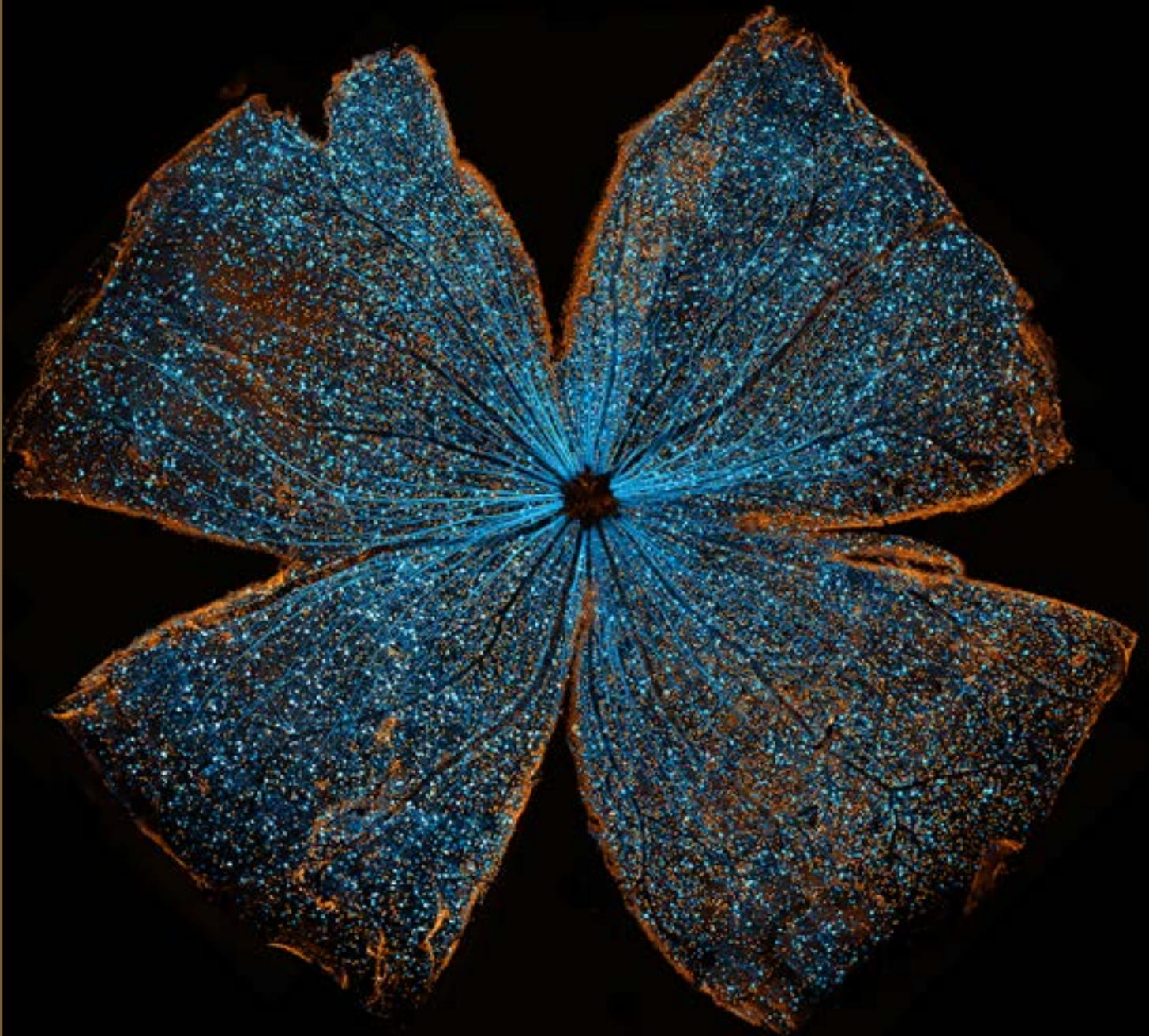


INTERNATIONAL RETINAL
RESEARCH FOUNDATION

IRRF

2021 ANNUAL REPORT





The IRRF 2021 Annual Report

Sandra Blackwood, Editor
Photos: Sandra Blackwood
Design: Robert Weathers

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Retinal Research Foundation

COVER: *High-resolution, wide-field montage of the entire surface of the mouse retina.* (Panuakdet Suwannatat, PhD, Department of Computer Science at UC Santa Barbara Neuroscience Research Institute; Gabriel Luna, BA, Research Specialist in Dr. Steven Fisher's lab in the Neuroscience Research Institute.)

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In 2021, the International Retinal Research Foundation (IRRF) Board of Directors approved grants for up to two years of funding.



The IRRF provides financial assistance for vision research to scientists in every corner of the world, while focusing on discovery of causes, preventions and cures of macular degeneration and diabetic retinopathy. More than ever, this support is vital to the ongoing work, which will affect the lives of many individuals and further scientific knowledge.

The following pages summarize IRRF funding commitments over the next two years for scientific study. Because eye diseases affect individuals worldwide, funding internationally has always been a priority and grant recipients are a diverse group of scientists from across the United States and overseas.

