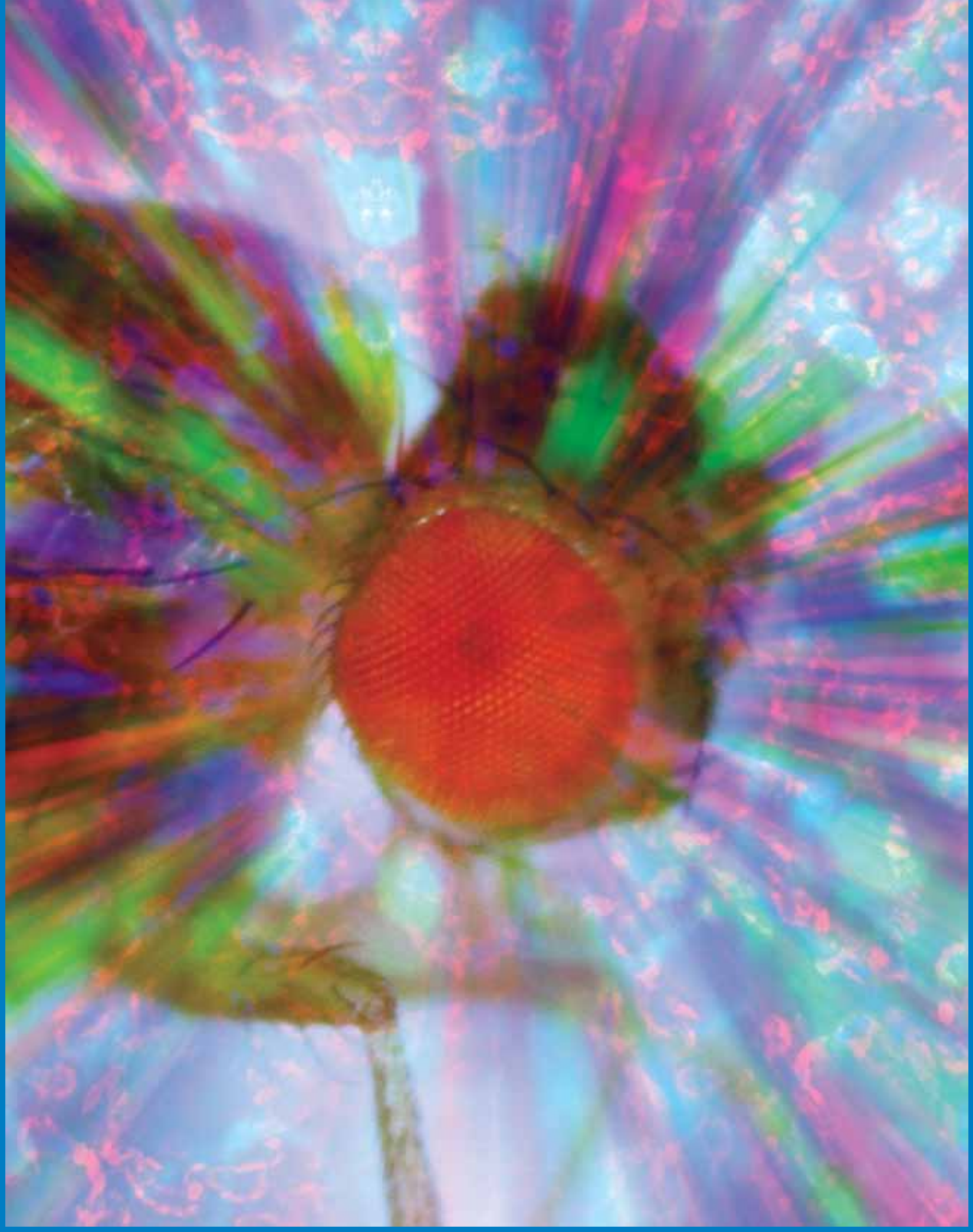
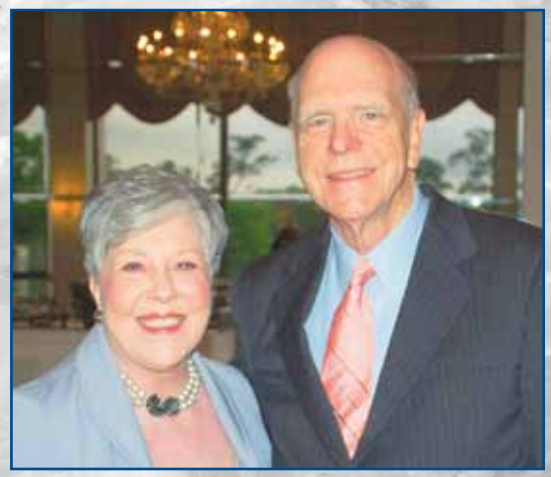


RETINA
RESEARCH FOUNDATION
2011 annual report

Dede Weil

Cecil Rix, PhD, Ames Smith and Shane Hudson

Bernard Hicks, MD, Rose Haché, Frank Eggleston, DDS, Shara Fryer and Kelli Kickerillo



Jacquelyn Royce and Ben Orman, MD

Ben Morton and Lynn Bernard

Cover photo courtesy of Nansi Jo Colley, PhD

TRP channels have emerged as key biological sensors functioning in many cellular processes including vision, taste, olfaction, hearing and touch. Despite their importance, virtually nothing is known about the folding and targeting of TRP channels during their biosynthesis. In the November 2011 issue of Neuron the Colley lab published work on a novel molecular chaperone, XPORT, which functions in the biosynthesis and trafficking of the *Drosophila* TRP channel and its G-protein coupled receptor, rhodopsin (Rh1).

This image shows the *Drosophila* compound eye, which is where the first TRP channel was discovered and characterized. In the background is an overlay of several immunofluorescently labeled tissue sections. XPORT protein is labeled in red. TRP or Rh1 are labeled in green, and nuclei are shown in blue.

Retina Research Foundation
Annual Report
2011

Table of Contents

Retina Research Foundation Board of Directors

Nancy Japhet and Arthur Willis, MD

John Dawson, Jr., and Bettie Lee

Bruce Mack, Alice McPherson, MD, and Richard Walton

President's Message

Alice McPherson, MD

Dear Friends,

In this age of rapid change, Retina Research Foundation (RRF) is proud to say that the change we methodically advance is research into causes and cures for blindness. "Slow and steady wins the race" is true, but often scientific advancement comes from unexpected quarters and in seemingly random sequence. The scientific process requires pursuing a diversity of avenues to achieve maximum success. The pace of progress may be frustratingly slow at times, but may then leap ahead in great bounds if the groundwork has been laid.

As you will see on page four of this report, RRF works in collaboration with the most outstanding organizations worldwide. Like spokes in a wheel, these collaborating organizations allow RRF to have the strength and solid foundation on which to build a carefully designed, balanced program of retina research:

- Pilot studies conducted by highly regarded scientists at leading universities;
- Established ongoing studies conducted by internationally recognized award recipients;
- Research Chairs and Professorships at leading universities and institutions;
- International fellowships that provide advanced subspecialty training to young scientists, who return to their home countries following training;
- Young scientist development and career advancement programs.

This diversity of research programs is intended to cast a wide net of investigation into sight preservation. The research sites shown on page five of this report list the local, national, and international sites for research projects that RRF has supported through the years. Our influence is worldwide because blindness knows no boundaries.

