronan alone does not account for the entire effect observed. Subsequently, he began to explore the contribution of another vitreous component, the large hyaluronan-binding proteoglycan versican and to examine the biochemical pathways influenced by its functional domains. Using the information gained from these studies, he is also examining a non-invasive delivery approach that uses microwafers loaded with nanoparticles to deliver therapeutic drugs or genes with the goal of further enhancing efficacy and reducing toxicity.

Harry E. Bovay, Jr. Research Project



Wenbo Zhang, PhD
Department of Ophthalmology & Visual Sciences
University of Texas Medical Branch at Galveston
Galveston, TX

Novel therapy for retinal neovascularization

Ischemic retinopathies are caused by impaired retinal blood supply in various diseases, such as diabetic retinopathy, retinopathy of prematurity, and retinal vascular occlusion. These conditions often result in irreversible vision loss due to the development and growth of abnormal new vessels after a period of retinal ischemia, a process referred to as retinal neovascularization. Data generated in 2018 suggest that pathogenic bacteria and probiotics may potentially affect retinal neovascularization differently via their disease-inducing products or beneficial metabolites, respectively. One manuscript based on data generated from RRF support has been published in IOVS, and three abstracts have been presented as a poster in the ARVO annual conference in May 2018.

Basic Research Projects

Timothy W. Corson, PhD
Eugene & Marilyn Glick Eye Institute
Indiana University School of Medicine
Indianapolis, IN

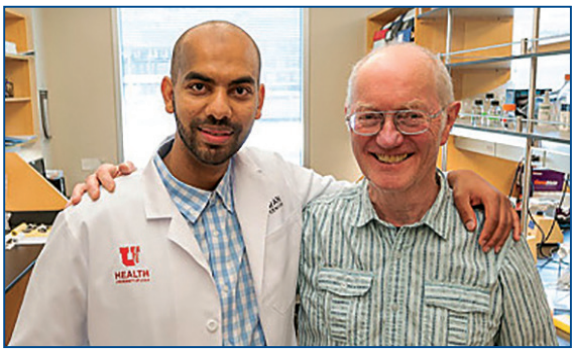
Screening homoisoflavonoids as soluble epoxide inhibitors for choroidal neovascularization

Dr. Corson (third from right) with his lab group

The overall goal of this project is to develop therapies for diseases like wet AMD by showing how soluble epoxide hydrolase (sEH) is important for abnormal blood vessel growth. Dr. Corson has developed a potent chemical called SH-11037 and tested this in combination with anti-VEGF therapy. He found sEH as a cellular target of SH-11037 and showed that sEH is present at high levels in human and mouse eyes with AMD-like features. Dr. Corson found that known sEH inhibitors can block new blood vessel growth in the eye and that a substrate (input) of sEH was antiangiogenic. In 2018, he assessed his library of novel chemicals and found candidates that perform as well as SH-11037 at blocking sEH, helping to build a "structure activity relationship" for blocking sEH function.

Research

Wolfgang B. Baehr, PhD
Department of Ophthalmology and Visual Sciences
University of Utah Health Science Center
Salt Lake City, UT



Dr. Baehr (right) and Dr. Ali Sharif, the team on the road to understanding LCA in INPP5E-Joubert Syndrome

The road to understanding INPP5E- Joubert Syndrome

Dr. Baehr's lab is interested in understanding mechanisms leading to non-syndromic and syndromic ciliopathies, focusing mainly on the retina. Mutations in INPP5E are associated with Joubert syndrome: mental retardation, truncal obesity, and retinal dystrophy (LCA). To date, the function of INPP5E is unclear. Dr. Baehr generated a mouse model in which INPP5E was deleted before birth. Phenotypic analysis shows that deletion of INPP5E affects multiple photoreceptor subcompartments, including the function of the ER and the structure of the Golgi apparatus. In particular, disc morphogenesis was impaired, presumably through changing the distribution of the phosphoinositides. Dr. Baehr's goal, using germline and retina-specific gene knockouts, is to identify the onset and cause of degeneration and devise gene-based therapies to ameliorate or cure the retina disease.

Yingbin Fu, PhD
Cullen Eye Institute
Baylor College of Medicine, Houston, TX

A unified mechanism for multiple forms of cone photoreceptor degeneration

The mechanism underlying cone death in Leber's congenital amaurosis (LCA) is not well understood. The large number of gene mutations involved and diverse functions affected create a challenge in designing LCA treatments. The goal of this application is to identify common mechanisms underlying cone death in order to find a common treatment strategy to protect cones and preserve vision across multiple forms of LCAs. Dr. Fu discovered a unified mechanism for cone degeneration in LCA. Namely, S-opsin aggregation induced endoplasmic reticulum (ER) stress is responsible for the rapid degeneration of "S-cones" (i.e., blue cones in human), and M-opsin degradation associated proteasome stress is a major contributor for "M-cone" (i.e., red/green cones in human) degeneration. This discovery has broad implications for cone degeneration in general.