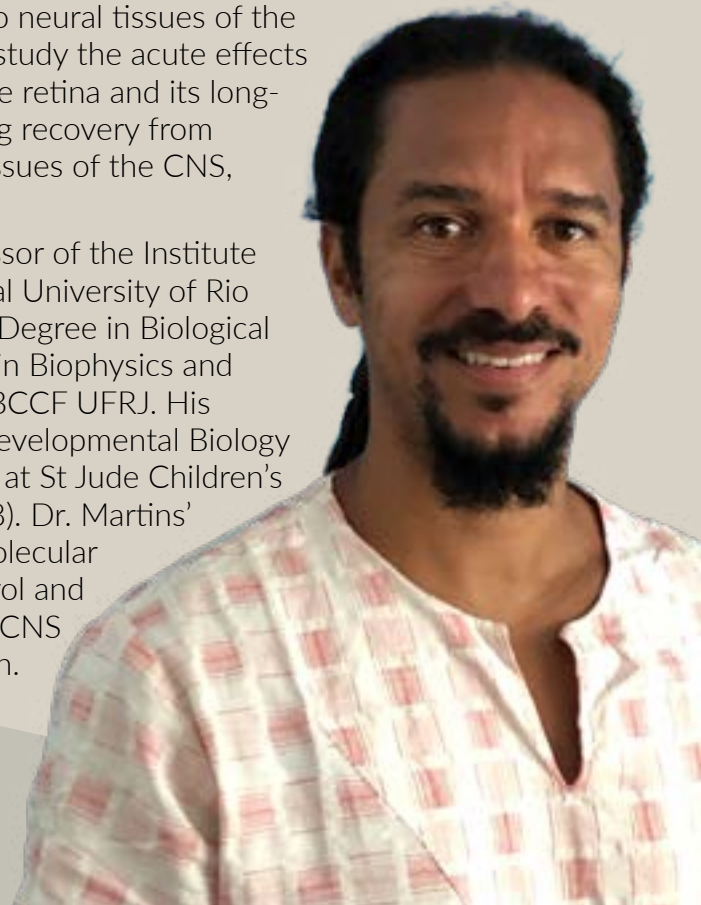
The Cellular and Molecular Basis of COVID-19 Effects in the Retina and Brain

Rodrigo Martins, PhD
Funded for Two Years

ABSTRACT: The novel coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is an absolute priority of the global health agenda. Although the predominant clinical presentation is respiratory disease, it is now clear that COVID-19 is a systemic disease, and neurological manifestations and retinal findings have been described. While most patients recover from COVID-19 within weeks, some experience complications that can last months after recovery. This condition, known as “long COVID”, is characterized by a variety of new or returning health problems, and 80% of infected patients may develop one or more long-term symptoms. In humans, the retina and other tissues of the CNS (central nervous system) are affected by COVID-19 during the symptomatic phase and after recovery. In this unprecedented scenario, animal models that mirror human disease caused by SARS-CoV-2 are crucial for medical countermeasures and for a better comprehension of the central nervous system (CNS) pathogenesis. Here, we plan to take advantage of a unique transgenic mouse model to better understand the consequences of COVID-19 to neural tissues of the CNS. In particular, we plan to study the acute effects of SARS-CoV-2 infection to the retina and its long-term consequences – following recovery from COVID-19 – to the specific tissues of the CNS, including the retina.

Dr. Martins is Associate Professor of the Institute of Biomedical Sciences, Federal University of Rio de Janeiro (UFRJ) and holds a Degree in Biological Sciences from UFRJ and MSc in Biophysics and Doctor of Science (2004) by IBCCF UFRJ. His postdoctoral training was in Developmental Biology and Tumorigenesis in the CNS at St Jude Children's Research Hospital (2005-2008). Dr. Martins' main scientific interests are molecular mechanisms of cell cycle control and DNA damage signaling during CNS development and degeneration.

Rodrigo Martins, PhD



PROJECT TITLE: *Generation of Induced-Retinal Ganglion Cells by Reprogramming Late Retinal Progenitors and Adult Müller Glia*

Donoso Awardee:

Mariana Souza da Silveira, PhD, Federal University of Rio de Janeiro (UFRJ) in Brazil, has also been selected to receive the second Larry A. Donoso, MD Award in Retinal Research after receiving the highest-ranking score in the 2021 grant review process, a criterion for the Award. The Award was created to honor IRRF Director, Larry A. Donoso, MD, PhD, to recognize his tireless efforts for the IRRF.

Mariana Souza da Silveira, PhD, Federal University of Rio de Janeiro (UFRJ) in Brazil, has been awarded two years of funding for her study and will collaborate with Dr. Alejandra Bosco, University of Utah, USA, who will act as co-principal investigator and who will help direct Aim 1 for the project. Dr. Bosco currently works in the laboratory of Monica Vetter, PhD, Chair, Department of Neurobiology at the University of Utah School of Medicine.



Mariana Souza da Silveira, PhD

Vision loss in glaucoma results from neurodegeneration of retinal ganglion cells (RGCs) and their optic nerve axons, which process and carry visual information from the eye to the brain. RGC loss is irreversible, given that the retina of humans and other mammals lack significant regenerative capacity. However, RGCs effectively regenerate in the adult fish retina from Müller glia (MG). Dr. Silveira is exploring the question, *could transcriptional reprogramming of MG reestablish this proliferative and neurogenic ability in the mammalian retina?* The identification of reprogramming factors sufficient to override the restriction and promote de novo neurogenesis of RGCs in vivo is key to design novel regenerative strategies for RGC replacement in glaucoma and other conditions that kill these neurons. Two Aims have been identified for this project.

AIM 1: Optimize Klf4 (Krüppel-like factor 4) reprogramming strategies of late retinal progenitors to generate mature iRGCs.

AIM 2: Establish whether rodent Müller glia can be reprogrammed via Klf4 to generate iRGCs *in vivo*.

Dr. Silveira's research experience is focused on retinal development. Recently, she started working in reprogramming as an approach for generating a specific cell type, the retinal ganglion cell (RGC).

