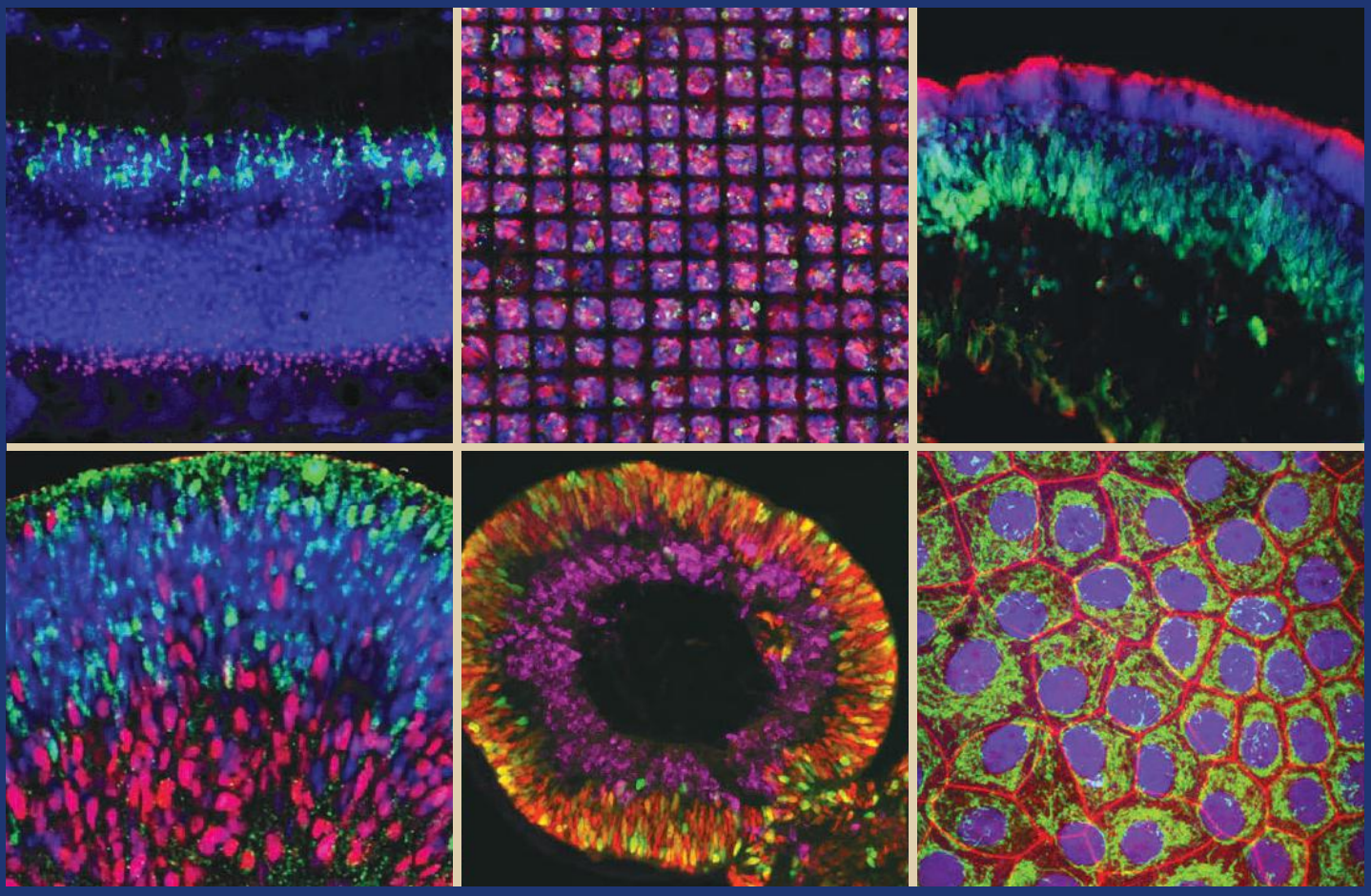
RETINA RESEARCH FOUNDATION



ANNUAL REPORT 2020

FUNDING PROGRAMS IN RESEARCH AND EDUCATION
TO REDUCE RETINAL BLINDNESS WORLDWIDE

Annual Report 2020

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Retina Research Foundation
Board of Directors 2020

Established in 1969

The mission of the Retina Research Foundation is to reduce retinal blindness worldwide by funding programs in research and education.

Dear Friends,

We will remember 2020 as a year radically different from any other during our lifetime. Fortunately, basic research in genetics and virology contributed to the unprecedentedly rapid development of novel and highly efficacious vaccine solutions, saving millions of lives. The speed of the COVID-19 vaccine development tests our whole paradigm of what is possible for realizing the promise of basic research in therapies advantageous to our future, shared benefit. The vital importance of investing in basic scientific research is more evident to the general public than ever before.

Reflecting on the past year, RRF is pleased to report that the diversified RRF research and educational programs weathered this challenging time well, and we hope that as you review the activities presented in this year's Annual Report, you will be heartened by the good news of the progress made toward eliminating vision loss due to retinal diseases. RRF researchers did not escape the pandemic's impact, but in response to laboratory closures and stay-at-home orders, they adapted to remote work and virtual meetings, and they returned to the bench as quickly as possible once restrictions eased. While away from their physical laboratories, scientists pivoted and worked on their publications, the primary media for sharing their research. RRF basic science researchers published more than typically possible, nearly doubling the annual number of manuscripts accepted by high-impact, peer-reviewed journals. Eleven scientists published 35 articles or abstracts, and two researchers patented numerous discoveries. Contributing to the greater body of scientific knowledge on the retina's function and retinal disease is a principal goal of our Foundation's work. These efforts lead to the sharing of data and insight essential to development of novel therapeutic approaches that will, one day, reduce the incidence of low-vision and blindness caused by retinal diseases.

Your support this past year was unwavering, and it enabled the expansion of the RRF basic research program while also increasing financial grant support to scientists, including the RRF Chairs and Professorships, at leading research universities and institutes. RRF and our affiliated vision scientists adjusted to accomplish our work in spite of the pandemic, and excellent work resulted. As RRF looks forward, we remain hopeful that our vision of ending blindness caused by retinal diseases will be realized, and we recognize that in this year in particular, there is much to be grateful for as we push forward to our goal.

With appreciation,

Alice McPherson M.D.

Research Program Overview - 2020

Retina Research Foundation supports an exemplary variety of programs in retina research all around the world. The following is a brief overview of RRF research supported in 2020, which illustrates the wide scope of the Foundation's 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 – Dana and Gil Petri Research Project
- Rui Chen, PhD – Manning Research Project
- Graeme Mardon, PhD – Miller Research Project
- Richard Hurwitz, MD – Wilson Research Project

University of Texas Medical Branch-Galveston, Galveston, TX
- Wenbo Zhang, PhD – Bovay Research Project

Texas A&M Health Science Center, Bryan, TX
- Lih Kuo, PhD – Gueymard Research Grant

University of Wisconsin, Madison, WI
- Curtis Brandt, PhD – Murfee Macular Degeneration Project

Indiana University, Indianapolis, IN
- Timothy Corson, PhD – Lawrence Research Project

University of Utah, John Moran Eye Center, Salt Lake City, UT
- Wolfgang Baehr, PhD – Humble Research Project

West Virginia University School of Medicine, Morgantown, WV
- Jianhai Du, PhD – Basic Research Project

University of Tennessee, Memphis, TN
- Francesco Giorgianni, PhD – Basic Research Project

Vanderbilt University, Nashville, TN
- Milam Brantley, MD, PhD – Basic Research Project

Northeastern University, Boston, MA
- James Monaghan, PhD – Basic Research Project

Carver College of Medicine, University of Iowa, Iowa City, IA
- Luke Wiley, PhD – Basic Research Project

Bascom Palmer Eye Institute, University of Miami, Miami, FL
- Hong Yu, PhD – Basic Research Project

RRF Cox Macula Society Research Grant – administered by The Macula Society
- Kathryn L. Pepple, MD, PhD - University of Washington School of Medicine, Seattle, WA

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
Krishanu Saha, PhD – Murfee Chair, McPherson Eye Research Institute
Barbara Blodi, MD – Albert Chair, McPherson Eye Research Institute

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
Russell N. Van Gelder, MD, PhD – University of Washington, Seattle, WA

RRF Paul Kayser International Award – presented by International Society for Eye Research (ISER)
Samuel M. Wu, PhD - Cullen Eye Institute, Baylor College of Medicine, Houston, TX

RRF Pyron Award – presented by American Society of Retina Specialists (ASRS)
Mark S. Humayun, MD, PhD – USC Roski Eye Institute, Los Angeles, CA

CL Schepens MD/AAO Award – presented by American Academy of Ophthalmology (AAO) and Schepens International Society (SIS)
Julia A. Haller, MD – Wills Eye Hospital, Philadelphia, PA

RRF Gonin Lecturer – presented by Club Jules Gonin – will be awarded in 2022

Gonin Medal – presented by International Council of Ophthalmology (ICO) – will be awarded in 2022

