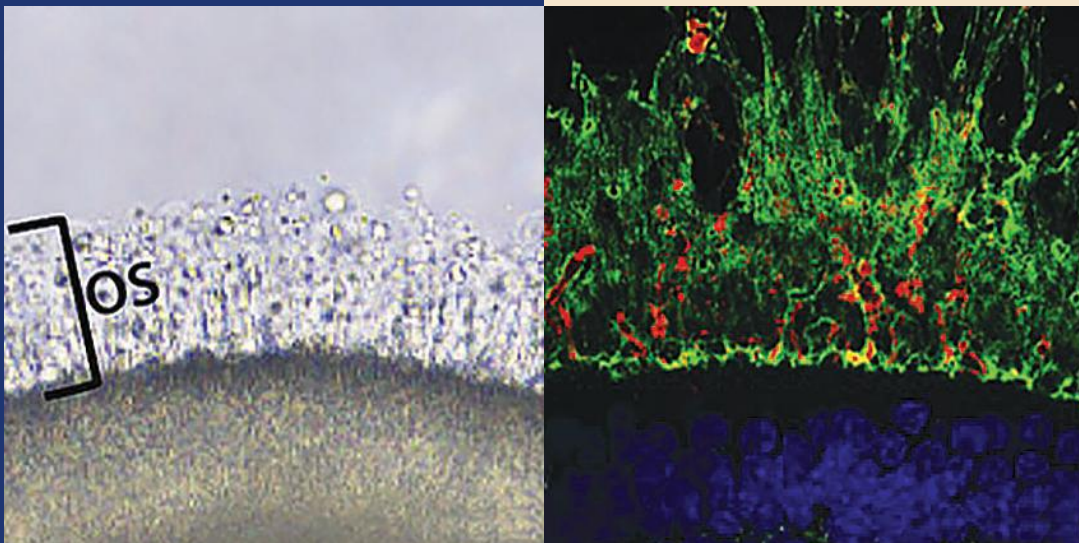
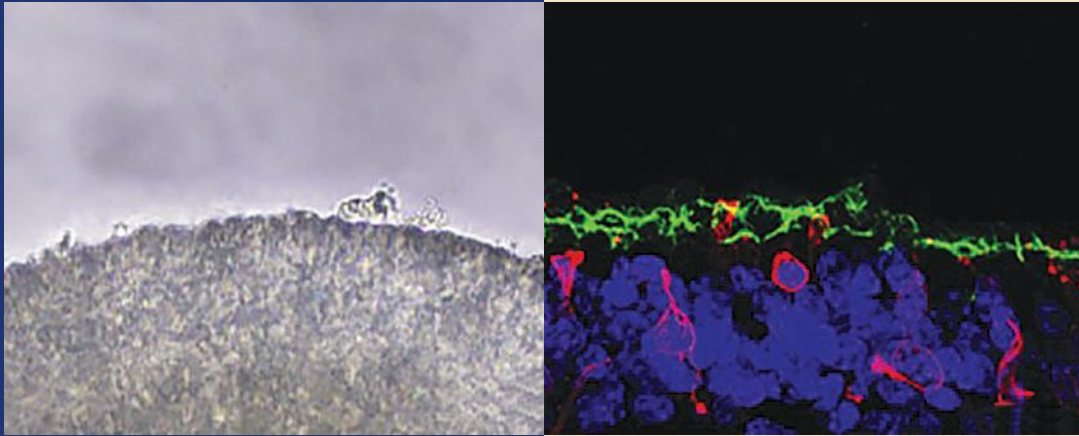




RETINA RESEARCH FOUNDATION



ANNUAL REPORT 2022

FUNDING PROGRAMS IN RESEARCH AND EDUCATION
TO REDUCE RETINAL BLINDNESS WORLDWIDE

Annual Report 2022

Table of Contents

Research Program Overview	2
Collaborating Organizations.....	4
Named and Basic Research Projects	6
Research Chairs and Professorships	17
Established Research Awards.....	22
International Fellowships	26
Research Initiatives	30
Special Events.....	31
Officers and Boards.....	32
Contributors.....	34
Financial Summary	38
In Memoriam	40



Established in 1969

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

Chairman's Message



Dear Friends,

The year 2022 was one of considerable change for Retina Research Foundation. A pivotal moment occurred when our Founder and President, Dr. Alice R. McPherson, determined to step away from the daily responsibilities of managing the Foundation, responsibilities she had admirably shouldered for the past 53 years. The Board of Managing Directors actively assumed these responsibilities and on behalf of the Board, I am pleased to share with you that we are in an exceptionally good position to continue the work of the Foundation into the foreseeable future. This is as it needs to be because the Foundation, with its focus on retina, continues to be a vital source of funding for vision research seeking to cure and prevent blindness caused by retinal diseases.

As you will learn on the pages ahead, RRF remains dynamic and impactful. Our research and educational programs are entirely restored to full implementation at pre-pandemic capacity. The basic research program continues to expand in scope, funding 20 pilot projects in 2022, and 25 pilot projects in 2023. Vision societies are again able to hold their meetings and share knowledge of advancements in the field, and at these international meetings, RRF's established awards and accompanying research grants were bestowed, six in total during 2022, recognizing excellence in retina research. For younger ophthalmology physician/researchers, our international fellowship programs progressed unimpeded throughout 2022 and into 2023, and travel awards were reinstated for in-person meeting participation. The RRF community also gathered. We were pleased, after much time apart, to hold the 2022 RRF Luncheon and Honorary Lectureship. Dr. McPherson enjoyed the opportunity to visit with many of you at the event, which ultimately proved to be our founder's last public appearance.

As was inevitable, we said a final goodbye to Dr. McPherson just following the end of the year, on January 16, 2023. We deeply feel her passing, and we miss her presence in the board room and at our events and functions. Her departure brings to a close a personal connection with her begun by my father, John C. Dawson, Sr., who joined the RRF Board of Managing Directors in 1973. Serving as chairman during that time, he

was instrumental in developing the structure and policies of the Foundation. Like many other families, dedication to RRF's mission spans generations. I am honored to serve as Chairman of the Board of Managing Directors, and it has been a distinct pleasure to have worked on the RRF Board and the Executive Committee beside Dr. McPherson for nearly three decades. Throughout the years, she guided us skillfully toward her vision for the Foundation, and infused her exceptionally high standards into our formal procedures and processes, with the expectation that RRF will continue, in perpetuity. All this is to say that, again, speaking on behalf of the RRF Board, all members are steadfastly committed to this important purpose of funding vision research. We will do everything in our power to realize Dr. McPherson's vision, which we share with you, and our success is enhanced by your continued interest and support. As we look forward, RRF is encouraged by the promise of future research breakthroughs, and together, you and all of us at RRF will not waiver in our commitment to realizing the ultimate goal, to end blindness caused by retinal diseases, as Dr. McPherson would have wanted.

With appreciation,

A handwritten signature in black ink, appearing to read "John C. Dawson, Jr.", written in a cursive style.

John C. Dawson, Jr.
Chairman



John C. Dawson, Jr.
Chairman

Alice R. McPherson, MD
Founder and President

Research Program Overview - 2022

Retina Research Foundation supports an exemplary variety of programs in retina research all around the world. The following overview of RRF research supported in 2022 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
- Institute for Vision Research Center, University of Iowa, Iowa City, IA
 - Seongjin Seo, PhD – Basic Research Project
- University of California, Irving, Irving, CA
 - Vladimir Kefalov, PhD – Basic Research Project
- University of Illinois at Chicago, Chicago, IL
 - Adrius Kazlauskas, PhD – Basic Research Project
- University of Arizona, Tuscon, AZ
 - Erika D. Eggers, PhD – Basic Research Project
- University of Kentucky, Lexington, KY
 - Ann C. Morris, PhD – Basic Research Project
- Augusta University, Medical College of Georgia, Augusta, GA
 - Ming Zhang, MD, PhD – Basic Research Project

RRF Cox Macula Society Research Grant – New Clinical Research Project

- Administered by The Macula Society
- Ajay E. Kuriyan, MD, MS – Wills Eye Hospital, Philadelphia, PA

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

Nader Sheibani, PhD – RRF Research Chair

David Gamm, MD, PhD – Humble Distinguished Director, McPherson Eye Research Institute

Kevin W. Eliceiri, PhD – Helmerich Chair, Assoc. Director, McPherson Eye Research Institute

Krishanu Saha, PhD – Murfee Chair, McPherson Eye Research Institute

Melissa Skala, PhD – Albert Chair, McPherson Eye Research Institute

Research Professorships – Ongoing Proven Research Projects

University of Wisconsin, Madison, WI

Sarah Gong, 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 and Ongoing Research

RRF Award of Merit – presented by The Retina Society

Edwin Stone, MD, PhD – University of Iowa, Iowa City, IA

RRF Pyron Award – presented by American Society of Retina Specialists (ASRS)

Mary Elizabeth Hartnett, MD – Byers Eye Institute, Stanford Medicine, Palo Alto, CA

CL Schepens MD/AAO Award – presented by American Academy of Ophthalmology (AAO) and in the spirit of Schepens International Society (SIS)

Philip Rosenfeld, MD, PhD – Bascom Palmer Eye Institute, University of Miami, Miami, FL

RRF Gonin Lecturer – presented by Club Jules Gonin

Ramin Tadayoni, MD, PhD, Université Paris Cité, Fondation Adolphe de Rothschild Hospital Paris, France

Gonin Medal – presented by International Council of Ophthalmology (ICO)

Stanley Chang, MD – Columbia University Medical Center, New York, NY

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

Steven Fliesler, PhD, SUNY - University of Buffalo, Buffalo, NY

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

International Fellowships – Advanced Subspecialty Training

RRF Helmerich International Fellowships – presented by Ophthalmology Foundation (OF) and administered by International Ophthalmological Fellowship Foundation e. V. (IOFF)

Chibuzo Barbara Ekumakama, MD – from Nigeria to MGM Eye Institute in Raipur, India

Amare Atoma Gelacha, MD – from Ethiopia to Pakistan Institute of Community Ophthalmology, Peshawar, Pakistan

Perpetua Odugbo, MD – from Nigeria to Jules Stein Eye Institute, UCLA, Los Angeles, CA

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

Natasha Ferreira Santos da Cruz, MD – from Brazil to Bascom Palmer Eye Institute, Miami, FL

Miguel N. Cruz Pimentel, MD – from the Dominican Republic to University of Toronto Toronto, Ontario, Canada

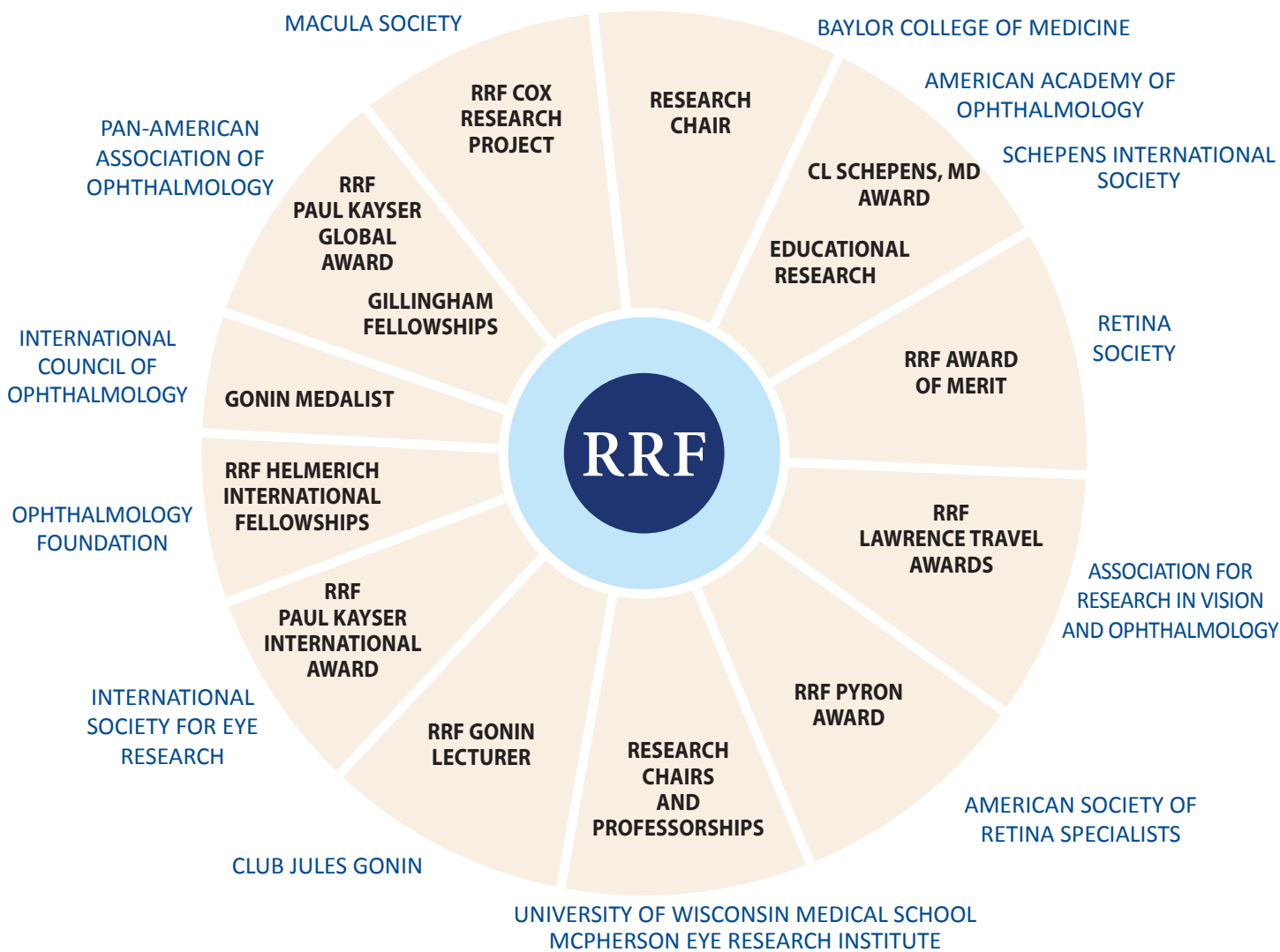
Research Initiatives – Educational and Travel Scholarships