Grant Recipient from The Macula Society

The RRF Margaret and Mills Cox Macula Society Research Project

Cagri Besirli, MD, PhD
University of Michigan, Dept. of Ophthalmology and Visual Sciences
Ann Arbor, MI

The Role of HK2 in Photoreceptor Metabolism and Survival

Dr. Besirli's research group is primarily focused on the metabolic regulation of photoreceptor death. Proteomic analysis of the subretinal fluid samples collected from children and adults with retinal detachment has identified key metabolic proteins as potential mediators of photoreceptor cell death. Based on this observation, Dr. Besirli has generated in vitro and in vivo models to study metabolic regulation of photoreceptor death and has demonstrated that metabolic reprogramming is a novel strategy for photoreceptor neuroprotection.

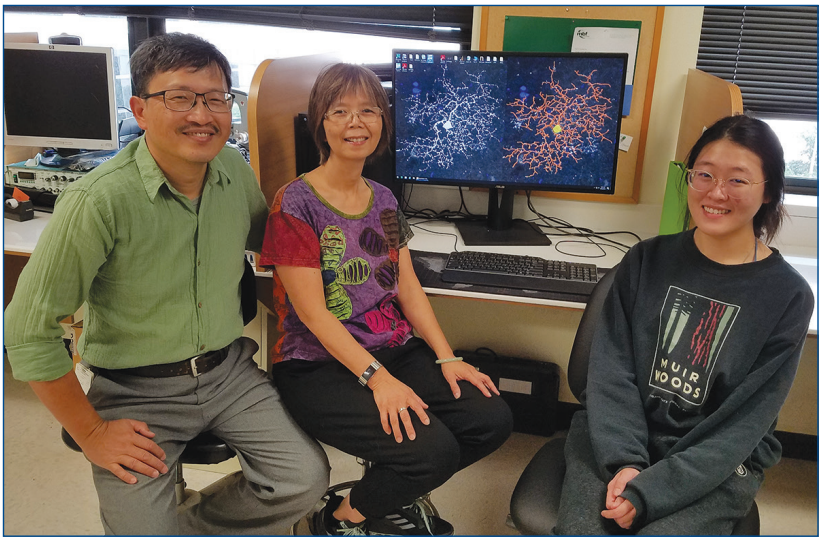
Research Chairs and Professorships

RRF now supports a total of six chairs and three professorships in retina research, which provide funds to vision scientists engaged in original excellent research that has the potential to increase understanding of the retina or retinal diseases.

RRF Research Chair

Ching-Kang Jason Chen, PhD
Depts. of Ophthalmology, Biochemistry and Molecular Biology, Neuroscience
Baylor College of Medicine
Houston, TX

Retinal ganglion cell diversity



Dr. Chen (left) with his research group

Dr. Chen's lab continues to investigate neuronal oscillation mechanisms in retinas of mice with degenerated photoreceptors. This endeavor provides knowledge on synaptic connectivity of oscillating and non-oscillating retinal ganglion cells (RGCs), which is also an important part of an ongoing effort to document the diversity of mouse RGCs. Recently, the lab generated an animal with silenced rod and cone photoreceptor inputs to the inner retina by targeted deletions of rod and cone transducin genes and surprisingly found in it that certain types of RGCs still retain light sensitivity. This exciting finding provides a new way to examine mouse RGC synaptic connectivity. The overall goal is to provide the vision research field with a catalog of genetically marked mouse inner retinal neurons to guide in depth investigations into retinal disease mechanisms and potential therapeutic interventions.

Walter H. Helmerich Chair

Kevin W. Eliceiri, PhD
Associate Director, McPherson Eye Research Institute
Director, Laboratory for Optical and Computational Instrumentation
University of Wisconsin, Madison, WI

Computational imaging of the cellular microenvironment

Dr. Eliceiri's research interests are in the areas of developing optical and computational approaches to study dynamic cellular processes such as those in the eye non-invasively. His current research focuses on the development of novel optical imaging methods and instrumentation for investigating the cellular microenvironment as well as the development of open source software for multidimensional imaging informatics. Specific interests include developing label free optical approaches for deeper imaging and sensing of the cellular microenvironment, new technologies for metabolic imaging as well as machine-learning-based analysis of cell morphology and dynamics. Recently his group developed a new computational imaging platform for label free studies of macrophages and microglial in intact tissues.