Paul Kayser/RRF Global Award – presented by Pan-American Association of Ophthalmology (PAAO) – will be awarded in 2023

International Fellowships – Advanced Subspecialty Training

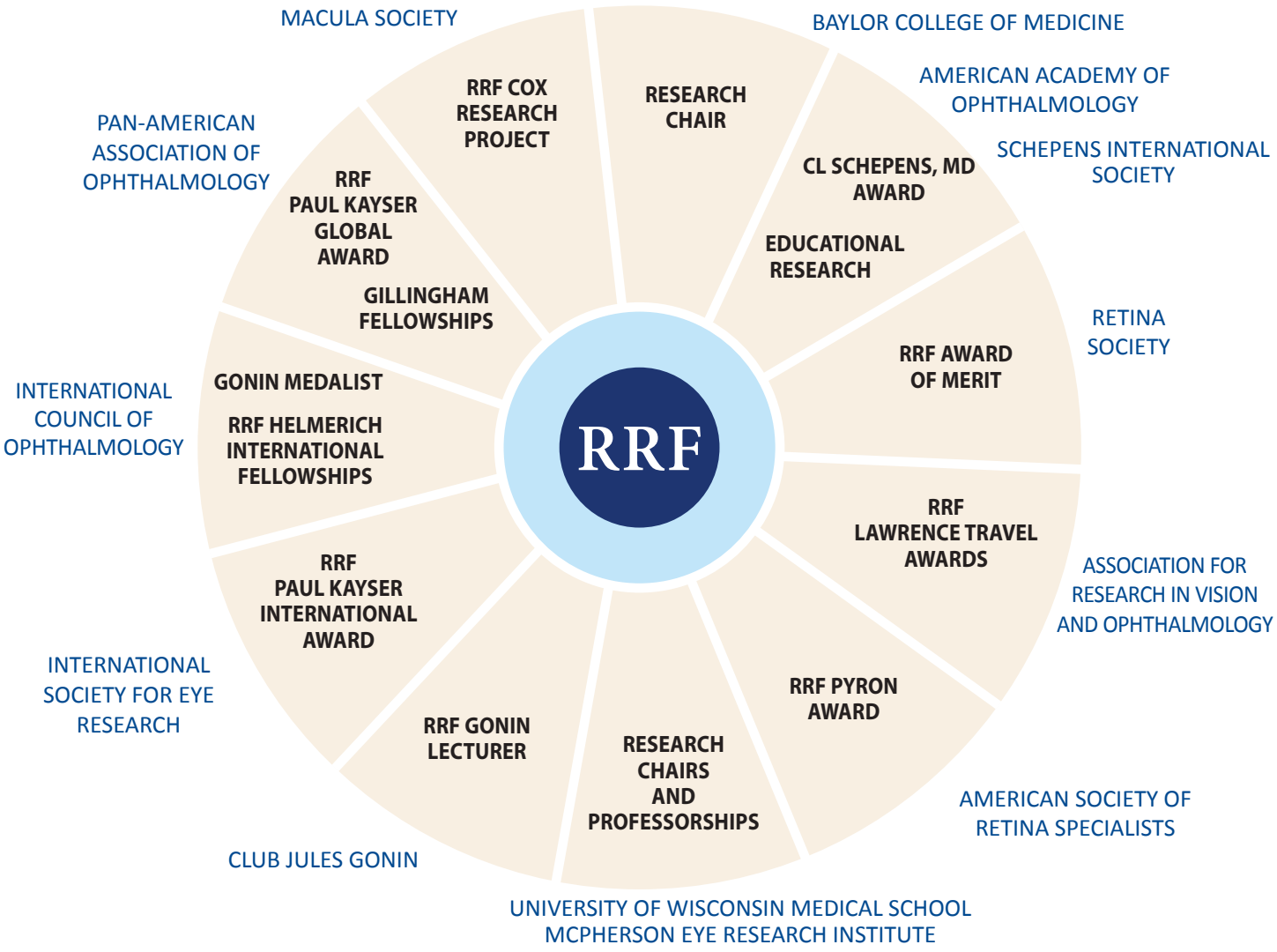
ICO – RRF Helmerich International Fellowships – administered by International Council of Ophthalmology Foundation (ICOF)
Estephania Feria Anzaldo, MD – from Mexico to Bascom Palmer Eye Institute, University of Miami, Miami, FL
Irmak Karac, MD – from Turkey to Byers Eye Institute, Stanford University, Palo Alto, CA

Gillingham Pan-American Fellowships – administered by Pan-American Association of Ophthalmology (PAAO)
Julia de Lima Farah, MD – from Brazil to the University of Calgary, Canada
Matias Soifer, MD – from Argentina to Duke Eye Institute, Durham, NC

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 Association for Research in Vision and Ophthalmology (ARVO) – will resume in 2021

Collaborating Organizations



COLLABORATING ORGANIZATION	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	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
Houston 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 : 62

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
Carver College of Medicine	Iowa City, IA
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
Northeastern University	Boston, MA
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 Tennessee	Memphis, TN
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
West Virginia School of Medicine	Morgantown, WV
Wills Eye Hospital	Philadelphia, PA
Wilmer Eye Institute	Baltimore, MD

Research

RRF increased basic grant funding in 2020, expanding the number of pilot study research projects conducted at leading research institutions to 16. Ten projects are named in recognition of individuals who have generously supported the mission of our organization. Basic science projects are experimental and designed to investigate previously unstudied or understudied avenues in an effort to break new ground and advance scientific knowledge. Findings may lead to ongoing studies in the future. In 2020, these basic science researchers contributed significantly to the body of knowledge with 35 publications submitted or published in peer review journals. Scientists' groundbreaking findings also resulted in the issue of new patents.

Named Basic Research Projects

The Kathryn and Latimer Murfee Macular Degeneration Project

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

Gene therapy for retinal degenerative diseases

The purpose of Dr. Brandt's project is to determine mechanisms of inflammation triggered by injection of viral gene delivery vectors in the eye and to improve the efficiency of gene delivery. Factors intrinsic to our cells act to prevent viral entry and growth and these also affect gene delivery vectors. Recently Dr. Brandt's lab confirmed that two of these factors inhibit gene delivery and that reducing the amount of these factors increases gene delivery efficiency. The research team has demonstrated that these factors are expressed in Muller cells and non-human primate retina tissue.

Joe M. and Eula C. Lawrence Research Project

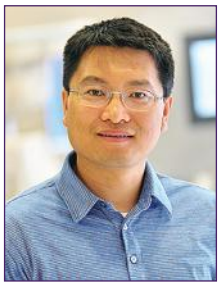
Timothy W. Corson, PhD
Department of Ophthalmology
Indiana University School of Medicine
Indianapolis, IN

Effect of sex differences in soluble epoxide hydrolase expression on choroidal neovascularization

Dr. Corson pursues development of new therapeutic approaches for treating ocular neovascularization, the abnormal blood vessel growth seen in diseases like wet age-related macular degeneration (AMD). The specific goal of his project is to explore an enzyme identified to be important for abnormal new blood vessel growth, soluble epoxide hydrolase (sEH), to definitively determine which cell types in the eye produce sEH and ascertain the effect on fatty acids when it is depleted, to guide therapeutic development. In previous years of RRF funding, Dr. Corson developed a potent chemical called SH-11037, and tested this in combination with standard anti-VEGF therapy. His work documented 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 characterized the molecular mechanism of how SH-11037 inhibits sEH, including identifying factors that increase its levels in the eye. After assessing his library of novel chemicals, he found candidates that perform as well as SH-11037 at blocking sEH, helping to build a "structure activity relationship" for blocking sEH function. In 2020, Dr. Corson showed differential expression in sEH between the sexes, and found that depletion of sEH with a genetic tool his laboratory developed reduces inflammatory signals. Dr. Corson's work resulted in the issue of two patents and numerous publications and abstracts.

The Corson Lab research team

W.O. Manning Research Project

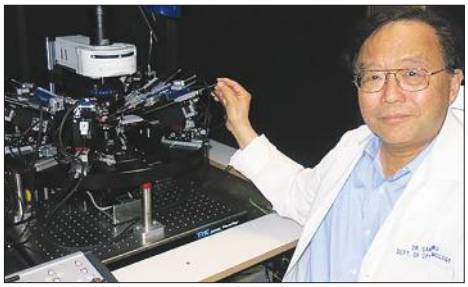


Rui Chen, PhD
Department of Molecular and Human Genetics
Baylor College of Medicine
Houston, TX

Identification and functional analysis of genes involved in retina diseases

The principal goal of Dr. Chen's project is to identify novel genes involved in Leber congenital amaurosis (LCA), perform respective gene disease mechanisms studies, and apply resulting knowledge to develop new therapeutic approaches. Dr. Chen chooses to study LCA because it is one of the most common causes of hereditary visual impairment in infants and children and is responsible for more than 5% of all retinal dystrophies. Due to its genetic heterogeneity, meaning that different genes or genetic mechanisms can cause LCA, accurate molecular diagnosis of a patient's observed LCA and administration of the appropriate interventions are essential for treatment. Because of its heterogeneity, LCA shares many common molecular mechanisms with other retinal dystrophies, such as Retinitis Pigmentosa and rare Bardet-Biedl Syndrome. By studying LCA, valuable understanding of other retinal degenerative dystrophies is gained as well. Subsequent functional analysis of these novel disease genes using model organisms is the first step toward both early diagnosis of individuals at risk as well as developing reagents for treatment of retinal disease, including gene and drug therapy. In 2020, Dr. Chen focused on performing functional studies. Dr. Chen generated animal models for REEP6 and TLCD38 and performed the functional studies of novel disease genes identified by his team and developing new therapeutic approaches. Dr. Chen generated animal models for REEP6 and TLCD38. Gene replacement therapy targeting these two genes has been developed into promising results. Dr. Chen's results led to three publications.