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

Retina-related educational programs for clinical and basic science

RRF Lawrence Travel Scholarships – administered by Association for Research in Vision and Ophthalmology (ARVO) – 28 in-person travel scholarships awarded in 2022

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 Schepens International Society	Charles L. Schepens, MD/AAO Award	2008
ICO/ICOF International Council of Ophthalmology	RRF Helmerich International Fellowships	2009
OF Ophthalmology Foundation/IOFF	RRF Helmerich International Fellowships	2021

TEXAS : 11

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

PAN AMERICAN : 23

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

INTERNATIONAL : 48

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
Hospital Fondation Rothschild	Paris, France
Institut de la Vision	Paris, France
Intercommunal Hospital of Crèteil	Crèteil, 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 : 67

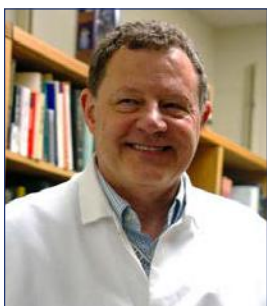
Augusta University College of Medicine	Augusta, GA
Bascom Palmer Eye Institute	Miami, FL
Beaumont Eye Institute/Hospital	Royal Oak, MI
Byers Eye Institute/Stanford University	Palo Alto, CA
California Institute of Technology	Pasadena, CA
Carver College of Medicine	Iowa City, IA
Case Western Reserve University	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	Worcester, MA
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 Arizona	Tucson, AZ
University of Buffalo/SUNY	Buffalo, NY
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 Illinois at Chicago	Chicago, IL
University of Iowa	Iowa City, IA
University of Kansas Medical College	Kansas City, KS
University of Kentucky	Lexington, KY
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

Today's robust basic research program has evolved from a single pilot study funded in 1973 for \$30,000. By the end of 2022, over 655 basic research pilot grant awards will have been awarded, and more than \$20 million will have been dedicated to funding basic retinal research through the RRF pilot study program. In 2022, RRF funded 20 pilot studies, including two newly added projects. Pilot studies are experimental, basic science studies, conducted at leading research institutions that are designed to investigate novel lines of inquiry into the causes of retinal diseases in an effort to obtain new understanding and to advance scientific knowledge. The hope is that these studies lead to future ongoing projects and, ultimately, new therapies. Ten established projects are named in recognition of individuals who have generously supported the RRF mission. During the year, RRF affiliated vision researchers contributed to the body of knowledge through publication of an impressive 15 manuscripts, submitted to or published in high-impact, peer review journals.

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

Dr. Brandt's research project goals are to reduce the impact of host cell restriction factors on viral vector transduction

efficiency and to understand the innate immune response to gene delivery vectors (gdvs) in order to improve gene therapy for human ocular diseases. In 2022, his laboratory examined the effect of activation of a common transcription factor on gdv efficiency in two human retinal cell lines. They determined the expression and cellular distribution of host cell restriction factors that recognize viral RNA and DNA, in human retinal cell lines and non-human primate (NHP) retina tissue. Dr. Brandt also demonstrated that knockdown of a mitochondrial protein linked to host cell restriction factor signaling could significantly increase gdv efficiency in a human Muller cell line.

Joe M. and Eula C. Lawrence Research Project



Timothy W. Corson, PhD
Department of Pharmacology
and Toxicology
Indiana University School of
Medicine
Indianapolis, IN

Role of soluble epoxide hydrolase in blood-retinal barrier function

The long-term goal of Dr. Corson's research is to find new therapeutic approaches for age-related macular degeneration (AMD), a disease characterized by abnormal blood vessel growth, and retinal pigment epithelium (RPE) dysfunction. The specific goal of the 2022 project was to explore soluble epoxide hydrolase (sEH), an enzyme identified to be important for abnormal new blood vessel growth, and to assess whether sEH regulates the permeability of blood vessel cells and RPE, to guide therapeutic development.

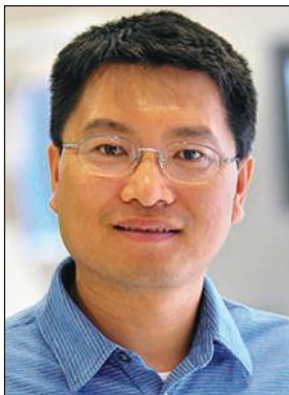
In previous years, Dr. Corson developed a potent chemical called SH-11037, and tested this in combination with standard anti-VEGF therapy. He found sEH as a cellular target of SH-11037, and showed that sEH is present at high levels in human and mouse eyes with AMD-like features. These sEH inhibitors can block new blood vessel growth in the

eye. Assessing their library of novel chemicals, Dr. Corson's group found candidates that perform as well as SH-11037 at blocking sEH, helping to build a "structure activity relationship" for blocking sEH function. Their research showed differential expression in sEH between the sexes, found that depletion of sEH with a genetic tool the Corson lab developed reduces inflammatory signals, and revealed RPE as a major source of this protein. In 2022, Dr. Corson's lab explored whether sEH regulates the permeability of blood vessels in culture, finding that sEH inhibition can decrease leakiness of blood vessels, one of the pathological features of wet AMD.



The Corson Research Lab Team

W.O. Manning Research Project



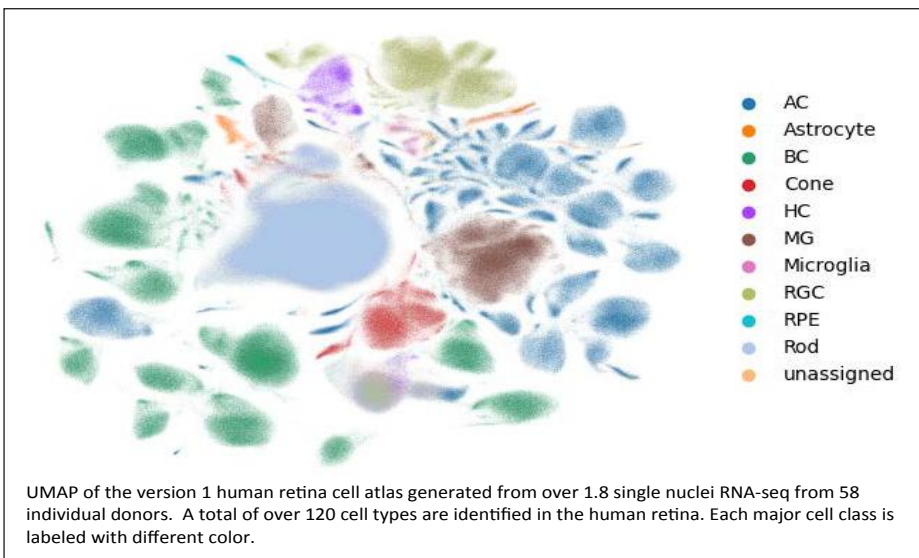
Rui Chen, PhD
 Department of Molecular and Human Genetics
 Baylor College of Medicine
 Houston, TX

Identification and functional analysis of genes involved in retina diseases

The ultimate goal of Dr. Chen’s research is to improve the ability to prevent, diagnose, and treat human retinal diseases. Dr. Chen identifies and conducts functional characterization of novel disease genes underlying human retinal disorders. Since many human eye disease genes are involved in normal eye development, the Chen laboratory utilizes animal model systems to study retinal development. Results obtained from these studies can be directly translated into the understanding of human retinal disease and form the basis of developing optimal treatment of human eye diseases.

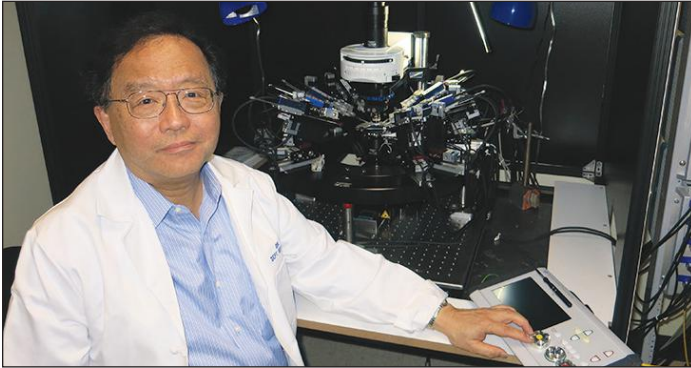
Dr. Chen previously completed panel sequencing for nearly 1000 Leber Congenital Amaurosis (LCA) patients. Nearly 750 patients received positive molecular diagnosis for their retinal

diseases, while 250 patients remained unsolved. Performing whole genome sequencing (WGS) on these remaining patients identified novel mutations that were previously missed. One type of mutation identified is a deep intronic cryptic splicing mutation, and this data was published in *Frontiers in Genetics*. Dr. Chen’s lab established a mutant mice model for a novel human retinal disease gene identified by his laboratory, *Tlcd3b*, and in the past year, his team tested the feasibility of performing gene therapy to rescue the photoreceptor degeneration phenotype. Results demonstrated that gene replacement therapy is effective in treating the *Tlcd3b* mutant mice, findings that pave the way for future human therapy development. The manuscript describing this work was published in *IVOS*. Dr. Chen’s research in 2022 yielded four publications in total.



The Chen Laboratory Team (Dr. Chen, standing front row, far right)

The Paul Kayser Research Project



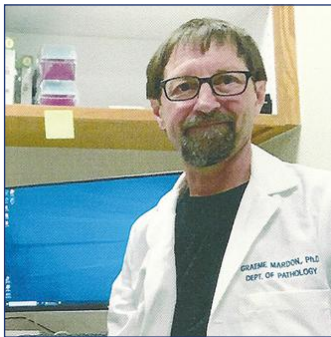
Samuel Wu, PhD

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)

Throughout 2022, Dr. Wu continued his research on the cellular and genetic mechanisms underlying retinal dysfunction and degeneration in glaucoma and age-related macular degeneration (AMD). Using the state-of-the-art, 8-channel patch clamp recording system for simultaneous recordings of multiple retinal neurons and studying the synaptic connectivity in normal and disease states, Dr. Wu's lab extended its studies to primate and other mammalian retinas. His team also researched receptive fields and motion selectivity of retinal ganglion cells (RGC) in normal, AMD and glaucoma retinas. These studies are essential to identifying targets for drug and gene therapies for treating RGC dysfunction in glaucoma and AMD. In 2022, Dr. Wu's lab completed four lines of research, resulting in the submission of two papers for publication. An additional two manuscripts are in preparation. Dr. Wu presented a poster at the Federation of American Societies of Experimental Biology (FASEB) meeting in June and he conducted a seminar for the Department of Biological Sciences at the University of Virginia, Charlottesville in September.

Bertha and I.L. Miller Research Project

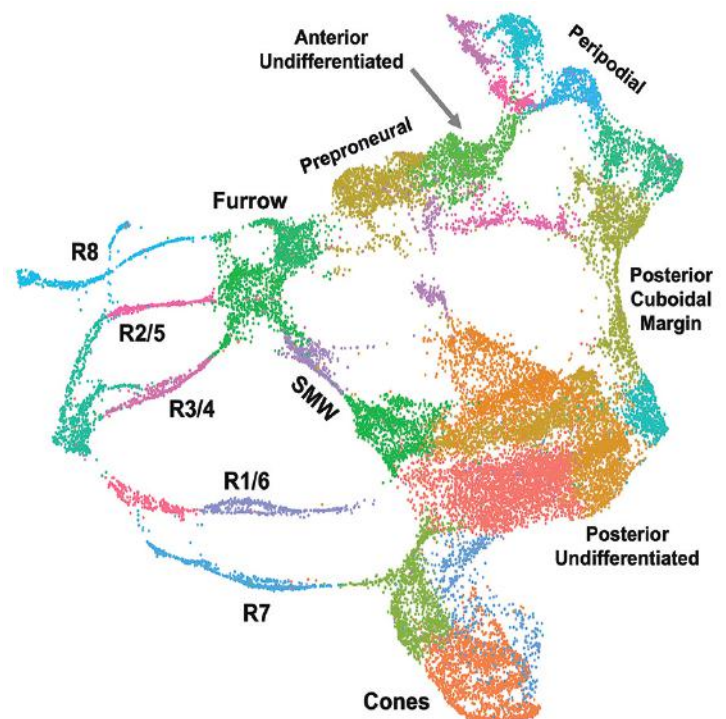


Graeme Mardon, PhD

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 and treatment for human retinal diseases. To that end, he uses the *Drosophila* eye as a powerful animal model system for deciphering conserved molecular mechanisms of retinal cell fate determination and development. An opportunity for transformative change in our ability to achieve these goals is presented by the advent of single cell genomics. We have generated extensive, high quality single cell RNA sequence (scRNA-seq) data from the normal developing *Drosophila* eye and in this proposal, we sought to obtain scRNA-seq data on retinas that are mutant for the *rough* gene. Although it has been known for more than 25 years that *rough* is required for normal photoreceptor differentiation, the molecular details are unknown. We have obtained deep scRNA-seq data and have found that two photoreceptors, R1 and R6, are largely missing from the developing eye. We are currently using this data to develop hypotheses for the molecular basis for this defect.



A cluster plot for the developing *Drosophila* eye that represent single-cell RNA-sequencing data. Each dot in the plot is one cell from the eye and cells that have similar gene expression cluster together. Streams of cells on the left side of the plot represent each of the photoreceptor subtypes in the fly eye.