Research Chairs and Professorships

RRF Research Chair

Nader Sheibani, PhD
Department of Ophthalmology & Visual Sciences
University of Wisconsin, Madison, WI

Regulation of ocular vascular development and neovascularization

Dr. Sheibani (standing, third from right) with his research team

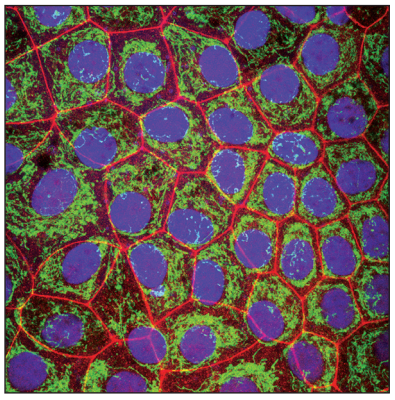
Dr. Sheibani's work focuses on mechanisms that maintain ocular vascular homeostasis. He demonstrated CYP1B1 is a major regulator of ocular redox hemostasis whose expression affects the angiogenic and inflammatory properties of vascular cells. Dr. Sheibani reported signature changes in different retinal layers content with diabetes, and showed increased mitochondrial oxidative stress in pericytes with high glucose. He also showed an important role for O-GlcNAcylation in metabolic stress and death of pericytes in high glucose. He demonstrated hypoxic-ischemic encephalopathy has a dramatic impact on retinal vascularization and function. Dr. Sheibani also reported a novel method for slow intravitreal delivery of potential therapeutic peptides. Reported in: TCMB (Jan 2018), Sci Rep (Jan and Jun 2018), Clin Sci (Apr 2018), Biophotonics (Sept 2018), IOVS (Aug 2018), Plos One (Oct 2018).

Emmett A. Humble Distinguished Directorship

David M. Gamm, MD, PhD
Director, McPherson Eye Research Institute
Dept. of Ophthalmology and Visual Sciences
University of Wisconsin, Madison, WI

Modeling and treating retinal disease with human induced pluripotent stem cells (hiPSCs)

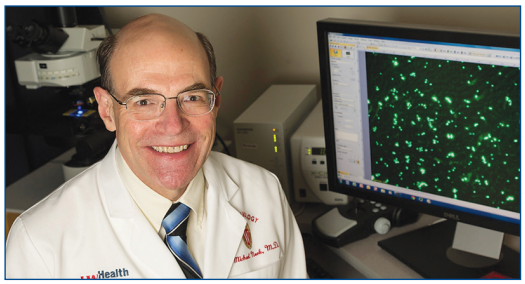
Dr. Gamm's lab has pioneered methods to generate retina cells from human pluripotent stem cells, which they are using to better understand how the retina is made and how best to employ this technology to preserve or restore vision in patients with age-related macular degeneration (AMD) and retinitis pigmentosa (RP). This past year, his lab further validated the authenticity of their lab-created photoreceptors and retinal pigment epithelium and began testing these critical cell types in animal models of retinal disease. Results from these studies will aid efforts to develop and test new therapies for patients with advanced AMD and RP, which is being pursued in conjunction with Opsis Therapeutics and FUJIFILM-Cellular Dynamics.



High magnification image of human retinal pigment epithelium (RPE) cells created from induced pluripotent stem cells. The colors highlight RPE nuclei (blue), connections between RPE cells (red), and mitochondria (energy-generating structures) within each RPE cell (green)

Research Chairs and Professorships

Kathryn and Latimer Murfee Chair



T. Michael Nork, MD
McPherson Eye Research Institute
Dept. of Ophthalmology and Visual Sciences
University of Wisconsin, Madison, WI

Functional and cellular mechanisms of ischemic retinal injury

Dr. Nork's laboratory is set up around developing and using animal models of retinal disease—especially retinal ischemia. Endpoints include both function (i.e., electrophysiology) and histopathology. He has been interested in learning how glaucoma affects the outer retina, and is now beginning to explore the effects of intraocular pressure (IOP)-related ischemia on the retina. The problem with glaucoma models of retinal ischemia is separating out the effects of elevated IOP and retinal ganglion cell loss possibly related to the observed effects on the photoreceptors. One approach Dr. Nork has been using is to use vasoconstrictors without elevated IOP. The real goal is to treat retinal disease, not simply to come up with animal models for it. Once we understand better the effects of retinal ischemia, it may be possible to ameliorate those by using long-acting vasodilators instead of vasoconstrictors.

Daniel M. Albert Chair

Barbara Blodi, MD
McPherson Eye Research Institute
Dept. of Ophthalmology and Visual Sciences
Medical Director, Fundus Photograph Reading Center (FPRC)
University of Wisconsin, Madison, WI

Adaptive optics imaging of human retinal function

Dr. Blodi is a retina specialist and one of the leaders of WAIVS (Wisconsin Advanced Imaging of Visual Systems), a newly established initiative to develop novel imaging systems of the visual pathway. The first WAIVS imaging system under development is Adaptive Optics, an imaging modality that is able to image individual photoreceptors in the human retina. In order to build this complex Adaptive Optics instrument, the WAIVS research group includes experts in retinal imaging, biomedical engineering, optics, physics and software development. Dr. Blodi is developing a standardized Adaptive Optics imaging protocol for human subjects in order to provide researchers well-defined guidelines in the acquisition and analysis of images.