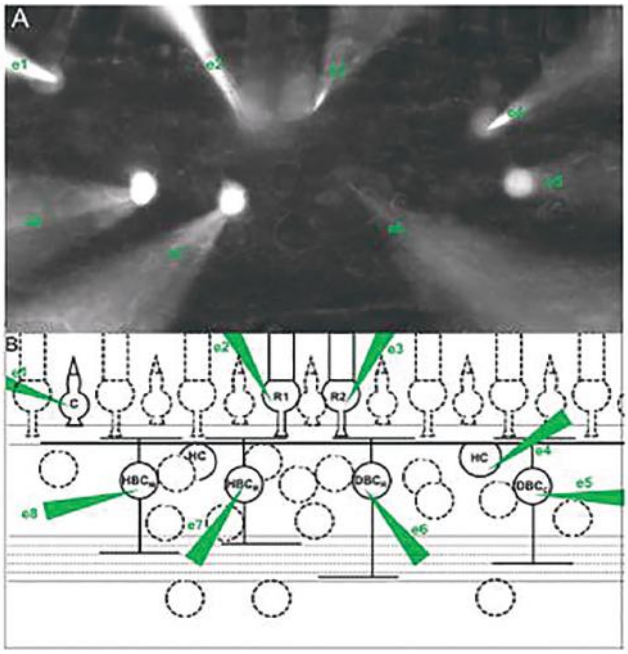
The Paul Kayser Research Project



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 intent of Dr. Wu's project is to understand how retinal neurons interact through study of the chemical and electrical synapses in healthy organisms contrasted with models of various disease states, including glaucoma and age-related macular degeneration, and to identify effective drug and gene therapy strategies to combat these retinal disorders. In 2020, Dr. Wu's lab published three papers and submitted three manuscripts in top international journals. These publications report on new discoveries of genetic dissection and glycinergic and GABAergic modulation of amacrine cells on retinal ganglion cell receptive fields in normal and model glaucoma mice, and the contrasting influence on synaptic pathways and pathogenesis of glaucoma and AMD. Dr. Wu's research will continue using the state-of-the-art eight-channel patch clamp recording system he invented to study synaptic connectivity between photoreceptors, bipolar cells, and ganglion cells in healthy animals and in animal models for glaucoma, age-related macular degeneration (AMD), retinitis pigmentosa (RP) and other retinal diseases.

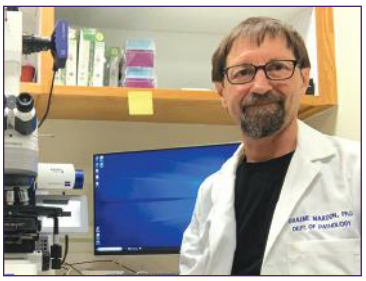


Synaptic interactions between photoreceptors, bipolar cells and horizontal cells in a living retinal slice.

A: *Two rods (R1 and R2), one cone (C), one horizontal cell (HC), two OFF bipolar cells (HBCM and HBCR) and two ON bipolar cells (DBCM and DBCC) recorded with the 8 patch electrode recording system. Patch electrodes and retinal neurons were filled with Lucifer yellow and e1-e8 are electrode numbers.*

B: *Schematic diagram of the retinal slice in A, the 8 recorded cells are shown in solid lines and the electrodes are marked with green triangles.*

Bertha and I.L. Miller Research Project



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

Genetic and molecular analysis of retinal development

Dr. Mardon's long-term objective is to improve prevention, diagnostics, and treatments for human retinal diseases that cause congenital blindness. His research team has been studying a causative gene associated with congenital blindness, named SPATA7, which encodes a novel adaptor protein whose mechanism of function is poorly understood. A detailed understanding of SPATA7 function in the eye could have broad implications. In 2020 Dr. Mardon completed his work on the mouse Kcnj13 gene, making significant breakthroughs concerning the retinal disease gene. In particular, he found that by using AAV-based gene therapy, he was able to significantly rescue the loss of Kcnj13 function in the eye, which leads to early dysfunction of the retina. These results suggest that gene therapy is a feasible approach to treating patients whose have mutations in this gene and therefore represents a major step forward in developing therapeutics for inherited blindness associated with this gene mutation. With the conclusion of this area of inquiry, Dr. Mardon will submit his results for publication in the coming year.

Emmett A. Humble Research Project

Wolfgang B. Baehr, PhD
Department of Ophthalmology and Visual Sciences
John Moran Eye Center
University of Utah
Salt Lake City, UT

The role of Arf-like protein 2 (ARL2) in photoreceptors

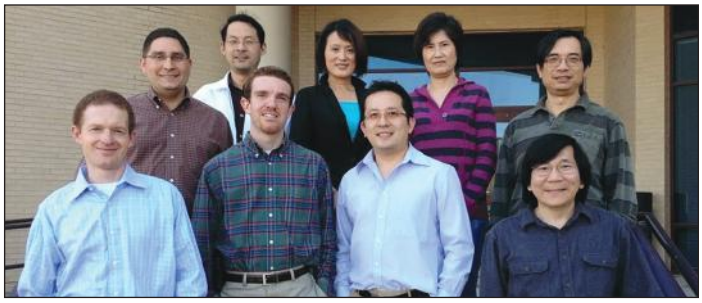
Dr. Baehr is interested in understanding the mechanisms leading to retina disease and in developing gene-based therapies to address photoreceptor degeneration. During 2020, Dr. Baehr's research focus pivoted to researching the role of INPP5E, a phosphatidylinositide phosphatase present in the process of disease development in retina photoreceptors. INPP5E mutations are associated with Joubert Syndrome and Retinitis Pigmentosa. Continuing a line of inquiry previously begun in 2018, Dr. Baehr made excellent progress and his research resulted in three publications in the year as well as submission of a paper to the Journal of Biological Chemistry entitled "Deletion of INPP5E in retina impairs axoneme formation and disc morphogenesis" that was published in March 2021.

Adolphe G. and Josephine Roberts Gueymard Research Project

Lih Kuo, PhD
Department of Medical Physiology
Texas A&M University Health Science Center
Bryan, TX

Activation of Endothelin-dependent RhoA/ROCK Pathway Elicits Retinal Microvascular Dysfunction in Diabetic Retinopathy

Dr. Kuo's research project is to elucidate the mechanisms responsible for the microvascular pathogenesis of diabetic retinopathy and to develop strategies and tools for the prevention and treatment of this sight-threatening disease. Proper function of the retina depends on adequate blood supply to the retina, and dysfunction of the retinal microcirculation could promote disease development. Dr. Kuo's research team found that in the diabetic retina, the synthesis of vasoconstrictor/inflammation agent endothelin-1 (ET-1) from endothelin converting enzyme (ECE) is elevated, and the RhoA kinase (ROCK) and arginase enzymes that regulate vascular activity are upregulated. The team's hypothesis is that activation of ECE/ROCK/arginase contributes to the microvascular dysfunction and retinopathy. Using a pig model, which resembles blood circulation in the human eye, Dr. Kuo identified vascular signaling pathways in the initiation and development of microvascular dysfunction in diabetic retina. His recent experiments suggested the involvement of reverse-mode sodium-calcium exchanger (NCX) in enhanced retinal venular constriction to ET-1 in diabetes or during high glucose insult. This abnormality can contribute to retinal edema, a major manifestation of diabetic retinopathy, by elevating capillary filtration and reducing fluid drainage from the venous circulation. Dr. Kuo speculates that activation of sodium-hydrogen exchanger-1 (NHE-1), a potential signaling protein upstream of NCX, by stress-activated protein kinases might contribute to venular dysfunction in the diabetic retina. Dr. Kuo's research was published in three peer-review journals in 2020.