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 mechanisms leading to retina disease and in developing gene-based therapies to address photoreceptor degeneration. In 2022, Dr. Baehr’s research project addressed the generation of novel, dominant mouse models expressing mutant ARL2. One model expresses ARL2(R15L) transgene under the

control of a powerful rod/cone promoter, and is expected to mimic autosomal dominant rod/cone dystrophy. The second model introduced a mutation in wild-type mouse by gene editing, and Dr. Baehr expected a more complex phenotype that includes micro- cornea, rod-cone dystrophy and optic nerve atrophy. Using prime editing (PE), a CRISPR-based strategy for precision genome editing, Dr. Baehr’s research is revolutionary, with the development potential of treating and repairing single nucleotide polymorphisms causing retina disease in mouse models.

Dr. Baehr’s research resulted in a publication in the peer-reviewed journal, PLoS Genetics in September, 2022: The role of Arf-like protein 2 (ARL2) in photoreceptors, and acknowledges support from RRF. The publication has been viewed nearly 1,300 times and cited seven times.

Adolphe G. and Josephine Roberts Gueymard Research Project

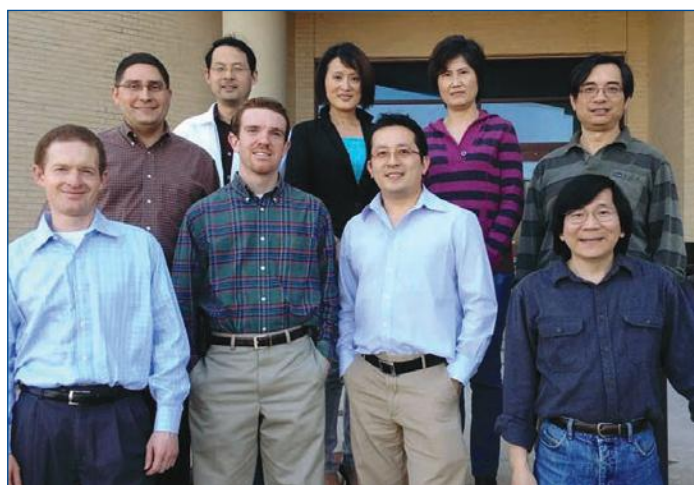


Lih Kuo, PhD
 Department of Medical
 Physiology
 Texas A&M University Health
 Science Center
 Bryan, TX

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

This project is to identify the mechanisms of the early development of diabetic retinopathy in retinal microcirculation and to identify strategies/tools for the prevention/treatment of this sight-threatening disease. Dr. Kuo found that the synthesis of vasoconstrictor/ inflammation agent endothelin-1 (ET-1) from vascular endothelin converting enzyme (ECE) is elevated and corresponds to the activation of RhoA kinase (ROCK) and arginase enzymes in pig retinal microcirculation with early diabetes. He hypothesizes that ECE/ROCK/arginase signaling contributes to microvascular dysfunction and the development of early retinopathy. In 2022, Dr. Kuo’s research yielded three publications detailing exciting pilot data. Dr. Kuo demonstrated that retinal blood flow is dysregulated before the development of neural retinal dysfunction in type

1 diabetes. He also demonstrated the therapeutic potential of stanniocalcin-1 (STC-1) in reducing photoreceptor degeneration, enhancing cone photoreceptor function, and improving retinal structural integrity through antioxidative and anti-inflammatory effects. Because diabetic retinopathy is closely associated with oxidative stress and inflammation, Dr. Kuo’s findings support that STC-1 might be an excellent drug candidate for preventing/treating retinal microvascular dysfunction during the development/progression of retinopathy in early diabetes before the establishment of overt neurovascular pathology.



Dr. Kuo’s Retinal Research Team (Dr. Kuo, front row, far right)

Mary Ellen Wilson Research Project



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

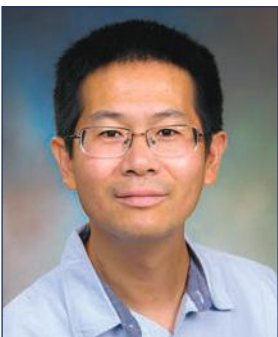
Immune consequences of gene therapy for ocular disorders

Dr. Hurwitz hypothesizes 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 has developed vector systems for delivering suicide gene therapy for retinoblastoma and for gene replacement

approaches for the treatment of Stargardt Disease. His strategy for either application of gene therapy uses a special nonpathogenic virus to deliver the correct genetic material to selected cells in the eye. The virus has been altered so that it cannot cause its usual symptoms, and much of the viral DNA has been removed and replaced with DNA containing therapeutic sequences. However, use of these vectors for delivery does pose a potential for local or systemic complications, and often the severity of these complications is dose related. Dr. Hurwitz is examining a variety of methods to increase the efficiency of the delivery and expression of the therapeutic gene including, using a novel non-invasive delivery method of micro-wafers similar to contact lenses that would eliminate the need for intraocular injections. His goal is to understand the immune consequences related to these therapies and to develop therapeutic delivery systems that minimize the risks to patient's vision while allowing effective clinical management of the disorder.

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

The goal of Dr. Zhang's project is to develop a novel, effective and inexpensive approach to selectively kill abnormal blood vessels in the retina without affecting normal blood vessels. The development and growth of abnormal new blood vessels often result from various diseases, such as diabetic retinopathy, retinopathy of prematurity and retinal vascular occlusion that cause irreversible vision loss.

In 2022, Dr. Zhang investigated a novel role of ER stress/PERK pathway in retinal neovascularization during ischemic retinopathy. His research demonstrated that PERK was activated in the retina during retinal ischemia, and inhibition of PERK with a specific inhibitor GSK2606414 reduced neovascularization while promoting vascular repair. Moreover, PERK inhibition in IR reduced the loss of retinal ganglion cells. Mechanistically, PERK inhibition preserved astrocyte network, prevented Müller cell

activation and downregulated the recruitment/proliferation of macrophage/microglia, although it did not affect the upregulation of canonical angiogenic pathways in IR. A manuscript based on data generated from RRF support has been published and four poster abstracts were presented at ARVO in May, 2022.



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

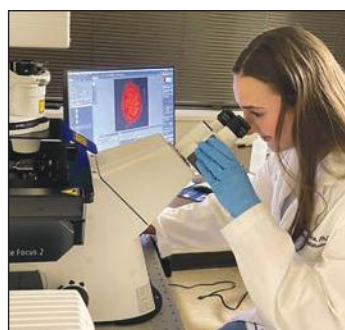
Age-related macular degeneration (AMD) is a major cause of blindness in the elderly. Choroidal neovascularization (CNV or wet AMD), the growth of abnormal leaky blood vessels beneath the retina, underlies 80-90% of legal blindness due to AMD. Up to half of patients have suboptimal responses to the current anti-vascular endothelial growth factor (VEGF) treatment. The objective of Dr. Fu's project is to develop a highly innovative and effective AIBP/apoA-I/anti-VEGF combination therapy for wet AMD by targeting three critical components: VEGF, endothelial cells, and macrophages.

In 2022, Dr. Fu successfully performed ophthalmic phenotyping of his mouse AMD model of anti-VEGF resistance, which exhibits features similar to anti-VEGF non-responders of human patients (i.e., arteriolar type CNV). This is the first study of its kind to use indocyanine green angiography (ICGA) to investigate CNV subtypes in AMD animal models. The project is highly significant because it makes it possible to correlate with human studies

regarding the relationship between CNV subtype and anti-VEGF responses. More importantly, Dr. Fu showed that the combination therapy was effective in treating anti-VEGF resistance by potently inhibiting arteriolar CNV while the current leading treatment, aflibercept monotherapy, was ineffective. These results were published in IOVS, in November 2022. This research lays the groundwork for further translational studies to move the novel AIBP/apoA-I/anti-VEGF combination therapy into the clinic.

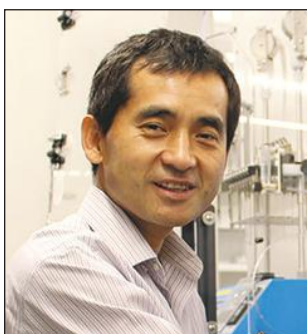


Members of the
Fu Laboratory



Dr. Fu reports that the research has also played a significant role in generating preliminary data for two large NIH grant submissions.

Basic Research Projects



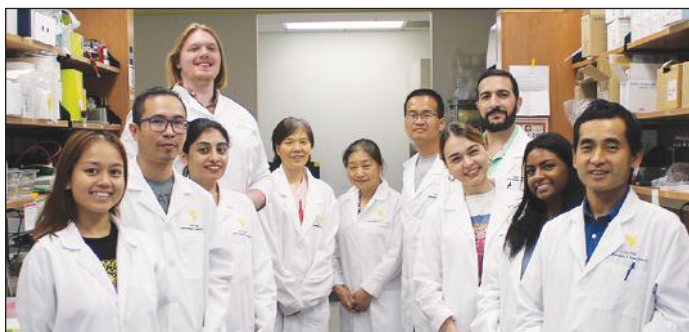
Jianhai Du, PhD
Department of Ophthalmology
West Virginia University
School of Medicine
Morgantown, WV

Nutritional strategies in age-related macular degeneration

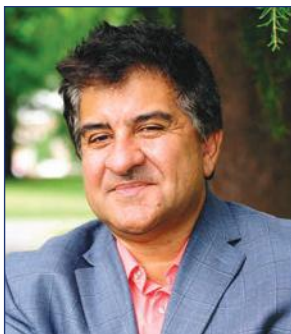
The goal of Dr. Du's project is to study the role of proline catabolism, the breaking down of this complex molecule into simpler ones that releases energy in the healthy and diseased retina, and to develop nutritional approaches to treat age-related macular degeneration.

In 2022, Dr. Du's laboratory made significant progress. They found proline dehydrogenase (PRODH) is critical for

the metabolic communication between the retinal pigment epithelium (RPE) and the neural retina. PRODH deficiency blocks the export of proline-derived nutrients from RPE to the retina, and PRODH is critical for both carbon metabolism in the mitochondrial Krebs cycle and nitrogen metabolism in producing neurotransmitters and amino acids in the retina. PRODH knockout mice have age-dependent visual decline.



The Du Laboratory Team (Dr. Du, front right)



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

**CD5L-mediated
autophagocytosis in RPE cells**

Dr. Giorgianni has discovered that patients affected by age-related macular degeneration (AMD) have antibodies circulating in their blood that can attack and damage proteins present in the eye. One of these targeted proteins, CD5L, might be important for the removal of compounds that are toxic to the eye. Dr. Giorgianni's research project investigating the function of CD5L in the retinal pigment epithelium (RPE), as related to the development of age-related macular degeneration (AMD), has now completed its fourth year. He believes that CD5L carries toxic compounds, especially those derived from cholesterol, and facilitates their degradation thus preventing their accumulation and damage to the RPE.

Dr. Giorgianni is working to definitively prove that the presence of CD5L inside the RPE cells accelerates the

degradation of a compound, derived from cholesterol, called OxLDL. He also will identify other proteins that combine with CD5L to degrade toxic OxLDL by leveraging analytical tools like the mass spectrometer that can identify and quantify proteins. Dr. Giorgianni's findings, published recently in the *Biochemistry and Biophysics Reports*, an open-access, online only, peer-reviewed international journal in the Life Sciences, will help to understand the molecular mechanisms that lead to AMD and could provide new leads for the development of new therapeutic strategies.



Dr. Giorgianni applies advanced mass spectrometry analytical instrumentation to elucidate the mechanisms that could be involved in the etiology of AMD.



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, two essential amino acids, 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 previous year data showed that citrulline and arginine induce an angiogenic response in retinal endothelial cells by activating eNOS, an essential mediator of retinal angiogenesis, to produce nitric oxide (NO) with no effect on arginase activity. These results have been submitted for publication. Additionally, Dr. Brantley demonstrated that inhibiting eNOS blocks citrulline and arginine-induced angiogenesis. His team showed that citrulline and arginine phosphorylate eNOS-activating signaling molecules AMPK and Akt, and that Akt inhibition ameliorates cell migration but not tube formation in retinal endothelial cells treated with citrulline and arginine. Finally, Dr. Brantley's lab further investigated the disruption of the protein, claudin-5, at the cell membrane and showed that citrulline and arginine increase retinal endothelial cell permeability.



James Monaghan, PhD
Biology Department
Northeastern University
Boston, MA

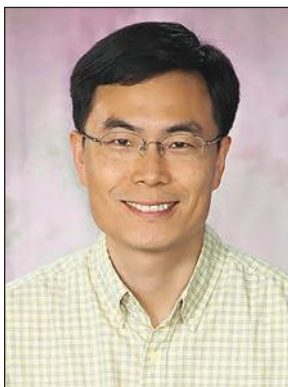
Analysis of notch signaling-mediated cell fate determination during regeneration of the neural retina

Dr. Monaghan researches the Mexican axolotl salamander to understand the molecular mechanisms that drive axolotl regeneration of retinal cells. Mammalian retina do not regenerate. Greater knowledge of the unique mechanisms of the axolotl that enable this regeneration may ultimately lead to better understanding of restoration and replacement of

damaged or missing cells, tissues and even entire body parts to full function beyond the species, including application to treating injuries and disease in humans.

In 2022, Dr. Monaghan finished the histological description of retinal regeneration, completed the first transcriptomic analysis and multiplexed imaging of gene expression, and confirmed that the Notch signaling pathway plays a critical role in retinal regeneration. Over the past two years, Dr. Monaghan's lab has also begun to identify the cell types activated and the molecular mechanisms driving the overall response.