Edwin and Dorothy Gamewell Professor

Photo by Todd Brown/Media Solutions

Jeremy Rogers, PhD
McPherson Eye Research Institute
Department of Biomedical Engineering
University of Wisconsin, Madison, WI

Optical instrumentation and technology platforms for the study and screening of retinal disease

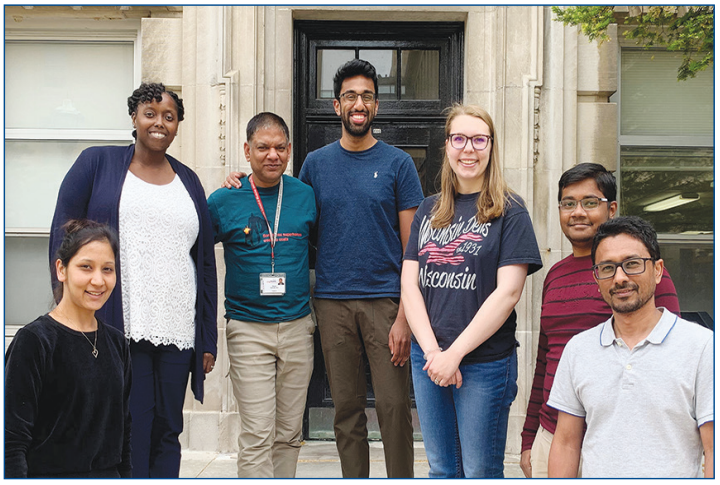
Dr. Rogers develops new imaging tools to aid in the diagnosis, treatment, and basic research of retinal disease. Imaging structure and function of retinal cells in a clinical setting is crucial to developing and monitoring new therapies. Dr. Rogers is developing technologies that exploit the intrinsic light scattering properties of cells, making these methods suitable for clinical imaging. His laboratory is currently building an Adaptive Optics Scanning Light Ophthalmoscope (AOSLO) that will enable imaging of individual photoreceptors and serve as a platform for developing next generation imaging capabilities to assess cell function. By developing new imaging methods based on light scattering and powered by computational simulations, he aims to create the tools needed to develop and monitor future stem cell or gene therapies.

Research Chairs and Professorships

M.D. Matthews Research Professor

Bikash Pattnaik, PhD
McPherson Eye Research Institute
Dept. of Pediatrics, Ophthalmology and Visual Sciences
University of Wisconsin
Madison, WI

Vision loss due to ion-channelopathy



Dr. Pattnaik (third from left) with his research team

Ion channels are proteins that help the diffusion of ions across the biological membrane. Mutation in several ion channels causes blindness. Dr. Pattnaik's research focus is on the inherited blindness due to defective inwardly rectifying potassium (Kir7.1) channel. These are present in the retinal pigment epithelium (RPE) cells in the back of the eye. Dr. Pattnaik's lab showed that induced pluripotent stem cells (iPSC) derived RPE cells from a Leber Congenital Amaurosis patient who had a defective Kir7.1 channel. After both gene therapy and drug treatment of the diseased iPSC-RPE cells and gene therapy in mice, the Kir7.1 channel had a normal function. His goal is to be able to manipulate the defective gene in these cells through cutting age gene-editing technology as a possible treatment for pediatric blindness.

Rebecca Meyer Brown Professor

Mrinalini Hoon, PhD
McPherson Eye Research Institute
Dept. of Ophthalmology and Visual Sciences
University of Wisconsin, Madison, WI

Synaptic connections in the developing and diseased retina

Dr. Hoon (second from left) with her research team

Dr Hoon's research is focused on elucidating the cellular and activity-dependent mechanisms that enable formation of correct neuronal connections ("synapses") in the developing retina and that damage retinal organization and function during disease and degeneration. The Hoon Lab combines high-resolution microscopy with single-cell electrophysiological and gene-sequencing approaches to reveal the synaptic and circuit re-organizations during phases of retinal "plasticity" encountered during developmental stages and when the circuit is damaged during retinal disease. Using transgenic mouse model systems that mimic developmental deficits or disease configurations, the Hoon Lab is determining inner retinal synaptic and circuit modifications, downstream of photoreceptor input, which will identify specific synaptic deficits in need of therapeutic attention.

Established Research Awards

These awards were presented to renowned scientists in recognition of their lifetime achievement.