The philosophy of RRF has been and continues to be achieving excellence each step along the way. These steps in excellence begin with the selection process for awards, grants or appointments and continue through the projects themselves that generate new insights and discoveries previously unknown, stimulating new avenues for scientific investigation.

One thing will never change – RRF is always striving to do better. In 2011, we completed a major redesign of our website, which we hope will be a window for you into our activities. An informed and supportive public is the best partner we can have as we work to achieve our mission of vision preservation.

With gratitude,

Alice McPherson, MD
President

Overview of Research - 2011

Retina Research Foundation supports an exemplary variety of programs in retina research around the world. Past and present RRF research sites now total 57 national and 51 international. The following is a brief recap of sites for RRF research funds in 2011, which illustrates the wide reach of RRF activities.

RRF Pilot Study Grants – Investigation of New Research Topics

Baylor College of Medicine, Houston, TX

- Samuel Wu, PhD - Gueymard Research Project
- Ramon Font, MD - Kayser Research Project
- Milan Jamrich, PhD - Lawrence Research Project
- Rui Chen, PhD - Manning Research Project
- Graeme Mardon, PhD - Miller Research Project
- Richard Hurwitz, MD - Wilson Research Project

UT MD Anderson Cancer Center, Houston, TX

- Louise Strong, MD - Humble Research Project

Texas A&M Health Science Center, Temple, TX

- Lih Kuo, PhD - Basic Research Grant

University of Wisconsin, Madison, WI

- Nansi Jo Colley, PhD - Murfee Macular Degeneration Project
- Barbara Klein, MD, MPH – Mueller Research Project
- Leonard Levin, MD, PhD - Basic Research Grant

RRF Macula Research Grant – Pilot Study Award

RRF Cox Research Project – administered by The Macula Society

- J. William Harbour, MD – Washington University School of Medicine, St. Louis, MO

Established Awards – Awards Recognizing Lifetime Achievement

RRF Award of Merit – presented by The Retina Society – Rome, Italy - Sept. 21 to 25

- Michael F. Marmor, MD – Eye Institute at Stanford, Stanford University, Palo Alto, CA

RRF Kayser International Award – presented by International Society for Eye Research (ISER)

- Will be presented again in 2012

RRF Pyron Award – presented by American Society of Retina Specialists (ASRS) – Boston, MA – Aug. 20 to 24

- Jean Bennett, MD, PhD – Stellar-Chance Labs, University of Pennsylvania, Philadelphia, PA
- Albert Maguire, MD – Scheie Eye Institute, University of Pennsylvania, Philadelphia, PA

C L Schepens MD/AAO Award – Co-Sponsored by RRF and Schepens International Society (SIS) – Orlando, FL - Oct. 21

- Stanley Chang, MD – Columbia University, New York, NY

RRF Gonin Lecturer – presented by Club Jules Gonin

Will be presented again in 2012

RRF Gonin Medalist – presented by ICO with Club Jules Gonin

Will be presented again in 2014

Research Chairs – Ongoing Proven Research Projects

University of Wisconsin, Madison, WI

Curtis Brandt, PhD – Helmerich Chair

Nader Sheibani, PhD – RRF Chair

Daniel Albert, MD, MS – Humble Distinguished Directorship

David Gamm, MD, PhD – Murfee Chair

Baylor College of Medicine, Houston, TX

RRF Chair – Yet to be named

Research Professorships – Ongoing Proven Research Projects

University of Wisconsin, Madison, WI

Arnold E. Ruoho, PhD – Gamewell Professor

Arthur S. Polans, PhD – MD Matthews Professor

Bikash Pattnaik, PhD – RM Brown Professor

International Fellowships – Advanced Subspecialty Training

ICO/Helmerich International Fellowships - administered by International Council of Ophthalmology Foundation (ICOF)

Lala Ceklic, MD, PhD – from Sarajevo to Bern University Hospital, Switzerland

Afsun Sahin, MD – from Turkey to Schepens Eye Research Inst., Harvard Univ., Boston, MA

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

Arturo Ramirez-Miranda, MD – from Mexico to Jules Stein Eye Institute, Los Angeles, CA

Caio Vinícius Saito Regatieri, MD – from Brazil to Schepens Eye Research Institute, Harvard Medical School, Boston, MA

Research Initiatives – Educational and Travel Scholarships

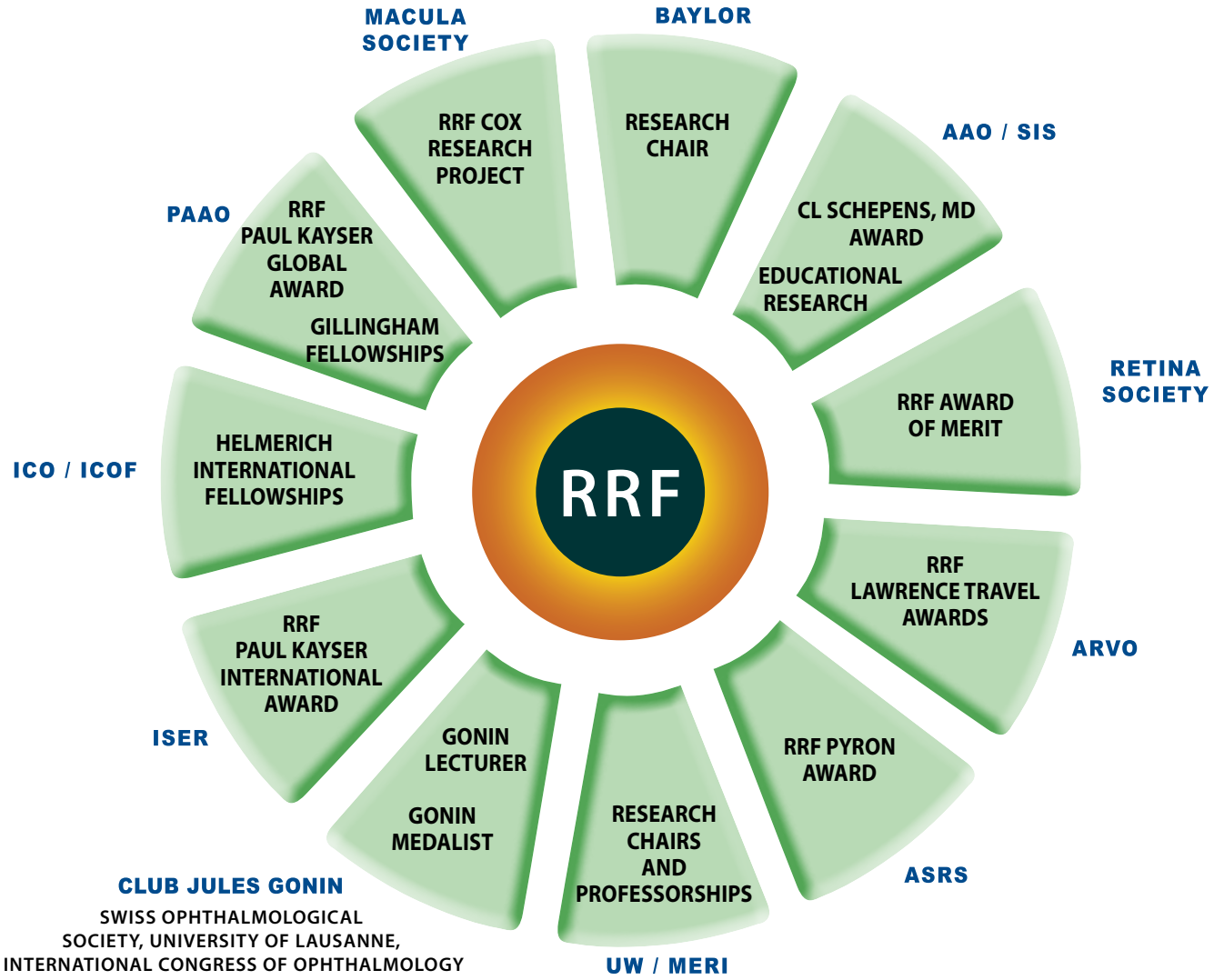
AAO Educational Trust Fund – administered by The Foundation of the American Academy of Ophthalmology (FAAO)

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)

Nineteen vitreoretinal scientists representing schools in thirteen states traveled to the ARVO Annual Meeting to present their scientific research.