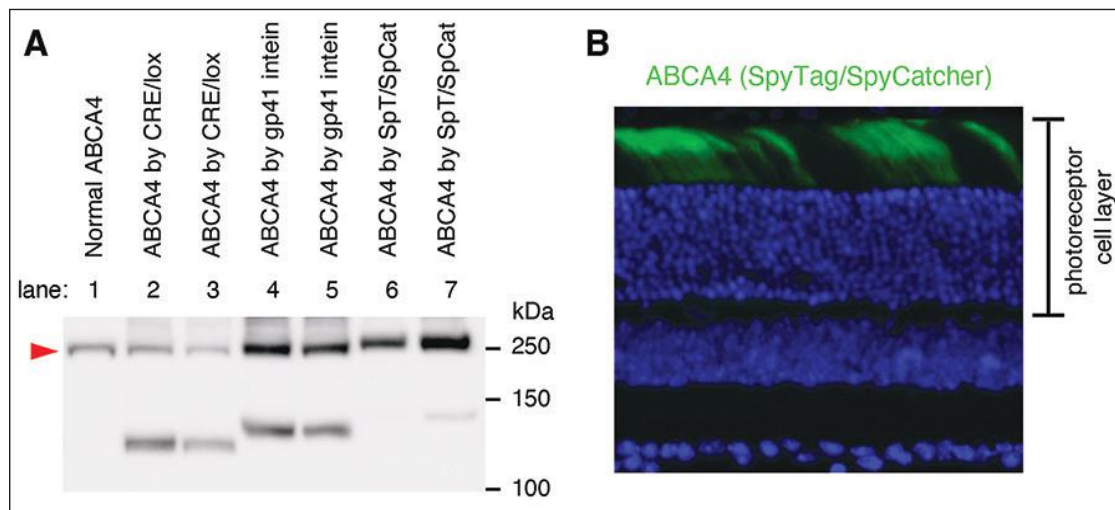
Dr. Monaghan's 2022 grant supported the work of graduate student, Anatasia Yandulskaya, whose dissertation was entitled, Cellular & Molecular Mechanisms of Retinal Regeneration in The Axoloti Salamander. Ms. Yandulskaya was awarded her PhD in May, 2022.



Seongjin Seo, PhD
Department of Ophthalmology and Visual Sciences
Institute for Vision Research Center, University of Iowa
Iowa City, IA

Novel dual AAV approaches for efficient delivery of large genes

The ultimate goal of Dr. Seo's research is to develop highly efficient, adeno-associated virus (AAV)-based large gene delivery systems for retinal gene therapy. While AAV is a safe and efficient gene delivery vehicle, its main drawback is the limited packaging capacity. In 2022, Dr. Seo focused on developing gene therapy vectors to treat ABCA4-associated retinal degeneration, responsible for 95% of the incidence of Stargardt disease, the most common inherited retinal disease. Dr. Seo established three approaches to deliver large genes using AAV and compared their reconstitution efficiencies in cultured mammalian cells for ABCA4 gene therapy vectors. One approach utilizes gp41 split intein-mediated protein trans-



A) The production of full-length ABCA4 proteins is visualized by a technique called Western blotting. Lane 1 shows the normal, full-length ABCA4 proteins (red arrowhead), while lanes 2-7 show ABCA4 proteins reconstituted via the CRE/lox (lanes 2-3), gp41 split intein (lanes 4-5), and SpyTag/SpyCatcher (lanes 6-7) systems. The hyphens and numbers on the right mark protein sizes. The molecular weight of full-length ABCA4 is ~260 kDa. **B**) The panel B image shows ABCA4 proteins (green; reconstituted by the SpyTag/SpyCatcher system) produced in a mouse eye after AAV vector delivery. It also shows that ABCA4 proteins are produced in the right cells (i.e., photoreceptors) and present in the right place (outer segments).

splicing to re-join protein fragments. The second approach utilizes a pair of high-affinity polypeptides (SpyTag and SpyCatcher) that form a covalent bond upon binding. The third uses the CRE/lox DNA recombination system to facilitate the reconstitution of therapeutic genes. Research has begun on testing the therapeutic efficacies of ABCA4 gene therapy vectors in an animal model.



Vladimir Kefalov, PhD
Department of Ophthalmology
and Visual Sciences
University of California, Irvine
Irvine, CA

Understanding how the G90D and G90V rhodopsin mutations cause blindness

The purpose of Dr. Kefalov's project is to identify the molecular mechanism by which two similar mutations in the visual pigment rhodopsin, Glycine 90 to Aspartate (G90D) and Glycine 90 to Valine (G90V), cause distinct visual disorders. Microspectrophotometric (MSP) measurements from mutant mice showed that the production and decay of photoactivated rhodopsin intermediates were greatly altered in both G90D and G90V mutants. Dr. Kefalov and his team also found that the level of chromophore-free opsin was low in wild type and G90D mouse retinas, but G90V mouse retinas contained a substantial fraction of free opsin. Consistent with that finding, treatment of dark-adapted retinas with exogenous 11-cis-retinal improved rod flash sensitivity in G90V but not G90D or wild type mice. These results demonstrate that while both G90D and G90V mutations disrupt the molecular properties of rhodopsin, only the G90V mutant desensitized rods due to the presence of free opsin. These findings were presented at the 2023 ARVO meeting in New Orleans.

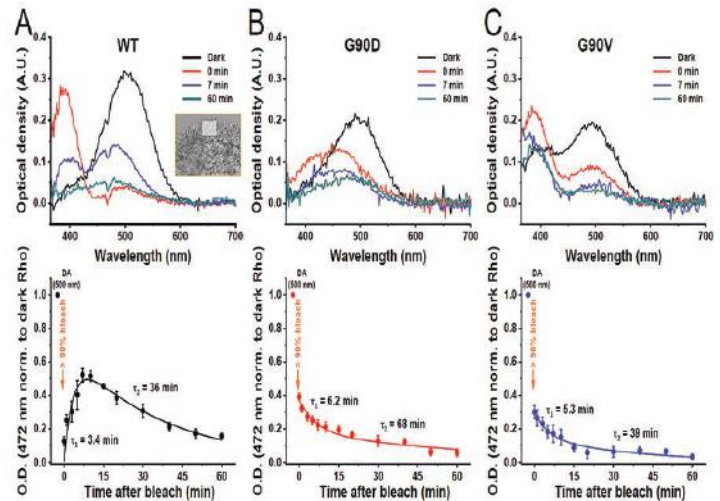


Figure legend. Production and decay of rhodopsin photobleaching products in WT, G90D, and G90V homozygous mouse retinas. Top: Representative raw microspectrophotometric (MSP) absorbance spectra from dark-adapted retina (black), after near complete bleach of the visual pigment (red), 7 min (blue), and 60 min (cyan) after the bleach of (A) WT, (B) G90D, and (C) G90V homozygous retinas. Inset in (A) shows the view under MSP of the measuring beam (light rectangle) on the retina edge. Bottom: Averaged (mean ± SEM) time course of Meta III, measured at 472 nm in (A) WT, (B) G90D, and (C) G90V retinas. The data were fitted with double exponential functions that yielded time constants of Meta III production and decay (WT) or decay only (G90D and G90V).



Andrius Kazlauskas, PhD
Department of Ophthalmology
and Visual Sciences
University of Illinois at Chicago
Chicago, IL

Hyperglycemia-induced mitochondrial adaptation

The long delay between the onset of diabetes mellitus (DM) and the development of retinopathy suggests the existence of systems that protect the retina from the deleterious effects of DM. Dr. Kazlauskas' lab recently published evidence for such a protective system. In the December 2022 issue of the *American Journal of Pathology*, they report that while exposing primary human retinal endothelial cells to hyperglycemia initially increased their vulnerability to oxidative stress-induced death, prolonged exposure induced adaptation, and thereby protected them from this DM-associated insult. Thus a key cell type within the retinal vasculature was capable of

adapting in order to endure hyperglycemia.

Dr. Kazlauskas' team considered if protection that was observed in cultured cells also occurred in living animal. To this end they studied diabetic mice in which the development of retinopathy is delayed from the onset of DM, just as it is in patients. DM induced protection of the retinal vasculature from oxidative stress-induced death. Furthermore, as the duration of DM was prolonged, protection was replaced with increased vulnerability, and the mice developed retinopathy. These observations indicate the existence of an endogenous system that protects the retina from DM-related damage. Identification of the molecular mediators of protection will enable development of novel therapeutic approaches to indefinitely delay the onset of retinopathy.

Anara Serikbaeva, PhD
student and Dr.
Kazlauskas in the lab.
The RRF-funded project
is the basis of Serikbaeva's
PhD thesis research.





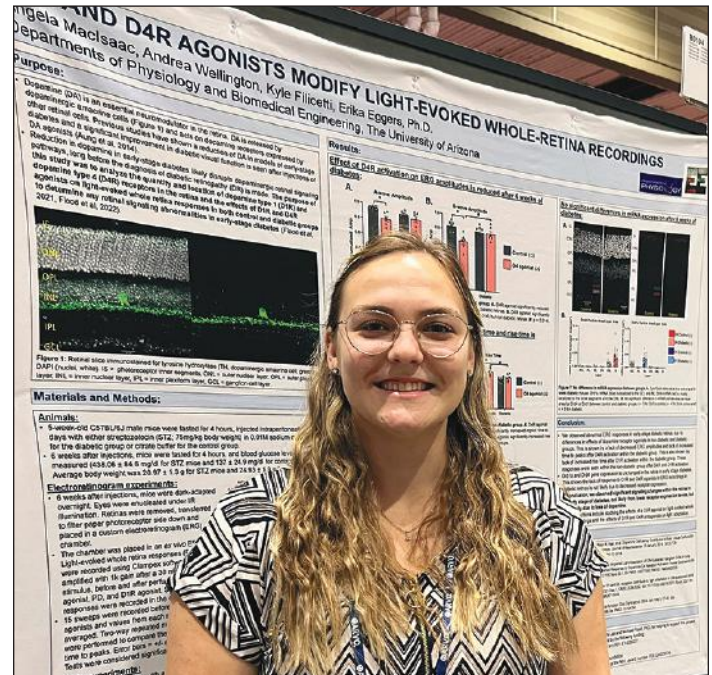
Erika D. Eggers, PhD
Department of Physiology & Biomedical Engineering
University of Arizona
Tucson, AZ

Investigation and modulation of inner retinal dysfunction in diabetes

Some of the earliest, identifiable retinal problems that diabetic patients experience include development of visual deficits in the function of dim light-activated rod pathways that are tied to diabetic retinopathy progression. Dr. Eggers researches whether the dim light-activated rod pathway is specifically vulnerable to diabetic damage and has shown that deficits of neurons in the inner retina are not due to cell death, but another unknown mechanism. Dr. Eggers focuses her research on low dopamine levels in diabetic retinas because dopamine is an important modulator to allow the retina to adapt to varying light levels. Her research hopes to identify the mechanism of dysfunction in order to develop targeted therapeutics to prevent the neuronal progression of vision loss.

Using the isolated retinal electroretinogram (iERG), Dr. Eggers's research found that six weeks of diabetes reduces the modulation of the entire retina by dopamine receptor 1 and 4. This aligns with previous results indicating that six weeks

of diabetes reduces Dopamine 4 receptor modulation of ganglion cells. The 2022 results validate using the iERG as a screening tool for examination of retinal modulators without requiring many retinas and/or individual neuron recordings. This work was presented as an abstract at ARVO 2023.



Angela MacIsaac, Eggers laboratory member, presents her work on dopamine receptor modulation of isolated ERGs in diabetes at ARVO 2023.



Ann C. Morris, PhD
Department of Biology
University of Kentucky
Lexington, KY

Retinal damage and regeneration in the African spiny mouse (*Acomys cahirinus*): a novel mammalian model for translational research

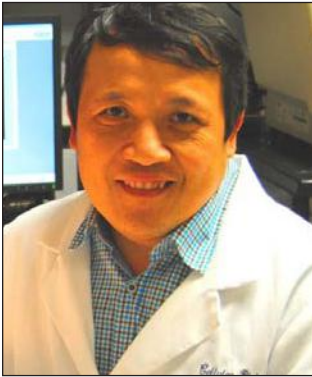
Some vertebrates such as fish and amphibians can regenerate their retinal neurons in response to injury; however, this ability was thought to be absent in mammals. In recent years, spiny mice (*Acomys*) have become the focus of intense research for their enhanced wound repair and regenerative ability in many tissues. Dr. Morris' RRF-funded research seeks to determine whether spiny mice can regenerate retinal neurons in response to damage – this would be the first demonstration of natural regenerative ability in the retina of any mammal.

In 2022, Dr. Morris and her team found that that in response to acute damage to inner retinal neurons, the spiny mouse mounts a pro-regenerative response that includes both cell proliferation and the induction of neurogenic gene expression, neither of which are observed in non-regenerating species such as the house mouse (*Mus musculus*). Excitingly, at 10 days after injury, the spiny mice show evidence of full recovery of inner retinal neurons. Further research in the spiny mouse model may lead to the identification of new



strategies to promote regeneration in human patients with retinal degenerative diseases.

Jess Bills, a graduate student in the Morris lab, is helping to study the regenerative capacity of the spiny mouse retina.



Ming Zhang, MD, PhD
Department of Cellular
Biology & Anatomy
Medical College of Georgia
Augusta University
Augusta, GA

**The roles of RIP kinase 3 in
the development of AMD-
like pathologies during
cytomegalovirus ocular
latency**

Dr. Zhang's research seeks understanding of the underlying causes that contribute to the development of AMD, which remain uncertain but are highly correlated with cell immunological/inflammatory mechanisms in the various tissue layers of the retina. *Receptor-interacting protein*

(RIP) kinases have emerged as modulators of inflammatory responses and play an important role in these tissues' specific innate immunity, autophagy and death-inducing processes. Dr. Zhang's studies will be the first to explore a possible viral cause of AMD as a result of latent ocular viral infection. Specifically, he proposes to research the impact of the human cytomegalovirus (HCMV), which infects 50 to 80% of the worldwide human population and is associated with some chronic diseases, and possibly may be a risk factor for AMD progression. The retinal choroid/RPE layers are a site of HCMV latency. The impact of his project findings will be far reaching. Dr. Zhang is testing the hypothesis that RIP3 contributes to the death and/or degeneration of ocular tissues using mouse models his team developed of cytomegalovirus ocular latency. The research findings in the first year of his project have generated results worthy of publication and a draft manuscript has been submitted for review.