The Award of Merit in Retina Research

Paul Sternberg, Jr, MD
Vanderbilt Eye Institute
Vanderbilt University Medical Center
Nashville, TN

Regenerative Visual Neuroscience: How It Will Transform Eye Care

In being chosen for the Award of Merit, Dr. Sternberg gave the Charles L. Schepens Lecture at the 51st Annual Scientific Meeting of The Retina Society in San Francisco, CA, which was held in September.

Dr. Sternberg maintains an active academic and research program, studying the pathogenesis of age-related macular degeneration. He has authored more than 250 scientific articles and 30 book chapters, and received research funding from the NIH, numerous foundations, and industry. Honors include the AAO Lifetime Achievement Award, the Heed Ophthalmic Foundation Award, Lew Wasserman Award of Merit from Research to Prevent Blindness, the Distinguished Service Award from ARVO, and the Sommer Prize from the EyeCare Foundation.

RRF Pyron Award for Outstanding Achievement in Retina Research

Joan W. Miller, MD
Mass Eye and Ear and Mass General Hospital
Harvard Medical School
Boston, MA

Treating AMD—Back to the Future

Dr. Miller presented the RRF Pyron Award lecture at the 36th Annual Meeting of the American Society of Retina Specialists (ASRS), which was held in Vancouver, BC, in July.

An internationally recognized expert on retinal disorders, Dr. Miller and her colleagues at Mass Eye and Ear developed verteporfin photodynamic therapy (PDT), the first pharmacologic treatment for retinal disease; co-discovered the role of vascular endothelial growth factor (VEGF) in neovascular eye disease; and demonstrated the therapeutic potential of VEGF inhibitors in neovascular eye disease.

Dr. Miller (center) with Drs. Timothy Murray and Mark Humayun, ASRS President

Paul Kayser International Award in Retina Research

Krzysztof Palczewski, PhD
UCI School of Medicine
Irvine, CA

Chemistry and Biology of Vision

The XXIII Biennial Meeting of the International Society for Eye Research (ISER), held in Northern Ireland, UK, in September was the setting for Dr. Palczewski's Plenary Lecture as recipient of the Kayser International Award.

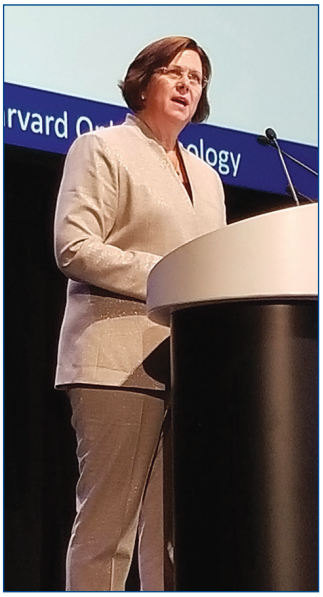
Dr. Palczewski has made major scientific contributions to the biology and chemistry of vertebrate vision. He and his colleagues are especially renowned for first solving the crystal structures of inactive and photoactivated bovine rhodopsin, a prototype for G protein-coupled receptors (GPCRs) that comprise the largest and most diverse family of human drug targets.

Established Research Awards

Charles L. Schepens, MD/AAO Award

Joan W. Miller, MD
Mass Eye and Ear and Mass General Hospital
Harvard Medical School
Boston, MA

Developing Therapies for AMD:
The Art and Science of Problem-Solving



In being selected for the Charles L. Schepens, MD/AAO Award, Dr. Miller gave the Charles L. Schepens, MD/AAO Lecture at the Retina Subspecialty Day of the American Academy of Ophthalmologists (AAO) Annual Meeting in Chicago, IL on October 26.

Dr. Miller has authored more than 200 original research articles and nearly 80 book chapters, review articles, or editorials. She is on the editorial board for the journals Ophthalmology and Ophthalmology Retina and an editor of several textbooks, including the 3rd edition of Albert and Jakobiec's Principles and Practice of Ophthalmology (Saunders). Her current studies focus on the genetics of age-related macular degeneration (AMD), strategies for early intervention in AMD, and neuroprotective therapies for retinal disease.

Club Jules Gonin Lecturer

Morten Dornonville de la Cour, MD
Glostrup Hospital
Copenhagen University
Denmark

Simulators in the Training of Surgeons – Is It Worth the Investment in Money and Time?

Dr. de la Cour gave the Jules Gonin Lecture at the XXXI Meeting of the Club Jules Gonin in Jersey, Channel Islands, in July.

Dr. de la Cour's research interests include epidemiology of retinal diseases and vitreoretinal surgery. One of his major contributions is the utilization and adaptation of the Danish National Patient Registry for ophthalmological problems. He conducts studies on transport of ions and water across the retinal pigment epithelium, including the identification of a molecular water pump in the apical membrane of the epithelium.