COLLABORATING ORGANIZATIONS



COLLABORATING ORGANIZATIONS	AWARD	DATE OF FIRST COLLABORATION WITH RRF
RETINA SOCIETY 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
SIS Schepens International Society	Charles L. Schepens, MD/AAO Award	1986
ASRS American Society of Retina Specialists	RRF Pyron Award	1988
PAAO Pan-American Association of Ophthalmology	Gillingham Fellowships Paul Kayser/RRF Global Award	1992
AAO American Academy of Ophthalmology	Educational Trust Fund	1993
MACULA SOCIETY Macula Society	RRF Cox Research Project	1993
CLUB JULES GONIN Club Jules Gonin, Swiss Ophthalmological Society, University of Lausanne, International Congress of Ophthalmology	Gonin Lecturer Gonin Medalist	1996
BAYLOR Baylor College of Medicine	Research Chair	1998
UW University of Wisconsin	Research Chairs and Professorships	1998
MERI McPherson Eye Research Institute	Research Chairs and Professorships	2007
ICO/ICOF International Council of Ophthalmology, ICOFoundation	ICO/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

NATIONAL : 46

Bascom Palmer Eye Institute	Miami, FL
California Institute of Technology	Pasadena, CA
Casey Eye Institute	Portland, OR
Cleveland Eye Clinic/Foundation	Cleveland, OH
Cole Eye Institute	Cleveland, OH
Columbia University	New York, NY
Cornell University Medical College	Ithaca, NY
Dean McGee Eye Institute	Oklahoma City, OK
Duke University Medical School	Durham, NC
Emory University Eye Center	Atlanta, GA
Eye Research Institute	Boston, MA
Eye Tech Pharmaceuticals	Worchester, MA
Greater Baltimore Medical Center	Baltimore, MD
Harvard Medical School	Boston, MA
Johns Hopkins University Medical School	Baltimore, MD
Joslin Diabetes Center	Baltimore, MD
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
St. Joseph's Hospital	Baltimore, MD
Stanford University Medical School	Palo Alto, CA
Tulane University Medical School	New Orleans, LA
Thomas Jefferson University	Philadelphia, PA
University of California	Berkeley, CA
University of California	Los Angeles, CA
University of California	San Francisco, CA
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 Southern California	Los Angeles, CA
University of Washington	Seattle, WA
University of Wisconsin Medical School	Madison, WI
Vanderbilt University	Nashville, TN
Washington University	St. Louis, MO
Wills Eye Hospital	Philadelphia, PA
Wilmer Eye Institute	Baltimore, MD
William Beaumont Hospital	Royal Oaks, MI

INTERNATIONAL : 30

Asahikawa Medical College	Asahikawa, Japan
Bern University Hospital	Bern, Switzerland
Eskisehir Osmangazi University	Eskisehir, Turkey
Eye Foundation Hospital	Laos, Nigeria
Hospital Ophthalmique	Lausanne, Switzerland
Institute de la Vision	Paris, France
Kasindo Eye Clinic	E. Sarajevo, Bosnia and Herzegovina
Keio University	Tokyo, Japan
L V Prasad Eye Institute	Hyderabad, India
Lariboisiere Hospital	Paris, France
Lidcombe Hospital	Sydney, Australia
Lund University	Lund, Sweden
Mashhad University Medical Services	Mashhad, Iran
Melles Cornea Clinic	Rotterdam, Netherlands
McGill University	Montreal, Canada
Montreal General Hospital	Montreal, Canada
Moorfields Eye Hospital	London, England
Osaka Medical School	Osaka, Japan
Research Institute of Ophthalmology	Cairo, Egypt
Royal College of Ophthalmologists	Edinburgh, Scotland
University of Cambridge	Cambridge, England
University of Iceland	Reykjavik, Iceland
University of Osaka	Osaka, Japan
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

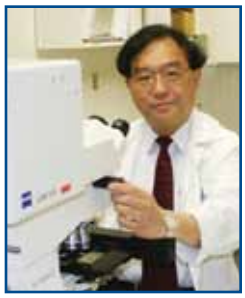
PAN AMERICAN COUNTRIES : 21

- Buenos Aires, Argentina
- Curitiba, Argentina
- La Paz, Bolivia
- Belo Horizonte, 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
- Mexico City, Mexico
- Nuevo León, Mexico
- Asunción, Paraguay
- Lima, Peru
- San Juan, Puerto Rico
- Montevideo, Uruguay
- Caracas, Venezuela

Research

RRF provided funding for 11 pilot study research projects conducted at leading research institutions. Pilot studies are experimental studies designed to "test the waters" or break new ground. Findings may lead to larger ongoing studies in the future. Eight of the projects have been named in recognition of generous support of gifts. This year the Carl G. Mueller, Jr. Research Project has been named in his memory and in honor of his long time leadership role and dedication to RRF.

Named Basic Research Projects



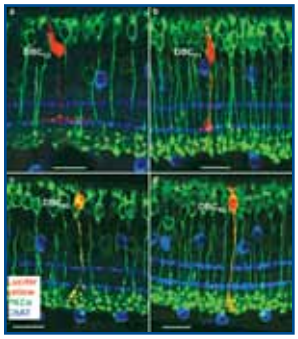
Adolphe G. and Josephine Roberts Gueymard Research Project

Samuel Wu, PhD

Cullen Eye Institute

Baylor College of Medicine, Houston, TX

Pharmacological and Genetic Mechanisms Underlying Retinal Cell Death in Glaucoma and Age-Related Macular Degeneration (AMD)



Confocal microscope photo of mouse retinal bipolar cells filled with Lucifer yellow (red) and counter-stained with PKCa (green) and ChAT (blue)

Dr. Wu's research is focused on molecular and synaptic mechanisms underlying retinal cell death in age-related macular degeneration (AMD) and glaucoma, and developing new gene therapy vectors for rescuing retinal degeneration in these diseases. His group has demonstrated that gene therapy prevents photoreceptor degeneration in a Bardet-Biedl Syndrome mouse model, and developed a new microinjection system for ocular delivery of pharmacological agents and viral/gene conjugates. His lab also designed new non-invasive devices for early detection of photoreceptor and ganglion cell dysfunction in animals and humans. They will use these new tools in conjunction with electrophysiological and pharmacological techniques to develop new treatment and prevention strategies. Dr. Wu's recent publications report new discoveries on the first successful gene therapy that prevents photoreceptor degeneration in a BBS animal model, and on physiological, pharmacological and genetic properties of healthy and diseased mouse retinas.