Macula Society Grant Recipient

The RRF Margaret and Mills Cox Macula Society Research Project



Ajay E. Kuriyan, MD, MS
Wills Eye Hospital
Philadelphia, PA

**Investigating the Role of
Monocarboxylate Transporter
4 (MCT4) and Lactate in
Proliferative Vitreoretinopathy**

Dr. Kuriyan is a member of the retina service at Wills Eye Hospital, and is an Associate Professor of Ophthalmology at Sidney Kimmel Medical College of Thomas Jefferson University. In his role, he cares for patients, conducts ground-breaking clinical research studies and trains clinical professionals at Wills Eye Hospital. Dr. Kuriyan's clinical

interests encompass the medical and surgical treatment of retinal disease, including retinal detachment surgery, drug therapy for macular degeneration and other diseases, treatment of hereditary retinal diseases and diabetic eye disease. He is actively involved as a clinical investigator in several collaborative trials and studies on various conditions, including age-related macular degeneration, diabetic retinopathy, refractory macular holes, retinal detachment repair, and novel retinal surgical techniques. He conducts translational research that focuses on proliferative vitreoretinopathy, a scar forming process that is the most common cause of recurrent retinal detachments. Dr. Kuriyan has authored and reviewed over 150 scientific publications and textbook chapters on vitreoretinal diseases, and he frequently is invited to present scientific papers and abstracts at national ophthalmic meetings. Dr. Kuriyan will share his research project findings at the 2024 annual meeting of the Macula Society.

Six academic chairs and three professorships are supported by RRF at nationally recognized research institutions in Houston, Texas, and Madison, Wisconsin. These vision scientists conduct original retina research that has the potential to increase understanding of the retina or retinal diseases. The projects provide funding for inspiring research opportunities for young vision scientists who benefit from opportunities to collaborate with top researchers across related academic disciplines.

RRF Research Chair at Baylor College of Medicine



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

RGC diversity viewed from a WAC's angle

Dr. Chen received NIH funding in 2022 to further his work on the function of the TH2-AC wide-field amacrine cell and the roles of trophoblast glycoprotein in the mouse retina. This timely support enabled the Chen lab to launch

a comprehensive survey of TH2-AC's postsynaptic retinal ganglion cell (RGC) partners using an optogenetic approach with some expected and surprising findings. First, it is known that TH2-AC releases GABA to control the activity of the W3B RGCs, a result we quickly confirmed early in the survey. Second, we were delighted to find several more RGC types whose action is also controlled by TH2-AC's release of the GABA inhibitory neurotransmitter, suggesting that TH2-AC controls not just one but many RGC types. The most intriguing of all is the discovery of several RGC types governed by the TH2-AC but not through its GABA release. We therefore fully expect to generate new knowledge in retinal circuitry and novel mouse resources from this five-year study. Finally, and as always, we cannot thank Dr. Alice McPherson and the RRF enough for their generous and lasting support of this line of investigation.

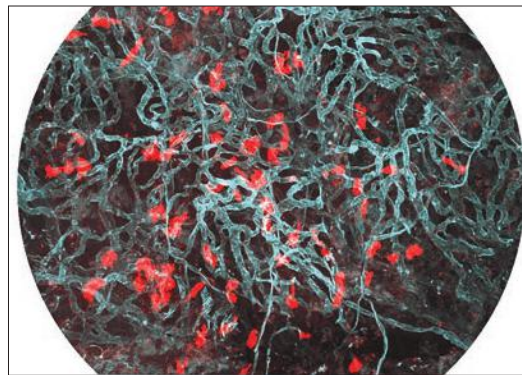
RRF Research Chair at University of Wisconsin



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

Ocular Vascular Development and Homeostasis

Dr. Sheibani's group showed that Bim expression is essential for clearance of mononuclear phagocytes and mitigation of scar formation in exudative AMD. Their Bim studies also demonstrated an important role for BIM involvement in branching morphogenesis of epithelium and endothelium. They showed Fingolimod, a drug used to treat MS, inhibits proangiogenic activity of choroidal endothelial cells in culture and choroidal neovascularization in vivo. They reviewed the role of CYP1B1 in ocular iron homeostasis and oxidative stress. They reported a novel method for staining of the vasculature and innate immune cells in the choroid of pigmented and albino mice. Dr. Sheibani was involved with reporting the negative impact of diabetes on tooth enamel and dentin microhardness and reviewed the important role of connective tissue growth factor as a key mediator of tissue fibrosis in the eye. *Reported in: Life (Basel) (Jan. 2022), Cells (March 2022), Arch Oral Biol (July 2022), Biomolecules (Sep. 2022), Cells (Sep. 22), Cells (Oct. 2022), J Ophthalmic Vis Res. (Nov. 2022).*

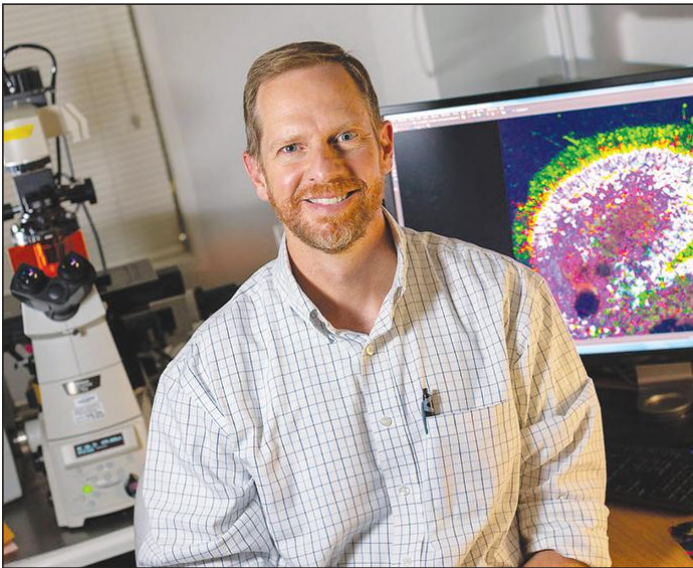


A novel method for visualization of choroidal mast cells and vasculature in pigmented mice. Please note degranulation of mast cells (red) and degeneration of choroidal vasculature (turquoise) in a mouse model of dry AMD.



Dr. Sheibani's Research Team

Emmett A. Humble Distinguished Directorship

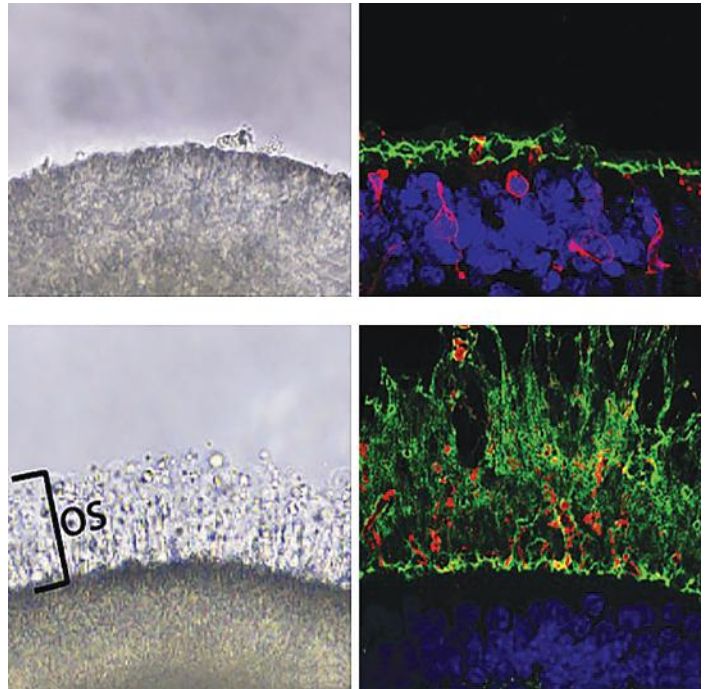


David M. Gamm, MD, PhD

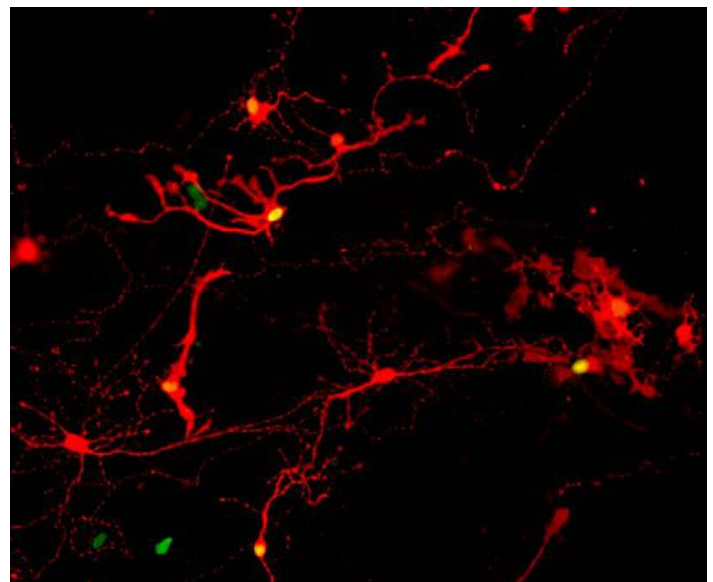
Distinguished Director, McPherson Eye Research Institute
Department of Ophthalmology and Visual Sciences
University of Wisconsin, Madison, WI

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

Dr. Gamm employs hiPSC technology to generate retinal organoids, which he uses to model human retinal diseases and develop therapies. In 2022, his lab developed a hiPSC-based model of retinitis pigmentosa caused by defects in IMPG2, a protein that protects the light-detecting outer segments of photoreceptors. They are now working on a gene therapy to treat this condition. Dr. Gamm, along with RRF chair holders Dr. Kris Saha and Dr. Bikash Pattnaik, also began a project to develop genome editing approaches to treat pediatric blindness and an inherited form of macular degeneration. Lastly, he is generating photoreceptors and retinal pigment epithelium (RPE) cells with the goal of treating patients with late-stage disease. Toward this end, Dr. Gamm and collaborators showed that hiPSC-derived cone photoreceptors can make new connections with other cells.



Retinal organoids carrying a mutation in the IMPG2 gene fail to generate photoreceptor outer segments (OS) (upper left panel). Following correction of the gene defect, the organoids are able to grow normal OS (lower left panel). The right panels highlight cell nuclei in blue, IMPG2 in green, and Rhodopsin (a rod photoreceptor protein) in red. Mayerl et al. *Stem Cell Rep* 2022.



Demonstration of new synapses connecting retinal cells derived from human pluripotent stem cells. Retinal cells capable of initiating a connection appear red with a yellow nucleus, while those that are the recipients of the connection are red only. UW–Madison image courtesy Gamm Laboratory.

Walter H. Helmerich Chair

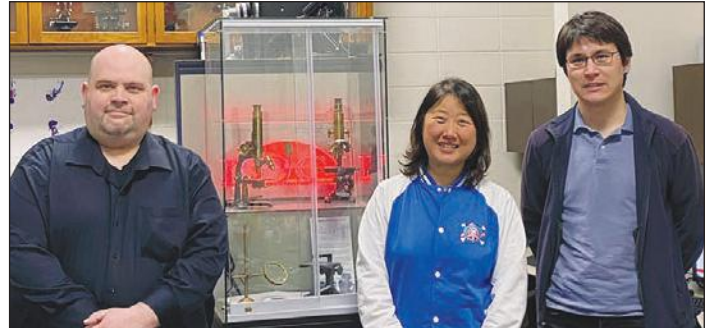


Kevin W. Eliceiri, PhD
 Associate Director
 McPherson Eye Research
 Institute
 Departments of Biomedical
 Engineering and Medical
 Physics
 University of Wisconsin
 Madison, WI

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 collaborating with computer scientists on deep learning approaches for smart imaging of cellular metabolism.



Members of the Eliceiri Laboratory Team

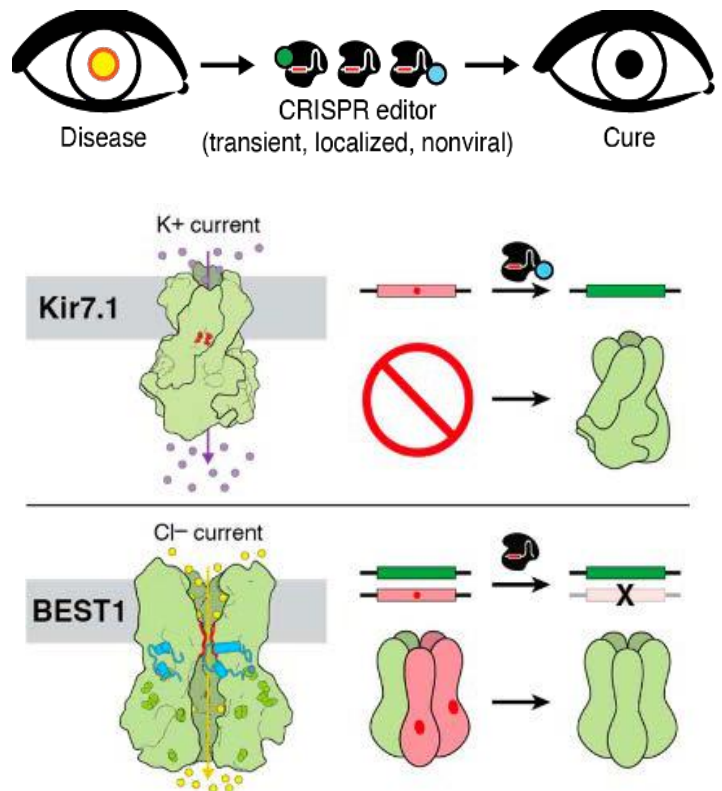
Kathryn and Latimer Murfee Chair



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

Dr. Saha leads a team of researchers at the University of Wisconsin, which has secured a \$29 million NIH grant to develop gene-editing therapies for two untreatable hereditary blindness diseases: Best Disease and Leber Congenital Amaurosis. Over the next five years, this team will use CRISPR technology and novel drug delivery systems to correct disease-causing mutations. The project will focus on the eye due to its accessibility and lower risk of adverse immune reactions. Two key challenges include achieving high efficiency in gene editing the retinal pigment epithelium (RPE) in situ and circumventing unintended off-target effects common with viral delivery systems. The team intends to employ nanotechnology for efficient drug delivery, with one approach focusing on biodegradable nanoparticles that can safely carry genome-editing tools. They will also partner with Spotlight Therapeutics to improve delivery using proteins and peptides. These non-viral gene editing approaches could offer a highly customizable platform to address many disease-causing mutations underlying channelopathies of the RPE.