Dr. Kuo and members of his research team

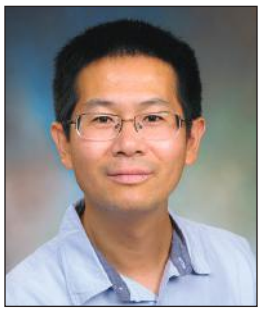
Mary Ellen Wilson Research Project

Richard L. Hurwitz, MD
Department of Pediatrics
Baylor College of Medicine
Houston, TX

Immune consequences of gene therapy for ocular disorders

Dr. Hurwitz's research hypothesis is that gene therapy protocols for both ocular and non-ocular disorders can be optimized based on understanding how the unique ocular environment influences the efficacy of the gene therapy treatment. He previously published an association of the vitreous component hyaluronan with the enhanced expression of potentially therapeutic genes transferred by adenoviral vectors. However, hyaluronan alone does not account for the entire effect observed. Subsequently in 2020, Dr. Hurwitz's research team began to explore the contribution of another vitreous component, the large hyaluronan-binding proteoglycan Versican. Preliminary evidence suggests that five expression constructs that span the G1 domain isolating and combining the known functional elements may affect transgene expression. Dr. Hurwitz also has a construct that expresses the EGF-like motif in the carboxyterminal G3 domain. These constructs may be useful in designing more efficient vectors and delivery systems to optimize gene therapy outcomes and limit toxicities, including immune consequences. Dr. Hurwitz's shared his research conclusions through an article in PLOS ONE in 2020.

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

Diseases such as diabetic retinopathy, retinopathy of prematurity, and retinal vascular occlusion can cause ischemic retinopathy, or damage to the optic nerve due to impaired retinal blood supply because of retinal vessel regression or vascular occlusion. These conditions affect a large population of patients and often result in irreversible vision loss due to the development and growth of abnormal new vessels in response to a period of retinal ischemia. This process is referred to as retinal neovascularization. The abnormal vessels are leaky and fragile, resulting in vitreous hemorrhage, epiretinal or subretinal fibrosis, and tractional retinal detachment. At present, therapies for retinal neovascularization are limited, not always effective, and have considerable side effects. The goal of this project is to develop a novel, effective and inexpensive approach to selectively kill abnormal blood vessels in the retina without affecting normal blood vessels. In 2020, Dr. Zhang assessed the potential role of gut microbiota in retinal neovascularization. Commensal gut microbiota exerts profound influence on digestion, dietary metabolism, endotoxemia, and immune responses. Using 16S rRNA sequencing to assess bacterial microbiota composition in the colon feces in a mouse model of oxygen-induced retinopathy (OIR), Dr. Zhang found that although total bacterial abundance in the colon was not changed in OIR mice, the microbiota composition was changed. This data suggests that decreases in probiotics were potentially involved in retinal neovascularization and warrants further investigation as to the role of gut microbiota in ischemic retinopathy. Dr. Zhang prepared a manuscript for submission and presented two posters at the virtual ARVO annual conference in May, 2020.

Dana and Gil Petri Research Project

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

A novel treatment strategy for age-related macular degeneration by targeting cholesterol transport

Age-related macular degeneration (AMD) is a major cause of blindness in the elderly and choroidal neovascularization (CVN), growth of abnormal leaky blood vessels beneath the retina, the wet type AMD, underlies 80-90% of legal blindness due to AMD. Up to one-fourth of patients have poor responses to current anti-VEGF treatment, and the long-term outcomes are suboptimal even among responders. The objective of Dr. Fu's project is to develop a highly innovative and effective AIBP/anti-VEGF combination therapy for wet AMD by targeting three critical components involved in CNV pathogenesis: VEGF, endothelial cells, and macrophages. In 2020, Dr. Fu's team quickly realized that the combination of AIBP and anti-VEGF therapy produces strong synergistic effect and provides superior therapeutic efficacy than either single treatment alone. Dr. Fu developed AMD models that can represent a broad spectrum of patients, ranging from anti-VEGF responders to non-responders by using different ages of CNV mice. He discovered that the combination of AIBP and anti-VEGF treatment effectively overcomes anti-VEGF resistance. Dr. Fu's work was published and picked up in multiple press releases, including the National Eye Institute (NEI). Significantly, a patent application for this invention was filed.

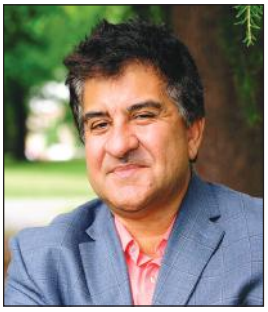
Basic Research Projects

Jianhai Du, PhD
Department of Ophthalmology
West Virginia University School of Medicine
Morgantown, WV

Nutritional strategies in age-related macular degeneration

The retina is one of the most energy demanding tissues in the human body, and proline metabolism in the retinal pigment epithelium (RPE) is important to maintaining the retinal metabolism and health. Dr. Du is interested in developing a nutritional approach to treating age-related macular degeneration, and he is investigating the role of proline metabolism in retinal function and viability. In 2020, his laboratory made significant progress in both areas. The research team generated inducible RPE-specific SLC6A20A knockout mice and whole body SLC6A20A mice. They found SLC6A20 and other proline metabolism genes are highly increased in the RPE. The inhibition of mitochondrial respiration in RPE blocked proline utilization to disrupt the nutrient transport to the retina. Additionally, Dr. Du found a proline-enriched diet increases the biosynthesis of glutathione and NADPH, protects from oxidative damage, and improves visual function in an acute AMD-like mouse model. Dr. Du's work was published in six journals during the year.

Dr. Du and his research team



Francesco Giorgianni, PhD
Department of Pharmaceutical Sciences
University of Tennessee Health Science Center
Memphis, TN

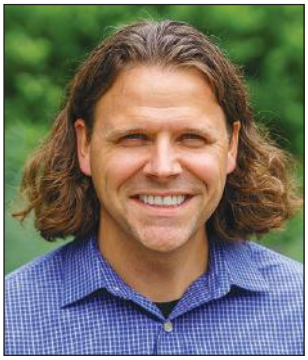
CD5L-mediated autophagocytosis in RPE cells

In 2020, Dr. Giorgianni continued research to further understand the role of CD5L in age-related macular degeneration (AMD). Dr. Giorgianni has discovered that elderly patients affected by AMD have antibodies circulating in their blood that can attack and damage proteins present in the eye. CD5L appears to be important for the removal of compounds that are toxic to the eye. To further demonstrate the function of CD5L, Dr. Giorgianni is investigating CD5L's impact on retinal pigment epithelium (RPE), tissue that is compromised in AMD patients. Dr. Giorgianni believes that CD5L removes toxic compounds, especially those derived from cholesterol, and that it facilitates the toxic compound's degradation and prevents their accumulation and resulting damage to the RPE. Dr. Giorgianni performed experiments to prove that the presence of CD5L inside the RPE cells accelerates the degradation of a compound, derived from cholesterol, called OxLDL. For this work, the laboratory is leveraging state-of-the-art bioannlytical methods, including high resolution (mass spectrometry) that can quickly identify and quantify proteins. Dr. Giorgianni is also identifying other necessary proteins that pair with CD5L to perform the degradation of toxic OxLDL. The findings from his proposed experiments will provide better understanding of the cellular mechanisms that lead to AMD and could result in new leads for the development of new therapeutic strategies. Dr. Giorgianni submitted one manuscript for publication in 2020 that was subsequently published.

Milam Brantley, MD, PhD
Department of Ophthalmology & Visual Sciences
Vanderbilt University
Nashville, TN

"The cellular mechanisms by which arginine and citrulline promote vision threatening diabetic retinopathy"

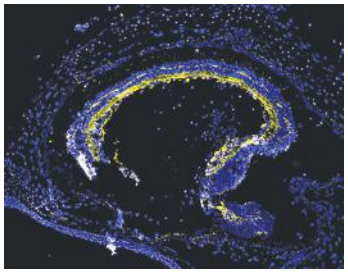
The purpose of Dr. Brantley's project is to understand precisely how arginine and citrulline alter the cells in the retina that are specifically involved in Diabetic Retinopathy (DR). His research aim is to determine exactly how arginine and citrulline function in retinal endothelial cells to cause retinopathy and how they may be used to modify current treatments for DR. These studies will help to develop new ways of treating, or even preventing, diabetic retinopathy. Dr. Brantley's data thus far suggest that treatment of retinal endothelial cells with arginine and citrulline leads to increased nitric oxide synthase activity and nitric oxide production. Arginine and citrulline in combination also reduce arginase activity. These data support Dr. Brantley's hypothesis that arginine and citrulline induce new blood vessel growth through the nitric oxide pathway.



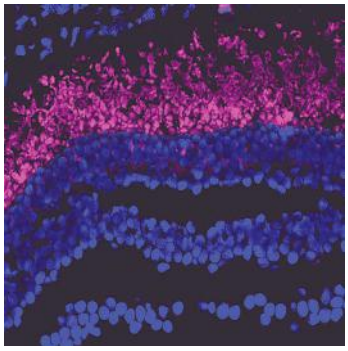
James Monaghan, PhD
Biology Department
Northeastern University
Boston, MA

"Analysis of notch signaling-mediated cell fate determination during regeneration of the neural retina"

Humans cannot recover from retinal damage, but Mexican axolotl salamanders can regenerate their entire retinas. Dr. Monaghan aims to understand cellular and molecular mechanisms that permit salamander retinal regeneration. The ultimate goal is to lay the foundation for translating those mechanisms into cures for degenerative diseases of the human retina. During 2020, Dr. Monaghan's research team developed a technique that reveals cell types in the axolotl retina and their gene activity, which will equip them to understand the molecular mechanisms behind regeneration. They collected preliminary data suggesting that the Notch signaling pathway may dictate what types of cells regrow in the new retina. Dr. Monaghan confirmed that the regenerated retina re-establishes its connection with the brain, which is necessary for its functionality. The team also showed for the first time that the axolotl retina contains a type of glial cells that may serve as stem cells during salamander retinal regeneration.