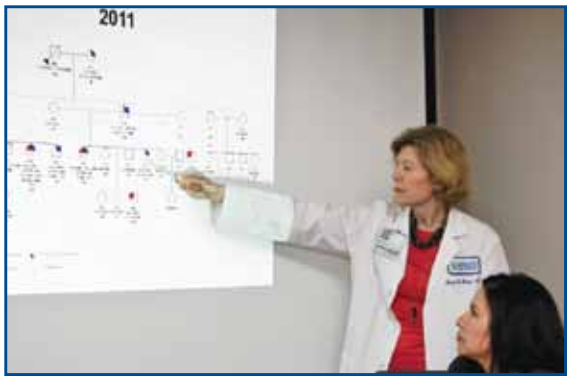
Emmett A. Humble Research Project

Louise C. Strong, MD

Genetics

University of Texas M.D. Anderson Cancer Center, Houston, TX

Genetic Etiology of Retinoblastoma



Shown is a family with retinoblastoma (RTB) in many members, with a gene mutation (mut) in all with RTB and others with no RTB. Since 1985, six additional cancers occurred in Rb1 mut carriers. This shows the role of Rb1 mut in many tumors and ages, and need for continued care of Rb1 mut families.

The overall goal of Dr. Strong's project is to characterize the genetic mechanisms of the non-ocular cancers that occur in hereditary retinoblastoma patients and their relatives. This is a significant health problem as the most frequent cause of death in hereditary retinoblastoma patients is a second malignant neoplasm; it is also an important biologic question, as the retinoblastoma "pathway" is considered to be critical to the development of most if not all cancers, and understanding the interactions between the Rb protein (the product of the retinoblastoma gene), other proteins that interact with Rb, and other molecular pathways may provide further insights into tumor development and may identify potential targets for therapy. Dr. Strong's program to date has ascertained some 127 hereditary retinoblastoma kindreds, including 36 in which at least one family member had a second malignant non-ocular neoplasm.

Research

The Paul Kayser Research Project

Ramon Font, MD

Cullen Eye Institute

Baylor College of Medicine, Houston, TX

Immunohistochemistry and Molecular Biology in Ophthalmic Pathology

Dr. Font's research interest is the pathogenesis and immunohistochemical profile of ophthalmic lesions involving the eye and ocular adnexa. Recently he has collected approximately 35 conjunctival lesions that have been classified as dysplasia. The lesions are classified as mild, moderate, and severe using a monoclonal antibody (Ki-67) to determine the percent of Ki-67 positive nuclei within the foci of dysplasia. In 2011, Dr. Font's laboratory completed a study of conjunctival lesion from a middle-aged woman who had Kaposi sarcoma of the conjunctiva associated with Human Herpes Virus type 8 (HHV-8), which was detected by immunohistochemical methods (the patient was HIV-positive). They collected 15 cases of microspordiosis of the cornea in which both eyes were simultaneously involved. The organisms (Vittaforma cornea) were identified mostly in the cytoplasm of the keratocytes and demonstrated quite nicely by the electron microscopy.

Joe M. and Eula C. Lawrence Research Project

Milan Jamrich, PhD

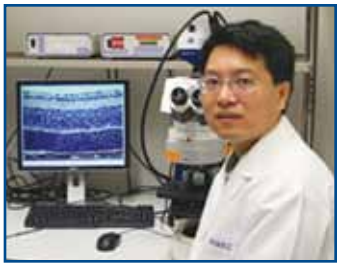
Molecular and Cellular Biology

Baylor College of Medicine, Houston, TX

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

Expression of the Pax6 - lacZ reporter in the head of an E16.5 wild type mouse embryo

The goal of Dr. Jamrich's project is to identify genes and developmental processes that are responsible for development and survival of vertebrate retinal cells. During eye development, the initially undifferentiated cells of the retina develop into a layered array of cell types with specific capabilities. The retinal gene Rx, initially isolated in Dr. Jamrich's laboratory, plays a critical role in eye formation. In 2011, Dr. Jamrich's laboratory strived to determine whether the two human RAX genes could rescue eye formation in mice lacking the mouse Rx gene. They made transgenic mice using two RAX genes. One of the transgenic mouse lines was carrying the human RAX1 gene, but this gene was not expressed in the transgenic mouse. The second line, carrying RAX2, was showing expression of this transgene but this gene was not able to rescue eye formation in Rx deficient mice.



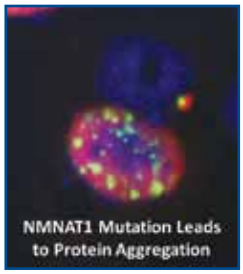
The W.O. Manning Research Project

Rui Chen, PhD

Molecular and Human Genetics

Baylor College of Medicine, Houston, TX

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



Protein aggregation assay in cell culture for NMNAT1 mutant allele

The goal of Dr. Chen's project is to identify novel genes involved in human retinal disorders and conduct functional analysis of genes involved in retinal development using model organism such as *Mus musculus* (house mouse). Understanding of molecular mechanisms of normal retina development is an essential part for better understanding the mechanisms and designing novel treatments of eye diseases. Dr. Chen's laboratory has applied the cutting edge sequencing technology in cloning disease genes underlying Leber congenital amaurosis (LCA) and retinitis pigmentosa (RP) and performed whole exome sequencing on a large cohort of patients. In the past year, Dr. Chen's group has made significant progress in identifying novel LCA/RP disease genes, including CEP164, KCNJ13, and NMNAT1. Follow up functional studies suggest potential novel disease mechanisms of LCA such as protein transportation and NAD homeostasis in photoreceptor cells function. Corresponding animal models are being established and will be used for further mechanistic studies and testing of potential treatments, including gene and drug therapy.

Research

The Kathryn and Latimer Murfee Macular Degeneration Project

Nansi Jo Colley, PhD
Ophthalmology and Visual Sciences
Eye Research Institute
University of Wisconsin, Madison, WI

Molecular Genetic Studies of Retinal Degeneration in Drosophila (cover photo)

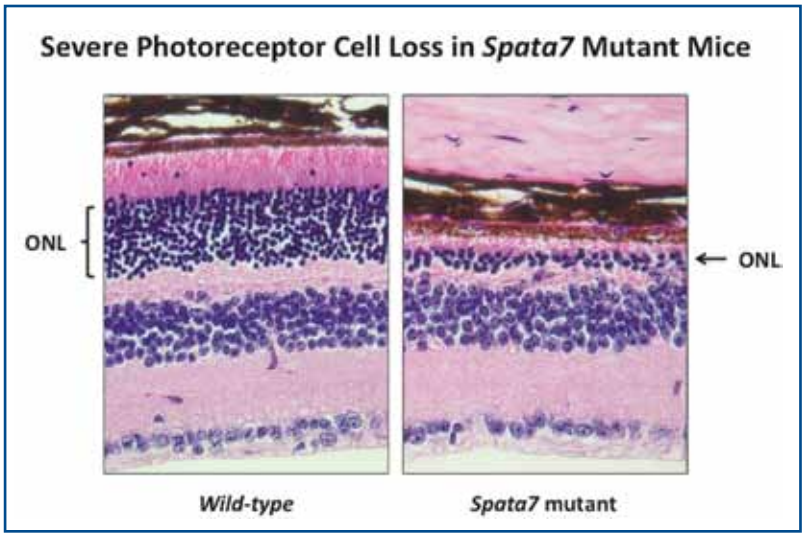
Dr. Colley's laboratory is focused on using *Drosophila* (fruit fly) as a model for studying hereditary human retinal diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD). An ongoing challenge in diagnosing and treating AMD and RP is that they are highly complex diseases with multiple subtypes, each with a distinct genetic and biochemical basis. *Drosophila* is a powerful animal model for studying inherited retinal degeneration disorders. In 2011, Dr. Colley conducted a large-scale forward genetic screen of both the second and third chromosomes to identify and characterize constituents of protein targeting and transport in *Drosophila* photoreceptor cells. Results identify XPORT (Exit Protein) as a key molecular chaperone for TRP (Transient Receptor Potential) and Rhodopsin. Defective transport of TRP and Rhodopsin occur when there are mutations in XPORT, which leads to retinal degeneration.