Alejandra Bosco, PhD



PROJECT TITLE: *Role of autophagy in photoreceptor cell homeostasis and disease*

Ivan Conte graduated in 1999, with a degree in Biology from University of Naples "Federico II". In 2004, he completed his Ph.D. studies on the molecular mechanisms underlying inherited retinal dystrophies in the laboratory of Prof. A. Ciccodicola also at the University of Naples. To broaden his interest in the visual system, he moved to the Institute of Neurobiology "Ramon y Cajal" in Madrid (Spain), working as a postdoc in the laboratory of Prof. P. Bovolenta, where he studied the development of retinal cells and mechanism behind retinal disease. In 2007, he moved to the laboratory of Prof. Banfi at Telethon Institute of Genetics and Medicine (TIGEM) and was honored for scientific achievements in Neurobiology by the President of the Italian Republic. Since 2012, he has directed his own laboratory in TIGEM. From 2019, he has held the position of Assistant Professor of Molecular Biology at University of Naples "Federico II".

Dr. Conte's IRRF-funded research will have a main goal of understanding of the biological mechanisms regulating cell clearance function in the retina and to translate cell clearance discoveries into novel therapeutic strategies for adRP. To achieve this goal three specific aims will be addressed:

AIM 1: Defining miR-211/Ezrin axis in cell clearance on human-iPSC-derived photoreceptors. The team will assess the contribution of miR-211 in regulating the Ezrin/AKT/mTOR signaling on autophagy.

AIM 2: Defining the role of miR-211/Ezrin axis in RPE/PR crosstalk, in vivo. A detailed analysis of the role of miR-211 on the AKT/mTOR-mediated control of autophagy in photoreceptor cells will be carried out.

AIM 3: Long-term in vivo evaluation of miR-211 therapeutic potential in retinal degeneration. The team aims to further assess the therapeutic treatment and investigate on efficacy of miR-211-mediated Ezrin inhibition in adult mice until 18 months.

TERMS: MIRN211 also known as mir-211 – MicroRNAs (miRNAs) are short (20-24 nt) non-coding RNAs that are involved in post-transcriptional regulation of gene expression in multicellular organisms by affecting both the stability and translation of mRNAs.

Ivan Conte, PhD
University of Naples
Naples, Italy



Ivan Conte, PhD

Emerging Lysosomal Functions for Photoreceptor Cell Homeostasis and Survival

ABSTRACT: Lysosomes are membrane-bound cell organelles that respond to nutrient changes and are implicated in cell homeostasis and clearance mechanisms, allowing effective adaption to specific cellular needs. The relevance of the lysosome has been elucidated in a number of different contexts. Of these, the retina represents an interesting scenario to appreciate the various functions of this organelle in both physiological and pathological conditions. Growing evidence suggests a role for lysosome-related mechanisms in retinal degeneration. Abnormal lysosomal activation or inhibition has dramatic consequences on photoreceptor cell homeostasis and impacts extensive cellular function, which in turn affects vision. Based on these findings, a series of therapeutic methods targeting lysosomal processes could offer treatment for blindness conditions. In this publication, findings on membrane trafficking, subcellular organization, mechanisms by which lysosome/autophagy pathway impairment affects photoreceptor cell homeostasis and the recent advances on developing efficient lysosomal-based therapies for retinal disorders are reviewed.

This study was conducted with IRRF Funds: Ivan Conte, PhD

Cells is an international, peer-reviewed, open access journal of cell biology, molecular biology, and biophysics, published semimonthly online by MDPI (Multidisciplinary Digital Publishing Institute, based in Basel, Switzerland).

Access this article: www.mdpi.com/2073-4409/11/1/60



Manuela Santo¹ and
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34, 80078 Pozzuoli, Italy



Development of a Novel Technology to Connect Patients with Vision Loss: The Low Vision Connect App

Bonnielin Swenor, PhD
Johns Hopkins School of
Medicine/SON

Funded for Two Years with
matching funds provided by the
American Macular Degeneration
Foundation (AMDF)



The goal of this proposal is to develop and test the “Low Vision Connect” application. This accessible mobile technology platform will connect patients with visual impairments in peer-to-peer mentoring relationships around a specified goal. The application provides a forum whereby people with vision loss related to living with low vision, and will provide opportunities to enhance self-efficacy by both obtaining and sharing knowledge and advice. Patients will be matched via a user-driven, flexible matching algorithm, meaning the user can identify and rank the characteristics on which to be matched for each pairing request. For example, a patient with age-related macular degeneration seeking advice on caring for grandchildren may want to connect with other grandparents or parents with retinal disease, given their likely common experiences.

The potential impact of this application is far-reaching, as this technology can be expanded to any disease or patient population and serve as a framework to enhance social interaction, self-efficacy and mental well-being.

Bonnielin Swenor is an associate professor at The Johns Hopkins School of Nursing, the Johns Hopkins School of Medicine Wilmer Eye Institute and in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health. She is the founder and director of the Johns Hopkins Disability Health Research Center, which aims to shift the paradigm from ‘living with a disability’ to ‘thriving with a disability’ through research, education, and policy.

Dr. Swenor’s research is motivated by her personal experience with low vision. Her work takes a data-driven approach to advancing health equity for people with disabilities. To achieve this, she focuses on three areas: (1) developing novel methods to assess and track health and healthcare inequities for people with disabilities; (2) testing innovative strategies to reduce these inequities, and (3) building approaches that promote disability inclusion in research and higher education.