The CRISPR Vision Program, led by Dr. Krishanu Saha, will develop new gene editing therapeutics that could treat inherited diseases, such as Best Disease and Leber Congenital Amaurosis. The genome editors will directly edit disease-causing mutations that lead to channelopathies.

Research Chairs and Professorships

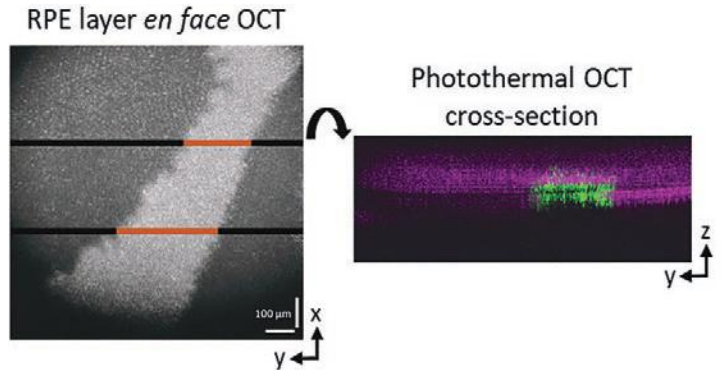
Daniel M. Albert Chair



Melissa Skala, PhD
McPherson Eye Research Institute
Morgridge Institute for Research
Department of Biomedical
Engineering
University of Wisconsin
Madison, WI

Optical imaging of retinal melanin

Dr. Skala's lab develops new optical imaging methods to monitor cell function in the retina, using sources of contrast already present in cells. These methods provide high-resolution biochemical information and are especially well suited for human use. Recently, her lab has developed photothermal optical coherence tomography (photothermal OCT) to monitor melanin levels in the retinal pigment epithelium (RPE). These tools are used to understand the role of melanin in healthy vision and to monitor early changes that precede vision loss in retinal diseases.



Photothermal optical coherence tomography (OCT) of retinal melanin in zebrafish. The retinal pigment epithelium (RPE) from standard OCT images shows a mosaic of melanin (light) and melanin-free (dark) regions in the front facing (*en face*) view of the retina (left). Photothermal OCT provides depth-resolved information on the presence of melanin (green) that is overlaid with standard OCT (pink) in a cross-sectional view of the retina. This imaging technique aims to understand the role of melanin in healthy vision and in vision loss.

Edwin and Dorothy Gamewell Professor

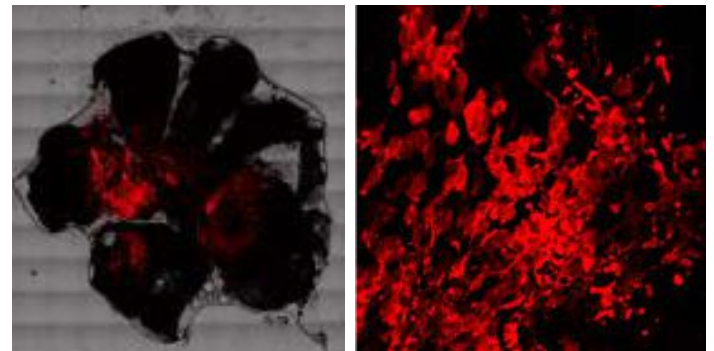


Shaoqin "Sarah" Gong, PhD
McPherson Eye Research Institute
Department of Ophthalmology
and Visual Sciences
Department of Biomedical
Engineering
Wisconsin Institute for
Discovery
University of Wisconsin
Madison, WI

Ocular Gene Therapy

Dr. Gong's lab designs, synthesizes, and optimizes non-viral drug and gene delivery systems. Judiciously engineered non-viral delivery nanosystems possess a number of advantages over viral vectors for gene therapy, including better biosafety profiles. Dr. Gong's lab recently developed a unique lipid

nanoparticle that can efficiently and safely deliver nucleic acids and/or genome editors to retinal pigment epithelium (RPE) cells both *in vitro* and *in vivo*. This research may lead to new gene therapy to fight blindness.



Lipid nanoparticle mediated delivery of Cre mRNA in Ai14 reporter mice led to strong tdTomato expression (Left, RPE floret; Right, magnified RPE floret region), suggesting efficient delivery of the mRNA.

M.D. Matthews Research Professor



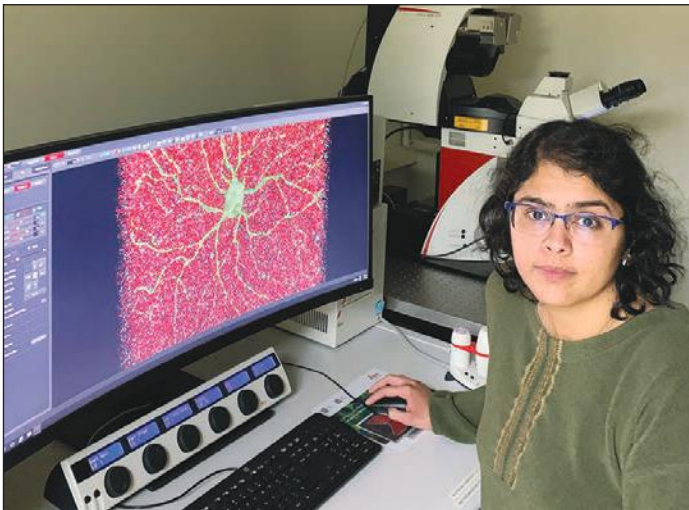
Bikash Pattnaik, PhD
McPherson Eye Research Institute
Department of Pediatrics,
Ophthalmology and Visual Sciences
University of Wisconsin, Madison, WI

Using rare diseases to push the limits of therapeutic discovery

Inherited retinal degeneration (IRDs) encompasses a group of genetically determined disorders that affect the structure and function of the retina, leading to progressive vision loss. Channelopathies, a subset of IRDs, arise from

dysfunction in ion channels critical for maintaining diverse physiological functions, starting with phototransduction. Dr. Pattnaik's research focuses on understanding the underlying mechanisms and developing effective therapies for channelopathies, which represent significant challenges in the field of ophthalmology. The lab discovered that mutations in a gene result in loss-of-function of an inwardly rectifying potassium channel (Kir7.1) in the retinal pigment epithelium (RPE). The lab demonstrated that small molecule drugs or biological molecules such as DNA and RNA could protect retina function by testing patient samples of induced pluripotent stem cells derived RPE (iPSC-RPE) and novel mouse models.

Rebecca Meyer Brown Professor



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

Mechanisms that alter inner retinal connections in photoreceptor diseases

Nerve cells in the retina rely on specialized junctions of communication to transfer information and maintain vision. Alterations in these connections underlies loss of vision in disease conditions. The Hoon Lab is studying the

molecular composition, ultrastructural organization and function of these neural connections in the retina in photoreceptor disease models to understand the substrates of dysfunction in the remaining inner retinal circuit. For this we are bringing together genetic and proteomic approaches with high resolution light and electron microscopy, single cell profiling and electrophysiology and contrasting models where photoreceptor signaling is perturbed with models that experience photoreceptor loss. Our findings will reveal the differential mechanisms regulating the maintenance and function of inner retinal connection types in photoreceptor diseases and alterations at the level of retinal output. Knowledge about specific connectivity alterations in photoreceptor disease conditions will reveal new therapeutic targets for recovery of visual function.



3D reconstruction of a retinal neuron (dark green) receiving input from several photoreceptor terminals (light green). These connections are disrupted in photoreceptor disease conditions.

Established Research Awards

These awards are presented to renowned scientists in recognition of their lifetime achievement. RRF's research and education mission is global in scope, and in 2022, three international awards were given.

The Award of Merit in Retina Research



Edwin M. Stone, MD, PhD
Institute for Vision Research
Carver College of Medicine
University of Iowa
Iowa City, IA

Curing Heritable Blindness

As the 2022 recipient of the Award of Merit in Retina Research, Dr. Stone gave the Charles L. Schepens Lecture at the Retina Society's 55th Annual Scientific Meeting held in Pasadena, CA in early-November.

Dr. Stone is the Director of the University of Iowa Institute for Vision Research and holds the Seamans-Hausner Chair of Molecular Ophthalmology in the University of Iowa's Carver College of Medicine. He is widely known for his work in defining the genetic basis of blinding eye diseases: ranging from two of the most common causes of blindness, macular degeneration and glaucoma, to much rarer conditions like retinitis pigmentosa and Leber congenital amaurosis. Dr.

Stone has been very active in removing the technical, legal and financial barriers between genetic discoveries and the patients who could benefit from them. He founded the Carver Nonprofit Genetic Testing Laboratory at the University of Iowa that provides low cost genetic tests to patients in every state of the U.S. and more than 60 other countries. He also created an open-access web-based teaching tool with thousands of downloadable full-resolution images to help physicians around the world improve their ability to diagnose Mendelian retinal diseases. His current research interest is in developing affordable gene- and stem-cell-based treatments for all molecular forms of inherited retinal disease.



RRF Pyron Award for Outstanding Achievement in Retina Research



Mary Elizabeth Hartnett, MD
Byers Eye Institute
Stanford University
Palo Alto, CA

Targeting Pathologic Signaling to Restore Homeostasis in Retinal Diseases

Dr. Mary Elizabeth Hartnett was recognized as the 2022 Pyron Award recipient during the ASRS Annual Meeting, held in July in New York City, where she presented the 27th annual RRF Gertrude D. Pyron Award lecture.

Dr. Hartnett is the Michael F. Marmor, MD Professor in Retinal Science and Diseases and is a Professor of Ophthalmology at Stanford University. Dr. Hartnett directs Pediatric Retina at Stanford University and is the principal investigator of a retinal angiogenesis laboratory, in which she studies causes and treatments for diseases, including retinopathy of prematurity and age-related macular degeneration. Previously affiliated with the University of Utah, she founded and directed Pediatric Retina at the John A. Moran Eye Center.

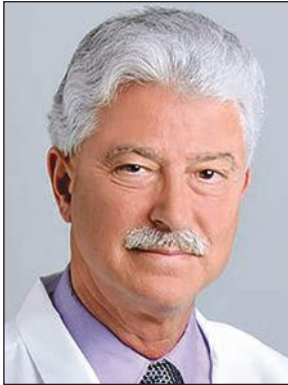
Dr. Hartnett's NIH-funded laboratory of vascular biology and angiogenesis has studied mechanisms causing pathology in age-related macular degeneration (AMD) and retinopathy of prematurity (ROP).

She has translated her work into clinical trials to evaluate new treatments for severe ROP. Her contributions represent a paradigm shift in the understanding and treatment of severe ROP.

Dr. Hartnett created the first-ever academic textbook on the subject, *Pediatric Retina*, an invaluable resource for residents and ophthalmologists internationally. Her prolific publication record includes 227 articles in peer-reviewed journals and over 40 book chapters. She reviews manuscripts for more than 20 eye and science journals and serves on the editorial boards of *PlosOne*, *Molecular Vision*, and the *American Journal of Ophthalmology*.

Dr. Hartnett has received numerous awards, including previous RRF awards, the 2019 Paul Kayser/RRF Global Award from the Pan-American Association of Ophthalmology, the 2017 RRF Cox Macula Research Project Award. She also has received the 2021 Suzanne Veronneau-Troutman Award, the most prestigious award for women in ophthalmology.

Paul Kayser International Award in Retina Research



Steven J. Fliesler, PhD
 Jacobs School of Medicine and
 Biomedical Sciences
 State University of New York
 (SUNY), University at Buffalo
 (UB)
 Buffalo, NY

**Hereditary Retinal Diseases:
 Cruisin' for a Bruising Down
 the Mevalonate Pathway**

Made possible by a gift to RRF in honor of Paul Kayser, the RRF Paul Kayser International Award in Retina Research, is presented by the International Society for Eye Research (ISER). This international award recognizes lifetime achievement by a vision scientist who has made a significant contribution to the understanding of vitreoretinal diseases or disorders, and it is given every two years. Dr. Fliesler received his award and presented a lecture at the XXV Biennial Meeting of the International Society for Eye Research (ISER), in Queensland, Australia in February, 2023.

Dr. Fliesler holds concurrent appointments as a professor in the Department of Biochemistry and in the Neuroscience Graduate Program at UB, as well as being a Research Career Scientist at the Buffalo VA Medical Center (VA Western NY Healthcare System). He currently serves as Vice-Chair of the SUNY Distinguished Academy Board, which builds and supports academic excellence of faculty.