Bertha and I.L. Miller Research Project

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

Genetic and Molecular Analysis of Retinal Development and Disease

Improving both the diagnoses and the treatments of Leber congenital amaurosis (LCA) is the goal of Dr. Mardon's project. Dr. Mardon has identified the causative gene associated with LCA3, named Spata7, and significantly these mutations are associated with both LCA and early-onset retinitis pigmentosa (RP), suggesting that a detailed understanding of Spata7 function could have broad implications in human retinal diseases. Using a mouse model he created for LCA3, Dr. Mardon's laboratory has shown that the severe reduction in the number of photoreceptor cells and little or no response to light in the absence of Spata7 function is due to the mislocalization of the visual pigment Rhodopsin. By removing both Spata7 and Rhodopsin, cell death is blocked, demonstrating that mislocalization of Rhodopsin is the key event leading to photoreceptor loss. This model is now validated for the next major goal: to develop gene therapy approaches.



By one year of age, Spata7 mutant mice present with a severe loss of photoreceptors, as seen by the large reduction in the outer nuclear layer (ONL) of the retina. These mice fully recapitulate the human LCA disease phenotype and are now being used for gene therapy studies.

Research

Mary Ellen Wilson Research Project

Richard L. Hurwitz, MD
Associate Professor of Pediatrics - Hematology and Oncology
Director, Retinoblastoma Center, Texas Children's Cancer Center
Baylor College of Medicine, Houston, TX

Immune Consequences of Gene Therapy for Ocular Disorders

Retinoblastoma (Rb), an ocular cancer that affects young children, can be caused by an inherited mutation. Children treated with chemotherapy or radiation therapy have a significantly increased risk of developing other types of cancer later in life. Some disorders that cause retinal degeneration such as Stargardt's Disease are also associated with errors in genetic material. These defects are manifest in the abnormal structure or function of proteins responsible for normal vision. If the mutation(s) in the affected gene is known, replacing the defective gene with a normally functioning gene could slow or even halt the degeneration. The vector systems that Dr. Hurwitz's laboratory has developed for suicide gene therapy for retinoblastoma and gene replacement approaches for treating Stargardt's Disease are being used to explore mechanisms of adenoviral-mediated transgene expression unique to the ocular environment.

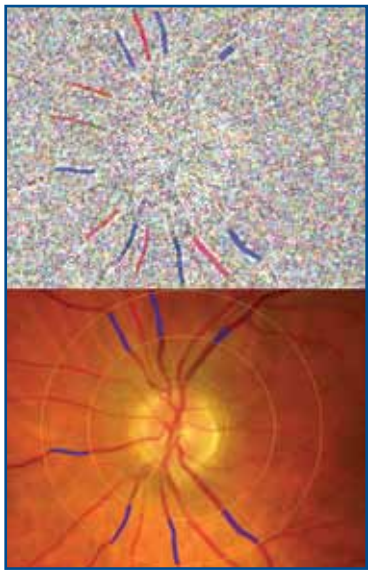
The Carl G. Mueller, Jr. Project

Barbara Klein, MD, MPH

Ophthalmology and Visual Sciences
University of Wisconsin School of Medicine and Public Health,
Madison, WI

Prevalence and Incident Changes in Retinal Vascular Caliber Associated with Medication and Supplement Use

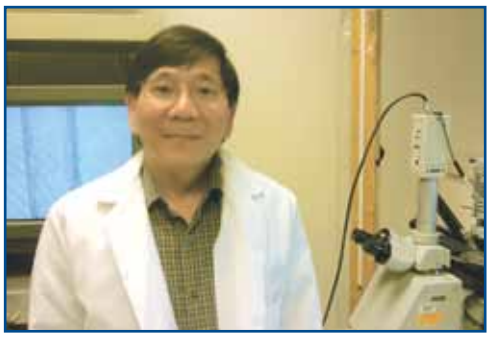
Retinal vessel diameters (RVD) are associated with cardiovascular diseases and also with other ocular diseases. For example, wider retinal venules are associated with the severity of diabetic retinopathy and one study has reported evidence of an association of RVD and age-related macular degeneration (AMD). A class of exposures that is often ignored in examining associations between cardiovascular endpoints and RVD is medications and supplements. Dr. Klein's laboratory has been reviewing all medications previously used as well as those currently used in the population. This was done in order to include new drugs and also to reclassify some medications/supplements that have recently been reported to have effects on microvascular caliber.



A splat model used during computer-aided measurement of retinal vessels (top) and the corresponding fundus image (bottom). Splat models elucidate retinal vessel patterns and help the grader to determine whether accurate measurements of the vessels can be obtained from the image. Red shaded areas indicate the locations of arterioles and blue shaded areas indicate the locations of venules.

Research

Basic Research Grants

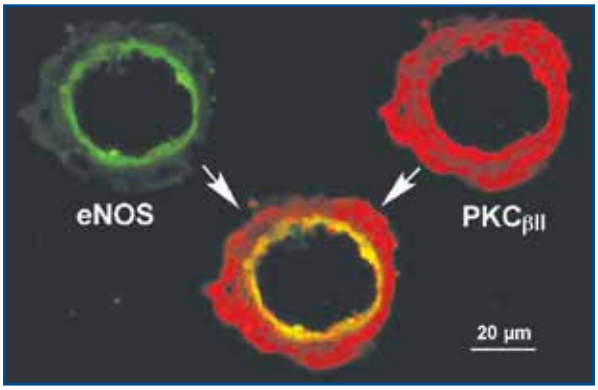


Lih Kuo, PhD

Departments of Systems Biology and Translational Medicine and Ophthalmology
Scott & White Memorial Hospital
Texas A&M Health Science Center, Temple, TX

Activation of Endothelin-dependent RhoA/ROCK by C-Reactive Protein Elicits Retinal Arteriolar Dysfunction

The purpose of Dr. Kuo's project is to understand the pathophysiology of inflammation and ischemia-associated retinal vascular dysfunction at molecular, cellular and intact tissue levels and to develop a therapeutic approach for disease treatment. Retinal vascular diseases are the leading causes of visual impairment in the USA, but the etiology and development of this vasculature-related ocular disease are not fully understood. Because the proper function of retina neuronal tissues depends upon the sufficient oxygen and nutrients supply via the microvascular system, the blood flow regulation by these microvessels is critically important and closely related to the disease development. Dr. Kuo's laboratory has developed a clinically relevant animal model for retinal ischemia to support the critical role of ET-1 system and RhoA kinase/ROCK in the development of vascular pathophysiology.