Bonnielin Swenor, PhD



PROJECT TITLE: *Dysregulated Lipid Metabolism and Senescence in Age-Related Macular Degeneration*

**2021 Alston Callahan,
MD Postdoctoral
Scholar**

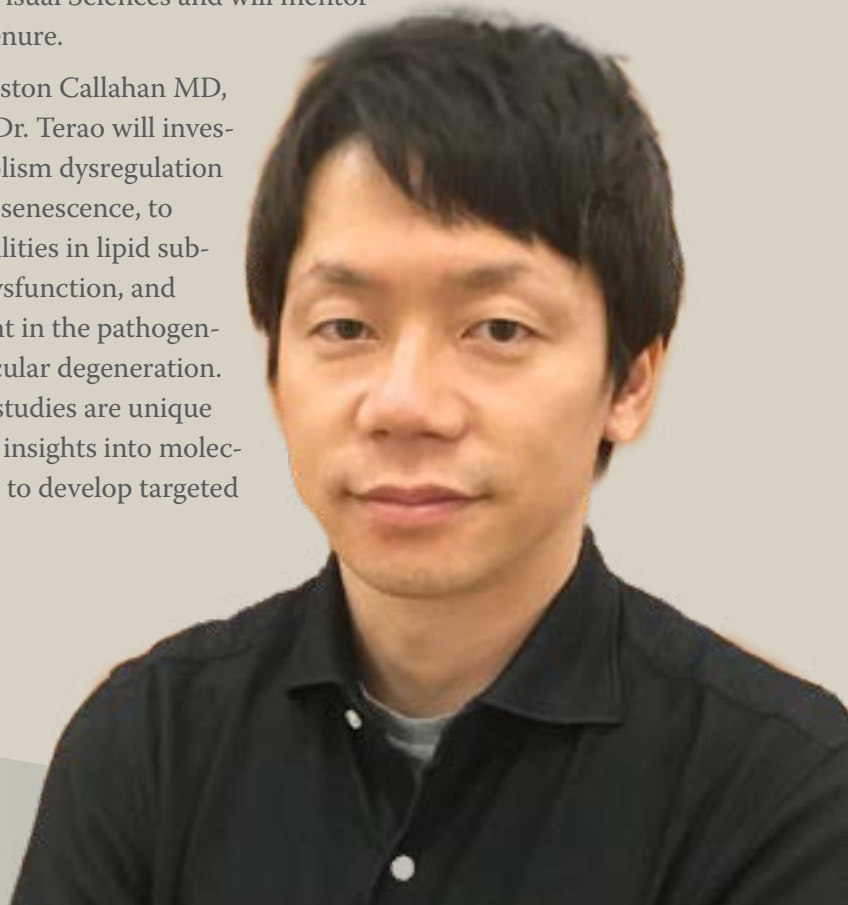
Ryo Terao, MD, PhD
*Washington University
School of Medicine in
St. Louis
Department of
Ophthalmology & Visual
Sciences
St. Louis, Missouri*

Dr. Terao received his MD from the University of Tsukuba, Japan and completed his internship at the University of Tsukuba Hospital. He trained as a resident in the University of Tokyo Hospital Japan. He then earned his PhD from the Graduate School of Medicine, University of Tokyo, Japan, under the supervision of Makoto Aihara, MD, PhD. Dr. Terao began training in basic science as a graduate student in the Department of Ophthalmology, focusing on bioactive lipid mediators in retinal diseases. This sparked his interest in how lipid metabolism affects retinal diseases. Throughout the PhD program, he has published several articles on bioactive lipids in retina.

Dr. Terao has received the Japanese Ophthalmological Society (JOS) Young Investigator Award, as well as the Bayer Japan Retina Award in 2020. After graduating in 2020, he joined the lab of Rajendra S. Apte, MD, PhD at Washington University School of Medicine in St. Louis as a postdoctoral research fellow. Dr. Apte currently holds the Paul A. Cibis Distinguished Professorship in the Department of Ophthalmology & Visual Sciences and will mentor Dr. Terao during his tenure.

As the IRRF 2021 Alston Callahan MD, Postdoctoral Scholar, Dr. Terao will investigate the lipid metabolism dysregulation and cellular aging and senescence, to uncover how abnormalities in lipid substrates cause retinal dysfunction, and how they are important in the pathogenesis of age-related macular degeneration. Says Dr. Apte, “These studies are unique and will provide novel insights into molecular pathways in order to develop targeted therapeutics in AMD.”

Ryo Terao, MD, PhD



PROJECT TITLE: *AAV-mediated Gene Augmentation Therapy for CRB1-Associated Retinal Degeneration*

After receiving his BSc at The University of Manchester and MSc at Brunel University, Dr. Quinn joined the lab of Dr. Jan Wijnholds at Leiden University, where he completed his PhD. Subsequently, Dr. Quinn joined Columbia University in New York as a postdoctoral research fellow, where he is mentored by Drs. Stephen H. Tsang and Irene H. Maumenee. Dr. Quinn's focus is to provide clinically translatable impact using iPSC-derived retinal organoid-based approaches for the understanding and treatment of retinal degenerative diseases. He is currently developing gene augmentation and prime editing therapeutics for the amelioration of the phenotypic, histopathological, and molecular changes in inherited retinal disease iPSC-derived retinal organoid models.

"My own experience as a mentor allows me to assess the potential of scientists at various levels of their career; in my view, Dr. Quinn is remarkably gifted," says Stephen H. Tsang, MD, PhD, Dr. Quinn's sponsor for the IRRF David and Loris Rich Postdoctoral Scholarship Award. Dr. Quinn's project, *AAV-mediated Gene Augmentation Therapy for CRB1-Associated Retinal Degeneration*, will be explored over the next year. Its primary objective is to develop and evaluate CRB1 (*Crumbs homologue-1*) gene augmentation therapeutics that can be utilized in a Phase I/IIa combined clinical trial. Dr. Quinn and his team have hypothesized that the concomitant overexpression of CRB1-A and CRB1-B in their cell-type-specific localizations will preserve retinal structure and function. It is anticipated that the tools developed in the proposal will lead to tangible clinical benefits for patients with retinal disorders.