His research is focused on inborn errors of cholesterol and isoprenoid metabolism and their impact on the development, structure and function of the retina, as well as on blast injury to the eye. He has published more than 150 peer-reviewed journal articles, book chapters and review articles, and is the editor of two books. His research program has been funded continuously for nearly 40 years by federal and private grants.



Dr. Fliesler is the Editor-in-Chief of *Experimental Eye Research*, the Deputy Editor-in-Chief of *Eye and Vision*, an Associate Editor for *Frontiers in Cell and Developmental Biology*, and serves on four other journal editorial boards, including *Molecular Vision* and the *Journal of Lipid Research*. He has received multiple honors and awards and has given multiple named lectures and keynote presentations at universities and scientific meetings in the U.S. and abroad. He has served as Councilor for North America, Treasurer, and President of the International Society for Eye Research (ISER).



Dr. Steven Fliesler and Dr. Samuel Wu, Baylor College of Medicine, 2022 and 2020 respective award recipients



Established Research Awards

Charles L. Schepens, MD/AAO Award



Philip J. Rosenfeld, MD, PhD
Bascom Palmer Eye Institute
University of Miami
Miami, FL

***Rediscovering AMD with
SS-OCT Imaging***

The 2022 RRF Charles L. Schepens, MD/AAO Award was given to Philip J. Rosenfeld, MD, PhD. He delivered the Schepens Lecture during the morning proceedings of the Retina Subspecialty day at the American Academy of Ophthalmology's annual meeting held in Chicago at the end of September.

Philip J. Rosenfeld MD, PhD is Professor of Ophthalmology at the Bascom Palmer Eye Institute of the University of Miami Miller School of Medicine. He is a retina specialist and a world-renown expert on age-related macular degeneration (AMD) and optical coherence tomography (OCT). He played a pivotal role in the development of anti-VEGF therapies for neovascular and exudative eye diseases. Of note, he pioneered the use of Avastin (bevacizumab) therapy for exudative eye diseases.

Dr. Rosenfeld has been involved in the clinical development of optical coherence tomography (OCT) instruments, and he pioneered the use of OCT-guided treatment with anti-VEGF therapy. Similarly, he championed the development of complement inhibitors for the treatment of dry AMD and

the development of novel OCT algorithms for the diagnosis and study of AMD in clinical trials, especially nonexudative (dry) AMD. Most recently, his research has been focused on the development and use of swept-source OCT angiography and novel algorithms to investigate retinal diseases with the goal of developing new OCT clinical trial anatomic endpoints for use in the study of novel AMD therapies.



Dr. Rosenfeld and
Dr. Harvey Flynn Jr.,
2016 Schepens Award
recipient.

Dr. Rosenfeld has published over 150 research manuscripts. He is the recipient of numerous awards and has been named to *The Ophthalmologist Power List* in 2014, 2016, 2018, 2019, 2020 and 2022.



Club Jules Gonin Lecturer



Ramin Tadayoni, MD, PhD
Université Paris Cité
Paris, France

The Jules Gonin Lecturer of the Retina Research Foundation is selected by members of Club Jules Gonin, and is presented at the Biennial meetings of Club Jules Gonin. The award is given in recognition of significant contributions to

the understanding and treatment of eye diseases. Ramin Tadayoni, MD, PhD, the 2020/2022 lecturer presented the Jules Gonin Lecture at XXXIIIrd Meeting of the Club in Dubrovnik, Croatia on September 9, 2022.

Dr. Ramin Tadayoni is a Professor of Ophthalmology at

the Université Paris Cité, France's leading multidisciplinary university, and Chairman of the Department of Ophthalmology at three Parisian hospitals: Lariboisiere, Saint Louis and Rothschild Foundation Hospitals, in France. He is very committed to education and has the honor of overseeing the training of clinical vitreoretinal and research fellows.

In addition to his clinical and management activities, Professor Tadayoni is the leader of French government funded EviRed research program on artificial intelligence for diabetic retinopathy, and he has authored over 200 scientific articles. Dr. Tadayoni is the EURETINA President Elect, past President of the French-speaking Retina Specialists Society (CFSR) and elected as associate of the "French National Academy of Surgery". He has been awarded HDR, the highest academic degree in France, and the American Academy of Ophthalmology Achievement Award.

The Gonin Medalist



Stanley Chang, MD
Columbia University Irving
Medical Center
New York, NY

The Evolution of Retinal Detachment Surgery after Jules Gonin

The Gonin Medal was instituted in 1937 in memory of Swiss-born Jules Gonin, MD, and it is the oldest and most prestigious medal in ophthalmology. Every four years, the International Council of Ophthalmology (ICO) Board of Trustees with the University of Lausanne and the Swiss Ophthalmological Society, elects the gold medalist. The diploma of the medal was delivered during a special ceremony at the Jules Gonin Eye Hospital in Lausanne Switzerland on March 24, 2022, and the gold medal, usually presented at the World Ophthalmology Congress, was virtually recognized at the 2022 Virtual Congress, which was held in September.

Stanley Chang, MD, is the K.K. Tse and Ku Teh Ying Professor of Ophthalmology at Columbia University Medical Center. From 1995-2012, he was Chair of Ophthalmology at the Edward Harkness Eye Institute, and he remains an active faculty member in clinical care, research and teaching at Columbia.



Dr. Chang commemorating the addition of his portrait to the tribute wall honoring Past Gonin Medalists, including Dr. Alice McPherson.

Dr. Chang has developed and pioneered several revolutionary surgical approaches to treat complicated forms of retinal detachment, improving outcomes for patients worldwide. He was the first to use perfluoropropane gas in the management of retinal detachments caused by scar tissue proliferation (PVR) on the retina. He developed perfluorocarbon liquids, a 'heavy liquid' used in flattening retinal detachment, and the related surgical techniques for vitreoretinal surgery. As a co-collaborator, he developed a panoramic viewing system and led the worldwide adaptation of this technique throughout the vitreoretina surgery community. The recipient of many international honors recognizing his lifetime achievements, Dr. Chang previously received the RRF Helmerich Prize from ASRS and the RRF Charles L. Schepens MD/AAO Award and Lectureship.



Photos courtesy of Columbia Viewpoint, Fall 2021/Winter 2022

One RRF established award was not bestowed in 2022. The Paul Kayser/RRF Global Award, given in conjunction with Pan-American Association of Ophthalmology (PAAO) will be awarded in March, 2023.

International Fellowships

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

RRF Helmerich International Fellowships

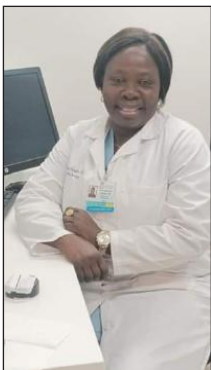
Since 2009, RRF has offered two international fellowships with income from an endowment created by Walter H. Helmerich, III. The 12-month fellowships provide advanced subspecialty training for young ophthalmologists from developing countries who are recommended by the head of a teaching or public service institution and are committed to returning to a position at a teaching institution or public service hospital in their home country following the fellowship. During 2022, three physicians received training as Helmerich International Fellows.



Dr. Chibuzo Barbara Ekumakama from Nigeria, received her fellowship training at MGM Eye Institute in Raipur, India. Her fellowship included practicing as an ophthalmologist in accordance with the educational principles of India, and she received an official degree certificate for Vitreoretina Subspecialty.



Dr. Amare Atoma Gelacha from Ethiopia, completed his fellowship in clinical (hand) training in uveitis under supervision of Prof. Sanaullah Jan and his team at the Pakistan Institute of Community Ophthalmology in Peshawar, Pakistan. His experience included examining and treating patients in the ophthalmology clinic.



Dr. Perpetua Odugbo from Nigeria, received a glaucoma fellowship at the Jules Stein Eye Institute, University of California, Los Angeles (UCLA), under the supervision of Dr. Joseph Caprioli.

Throughout her fellowship, Dr. Odugbo actively participated in glaucoma conference series, research meetings, microsurgical trainings, and clinic and operating room rotations.

She was involved with three research projects, one of which was completed and the results were presented as a poster at the annual conference of the *Association for Research in Vision and Ophthalmology (ARVO)*, New Orleans, Louisiana, in May, 2023.



Dr. Odugbo writes, “The privilege greatly enhanced my knowledge and professional skills for glaucoma care. [Following my graduation], I returned to Nigeria and have resumed work. I hope to make positive and measurable impacts on glaucoma care, transfer knowledge and skills to ophthalmologists-in-training and conduct more glaucoma related research.”



Gillingham Pan-American Fellowships

A collaboration with the Pan-American Association of Ophthalmology (PAAO), the RRF Gillingham Fellowships program offers two, six-month fellowships to Latin American ophthalmologists for training at leading institutions in the United States or Canada. The 2022 Gillingham Fellows are:



Natasha Ferreira Santos da Cruz (Brazil)

Accepted for a Pediatric Retina Fellowship at Bascom Palmer Eye Institute, Miami, Florida, USA.

Dr. Natasha Cruz spent her Gillingham fellowship at Bascom Palmer Eye Institute in Miami for a Pediatric Retina Research Fellowship under the supervision of Dr. Audina “Nina” Berrocal. She reports that it was a wonderful experience and the best year of her life because of the entirety of her mentorship and training, and in particular the close relationship she developed with Dr. Berrocal who is a pioneer in gene therapy and retinopathy of prematurity (ROP) treatment.

Dr. Cruz’s fellowship offered experience in the clinic, the operating room and retinopathy of prematurity rounds (ROP rounds). In addition, she participated in weekly in grand rounds, conducted research and attended retina and imaging conferences.

“To be able to be in the room/OR with Dr. Berrocal made all the difference in my doctor-patient relationships. It meant learning to listen more closely to the patient. It meant paying attention to details such as the patient’s social situation, the family history and dynamics, and a child’s sports choice. It taught me to trust my instinct when it tells me that an eye is worth fighting for. But it also taught me to be more

conservative with the treatments. It made me more sensitive while talking to parents and patients about their diseases, what to expect in the long term, possible treatments, and – most importantly – about never giving up because medicine advances every day.”

Dr. Cruz participated as part of the clinical research team in research related to ROP research lines, fluorescein angiography and OCT-A. Her efforts resulted in several papers, some already published, others submitted or accepted for publication. She also gained experience presenting her research at the retina meetings she attended.



Industry wetlab with Dr. Berrocal

International Fellowships

Gillingham Pan-American Fellowships

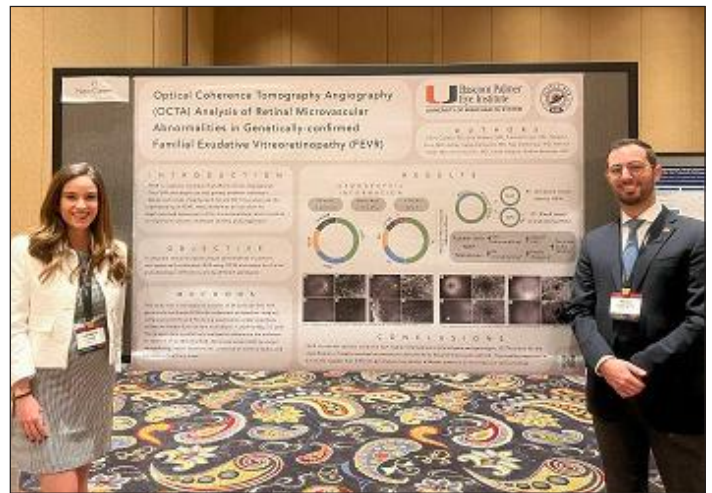
Dr. Cruz writes, “This was certainly a wonderful experience that increased not only my knowledge on pediatric retina, but also my skills as a person. I fulfilled my goals completely and I would absolutely recommend this fellowship to other ophthalmologists interested in pediatric retina. I will return to Brazil with a heavy heart. But I’ll carry with me incredible knowledge and skills that I hope will contribute in some way to my country and to my patients.”



ASRS 2022 with Dr. Audina Berrocal and Dr. Nimesh Patel



Bascom Palmer ROP Team



Poster presentation at VBS 2023 with Dr. Piero Carletti



Dr. Natasha Cruz with Dr. Nina Berrocal



Gillingham Pan-American Fellowships



Miguel N. Cruz Pimentel (Dominican Republic)
Accepted for a Vitreoretinal Surgery Fellowship at the University of Toronto, Toronto Western Hospital, Toronto, Ontario, Canada

During his extended Gillingham Fellowship, Dr. Pimentel completed his training in vitreous-retinal surgery at the University of Toronto under the direction of Dr. Efram Mandelcorn.

Dr. Pimentel writes, “my training allowed me to learn multiple surgical techniques for managing vitreous-retinal pathologies. I performed more than 600 retinal surgeries to treat retinal detachments, macular holes, epiretinal membranes, diabetic retinopathy, and the removal of intraocular foreign bodies, among other retina disorders. Outside the operating room, I provided clinical care to hundreds of patients with retinal vascular diseases such as age-related macular degeneration, vein occlusions, diabetic macular edema and diabetic retinopathy.”



The surgical team, including Dr. Kenneth Eng (far right) involved in scleral buckle surgery for retinal detachment at Sunnybrook Health Science Centre, Toronto.

Dr. Pimentel had the opportunity to participate in multiple research projects that were ultimately published in indexed journals, over 10 in all, some as first author. He was a participating author in three book chapters on Susac Syndrome, Drainage of Hemorrhagic Choroidal Detachment, Systemic Medication Retinal Toxicity and Side Effects. As an academic, complementing the surgical and clinical side of his practice with research is something he plans to continue throughout his professional career.

Additionally, Dr. Pimentel gained experience presenting his surgical cases at a number of North American meetings, including the Vit Buckle Society, Las Vegas 2022, the Fellows



Presenting a surgical case at the 10th Annual Vit Buckle Meeting in Las Vegas, March, 2022



Presenting at the Fellows Fighting Forum 2022, Chicago

Forum 2022 where he emerged as a 2022 Fellow Award Champion, the Retina Case Conference Canada 2022, and the Canadian Retina Society 2023.