Diminished nitric oxide (NO) synthesis from NO synthase (eNOS) and protein kinase C (PKC) activation contribute to several retinal diseases. PKCβII (red) localizes in both smooth muscle and endothelium, whereas eNOS (green) occurs in endothelium of arterioles. Endothelial co-localization of PKCβII and eNOS highlights possible PKCβII regulation of NO production.

Leonard Levin, MD, PhD

Dept. of Ophthalmology and Visual Science
University of Wisconsin, Madison, WI

Pharmacological Protection of Endothelial Cells For Retinal Vascular Disease

Many blinding retinal diseases result from abnormalities of blood vessels. In some diseases or as the result of radiation, the initial event is damage to endothelial cells, the cells that line the inside of the blood vessels. Dr. Levin has demonstrated that this endothelial cell death can be slowed down in a transgenic mouse where endothelial cell death is blocked with an anti-death protein. These drugs block endothelial cell death in tissue culture induced by radiation and by free radicals, helping protect cells that line blood vessels in the retina from radiation. The retinal damage from radiation has no effective treatment at present, and these new drugs are an encouraging sign that such a treatment may one day be possible. This study may eventually result in treatments for what is currently an incurable retinal disease and may also yield insights to other small vessel retinopathies such as diabetes.

Grant Recipient from The Macula Society

The Margaret and Mills Cox Macula Research Project
J. William Harbour, MD
Director, Ocular Oncology Service
Washington University School of Medicine
St. Louis, MO

Development of a Blood Test to Diagnose Uveal Melanoma

Dr. Harbour's research has contributed to the understanding of retinoblastoma, the main eye cancer of childhood, as well as ocular melanoma, the most common cancer of the eye in adults. Unfortunately, almost half of patients with ocular melanoma are at risk of dying from the fatal spread of this disease to other organs. Dr. Harbour's group recently discovered that mutation of one specific metastasis suppressor gene seems to cause the melanoma to spread and become lethal. Having identified this genetic defect, Dr. Harbour's group is developing new tests that will detect the spread of melanoma cells at a very early stage, when treatments are likely to be more effective.

Established Research Awards

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

The Award of Merit in Retina Research
Michael F. Marmor, MD
Byers Eye Institute at Stanford, Stanford University
Palo Alto, CA

The Art of Retina

In being chosen for the Award of Merit, Dr. Marmor gave the Charles L. Schepens Lecture on September 23 at the Annual Scientific Meeting of The Retina Society in Rome, Italy.

Dr. Marmor is known for pioneering work on the physiology and pathophysiology of the retina and RPE. In the early 1970s Dr. Marmor recognized the importance of the RPE as a vital tissue for retinal health. He played an important role in bringing this awareness to ophthalmology, writing many articles and the first comprehensive texts on the RPE. His clinical work has focused on retinal and macular dystrophies, toxic retinopathy and clinical electrophysiology.

Another aspect of Dr. Marmor's work lies at the interface between vision and art. He has written a number of articles and three books on art that explore the nature of vision and the effects of eye disease with respect to art. He also has written about ophthalmic history.

Established Research Awards

Gertrude Pyron Award for Outstanding Achievement in Retina Research

Jean Bennett, MD, PhD
Professor of Ophthalmology
University of Pennsylvania School of Medicine
Philadelphia, PA

Albert Maguire, MD
Scheie Eye Institute
Department of Ophthalmology
University of Pennsylvania School of Medicine
Philadelphia, PA

The Evolution of Retinal Gene Therapy: From DNA to FDA

As the Pyron Award recipients, Dr. Bennett and Dr. Maguire presented their lecture on August 21 at the Annual Meeting of the American Society of Retina Specialists (ASRS), which was held in Boston, Massachusetts.

Dr. Bennett and Dr. Maguire worked as a team to accomplish one of the first successful demonstrations of gene therapy in humans. Dr. Bennett bred a virus to carry to the gene, and Dr. Maguire injected it into the eye. The team successfully restored much of the vision in patients who have Leber's congenital amaurosis, in which a mutated gene prevents the retina from manufacturing a nutrient vital to eye health. The hardest part was finding a virus that would deliver normal copies of the defective gene – harmlessly. The technique eventually could be tried to treat macular degeneration.

Charles L. Schepens, MD/AAO Award

Stanley Chang, MD
Edward S. Harkness Professor
Chairman of Ophthalmology
Columbia University
New York, NY

Is Double Peeling for Epiretinal Membranes Necessary?

In being selected for the Charles L. Schepens, MD/AAO Award, Dr. Chang gave the Charles L. Schepens, MD/AAO Lecture at the Retina Subspecialty Day of the American Academy of Ophthalmologists (AAO) Annual Meeting in Orlando, Florida, on October 21.

Dr. Chang has developed and pioneered the use of several revolutionary surgical approaches to treat complex forms of retinal detachment, improving outcomes for patients worldwide. He was the first to use perfluoropropane gas in the management of retinal detachments made worse by scar tissue proliferation (PVR), and developed use of perfluorocarbon liquids during vitreoretinal surgery. With this development, the treatment of giant retinal tears and large relaxing retinotomies became a routine procedure.

Research Chairs and Professorships

Five chairs in retina research provide funds to vision scientists engaged in original excellent research that has the potential to increase understanding of the retina or retinal diseases. Four chairs have been established at University of Wisconsin and one at Baylor College of Medicine. Funding is provided by gifts from Margaret and Mills Cox, Gertrude D. Pyron, W. H. Helmerich, III, Kathryn and Latimer Murfee, and gifts given in honor of Emmett A. Humble, RRF Board Chairman for many years.

Walter H. Helmerich Chair

Curtis R. Brandt, PhD

Ophthalmology and Visual Science
University of Wisconsin School of Medicine and Public Health, Madison, WI

Gene Therapy for Retinal Degenerative Diseases

Viral-based gene delivery vectors are being extensively investigated for therapeutic use in a wide variety of ocular diseases. Because many viruses are human pathogens, our host defense systems can be activated even when replication-defective viruses are used for gene delivery. This response has a number of negative consequences that can affect therapeutic use of the vector, including activation of an immediate inflammatory response. For ocular gene therapy to move forward in people, developing strategies to block the effect by identifying the cause of the inflammatory response is necessary. Dr. Brandt's lab is studying several pre-inflammatory signaling molecules that could be the signal that initiates the process.

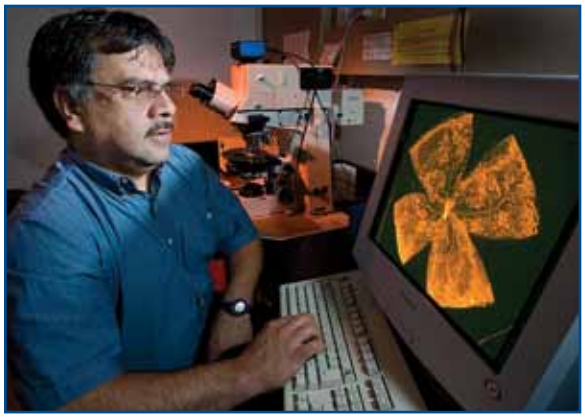
RRF Chair

Nader Sheibani, PhD

Ophthalmology and Visual Science
University of Wisconsin School of Medicine and Public Health, Madison, WI

Understanding the Molecular and Cellular Mechanisms that keep Retinal Vascularization in Check

The growth of new blood vessels from pre-existing capillaries (angiogenesis) contributes to the pathogenesis of many diseases, including retinopathy of prematurity, diabetic retinopathy, and age-related macular degeneration. Understanding the molecular and cellular mechanisms that regulate angiogenesis and how their alterations contribute to growth of new blood vessels, has significant clinical impact. Dr. Sheibani is working to develop new modalities to treat a variety of eye diseases with a neovascular component.