**2021 Loris and David Rich
Postdoctoral Scholar
Peter M.J. Quinn, PhD
Columbia University
New York, New York**

Peter M.J. Quinn, PhD



PROJECT TITLE: *CRISPR-mediated Müller glial reprogramming*

Dr. Hooper received his undergraduate degree in chemistry and biology from Eastern Washington University, and then completed his PhD at University of Florida in chemistry and biology. A postdoctoral fellowship followed from University of Washington in Seattle. Dr. Hooper's research interests have focused on preventing, and ideally reversing blindness caused by the death of retinal neurons following his studies in retinal regeneration and glial reprogramming.

As a postdoctoral researcher, Dr. Hooper has been working in the area of Müller glia reprogramming in Dr. Thomas Reh's lab at Washington University in Seattle. Their recent work is significant, and shows that Müller glia can regenerate functional retinal neurons. The primary goal is to generate visual neurons important for retinal disease. To this end, Dr. Hooper has learned to overexpress transcription factors using CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) activation, generate and analyze high throughput single cell genomics data and package adeno associated viral vectors.

Dr. Hooper is co-author on four recently published papers, and is currently in the process of writing two papers of his own.

As the International Retinal Research Foundation Charles D. Kelman, MD Postdoctoral Scholar, Dr. Hooper will expand his training by focusing on retinal regeneration and will expand his development of the specific genetic combinations to use CRISPR activation methods to reprogram cells. Dr. Thomas Reh, who will be Dr. Hooper's mentor during the next year says of Dr. Hooper, "He is an outstanding candidate for the IRRF Scholar Award, as he is highly motivated for a career in academic science and is a technical innovator who is determined to succeed."

CRISPR, or Clustered Regularly Interspaced Short Palindromic Repeats, is the basis of a revolutionary gene editing system. One day, it could make it possible to develop cures for chronic disease.

2021 Charles D. Kelman,
MD Postdoctoral Scholar
Marcus Hooper, PhD

Marcus Hooper, PhD



Association for Research in Vision and Ophthalmology

In 2002, the ARVO Foundation established and awarded its first travel grants. As of 2021, the Foundation had supported travel expenses for over 2,000 young researchers from around the world to report their work at the ARVO Annual Meeting, held in the United States. The Foundation currently offers 34 named travel grants that support over 185 researchers annually.

ARVO Travel Grants are awarded based on abstracts submitted to the ARVO Annual Meeting. Grants are awarded to the highest scored abstract that meets the travel grant criteria.

The International Retinal Research Foundation (IRRF) is proud to support the **Ramon F. Dacheux II Memorial Travel Grant**, a memorial to Dr. Dacheux, who was a professor in the department of ophthalmology at the University of Alabama at Birmingham (UAB). Dr. Dacheux was a driving force during the formation and establishment of the IRRF in 1997 and is remembered as an outstanding scientist. This grant is awarded to student researchers conducting basic science research in visual neuroscience.

In 2021, three Ramon F. Dacheux II Memorial Travel Grants were awarded:

Miranda L. Scalabrino, PhD, (Left) Duke University, Chapel Hill, North Carolina USA.

Dr. Scalabrino's background is in retinal gene therapy, developing a treatment for an animal model of an inherited retinal disease and engineering novel AAV capsid variants. Currently, she studies retinal circuitry functionality both in healthy tissue and models of degenerative retinal disease. Particularly, Dr. Scalabrino hopes to understand how different bipolar cell types shape visual processing, and how that processing is impaired once connectivity between photoreceptors and bipolar cells is lost in advanced forms of disease.

Dr. Scalabrino commented, "I am so grateful to the sponsor for providing the travel grant and selecting me as a recipient! Attending ARVO has been an essential part of my career as a scientist and I sincerely appreciate that the sponsor enabled my attendance."

Miranda L. Scalabrino, PhD



(ARVO) Foundation Travel Grants

Andrew Boal, BA, (below right) Vanderbilt University, Nashville, Tennessee USA.

At the time of the Award, Andrew Boal, BA was enrolled in the Medical Scientist Training Program at Vanderbilt School of Medicine and was assigned to the David Calkins Lab. Research interests include studying the neurologic basis of vision and diseases that affect the visual system. In the Calkins Lab, he studied the role of astrocytes in glaucoma and neurodegeneration.

Andrew Boal commented, "I had the opportunity to be nominated for the outstanding poster award, which was a wonderful honor. Thank you so much for your generosity! Your sponsorship provided a wonderful opportunity to further my education and professional development."

Solomon Gibson, BS, (Picture not available) Baylor College of Medicine, Houston, Texas USA.

Solomon is a Pre-Doctoral Fellow — Graduate Student

Solomon Gibson commented, *"I networked with brilliant scientists and gained insight that will help me with my own thesis work. I listened to great talks and read through many posters, allowing me to deepen my knowledge and gain more appreciation for my field. I am sincerely appreciative for this opportunity. Your donation allowed me to attend ARVO for the first time, but definitely not the last. I expect to come back next year with a paper under my belt and more data to showcase. Thank you again for your sponsorship."*



Andrew Boal, BA

The International Retinal Research Foundation Establishes the IRRF/Paul Sternberg, Jr., MD Directorship in Ophthalmology Through a \$2 million Pledge

In the Spring of 2021, the Directors of the International Retinal Research Foundation (IRRF) chose to establish an endowed Directorship in Honor of Dr. Paul Sternberg as lasting recognition for his longstanding contributions as a member of the IRRF board and devoted friend of the organization. The IRRF has benefitted from Dr. Sternberg's many hours of support and his tireless work as the Director of Research Funding.