The Mexican axolotl salamander can regenerate its retina even after a serious injury. Here, a new retina is growing back in the axolotl eye (in blue), and regenerated nerves (in yellow) are already connecting the three retinal layers.



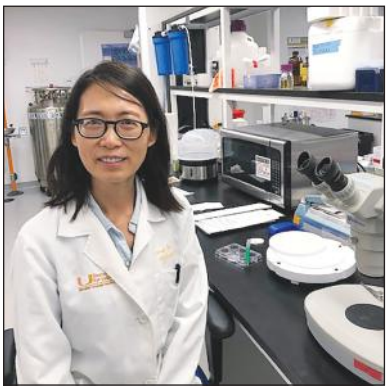
Like in humans, the axolotl salamander retina contains three distinct layers of cells (in blue). One of those layers consists of light-sensitive nerve cells called photoreceptors. With the help of a protein named rhodopsin (in purple), photoreceptors capture light, convert it to electric signals, and send them to nerve cells in the other two retinal layers.

Luke Wiley, PhD
Department of Ophthalmology and Visual Sciences
Institute for Vision Research Center, Carver College of Medicine
Iowa City, IA

"Evaluating the tropism and transduction efficiency of chimeric helper-dependent adenoviral vectors for delivery of large genes"

Dr. Wiley's long-term goal is to develop safe and effective gene therapies for inherited retinal degeneration. However, the two most common causes of retinal degeneration are mutations in genes too large to fit into an known adeno-associated viruse vectors. During the 2020 grant period, Dr. Wiley's research purpose was to identify a vector that has a sufficient carrying capacity for large genes, can specifically target human photoreceptor cells, and demonstrates high transduction efficiency for human photoreceptors. Preliminary data from single cell RNA-sequencing of human donor retinas and in vitro transduction of induced pluripotent stem cell-derived photoreceptor precursor cells suggested that two chimeric helper-dependent adenoviruses, HDAd5/3 and HDAd5/35, held great potential for targeting photoreceptors compared to HDAd5. Subsequently, Dr. Wiley's research team determined the tropism and transduction efficiency of the two chimeric helper-dependent adenoviruses in human donor retinal explants, and the tropism, transduction efficiency and immunogenicity of HDAd5/3 and HDAd5/35 in wild-type rats. Despite the promising observation of higher transduction in induced pluripotent stem cell-derived photoreceptor precursor cells, both HDAd5/3 and HDAd5/35 failed to transduce human photoreceptors, instead targeting some Müller glia and robustly transducing the ganglion cell/nerve fiber layers. Dr. Wiley presented his findings in a poster abstract during ARVO's virtual meeting in May, 2020.

Dr. Wiley and members of his research team



Hong Yu, PhD
Department of Ophthalmology
Bascom Palmer Eye Institute
University of Miami
Miami, FL

"Modification of mitochondrial DNA using targeted CRISPR/Cas9"

Mutations in mitochondrial DNA lead to a spectrum of neurodegenerative diseases for which no effective treatment exists. Dr. Yu has chosen to focus on ATP6T8993G, one of the most severe mitochondrial gene mutations, which is responsible for Maternally Inherited Leigh Syndrome (MILS) and Neurogenic muscle weakness, Ataxia, and Retinitis Pigmentosa (NARP).These diseases are notorious for causing death and blindness in children and young adults.

Gene editing provides a promising treatment for these disorders; however, tools that exist for mtDNA manipulation are limited and inefficient. Dr. Yu's research seeks to overcome these limitations by developing and validating a novel genetic delivery system to facilitate a precise modification of mtDNA in stem cells. During the 2020 grant period, Dr. Yu successfully delivered CRISPR-Cas9 components into mitochondria using a mitochondrial targeting system, which facilitated a successful mtDNA editing into a NARP cybrid cell line, a cytoplasmic hybrid of enucleated cells with mutated mtDNA and normal cells without mtDNA. The data generated from Dr. Yu's work thus far partially contributed to a NIH R01 application.

Macula Society Grant Recipient

The RRF Margaret and Mills Cox Macula Society Research Project

Kathryn L. Pepple, MD, PhD
University of Washington School of Medicine
Seattle, WA

"Retinal microglia and innate lymphoid cells in post-infectious uveitis."

Dr. Pepple specializes in and researches uveitis, a form of eye inflammation that affects the middle layer of tissue in the eye wall. Uveitis is a significant cause of vision loss in the U.S. In fact, it is the second leading cause of blindness in the working-age population and represents an important public health concern. Dr. Pepple pursues understanding the role the innate immune system, comprised of retinal microglia and innate lymphoid cells, plays in ocular inflammation in order to develop new therapies to treat patients with uveitis. Retinal microglia are a specialized population of macrophages found in the eye and other parts of the central nervous system that remove damaged neurons and infections and are important for maintaining healthy tissues. Innate lymphoid cells are fast-responding white blood cells, counterparts to T-cells, which detect changes in the microenvironment that may cause tissue damage. These cells shape subsequent adaptive immunity. Uncontrolled inflammation in patients with uveitis leads to severe visual loss and blindness. Current treatments are suboptimal, non-specific, and have high rates of complications, some of which can be life- threatening. Dr. Pepple will share her research findings at the 2022 annual meeting of the Macula Society.

RRF supports six chairs and three professorships in retina research. These vision scientists are engaged in outstanding and original research that has the potential to increase understanding of the retina and retinal diseases. These laboratories at esteemed research institutions also offer inspiring inquiry opportunities for young scientists.

RRF Research Chair

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

Transducin- and Melanopsin-Independent Phototransduction

The Chen laboratory in 2020 takes on a new research direction to study a novel light sensing pathway. This direction is based on unexpected but exciting findings from a triple knockout mouse the lab generated. The mouse model that lacks all currently known retinal light sensing pathways in rod, cone and intrinsically photosensitive retinal ganglion cells. By recording hundreds of inner retinal neurons from this triple knockout mouse, Dr. Chen's team found that all the neurons retain light sensitivity. Dr. Chen named this novel light sensing pathway "Transducin- and Melanopsin-Independent Phototransduction (TMIP)" and is currently using genetic and pharmacological means to investigate TMIP's physiological function and relationship to the three known retinal light sensing pathways. Phototransduction pathways have been studied for more than seven decades and rod phototransduction is hailed in many Biochemistry and Neuroscience textbooks as the canonical heterotrimeric G-protein signaling pathway. Therefore, the existence of TMIP in mammalian retina is a welcome surprise and a very important discovery to the field as TMIP can explain incomplete achromatopsia, or absence of color vision, in patients with mutated transducin and CNG channel genes. TMIP may also affect the development of the postnatal retina at a time when rod and cone phototransduction is yet to emerge in the developing retina. Dr. Chen hopes to advance the phototransduction and retinal development fields by elucidating TMIP's signaling mechanism and cellular origins. He will also explore its utility as a novel therapeutic modality to combat human blinding diseases.

Dr. Chen's research team

Walter H. Helmerich Chair

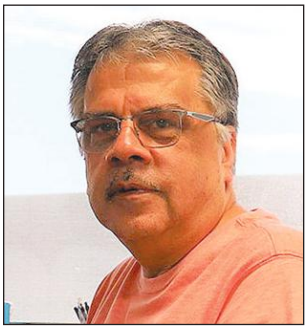
Kevin W. Eliceiri, PhD
Associate Director,
McPherson Eye Research Institute
Departments of Biomedical Engineering and Medical Physics
University of Wisconsin
Madison, WI

Computational Imaging of the Cellular Microenvironment

Dr. Eliceiri's research interests are in the areas of developing optical and computational approaches to non-invasively study dynamic cellular processes like those in the eye. His current research focuses on the development of novel optical imaging methods and instrumentation for investigating the cellular microenvironment, and 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 technologies for multi-scale and multimodal imaging. Recently his group has been developing machine learning based approaches for automated retinal vein occlusion image analysis in OCT images.