Research Chairs and Professorships

Emmett A. Humble Distinguished Directorship
Daniel Albert, MD, MS
Director, Eye Research Institute
University of Wisconsin, Madison, WI

Dr. Albert is the founding Director of the UW Eye Research Institute, which fosters a multi-disciplinary community of scholars working in collaboration to advance knowledge about the science and art of vision and apply it to the prevention of blindness. Bringing together scientists and scholars from diverse disciplines stimulates scientific progress through contact with new or disparate perspectives, exchange of ideas and insights, and application of innovative technologies and advanced methodologies.

Dr. Albert's research focuses on ocular tumors, specifically melanoma and retinoblastoma. His work with retinoblastoma utilizes transgenic mouse models of the tumor to investigate the molecular biology of the disease and to learn whether vitamin D analogs produce tumor regression in these animal models. He also studies melanoma in a transgenic mouse model. His other interests include medical ethics and the history of medicine and ophthalmology.

Kathryn and Latimer Murfee Chair
David M. Gamm, MD, PhD
UW Eye Research Institute
University of Wisconsin, Madison, WI

Deriving Photoreceptors from Human Embryonic Stem Cells

Dr. Gamm's research focus is the study of inherited and acquired eye diseases that culminate in the degeneration of photoreceptors and retinal pigment epithelium. Dr. Gamm has established a subretinal transplant system within a newly developed animal research facility complete with surgical stations and specialized equipment needed to conduct this work. This system allows him to test strategies for replacing retinal cells, such as photoreceptors, in rat models of retinal degenerative disease.

Dr. Gamm's laboratory has succeeded in creating structures from the most primitive stage of retinal development using embryonic stem cells and stem cells derived from human skin. His success in producing multiple retinal cell types from induced pluripotent stem (iPS) cells has led to development of human retinal disease-specific models, advancing stem cell-based therapies and could lead to better treatment methods for patients as a result. These iPS lines will aid in the study of the pathogenesis of retinal dystrophies and provide a means to test pharmacologic agents and develop customized stem cell treatment strategies.

The RRF Chair at Baylor College of Medicine has yet to be named.

Research Chairs and Professorships

Edwin and Dorothy Gamewell Professor
Arnold E. Ruoho, PhD
UW Eye Research Institute
University of Wisconsin, Madison, WI

Retinal Neuroprotection by the Sigma-1 Receptor Chaperone

Dr. Ruoho's research is directed at understanding the molecular mechanisms underlying neurotransmitter release and receptor activation. He has discovered a new class of compounds that are high-affinity inhibitors of the Sigma-1 receptor, a transmembrane chaperone protein expressed in many different tissue types and particularly concentrated in multiple layers of the retina. Sigma-1 may be utilized to diminish neurodegeneration of retinal photoreceptors and ganglion cells. His goal is to prevent blindness by applying pharmacological and genetic approaches that will enhance the biological activity of the Sigma-1 receptor in the retina.

M.D. Matthews Research Professor
Arthur S. Polans, PhD
UW Eye Research Institute
University of Wisconsin, Madison, WI

Studies of the Resveratrol-Stimulated Calcium Response in Endothelial Cells

There are significant problems associated with current treatment regimens for cancer, such as the use of radiation and chemotherapy agents. Dr. Polans' lab has demonstrated that resveratrol, a natural plant product, can inhibit tumor growth in different mouse models of uveal melanoma, retinoblastoma and other types of cancer and can cause tumor regression when the bioavailability of the compound is increased. The same compounds that are useful in reducing tumor growth may now be used to treat other neovascular diseases of the eye, including forms of AMD, diabetic retinopathy and retinopathy of prematurity.

Rebecca Meyer Brown Professor
Bikash Pattnaik, PhD
UW Eye Research Institute
University of Wisconsin, Madison, WI

Mechanisms Underlying Kir 7.1 Mutation Causing Snowflake Vitreoretinal Degeneration (SVD)

Macular degenerative diseases are hard to study because the aging process and consequences are hard to replicate in a laboratory setup. Studying disease mechanism of genetic eye diseases with parallel retinal degenerative phenotype is the best possible alternative. Snowflake vitreoretinal degeneration (SVD) is a genetic disorder due to a mutation in the RPE potassium channel causing pigment appearance on the retina. Dr. Pattnaik has made significant advances in understanding of the disease cause in SVD.

International Fellowships

RRF funds two programs of international fellowships, one a 12-month fellowship and the other a six-month fellowship.

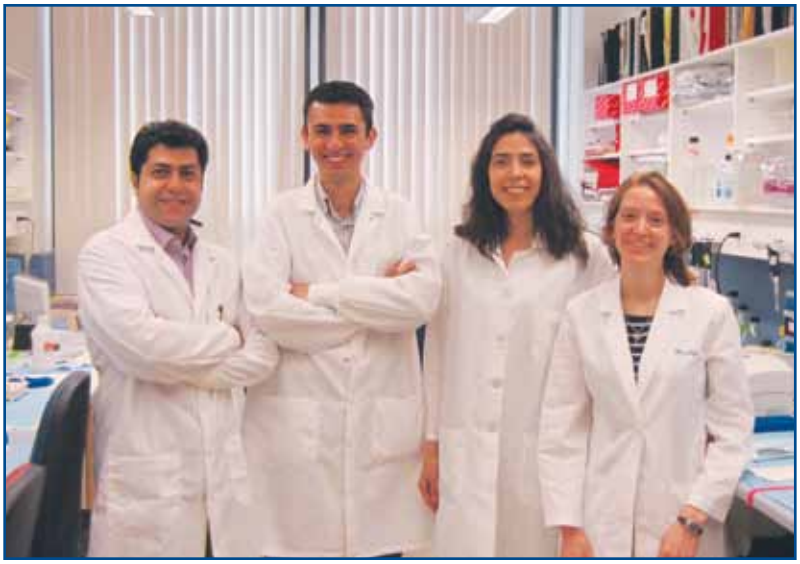
ICO/Helmerich International Fellowships

The International Council of Ophthalmology (ICO), in cooperation with the International Council of Ophthalmology Foundation (ICOF), and Retina Research Foundation have established two international fellowships with income from an endowment created by Walter H. Helmerich, III. These two, 12-month fellowships of $25,000 each provide advanced subspecialty training for young ophthalmologists from developing countries who are recommended by the head of a teaching or public service institution and who are committed to returning to a position at a teaching institution or public service hospital in their home country following the fellowship.

2011 Helmerich Fellows:

Lala Ceklic, MD, PhD, from Bosnia and Herzegovina, for training in retina and vitreoretinal surgery at Bern University Hospital in Switzerland. After fellowship Dr. Ceklic will return to the position of Chief of the Eye Department "Kasindo" Clinical Center of Eastern Sarajevo.

Afsun Sahin, MD, from Turkey, for training in corneal disease and surgery at the Schepens Eye Research Institute at Harvard University. After fellowship Dr. Sahin will return to teaching and research at the University Medical School in Eskisehir, Turkey.