Recognizing that the Vanderbilt Eye Institute (VEI) is one of the fastest-growing ophthalmology programs in the country and the recipient of consistent transformational funding from the National Eye Institute, the IRRF Directors feel strongly that this investment will add to VEI's status as an international leader in the field of vision research and in training the vision scientists of tomorrow. Additionally, it adheres to the IRRF's original mission of accelerating and sustaining targeted research efforts into discovering the causes, preventions and cures of macular degeneration of the retina and diabetic retinopathy. The IRRF/Paul Sternberg, Jr., MD Directorship will support a senior retina faculty member engaged in seminal work in the field. This leading investigator will be engaged in research, teaching and patient care – with an emphasis on collaborative work

that will help bring discovery from the bench to the bedside.

Dr. Sternberg has a long history of leadership in ophthalmology, highlighted by serving as President of the American Academy of Ophthalmology, President of the Macula Society, President of the Association of University Professors of Ophthalmology and Chair of the Board of Governors for the Association for Research in Vision and Ophthalmology (ARVO) Foundation. In addition, he has served on the Board of Scientific Counselors for the National Eye Institute, the Board of Directors of the International Retinal Research Foundation, the Board of Directors of the Tennessee Academy of Ophthalmology and has been President of the Society of Heed Fellows. Honors include the Merit in Retinal Research from the Retina Society, the Heed Ophthalmic Foundation Award, The Founder's Lecture from the American Society for Retina Specialists, and both the J. Donald M. Gass Medal and the Arnall Patz Medal from the Macula Society.

The IRRF/Paul Sternberg, Jr., MD Directorship is being gifted in recognition of Dr. Sternberg's planned retirement as chair of the Department of Ophthalmology and Visual Sciences at the Vanderbilt Eye Institute in 2023, at which time, it will thereafter be known as the Paul Sternberg, Jr., MD Directorship in Ophthalmology.

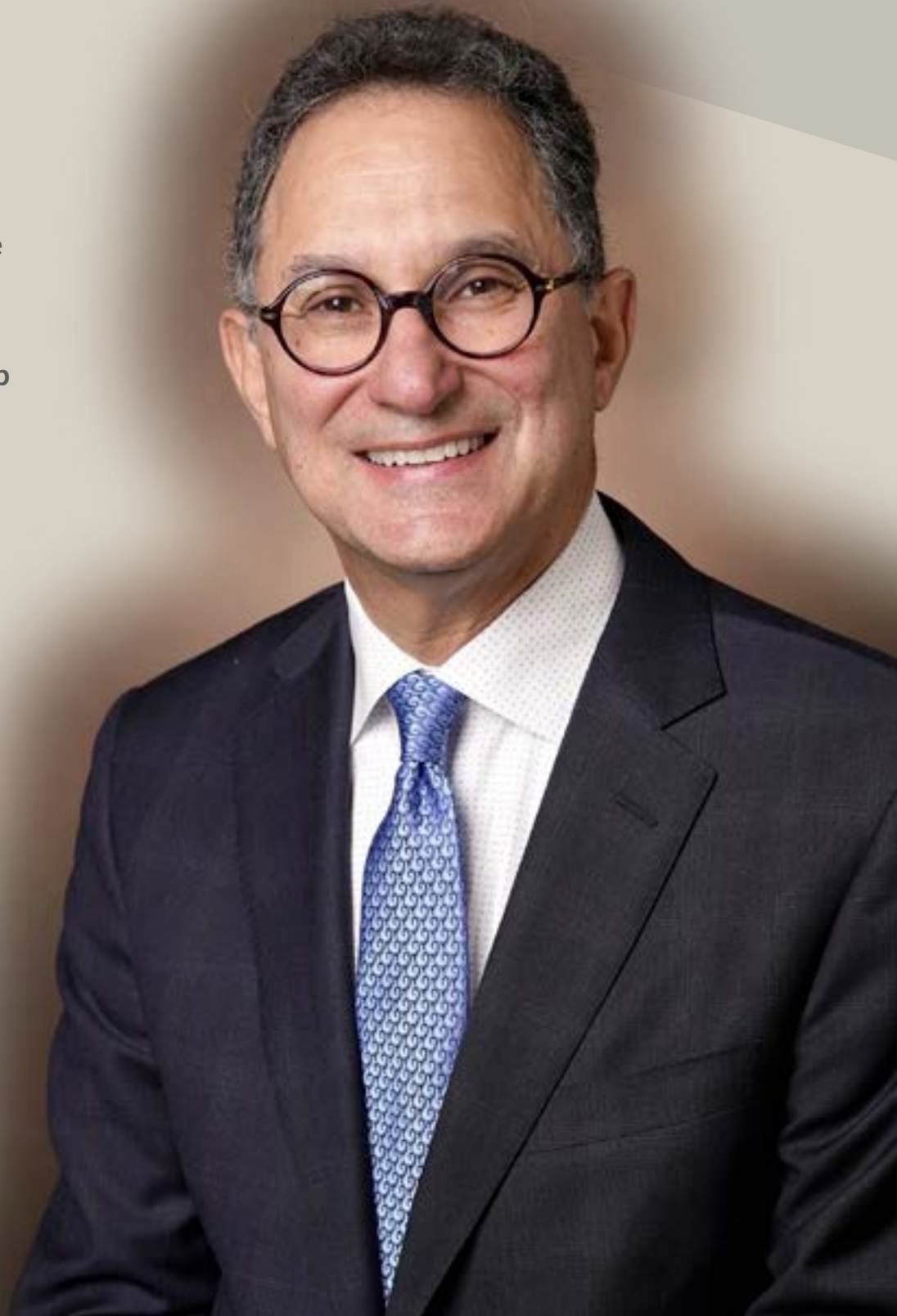
Paul Sternberg, Jr., MD

**G.W. Hale Professor and
Chairman, Vanderbilt Eye
Institute**

**Chief Medical Officer,
Vanderbilt Medical Group**

**Chief Patient Experience
and Service Officer**

**Associate Dean for
clinical Affairs,
Vanderbilt School
of Medicine**



Paul Steinberg, Jr., MD

Safety Evaluation of Photoacoustic Tomography System for Intraocular Tumors



Guan Xu; Nahed Khan; Ahmed Almazroa; Mercy Pawar; **Cagri Besirli**; Yannis M. Paulus; Xueding Wang; Hakan Demirci