Despite the intensity of his training, Dr. Pimentel became involved in multiple educational activities as part of the resident education program at the University of Toronto and in other Latin American countries, including Costa Rica and his home country, the Dominican Republic.



Moderating a question-and-answer session in Santo Domingo

Important to his future aspirations, Dr. Pimentel also had the opportunity to teach residents at the University of Toronto, including wet labs instruction on performing scleral buckling and pneumatic retinopexy. During his graduation ceremony, he was recognized for his dedication to teaching residents at the University of Toronto. He said, “this recognition motivates me to reaffirm my commitment to educating new generations in ophthalmology and my decision to pursue a career as an academic professor in the field of retinal diseases.”

Receiving the Lim Family Memorial Award from Dr. Efram Mandelcorn. Excellence in clinical, surgical and interpersonal skills. Department of Ophthalmology and Vision Sciences, University of Toronto, 2023



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 and vision scientists worldwide.

American Academy of Ophthalmology Educational Trust Fund

In collaboration with the American Academy of Ophthalmology, this educational program provides ophthalmologists with educational 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 2022 was \$50,000, and made possible the development and updates to basic and clinical science courses on retina and vitreous. These resources are available to clinicians as part of AAO's CME activities on the One® Network, the Academy's global platform for ophthalmic education.

RRF Lawrence Travel Scholarships

In 1992, a gift from Joe M. and Eula C. Lawrence provided funding for the creation of the Lawrence Travel Scholarship program. Administered for RRF by the Association for Research in Vision and Ophthalmology (ARVO), the program provides travel-expense scholarships to young vitreoretinal scientists for attending ARVO's annual meeting and participating in presentation of scientific works. This opportunity to present their papers or posters and to interact with their research peers is an important career development opportunity and quickens the pace of research progress.

The ARVO meeting was held in Denver in 2022, and RRF sponsored 28 travel grants. Hailing from the country's most prestigious research institutions, these young scientists participated in poster presentations with the additional ability to browse the latest research online by scientific section, author, title, or by key words within an abstract or poster. RRF grant recipients shared how stimulating and thought provoking they found the experience of presenting their research and learning about the research of others, further signaling the importance of travel scholarships to professional development and the dissemination of vision research data and knowledge.



Retina Research Foundation 2022 Luncheon



After a hiatus caused by the COVID-19 pandemic, The RRF community of leaders, scientists, supporters and friends again gathered on May 11th for the 2022 RRF Luncheon and Honorary Lecture, providing an opportunity to celebrate RRF's achievements in vision preservation since its founding in 1969 and to educate attendees about new advances in science and academics.

Extending the long-held tradition of inviting speakers who are outstanding leaders of the academic and medical community, RRF Board Director and former Houston Methodist President and CEO, Ron Girotto, introduced the honorary speaker, Dr. Marc Boom, President and CEO of Houston Methodist, a hospital system with more than 2,300 beds and 27,000 employees and world-renowned

research institute. Dr. Boom shared insights on Houston Methodist's national leadership role in educating the public about COVID-19 and the need for vaccines, Houston Methodist's pre-clinical and translational academic research programs, including leading-edge clinical trials, research leading to providing patients with the safest and highest quality care possible.



Marc L. Boom, MD,
2022 RRF Honorary
Lecturer



Ron Girotto,
RRF Board Director,
Houston Methodist
President and CEO,
Emeritus

BCM Vision Research Symposium 2022

In support of RRF's educational goals, RRF sponsored an inaugural vision research symposia convened by Baylor College of Medicine (BCM) in December. Held virtually and offered free to all participating vision scientists, the symposia was organized by RRF pilot grant scientist, Dr. Yingbin Fu, and Dr. Wei Li, both members of the Cullen Eye Institute at BCM. Sessions highlighted the latest, cutting-edge retina research, retinal wiring, glaucoma, ocular angiogenesis and corneal diseases. Presentations included Dr. David Gamm, the Distinguished Director of the McPherson Eye Research Institute as the keynote address, along with speakers from Baylor and nationally recognized vision institutes. Over 150 scientists registered with nearly two-thirds attending the Saturday event. Attendees indicated they appreciated the excellent, high-quality science and vigorous discussion that followed each presentation.

Baylor Medicine

Cullen Eye Institute invites you to join us for our inaugural Vision Research Symposium. This exciting symposium will be held VIRTUALLY ON ZOOM. The symposium is open to all vision scientists. The registration is free. We look forward to "meeting" you in the symposium!

BCM VISION RESEARCH SYMPOSIUM 2022

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RETINA RESEARCH FOUNDATION

COMBINED STATEMENT OF FINANCIAL POSITION

December 31, 2022

(with summarized financial information as of December 31, 2021)

	General Funds			Endowment Funds			2022 Total All Funds	2021 Total All Funds (Memorandum Only)
	Without Donor Restrictions	With Donor Restrictions	Total	Without Donor Restrictions	With Donor Restrictions	Total		
	Assets							
Cash and cash equivalents	\$ 791,475	\$ 67,500	\$ 858,975	\$ -	\$ 346,585	\$ 346,585	\$ 1,205,560	\$ 1,709,316
Contributions receivable	100	100,000	100,100	-	120,000	120,000	220,100	163,550
Investments	2,936,786	-	2,936,786	4,934,746	55,374,976	60,309,722	63,246,508	72,857,065
Furniture and equipment, net of accumulated depreciation of \$11,787	14,101	-	14,101	-	-	-	14,101	14,749
Intangible assets	12	-	12	-	-	-	12	12
Other assets	6,651	-	6,651	-	-	-	6,651	10,209
Total assets	\$ 3,749,125	\$ 167,500	\$ 3,916,625	\$ 4,934,746	\$ 55,841,561	\$ 60,776,307	\$ 64,692,932	\$ 74,754,901
Liabilities and net assets								
Accounts payable	\$ -	\$ -	\$ -	\$ -	\$ 71,176	\$ 71,176	\$ 71,176	\$ 81,976
Grants payable	100,000	-	100,000	-	-	-	100,000	150,000
Total liabilities	100,000	-	100,000	-	71,176	71,176	171,176	231,976
Net assets	3,649,125	167,500	3,816,625	4,934,746	55,770,385	60,705,131	64,521,756	74,522,925
Total liabilities and net assets	\$ 3,749,125	\$ 167,500	\$ 3,916,625	\$ 4,934,746	\$ 55,841,561	\$ 60,776,307	\$ 64,692,932	\$ 74,754,901

RETINA RESEARCH FOUNDATION

COMBINED STATEMENT OF ACTIVITIES AND CHANGES IN NET ASSETS

For the year ended December 31, 2022
(with summarized financial information for the year ended December 31, 2021)

	General Funds			Endowment Funds			2022 Total All Funds	2021 Total All Funds (Memorandum Only)
	Without Donor Restrictions	With Donor Restrictions	Total	Without Donor Restrictions	With Donor Restrictions	Total		
Revenues								
Contributions	\$ 116,795	\$ 106,000	\$ 222,795	\$ -	\$ 319,017	\$ 319,017	\$ 541,812	\$ 1,939,820
Investment income, net	108,500	-	108,500	186,419	2,112,579	2,298,998	2,407,498	1,592,383
Realized and unrealized gains (loss) on investments, net	(458,510)	-	(458,510)	(835,254)	(9,393,533)	(10,228,787)	(10,687,297)	8,262,872
Mineral interest income and other income	30,242	-	30,242	-	-	-	30,242	11,237
Income transferred from Endowment Fund investments	1,855,882	82,500	1,938,382	(158,059)	(1,780,323)	(1,938,382)	-	-
Net assets released from restrictions - satisfaction of program and timing restrictions	333,000	(333,000)	-	-	-	-	-	-
Total revenues	1,985,909	(144,500)	1,841,409	(806,894)	(8,742,260)	(9,549,154)	(7,707,745)	11,806,312
Expenses								
Program services								
Research projects and grants	2,103,112	-	2,103,112	-	-	-	2,103,112	1,749,132
Supporting services								
Management and general	190,312	-	190,312	-	-	-	190,312	158,272
Total expenses	2,293,424	-	2,293,424	-	-	-	2,293,424	1,907,404
Changes in net assets	(307,515)	(144,500)	(452,015)	(806,894)	(8,742,260)	(9,549,154)	(10,001,169)	9,898,908
Net assets, beginning of year	3,956,640	312,000	4,268,640	5,741,640	64,512,645	70,254,285	74,522,925	64,624,017
Net assets, end of year	\$ 3,649,125	\$ 167,500	\$ 3,816,625	\$ 4,934,746	\$ 55,770,385	\$ 60,705,131	\$ 64,521,756	\$ 74,522,925

In Memoriam

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Remembering Alice Ruth McPherson, MD

Alice Ruth McPherson, MD, passed away peacefully on the evening of January 16, 2023. Born on June 30, 1926 in Saskatchewan, Canada, the first daughter of Gordon and Viola McPherson, Alice McPherson spent much of her childhood in Minnesota and Wisconsin. Knowing she wanted to become a physician, she earned her undergraduate studies degree in 1948, medical degree in 1951, and completed her ophthalmologic residency in 1955, all from the University of Wisconsin.

Her focus in retina was motivated by low cure rates of retinal detachment in the early 1950s. In 1959, she completed a fellowship in retinal diseases and retinal surgery at the Massachusetts Ear and Eye Infirmary at Harvard University Medical School under the supervision of Charles L. Schepens, MD, considered to be the father of modern retinal surgery. She was one of the first fellows of Dr. Schepens and the first-ever female vitreoretinal fellow. Her admiration for Dr. Schepens, who became a mentor and a friend, informed many of her professional and philanthropic actions throughout the remainder of her life.

In 1958, Dr. McPherson married Anthony “Tony” Mierzwa and, when her training with Dr. Schepens ended, they made the decision to move to Houston, Texas. Dr. McPherson said, “The three best decisions I ever made were ophthalmology, Tony and Texas.”

Dr. McPherson’s retina expertise led her to become one of the world’s leading vitreoretinal specialists and retinal surgeons. Her scientific contributions included ground-breaking procedures. She vigorously advocated for the use of numerous retinal surgical procedures from their earliest implementation, including scleral buckling procedures, cryotherapy, xenon arc, laser photocoagulation, and vitrectomy, now accepted as basic elements of retinal disease treatment. Dr. McPherson pioneered the treatment of retinopathy of prematurity, and she was an early proponent of photocoagulation in the treatment of diabetic retinopathy. This was a highly debated approach, later proven correct by the large, randomized prospective National Eye Institute Diabetic Retinopathy Study. She trained over 100 vitreoretinal fellows, and her retina practice spanned more than 70 years, during which time she always did the best she could for her patients. Dr. Alice McPherson was devoted to her patients, and they to her.

With the establishment of her private practice and her professorship appointment at the Baylor College of Medicine in Houston, Dr. McPherson founded the first retina service in Texas and, more broadly, in the south. Simultaneously, she became the first full-time female retina specialist in the United States and the world. She remained committed to Baylor College of Medicine to the end of her life, and she ensured continuous funding of vision scientists affiliated with the College’s Cullen Eye Institute for many decades.

Dr. McPherson was a founding charter member and later the first female president of the Retina Society, the founding president of



the University of Wisconsin Ophthalmology Alumni Association, and the first female chair of the Pan-American Association of Ophthalmology Foundation. Dr. McPherson was the first American woman to be accepted into the prestigious European Club Jules Gonin, and she made ophthalmic history as the first woman selected to receive the Jules Gonin Medal, the highest achievement in ophthalmology. Most recently, Dr. McPherson was the inaugural recipient of the Retina Hall of Fame Award, bestowed in recognition of her inventive contributions in the retina field and her dedication to retina research. Never giving much thought to being the first in so many aspects of her life, Dr. McPherson was always self-effacing. She said, “It’s all about working together, sharing ideas, educating and inspiring others—men and women alike—to join our mission to save and prolong eyesight.”

In 1969, Dr. McPherson founded the Retina Research Foundation (RRF) in Houston, Texas, dedicated to the eradication of retinal disease by funding basic retinal research. She reflected, “As I gained experience in academic ophthalmology and clinical research, I became increasingly convinced that the most important contribution I could make would be to establish an organization that could help develop and sustain innovative retinal research. RRF moved from a dream, to a concept, to a reality.” This endeavor gave her much satisfaction, and under her leadership as President and Scientific Adviser, RRF funded well over 1,000 basic research grants and helped to launch the careers of many major vision researchers in the United States and abroad. RRF established major awards in collaboration with the leading ophthalmologic societies, chairs and professorships at universities and research institutions, travel grants for young scientists, and international fellowships of advanced subspecialty training. From its founding, the Foundation has awarded over \$40 million to retina research.

Dr. McPherson’s vision and support were essential to the formation of the University of Wisconsin Eye Research Institute, renamed the McPherson Eye Research Institute in her honor in 2012. Always keenly interested in the scientific pursuits of the Institute, which leads collaborative efforts amongst researchers in vision-related fields across the Madison campus, Dr. McPherson remained actively engaged with its leadership and scientists. She highly valued her relationships with the Institute’s successive Emmett A. Humble Distinguished Directors, Dr. Daniel M. Albert and since 2012, Dr. David M. Gamm.

It was Dr. McPherson’s unique combination, an elegant, caring, and brilliant woman of many firsts and great accomplishments, that made her a legend, a visionary whose imprint will be remembered through the advancements achieved in retina research, in the education and encouragement of her ophthalmology colleagues, and in the compassionate care of the many, many patients to which she dedicated her life. Ever humble, Dr. McPherson desired no recognition of her passing, however, her life-long actions ensure that her commitment to retina research will continue through the organizations she championed.



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retinaresearchfnd.org