The Gonin Medal

Jean-Jacques De Laey, MD, PhD
Ghent University Hospital
Ghent, Belgium

Paraneoplastic Retinopathies

Every four years the Gonin Medalist is selected by the International Council of Ophthalmology (ICO) Board of Trustees in collaboration with the University of Lausanne and the Swiss Ophthalmological Society. The Diploma of the Gonin Medal was presented to Dr. De Laey at the Jules Gonin Eye Hospital in Lausanne, Switzerland, following his Gonin Medal Lecture in February. The Gonin Medal was awarded at the Opening Ceremony of the World Ophthalmology Congress in Barcelona, Spain, in June.

Dr. De Laey is committed to the cause of education and training in ophthalmology both in Europe and around the world.

International Fellowships

RRF funds two programs of international fellowships, one a twelve-month fellowship and the other a six-month fellowship.

ICO - RRF Helmerich International Fellowships

The International Council of Ophthalmology (ICO), in cooperation with the International Council of Ophthalmology Foundation (ICOF), and Retina Research Foundation, has established two international fellowships with income from an endowment created by Walter H. Helmerich, III. This year two, 12-month fellowships provide advanced subspecialty training for young ophthalmologists from developing countries who are recommended by the head of a teaching or public service institution and are committed to returning to a position at a teaching institution or public service hospital in their home country following the fellowship.

Hassan Mansoor, MD, from Pakistan, for training in Cornea and External Diseases with Prof. Chee Soon Phaik at Singapore National Eye Center in Singapore. Dr. Mansoor will complete his fellowship year in June 2019. Following his training, he will return to Al Shifa Trust Eye Hospital in Rawalpindi, Pakistan as Clinical Registrar.

Supalert Prakhunhungsit, MD, from Thailand for training in Retinopathy of Prematurity (ROP) and Pediatric Retina with Dr. Audina Berrocal at Bascom Palmer, in Miami, FL. Dr. Prakhunhungsit will complete his fellowship year in March 2019. Following his training, he will return to Siriraj Hospital, Mahidol University, in Bangkok, Thailand as Vitreoretinal Specialist and Instructor.

Gillingham Pan-American Fellowships/PAAO

This program is administered for RRF by the Pan-American Association of Ophthalmology (PAAO). Two, six-month fellowships were awarded this year to Latin American ophthalmologists for training at leading institutions in the United States.

Claudio Ignacio Perez Valenzuela, MD, from Santiago, Chile, to University of California San Francisco (UCSF) in San Francisco, CA, for training in Glaucoma with Shan Lin, MD.

Jaime David Martinez, MD, from Aguascalientes, Mexico, to Bascom Palmer Eye Institute in Miami, FL, for training in Cornea with Guillermo Amescua, MD.

Research Initiatives

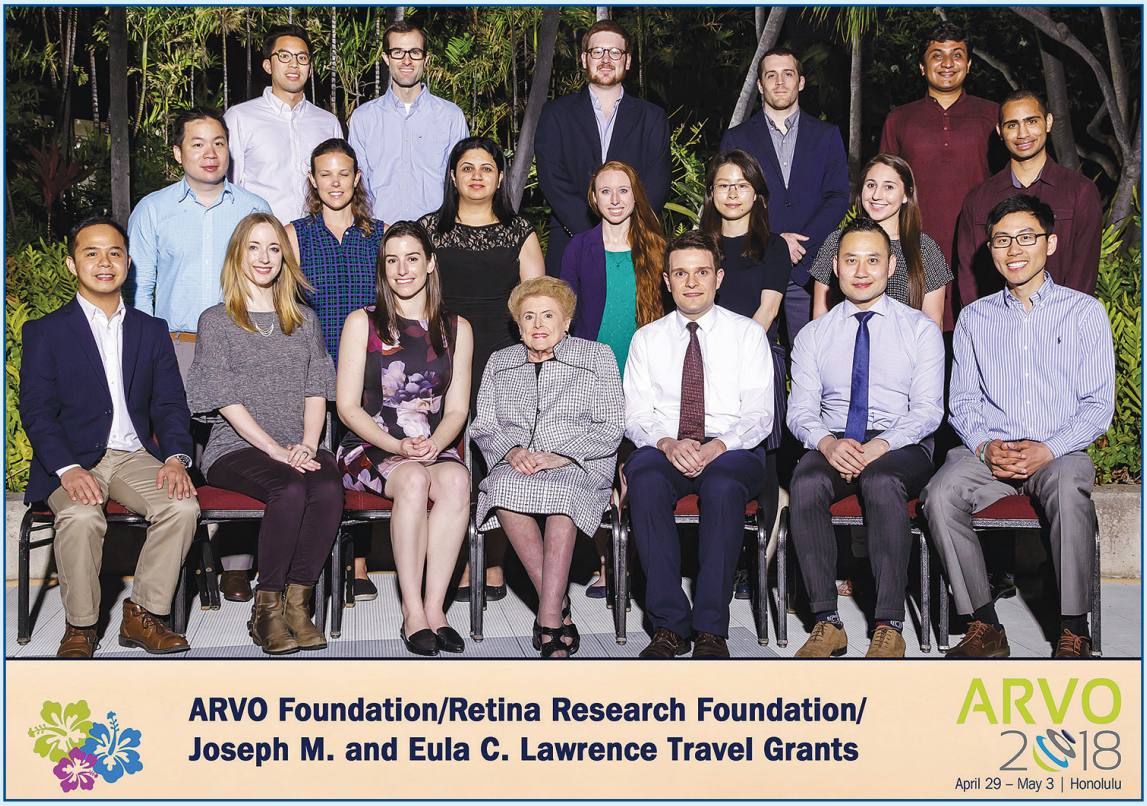
RRF has endowed gifts with earnings applied to translational research and education to bring laboratory knowledge to the clinical level.