Translational Vision Science & Technology, March 2022, Vol. 11, 30,

Doi:<https://doi.org/10.1167/tvst.11.3.30>

ABSTRACT: Photoacoustic tomography (PAT) has demonstrated the ability to characterize molecular components and architectural heterogeneities of intraocular tumors in enucleated human globes and in animals in vivo. Although laser safety levels have been established for illumination through the cornea, the safety limit for PAT illumination through the sclera has not been investigated. The purpose of this study is to examine if the energy level used in intraocular Pat results in ocular damage.

Methods: Rabbit eyes were exposed to pulsed laser illumination at 20 mJ/cm² at the scleral surface. Eyes were examined at 1, 7, and 28 days after the laser exposure. Examination procedures included white light and fluorescence fundus imaging, optical coherence tomography (OCT), electroretinography (ERG), and histology with hematoxylin and eosin (H&E) staining as well as terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling (TUNEL staining).

RESULTS: Fundus imaging and OCT of rabbit eyes at 1, 7, and 28 days following exposure of the laser illumination of the PAT system did not reveal any damage to the retinal structures. ERG showed no significant difference between the experimental and control eyes. Similarly, H&E histology did not show abnormalities in either the scleral tissue where the laser illumination was delivered or in the retinal layers. No sign of apoptosis in the layers of the retina, choroid, or optic nerve was found on TUNEL staining.

CONCLUSIONS: Similar to the application of PAT to other organs, the proposed laser illumination energy level at 20 mJ/cm² does not impose detectable harm to the ocular tissue.



Cagri Besirli, MD, PhD, W.K. Kellogg Eye Center,

University of Michigan.

Dr. Besirli received IRRF funding 2019 – 2021 for his study, *PKM2 metabolic reprogramming to prevent photoreceptor death in a preclinical model of macular degeneration*.

Area of Practice: Gene therapy for inherited retinal diseases; disease and surgery of the retina and vitreous, including retinal detachment, diabetic retinopathy, age-related macular degeneration, retinal vascular disease, ocular trauma, ocular inflammation, macular and submacular surgery, and surgical management of complex retinal detachment; medical and surgical management of acquired and inherited pediatric retinal disorders, including retinopathy of prematurity (ROP), familial exudative vitreo-retinopathy (FEVR), Coats' disease, retinal detachment and ocular trauma.

Oxidative Stress Resistance 1 Gene Therapy Retards Neurodegeneration in the *rd1* Mutant Mouse Model of Retinopathy

(*Investigative Ophthalmology & Visual Science*, September 2021, Vol.62, 8)

Authors: Bhubanananda Sahu; Laura Moreno Leon; Wei Zhang; Nikita Puranik; Ramesh Periasamy; Hemant Khanna; **Michael Volkert**

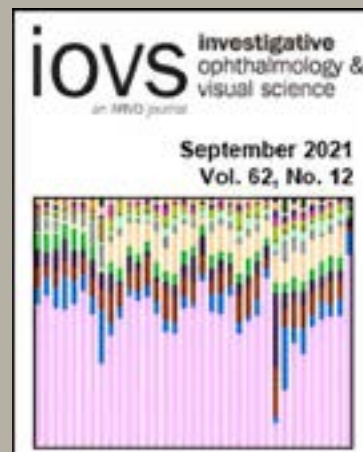
PURPOSE: Oxidative stress is a major factor underlying many neurodegenerative diseases. However, antioxidant therapy has had mixed results, possibly because of its indiscriminate activity. The purpose of this study is to determine if the human OXR1 (hOXR1) antioxidant regulatory gene could protect neurons from oxidative stress and delay photoreceptor cell death.

METHODS: The cone-like 661W cell line was transfected to stably express the hOXR1 gene. Oxidative stress was induced by the addition of hydrogen peroxide (H₂O₂). Intracellular levels of reactive oxygen species (ROS), caspase cleavage, and cellular resistance to oxidative stress were determined and compared between the control and hOXR1 cells. For in vivo analysis, AAV8-hOXR1 was injected subretinally into the *rd1* mouse model of retinal degeneration. Functional and structural integrity of the photoreceptors were assessed using electroretinography (ERG), histology, and immunofluorescence analysis.

RESULTS: Expression of hOXR1 increased cellular resistance and reduced ROS levels and caspase cleavage in the 661W cell line after H₂O₂ -induced oxidative stress. Subretinal injection of AAV8-hOXR1 in the *rd1* mice improved their photoreceptor light response, expression and localization of photoreceptor-specific proteins, and delayed retinal degeneration.

CONCLUSIONS: Our results suggest that OXR1 is a potential therapy candidate for retinal degeneration. Because OXR1 targets oxidative stress, a common feature of many retinal degenerative diseases, it should be of therapeutic value to multiple retinal degenerative diseases.

<https://iovs.arvojournals.org/article.aspx?articleid=2777889>



Michael Volkert, PhD is a scientist at the University of Massachusetts Chan Medical School and a professor of Microbiology and Physiological Systems. He is also a member of the UMass Chan NeuroNexus Institute and the Advanced Ocular Therapy Program. The IRRF supported his project, Gene Therapy for the Treatment of Oxidative Stress-Induced Retinal Degeneration, the results of which contributed to this publication.