Courtesy: McPherson Eye Research Institute

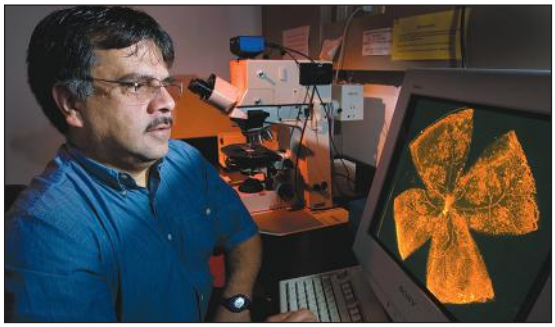
RRF Research Chair



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

Regulation of Ocular Vascular Development and Neovascularization

Dr. Sheibani recently reported a novel modality for noninvasive detection of early retinal vascular changes during diabetes using fundus images. He showed myeloid-derived thrombospondin-1 contributes to abdominal aortic aneurysm through suppression of TIMP-1. He demonstrated the important role of TXNIP in high fat-diet induced retinal vascular dysfunction. He also reported that the expression of Cyp1b1 in retinal astrocytes significantly impacts their adhesion and migration, while Bim expression regulate their inflammatory phenotype. He showed the antiangiogenic activity of his PEDF peptides in oxygen-induced ischemic retinopathy (OIR) and reported the long-term impact of OIR on retinal morphology and function. He was involved with reporting of Schlemm's canal and limbal vascular network in vivo imaging in mouse using Vis-OCT. Reported in: Sci Report (Oct. 2020), ATVB (Dec. 2020), Int J Mol Sci (June 2020), Exp Eye Res (June 2020), Plos One (May 2020 and April 2020), Mol Vis (April 2020), IOVS (Feb. 2020).



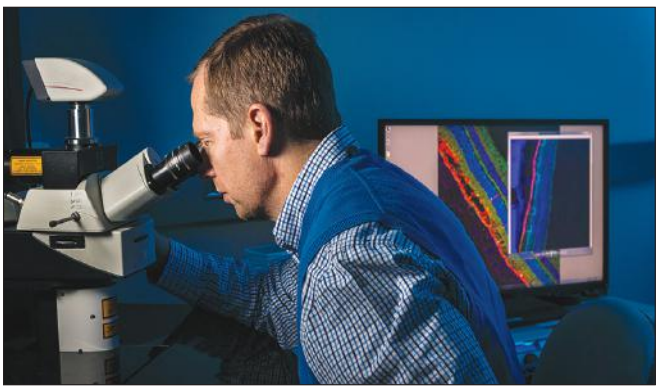
Dr. Sheibani examining a mouse retinal whole-mount for neovascularization after oxygen-induced ischemic retinopathy

Emmett A. Humble Distinguished Directorship

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

Modeling and Treating Retinal Disease with Human Induced Pluripotent Stem Cells (hiPSCs)

Dr. Gamm pioneered the use of human induced pluripotent stem cells (hiPSCs) to generate 3-dimensional retinal organoids in a laboratory dish, which he uses to model dozens of human retinal diseases and test drug and gene therapies. He is also employing his technology to generate clinical-grade photoreceptors and retinal pigment epithelium (RPE) cells on an industrial scale in conjunction with Opsis Therapeutics (Madison, WI), with the goal of treating patients with late-stage retinitis pigmentosa and age-related macular degeneration. Toward this end, he and his collaborators at UW-Madison recently engineered custom scaffolds, or patches, that can deliver these stem cell-derived photoreceptors and RPE to precise regions within the human retina. In so doing, Dr. Gamm's team is paving the way for hiPSC therapies for retinal disease.



Dr. Gamm reviewing results from a human photoreceptor transplant experiment

Kathryn and Latimer Murfee Chair

Krishanu Saha, PhD
McPherson Eye Research Institute
Departments of Biomedical Engineering and Pediatrics;
Wisconsin Institute for Discovery University of Wisconsin
Madison, WI

Bioengineering of Novel Cell and Gene Therapies for the Retinal Disorders

The goal of Dr. Saha's lab is to develop new, personalized therapies and human disease models using novel biomaterials and genetic engineering techniques. His lab has developed an array of engineering approaches that seek to generate new cells, organoids, and tissues from patient samples, as well as a suite of gene-editing technologies to knockout, correct, or insert transgenes into human cells. The lab is currently looking to expand and apply its CRISPR gene-editing tools in the eye, specifically to target retinal pigment epithelial cells and photoreceptors. Their work is integral to national efforts involving cell therapy and genome editing: the NSF Center on Cell Manufacturing (CMaT) and the NIH Somatic Cell Genome Editing (SCGE) Consortium.

Daniel M. Albert Chair

Barbara Blodi, MD
McPherson Eye Research Institute
Department of Ophthalmology and Visual Sciences
Medical Director, Fundus Photograph Reading Center
University of Wisconsin
Madison, WI

Clinical Trials for Macular Degeneration, Diabetic Retinopathy, and other Retinal Diseases

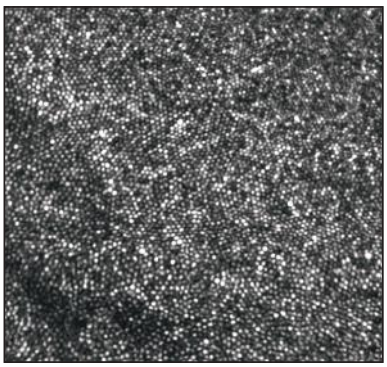
Dr. Blodi is a retina specialist and one of the leaders of WAIVS (Wisconsin Advanced Imaging of Visual Systems), an initiative to develop novel imaging systems of the visual pathway. The WAIVS Adaptive Optics (AO) imaging system, was created by a team of engineers and visual scientists. Adaptive Optics is a custom-built imaging system requiring micron precision to obtain and accurately align in vivo images of human retinal photoreceptors. The system can obtain images of in vivo rods and cones. Dr. Blodi continues to work on a clinical trial that will compare the AO images to standardize AO image capture, grading protocol, and evaluation. This is a crucial first step to make the technology useful for multicenter clinical research, with the goal of having an imaging tool that will assist the ophthalmology community in developing new treatments for macular degeneration and inherited retinal diseases.

Edwin and Dorothy Gamewell Professor

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

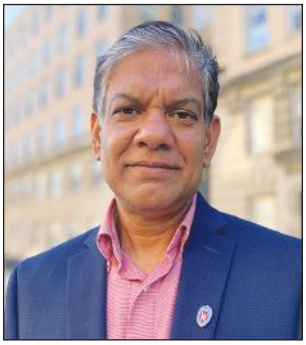
Optical Instrumentation and Technology Platforms for the Study and Screening of Retinal Disease

Dr. Rogers develops imaging methods and instruments to aid in the diagnosis, treatment, and basic research of retinal disease. Advances in diagnosis and therapy are now at the cellular scale and require new imaging technology with the resolution and contrast to visualize cells in a clinical setting. Dr. Rogers is building on Adaptive Optics Scanning Light Ophthalmoscope technology to improve both resolution and contrast of retinal cells by exploiting the intrinsic light scattering properties of cells. Computational modeling and machine learning methods are used to optimize instrument design. By characterizing the time dependent changes in the phase of scattered light, Dr. Rogers is also working to image retinal cell function based on dynamic phase contrast in optical coherence tomography (OCT).



UW-Madison's Adaptive Optics Scanning Light Ophthalmoscope captures its first images of the photoreceptor mosaic in a person. The cone cells shown here cannot be resolved using conventional imaging methods, but come into clear focus with this custom instrument.

M.D. Matthews Research Professor



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

Vision loss due to ion-channelopathy

Genetic eye diseases are the predominant, leading cause of blindness across all ages, from infants to adults. Dr. Pattnaik's research focus is on the basic biology that governs ion channel function, molecular mechanisms of disease and novel therapies, and diagnostic use of visual function tests. Key discoveries include the discovery of novel gene defects that cause blindness due to mutations in an inwardly rectifying potassium channel (Kir7.1). This protein is present in the retinal pigment epithelium (RPE) and helps with the diffusion of potassium across the cell. To model LCA16 blindness, Dr. Pattnaik's team used both induced pluripotent stem cells (iPSC) derived RPE cells from a Leber Congenital Amaurosis patient and in mice with Kir7.1 knock-down. Dr. Pattnaik's lab has developed a gene-therapy treatment for patients that is in advance stage clinical translation through Hubble Therapeutics. Using a particular nonsense mutation disease model, Dr. Pattnaik's lab is pursuing small molecule drugs, or biological molecules such as DNA or RNA that can be targeted to RPE cells as other possible treatments for pediatric blindness caused by defects in both the RPE cells and the photoreceptors.

Rebecca Meyer Brown Professor

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

Remodeling of inner retinal connections during photoreceptor degeneration.

Photoreceptor degeneration occurs in several blinding diseases. When photoreceptors degenerate, the second order neurons that connect with photoreceptors, lose their primary input and can begin to remodel. By combining genetic tools with high resolution microscopy and electrophysiology, the Hoon Lab is determining how the second order neurons remodel their arbors and connections in the inner retina during photoreceptor degeneration. Interestingly, certain connections persevere even after complete photoreceptor loss, whereas other kinds of connections (including neighboring connections on the same cell) lose functionality as soon as photoreceptor loss commences. Understanding the alterations of specific inner retinal connections during photoreceptor degeneration will reveal new therapeutic targets to re-instate visual function in a degenerating circuit.

Dr. Hoon, lower left, and members of the Hoon Lab.