American Academy of Ophthalmology Educational Trust Fund

This educational program is administered for RRF by the American Academy of Ophthalmology, and upgrades clinical research skills in the field of retina. The 2018 funding for this program was $50,000.

RRF Lawrence Travel Scholarships

This program is administered by the Association for Research in Vision and Ophthalmology (ARVO) and is made possible by a gift to RRF from Joe M. and Eula C. Lawrence. A total of $24,000 was funded to provide travel expenses for young vitreoretinal scientists to attend the ARVO Annual Meeting to present their papers or posters. This year the meeting was held in Honolulu, Hawaii.



Dr. Alice McPherson is seated, center, with this year's RRF Lawrence Travel Grant recipients

In 2018, twenty-two ophthalmology students were selected from these schools:

University of Utah, Salt Lake City, UT
Duke University School of Medicine, Durham, NC
University of California, San Diego, CA
Vanderbilt University, Nashville, TN
Mayo Clinic, Rochester, MN
University of California, Berkeley, CA
University of Tennessee Health Science Center, Memphis, TN
University of Washington, Seattle, WA
University of Rochester, NY
School of Medicine, University of Alabama at Birmingham, AL
Ohio State University, Columbus, OH
Joslin Diabetes Center, Boston, MA
Medical College of Wisconsin, Milwaukee, WI
Johns Hopkins University School of Medicine, Baltimore, MD
George Washington Univ. School of Medicine, Washington, DC
Tufts University School of Medicine, Boston, MA
Indiana University, Indianapolis, IN
Weill Cornell Medicine, New York City, NY
University of California, San Francisco, CA

Dedication of Dr. McPherson's 2014 Gonin Medal Archival Display at McPherson Eye Research Institute, Madison, WI

Dr. Alice McPherson has donated her Gonin Medal and diploma to the University of Wisconsin-Madison, and these historically important items are now displayed in an archival exhibition case in the Mandelbaum & Albert Family Vision Gallery at the entrance to the McPherson ERI's offices and research labs. The display will be part of the permanent archives of the University. Nine RRF Board members traveled to Madison, Wisconsin, in May for the dedication ceremony.

Dean Robert Golden, Dr. Alice McPherson, and Dr. David Gamm at the Dedication of the Gonin Medal Display Case

The Gonin Medal was instituted in 1937 in memory of Swiss-born Jules Gonin, MD. It is the oldest and most prestigious medal in ophthalmology. Every four years, the International Council of Ophthalmology (ICO) Board of Trustees elects the gold medalist. The diploma of the medal is delivered during a special ceremony in Lausanne, Switzerland, and the gold medal is presented at the World Ophthalmology Congress. In 2014, Dr. McPherson was selected for this high honor in recognition of her lifetime accomplishments as physician, teacher, scholar, leader, and pioneer dedicated to the study and treatment of retinal diseases.

University of Wisconsin-Madison Chancellor Rebecca Blank and Dr. McPherson

RRF Board of Directors with Dr. David Gamm (second from left)

Dr. McPherson Honored at ARVO

Dr. Alice McPherson and Retina Research Foundation were honored at the 2018 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in Honolulu, Hawaii, for creating and funding the RRF Lawrence Travel Grants. Since 1993, RRF has made it possible for 623 young scientists to attend ARVO annual meetings to present their papers and posters. This was a pioneering program at that time, and has caught on in a big way over the years. Founded in 1928, ARVO is the largest and most respected eye and vision research organization in the world.