Dr. Afsun Sahin (second from left)

Gillingham Fellowships/PAAO

Established by W. J. Gillingham, this program is administered for RRF by the Pan-American Association of Ophthalmology (PAAO). Two six-month fellowships, providing stipends of $10,000 each, were awarded this year to Latin American ophthalmologists for training at leading institutions in the United States.

Caio Vinícius Saito Regatieri, MD
From São Paulo, Brazil
Harvard Medical School, Schepens Eye Research Institute, Boston, MA

Training in Retina (Retina Stem Cell) with Michael Young, PhD

Arturo Ramírez-Miranda, MD
From Mexico City, Mexico
Jules Stein Eye Institute, UCLA, Los Angeles, CA

Training in Cornea, External Disease & Refractive Surgery with Anthony Aldave, 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

Educational programs administered for RRF by the American Academy of Ophthalmology are funded by the endowed gifts from Laura I. Cannon, Burt L. Risley, and the Schlichting Family. This program will upgrade clinical research skills in the field of retina. The 2011 funding for this program was $45,020.

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 $20,000 was funded to provide travel expenses for the students to attend the ARVO Annual Meeting in May in Ft. Lauderdale, FL, to present their papers or posters.

Nineteen ophthalmology students were selected from these schools in 2011:

Case Western Reserve University – Cleveland, OH
Cincinnati Children's Hospital – Cincinnati, OH
Columbia University College of Physicians & Surgeons – New York, NY
Indiana University – Bloomington, IN
Purdue University Indiana – West Lafayette, IN
John Hopkins School of Medicine – Baltimore, MD
John Hopkins University – Baltimore, MD
Massachusetts Eye and Ear Infirmary, Harvard Medical School – Boston, MA
National Eye Institute – Bethesda, MD
National Instititues of Health – Bethesda, MD
Oregon Health & Science University – Portland, OR
Texas A&M Health Science Center – Temple, TX
University of California Berkeley – Berkeley, CA
University of Colorado Anschutz Medical Center – Denver, CO
University of Illinois at Chicago – Chicago, IL
University of Oklahoma Health Sciences Center – Oklahoma City, OK
University of Utah – Salt Lake City, UT
Vanderbilt University – Nashville, TN

Retina Research Foundation Joseph M. and Eula C. Lawrence Travel Grant Recipients

COMBINED STATEMENT FINANCIAL POSITION

RETINA RESEARCH FOUNDATION
COMBINED STATEMENT OF FINANCIAL POSITION
DECEMBER 31, 2011
(With Summarized Information as of December 31, 2010)

	General Funds			Endowment Funds				2011	2010
	Unrestricted	Temporarily Restricted	Total	Unrestricted	Temporarily Restricted	Permanently Restricted	Total	Total All Funds	Total All Funds (Memorandum Only)
ASSETS									
Cash and Cash Equivalents	$ 486,160	$ 75,000	$ 561,160	$ -	$ 326,320	$ -	$ 326,320	$ 887,480	$ 572,141
Contributions Receivable	22,720	10,000	32,720	-	-	-	-	32,720	21,097
Investments	1,066,920	-	1,066,920	2,659,585	18,358,805	17,273,637	38,292,027	39,358,947	40,932,210
Furniture and Equipment, Net of Accumulated Depreciation of $5,282)	13,070	-	13,070	-	-	-	-	13,070	13,150
Charitable Remainder Trust	-	-	-	-	-	306,304	306,304	306,304	311,351
Intangible Assets	12	-	12	-	-	-	-	12	12
TOTAL ASSETS	$ 1,588,882	$ 85,000	$ 1,673,882	$ 2,659,585	$ 18,685,125	$ 17,579,941	$ 38,924,651	$ 40,598,533	$ 41,849,961
LIABILITIES AND NET ASSETS									
Accounts Payable	$ 2,324	$ -	$ 2,324	$ -	$ 70,467	$ -	$ 70,467	$ 72,791	$ 79,031
COMMITMENTS AND CONTINGENCIES									
NET ASSETS	1,586,558	85,000	1,671,558	2,659,585	18,614,658	17,579,941	38,854,184	40,525,742	41,770,930
TOTAL LIABILITIES AND NET ASSETS	$ 1,588,882	$ 85,000	$ 1,673,882	$ 2,659,585	$ 18,685,125	$ 17,579,941	$ 38,924,651	$ 40,598,533	$ 41,849,961

The accompanying notes are an integral part of these combined financial statements.

COMBINED STATEMENT NET ASSETS

RETINA RESEARCH FOUNDATION
COMBINED STATEMENT OF ACTIVITES AND CHANGES IN NET ASSETS
FOR THE YEAR ENDED DECEMBER 31, 2011
(With Summarized Financial Information for the Year Ended December 31, 2010)

	General Funds			Endowment Funds				2011	2010
	Unrestricted	Temporarily Restricted	Total	Unrestricted	Temporarily Restricted	Permanently Restricted	Total	Total All Funds	Total All Funds (Memorandum Only)
REVENUES:									
Contributions	$ 135,725	$ 41,000	$ 176,725	$ -	$ -	$ 428,930	$ 428,930	$ 605,655	$ 325,539
Interest, Dividend and Distribution Income	27,496	-	27,496	68,373	918,073	-	986,446	1,013,942	988,597
Realized and Unrealized Gains (Losses) on Investments, Net	(40,976)	-	(40,976)	(102,142)	(1,359,829)	-	(1,461,971)	(1,502,947)	3,815,851
Mineral Interest Income and Other Income	123,037	-	123,037	-	-	-	-	123,037	91,100
Change in Value of Split-Interest Agreement	-	-	-	-	-	(17,969)	(17,969)	(17,969)	11,331
Income Transferred from Endowment Fund Investments	897,531	75,000	972,531	(67,420)	(905,111)	-	(972,531)	-	-
Net Assets Released from Restrictions-Satisfaction of Program Restrictions	186,000	(186,000)	-	-	-	-	-	-	-
Total Revenues	1,328,813	(70,000)	1,258,813	(101,189)	(1,346,867)	410,961	(1,037,095)	221,718	5,232,418
EXPENSES:									
Program Services:									
Research Projects and Grants	946,255	-	946,255	-	-	-	-	946,255	1,067,342
Public Education	36,090	-	36,090	-	-	-	-	36,090	31,945
Career Development and Awards	79,843	-	79,843	-	-	-	-	79,843	174,164
Total Program Services	1,062,188	-	1,062,188	-	-	-	-	1,062,188	1,273,451
Supporting Services:									
Management and General	96,112	-	96,112	19,501	260,298	-	279,799	375,911	374,403
Fund Raising	28,807	-	28,807	-	-	-	-	28,807	27,455
Total Supporting Services	124,919	-	124,919	19,501	260,298	-	279,799	404,718	401,858
Total Expenses	1,187,107	-	1,187,107	19,501	260,298	-	279,799	1,466,906	1,675,309
Changes in Net Assets	141,706	(70,000)	71,706	(120,690)	(1,607,165)	410,961	(1,316,894)	(1,245,188)	3,557,109
Net Assets, Beginning of Year	1,444,852	155,000	1,599,852	2,780,275	20,221,823	17,168,980	40,171,078	41,770,930	38,213,821
Net Assets, End of Year	$ 1,586,558	$ 85,000	$ 1,671,558	$ 2,659,585	$ 18,614,658	$ 17,579,941	$ 38,854,184	$ 40,525,742	$ 41,770,930

The accompanying notes are an integral part of these combined financial statements.

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