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

The Award of Merit in Retina Research

Russell N. Van Gelder, MD, PhD
UW Medicine Eye Institute
University of Washington
Seattle, WA

Prospects for Vision Restoration in Outer Retinal Degeneration

Dr. Van Gelder is an active clinician-scientist and teacher. His research has been continuously funded by the NIH since 1999. While Dr. Van Gelder specializes in uveitis, his laboratory has been at the forefront of two fields, pathogen detection in uveitis and non-visual photoreception that focuses on how ganglion cells can sense light and how these discoveries can be used to treat blindness. His Award of Merit lecture discussed some of the most promising aspects of restoring sight to patients blinded by age-related macular degeneration and retinitis pigmentosa. Dr. Van Gelder finds hereditary retinal degeneration among the most challenging of diseases because the human retina does not regenerate damaged or destroyed cells. Current approaches to vision restoration: stem cell replacement of damaged cells; electronic chips to simulate and transmit light receptivity to the brain; and light sensing protein (Optogenetic) gene therapy, all face significant challenges to becoming established therapies. Dr. Van Gelder is pursuing a different approach to restoring retina function. His lab is investigating the therapeutic potential of synthetic small molecule photoswitches for restoring light sensitivity to degenerated retinas. Dr. Van Gelder is hopeful this research will transition to human clinical trials in the next several years.

Nationally, Dr. Van Gelder has served as President of the American Academy of Ophthalmology, having previously served as chair of the AAO Council. He currently serves on the National Advisory Eye Council of the NEI and as one of five committee members of the Audacious Goals Initiative, and on the Council of Councils of the NIH Director. He is also past president of the American Uveitis Society and President of the Association of University Professors of Ophthalmology.

RRF Pyron Award for Outstanding Achievement in Retina Research

Mark S. Humayun, MD, PhD
USC Roski Eye Institute
University of Southern California (USC)
Los Angeles, CA

Dr. Mark Humayun was recognized as the 2020 RRF Pyron Award recipient during the July virtual annual meeting of the American Society of Retina Specialists (ASRS). Due to the meeting's virtual format, Dr. Humayun will deliver his Pryon lecture at a future annual meeting.

Dr. Humayun considers the development of advanced implants for retinal diseases to be his major contribution to the field of visual sciences. He assembled a team of multidisciplinary experts to develop the first FDA-approved artificial retina, Argus II, for sight restoration. The advanced bioelectronic implant uses controlled electrical pulses to stimulate the remaining retinal neurons in the setting of total photoreceptor loss. It has restored partial sight to totally blind patients with retinitis pigmentosa enabling them to see large letters and objects.

Dr. Humayun is also the inventor of a bioengineered scaffold with stem cell derived retinal pigment epithelium (RPE). This implant, the CPCB1, is positioned subretinally and is for patients with advanced, dry macula degeneration. It assists with re-establishing host photoreceptor function by providing a healthy layer of RPE. CPCB1 has completed phase1/2a clinical trials. The results to date show an unprecedented gain after implantation in visual acuity in very advanced legally blind (20/200 or worse) patients.

Dr. Humayun is an internationally recognized pioneer in vision restoration. He holds more than 125 issued patents, and has authored over 250 peer-reviewed publications. For his extraordinary contributions, Dr. Humayun was awarded the U.S.'s highest technological achievement award, The National Medical of Technology and Innovation by President Barack Obama in 2016. Dr. Humayun has previously received the 2009 RRF Award of Merit, given by The Retina Society.

Charles L. Schepens, MD/AAO Award

Julia A. Haller, MD
Wills Eye Hospital
Philadelphia, PA

Retina in the Pandemic: Hear Our Roar

The 2020 RRF Charles L. Schepens, MD/AAO Award was given to Julia A. Haller, MD, Ophthalmologist-in-Chief at Wills Eye Hospital, Philadelphia, PA. Dr. Haller is one of the world's most renowned retina surgeons. Her award lecture, Retina in the Pandemic: Hear Our Roar, was delivered during the American Academy of Ophthalmology's (AAO) virtual annual meeting, Friday, November 13, 2020. Dr. Haller discussed how Wills Eye Hospital's doctors and clinics dealt with the challenges of providing patient care during the COVID-19 pandemic, including a significant and lasting increased use of telemedicine solutions as a way to maintain contact with patients when in-person visits are not possible. The use of the technology proved to be extremely effective and efficient in providing the expected high standards of care, so much so that moving forward, telemedicine will be a permanent and expanded part of provider care.

Dr. Haller is a member, National Academy of Medicine, numerous international scientific advisory boards, and sits on the Board of Trustees of the Association of University Professors of Ophthalmology. She is the president of Women in Medicine Legacy Foundation.

Dr. Haller has published over 400 scientific articles and book chapters and her research interests are in diabetic retinopathy, age-related macular degeneration, retinal pharmacology, health care disparities and gender equality.

Paul Kayser International Award in Retina Research

Samuel M. Wu, PhD
Cullen Eye Institute, Baylor College of Medicine
Houston, TX

A2 Amacrine Cell mediated Signaling Pathways in Healthy and Diseased Mammalian Retinas

Dr. Wu, was selected as the 2020 recipient of the Paul Kayser International Award by the International Society of Eye Research (ISER), an award given in collaboration with RRF since 1986. His presentation lecture was given during a virtual webinar in December, 2020. Dr. Wu explores the detailed molecular and synaptic mechanisms underlying retinal function and eye diseases. His laboratory pioneers investigations on rod and cone photoreceptor interactions and parallel information pathways in the retina and has made discoveries on how individual ion channels, receptors, synapses and gene products carry out retinal function in normal animals and dysfunction in mouse models for eye diseases such as retinitis pigmentosa, glaucoma and Bardet Biedl Syndrome. For nearly four decades RRF has significantly contributed to Dr. Wu's research and laboratory, which is considered one of the most highly advanced in the world.

Three RRF established awards were not bestowed in 2020. The Gonin Lecturer given in collaboration with Club Jules Gonin and the Gonin Medal given in conjunction with the International Council of Ophthalmology both will be awarded in 2022. The Paul Kayser/RRF Global Award, given in conjunction with Pan-American Association of Ophthalmology (PAAO) will be awarded in 2023.

RRF funds two programs of international fellowships, one a 12-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. The 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.

The 2020 Fellows are:

Estephania Feria Anzaldo, MD from Mexico who will serve a training fellowship in retinopathy of prematurity and pediatric retina under the supervision of Dr. Berrocal at Bascom Palmer Eye Institute, University of Miami in Florida. Her fellowship began in August 2020 and will end July 2021.

Irmak Karac, MD, from Turkey who will serve a training fellowship in retina and uveitis under Dr. Quan Dong Nguyen and Dr. Diana V. Do at the Byers Eye Institute, Stanford University, Palo Alto, CA from May 2020 to April 2021.

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 or Canada. Fortunately, this year's fellows had already arrived at their host institutions prior to the imposition of COVID-19 related travel restrictions and were able to receive their training as planned.

Julia de Lima Farah, MD from Brazil, trained in Retina at Alberta Health Services, The University of Calgary, Canada, with Dr. Amin Kherani and Dr. R. Geoff Williams. For Dr. Farah, flying north to Canada was well worth the trip; training in such a high quality and efficient public health system was a great experience. She worked in a high volume, retina surgery practice and learned from a team of retinal surgeons, uveitis specialists, and ocular oncologists using the most advanced technology available.

Dr. Amin Kherani, Dr. Farah and Dr. R. Geoff Williams

She provided retinal disease emergency care, and gained experience interpreting advanced retinal imaging, teaching rounds, and developing research protocols.

"Receiving the Gillingham Fellowship award from the PAAO was very impactful. I thank PAAO and the Retina Research Foundation, who sponsors this fellowship award. I am looking forward sharing the great training and knowledge I have had the privilege to receive."
Julia de Lima Farah, MD

Matias Soifer, MD from Argentina, trained in Cornea and Ocular Immunology and Clinical Research, at the Foster Center for Ocular Immunology, Duke Eye Institute, Duke University with Dr. Victor Perez. Dr. Soifer published a paper, *Matrix Metalloproteinase9 Positivity Predicts Long Term Decreased Tear Production*, during his fellowship, which was extended into 2021 due to the pandemic.

Research Initiatives

Stewardship of endowed gifts enables RRF to generously fund programs in translational research and education, disseminating basic research laboratory knowledge to practicing ophthalmologists worldwide.

American Academy of Ophthalmology Educational Trust Fund

Administered for RRF by the American Academy of Ophthalmology, this educational program provides ophthalmologists the world over with the resources needed to enhance their clinical research skills in the field of retina, and empower them with knowledge of the latest advancements necessary to treat patients more effectively. The funding level for this educational effort in 2020 was $50,000.

RRF Lawrence Travel Scholarships

The Lawrence Travel Scholarship 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. The program provides travel expense scholarships to young vitreoretinal scientists for attending ARVO's annual meeting and participating in presentation of scientific works. While RRF had anticipated increasing support for this program to $30,000, due to travel restrictions, ARVO elected to hold a virtual meeting, in June, 2020. While no travel scholarships were awarded for the ARVO poster presentations, young scholars were able to submit presentations for sharing in a virtual, online format. The virtual meeting was well attended with a high level of participation from all over the globe.