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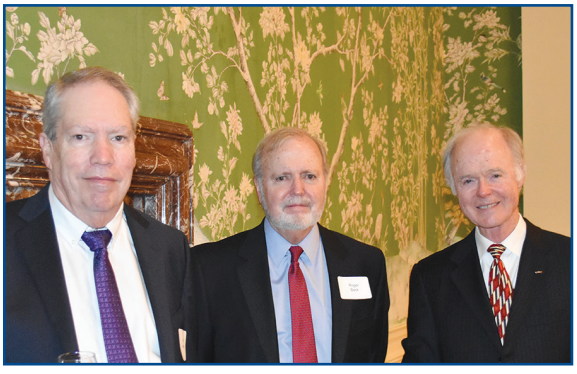

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Dr. Shawn Kavoussi with Dean Malouta and Rose Haché

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RETINA RESEARCH FOUNDATION
COMBINED STATEMENT OF FINANCIAL POSITION

December 31, 2018
(with summarized financial information as of December 31, 2017)

	General Funds			Endowment Funds			2018	2017 Total
	Without Donor Restrictions	With Donor Restrictions	Total	Without Donor Restrictions	With Donor Restrictions	Total	**Total All Funds**	All Funds (Memorandum Only)
Assets								
Cash and cash equivalents	$ 1,074,732	$ 39,500	$ 1,114,232	$ -	$ 846,895	$ 846,895	**$ 1,961,127**	$ 2,038,754
Contributions receivable	58,445	2,000	60,445	-	10,000	10,000	**70,445**	54,715
Investments	1,310,820	-	1,310,820	3,225,511	45,275,180	48,500,691	**49,811,511**	53,857,960
Furniture and equipment, net of accumulated depreciation of $10,276	18,654	-	18,654	-	-	-	**18,654**	20,516
Intangible assets	12	-	12	-	-	-	**12**	12
Total assets	$ 2,462,663	$ 41,500	$ 2,504,163	$ 3,225,511	$ 46,132,075	$ 49,357,586	**$ 51,861,749**	$ 55,971,957
Liabilities and net assets								
Accounts payable	$ 17,737	$ -	$ 17,737	$ -	$ 58,647	$ 58,647	**$ 76,384**	$ 68,958
Commitments and contingencies								
Net assets	2,444,926	41,500	2,486,426	3,225,511	46,073,428	49,298,939	**51,785,365**	55,902,999
Total liabilities and net assets	$ 2,462,663	$ 41,500	$ 2,504,163	$ 3,225,511	$ 46,132,075	$ 49,357,586	**$ 51,861,749**	$ 55,971,957

RETINA RESEARCH FOUNDATION
COMBINED STATEMENT OF ACTIVITIES AND CHANGES IN NET ASSETS

For the year ended December 31, 2018
(with summarized financial information for the year ended December 31, 2017)

	General Funds			Endowment Funds			2018	2017 Total
	Without Donor Restrictions	With Donor Restrictions	Total	Without Donor Restrictions	With Donor Restrictions	Total	**Total All Funds**	All Funds (Memorandum Only)
Revenues								
Contributions	$ 202,014	$ 189,500	$ 391,514	$ -	$ 144,750	$ 144,750	**$ 536,264**	$ 522,634
Investment income, net	51,488	-	51,488	91,006	1,309,800	1,400,806	**1,452,294**	1,260,207
Realized and unrealized (losses) gains on investments, net	(113,539)	-	(113,539)	(279,384)	(3,992,090)	(4,271,474)	**(4,385,013)**	3,587,859
Mineral interest income and other income	23,960	-	23,960	-	-	-	**23,960**	19,879
Income transferred from Endowment Fund investments	1,190,733	99,000	1,289,733	(84,429)	(1,205,304)	(1,289,733)	**-**	-
Net assets released from restrictions - satisfaction of program restrictions	364,000	(364,000)	-	-	-	-	**-**	-
Total revenues	1,718,656	(75,500)	1,643,156	(272,807)	(3,742,844)	(4,015,651)	**(2,372,495)**	5,390,579
Expenses								
Program services								
Research projects and grants	1,580,183	-	1,580,183	-	-	-	**1,580,183**	1,294,559
Supporting services								
Management and general	164,956	-	164,956	-	-	-	**164,956**	158,692
Total expenses	1,745,139	-	1,745,139	-	-	-	**1,745,139**	1,453,251
Changes in net assets	(26,483)	(75,500)	(101,983)	(272,807)	(3,742,844)	(4,015,651)	**(4,117,634)**	3,937,328
Net assets, beginning of year	2,471,409	117,000	2,588,409	3,498,318	49,816,272	53,314,590	**55,902,999**	51,965,671
Net assets, end of year	$ 2,444,926	$ 41,500	$ 2,486,426	$ 3,225,511	$ 46,073,428	$ 49,298,939	**$ 51,785,365**	$ 55,902,999

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Retina Research Foundation
1977 Butler Boulevard
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email: rrf@retinaresearchfnd.org
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