New Education Initiative in 2020

AAO Museum of the Eye

In 2020, RRF, in furtherance of its educational program goals, committed to supporting the American Academy of Ophthamology Museum of the Eye. The museum is dedicated to the science of sight. Open to the general public, the museum will offer interactive, high-tech exhibits and access to a rotating exhibit from the vast collection of historical ophthalmic artifacts. Up until now, the 38,000 piece collection was only available online or by appointment. RRF is specifically supporting the Retina Gallery where individuals can learn about the most miraculous tissue of the eye, the retina, and explore the latest innovations saving sight today. The AAO Museum of the Eye is located at the AAO headquarters in San Francisco, CA and will open in the summer of 2021.

Courtesy of American Academy of Ophthalmology

Courtesy of American Academy of Ophthalmology

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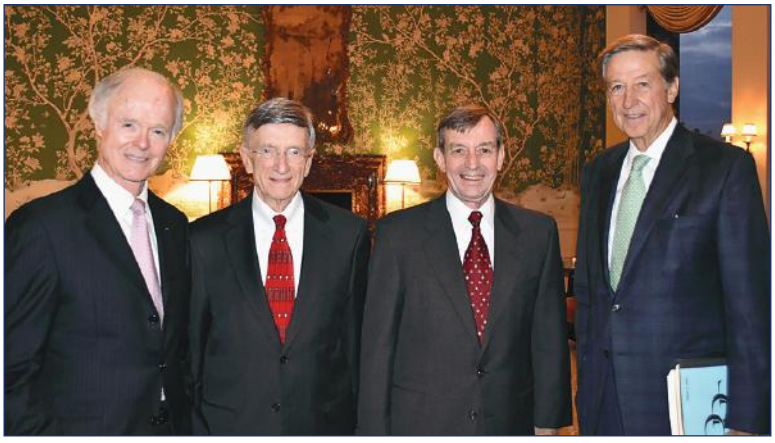

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RETINA RESEARCH FOUNDATION
COMBINED STATEMENT OF FINANCIAL POSITION

December 31, 2020
(with summarized financial information as of December 31, 2019)

	General Funds			Endowment Funds			2020	2019 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	$ 772,279	$ 80,000	$ 852,279	$ -	$ 2,447,313	$ 2,447,313	**$ 3,299,592**	$ 4,341,185
Contributions receivable	36,137	-	36,137	-	110,000	110,000	**146,137**	132,482
Interfund receivable	-	-	-	-	-	-	**-**	46,010
Investments	2,647,448	-	2,647,448	5,085,077	53,680,755	58,765,832	**61,413,280**	55,413,401
Furniture and equipment, net of accumulated depreciation of $8,895	14,932	-	14,932	-	-	-	**14,932**	16,793
Intangible assets	12	-	12	-	-	-	**12**	12
Other assets	15,235	-	15,235	-	-	-	**15,235**	20,358
Total assets	$ 3,486,043	$ 80,000	$ 3,566,043	$ 5,085,077	$ 56,238,068	$ 61,323,145	**$ 64,889,188**	$ 59,970,241
Liabilities and net assets								
Accounts payable	$ -	$ -	$ -	$ -	$ 65,171	$ 65,171	**$ 65,171**	$ 67,855
Grants payable	200,000	-	200,000	-	-	-	**200,000**	-
Interfund payable	-	-	-	-	-	-	**-**	46,010
Total liabilities	200,000	-	200,000	-	65,171	65,171	**265,171**	113,865
Net assets	3,286,043	80,000	3,366,043	5,085,077	56,172,897	61,257,974	**64,624,017**	59,856,376
Total liabilities and net assets	$ 3,486,043	$ 80,000	$ 3,566,043	$ 5,085,077	$ 56,238,068	$ 61,323,145	**$ 64,889,188**	$ 59,970,241

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

For the year ended December 31, 2020
(with summarized financial information for the year ended December 31, 2019)

	General Funds			Endowment Funds			**2020 Total All Funds**	2019 Total All Funds (Memorandum Only)
	Without Donor Restrictions	With Donor Restrictions	Total	Without Donor Restrictions	With Donor Restrictions	Total		
Revenues								
Contributions	$ 161,996	$ 124,500	$ 286,496	$ 1,216,115	$ 192,499	$ 1,408,614	**$ 1,695,110**	$ 959,863
Investment income, net	33,640	-	33,640	86,660	1,271,132	1,357,792	**1,391,432**	1,680,513
Realized and unrealized gains on investments, net	182,525	-	182,525	232,868	3,393,241	3,626,109	**3,808,634**	7,131,008
Mineral interest income and other income	9,214	-	9,214	-	-	-	**9,214**	21,113
Income transferred from Endowment Fund investments	1,680,080	55,000	1,735,080	(111,991)	(1,623,089)	(1,735,080)	**-**	-
Net assets released from restrictions - satisfaction of program restrictions	184,500	(184,500)	-	-	-	-	**-**	-
Total revenues	2,251,955	(5,000)	2,246,955	1,423,652	3,233,783	4,657,435	**6,904,390**	9,792,497
Expenses								
Program services								
Research projects and grants	1,969,509	-	1,969,509	-	-	-	**1,969,509**	1,492,785
Supporting services								
Management and general	167,240	-	167,240	-	-	-	**167,240**	228,701
Total expenses	2,136,749	-	2,136,749	-	-	-	**2,136,749**	1,721,486
Changes in net assets	115,206	(5,000)	110,206	1,423,652	3,233,783	4,657,435	**4,767,641**	8,071,011
Net assets, beginning of year	3,170,837	85,000	3,255,837	3,661,425	52,939,114	56,600,539	**59,856,376**	51,785,365
Net assets, end of year	$ 3,286,043	$ 80,000	$ 3,366,043	$ 5,085,077	$ 56,172,897	$ 61,257,974	**$ 64,624,017**	$ 59,856,376

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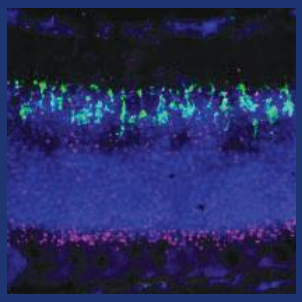

Photo courtesy of Timothy W. Corson, PhD, RRF Joe M. and Eula C. Lawrence Project Researcher, Indiana University School of Medicine, Bomina Park, Corson laboratory

Expression of soluble epoxide hydrolase (Ephx2) mRNA in mouse eyes with laser-induced choroidal neovascularization. Ephx2 is in magenta, Apoe (Müller cell marker) is in green, and nuclei are in blue.

Photo courtesy of David M. Gamm, MD, PhD, RRF Emmett A. Humble Distinguished Director, McPherson Eye Research Institute

An image of a photoreceptor scaffold "ice cube tray" (ICT) design with photoreceptors shown in red, as published in Science Advances, 2021.

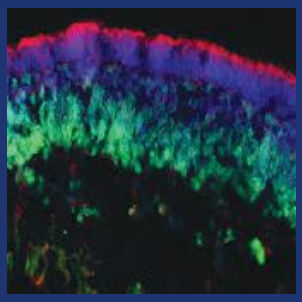

Photo courtesy of Rui Chen, PhD, RRF W.O. Manning Project Researcher, Baylor College of Medicine

Human embryonic stem cell derived retinal organoid stained with DAPI (blue), RHO (red) and SOX9 (green). Multi-layer structure is observed in the organoid, mimicking the retina in vivo.

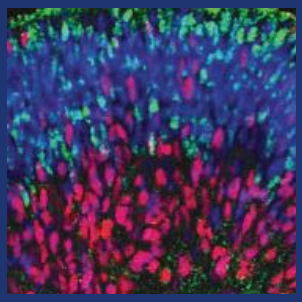

Photo courtesy of David M. Gamm, MD, PhD, RRF Emmett A. Humble Distinguished Director, McPherson Eye Research Institute

Cross section of a multi-layered retinal organoid generated from human induced pluripotent stem cells.

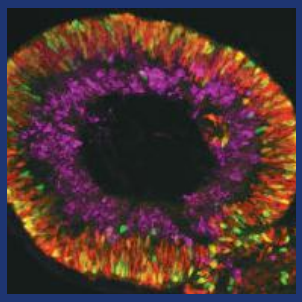

Photo courtesy of David M. Gamm, MD, PhD, RRF Emmett A. Humble Distinguished Director, McPherson Eye Research Institute

Cross section of an early retinal organoid generated from human induced pluripotent stem cells. Dividing retinal progenitor cells are shown in red and green and ganglion cells are shown in purple.

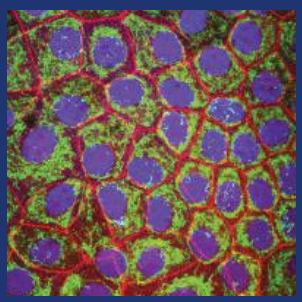

Photo courtesy of David M. Gamm, MD, PhD, RRF Emmett A. Humble Distinguished Director, McPherson Eye Research Institute

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).

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