Vanderbilt Eye Institute

International Retinal Research Foundation Vision Research Center at Vanderbilt Eye Institute

The Directors of the International Retinal Research Foundation (IRRF) announce the creation of the *International Retinal Research Foundation Vision Research Center* at Vanderbilt Eye Institute in Nashville. The \$8 million gift is an expansion of the IRRF/Paul Sternberg, Jr., MD Directorship established in the spring of 2021, and will create multiple funds to support a vision research center in the Department of Ophthalmology and Visual Sciences. With the aging of our population, along with the increasing rates of obesity, diabetes and other metabolic health issues, diseases affecting the retina have emerged as a major health care concern, particularly in the southeastern United States. This partnership will support new research desperately needed to inform novel mechanisms of disease susceptibility and progression and to identify and test translational therapies to protect the vision of hundreds of thousands of individuals each year.

The Center's purpose will be to promote retinal vision research designed to achieve clinical solutions for patients suffering from retinal and optic nerve diseases. To accomplish this, multiple funds will be established to support the Center enabling the IRRF to carry out its mission by providing direct financial support for vision

research and collaboration with outstanding research organizations.

Proposed funds include:

- **David and Loris Rich Research Fund to support research in age-related macular degeneration and other retinal degenerative diseases (\$3 million);**
- **International Retinal Research Foundation Research Fund to support research in diabetic retinopathy and other retinal vascular diseases (\$3 million);**
- **International Retinal Research Foundation Capital Fund to support physical space and equipment necessary for the work of the International Retinal Research Foundation Vision Research Center (\$2 million)**

In addition to the above funds from IRRF, Vanderbilt Eye Institute has committed an additional \$2,000,000 endowed institutional investment to be divided equally between the David and Loris Rich Research Fund and the International Retinal Research Foundation Research Fund, bringing each Fund to \$4 million.

IRRF Board Member Cynthia Toth, MD named Vice Chair for Clinical Research

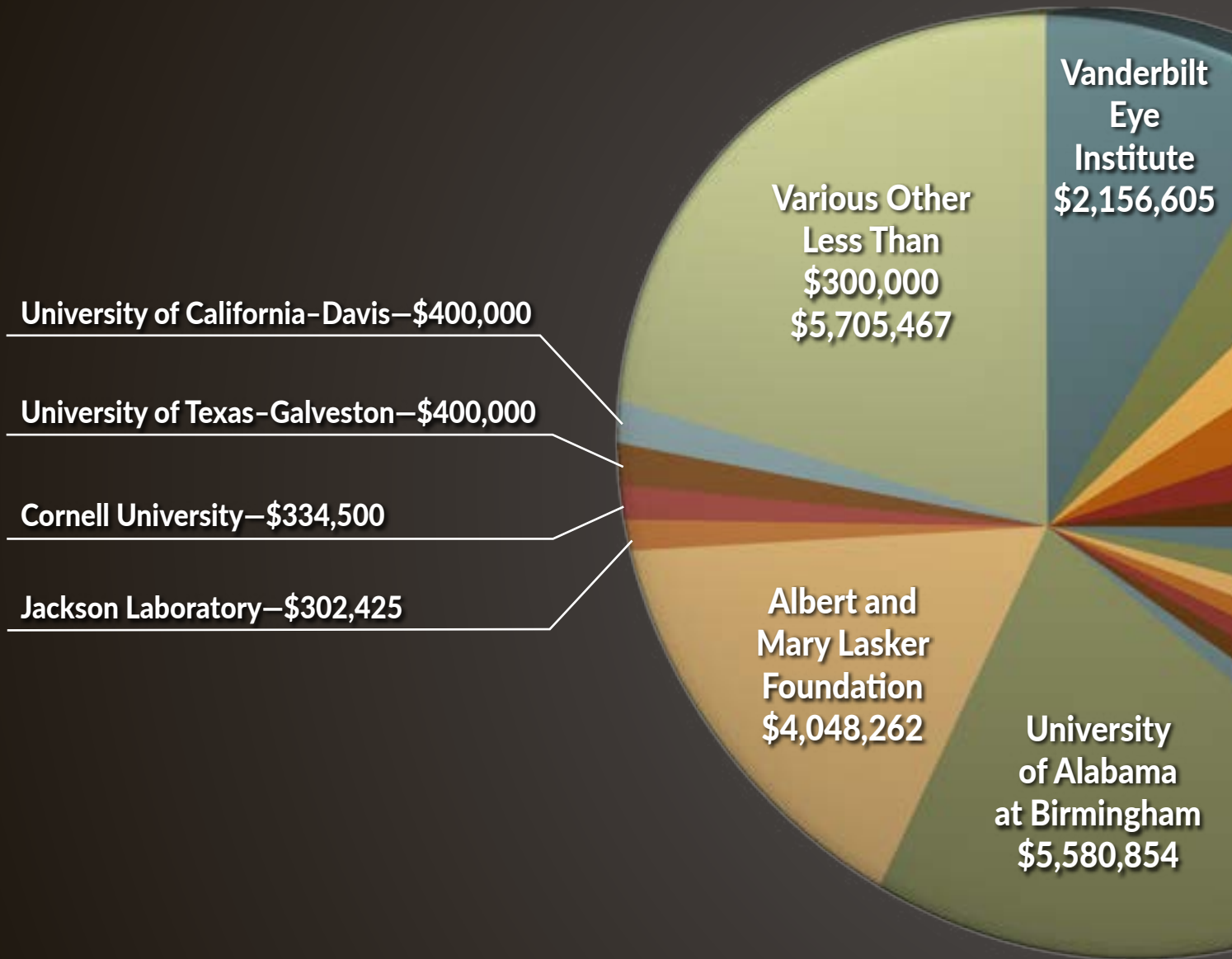
Cynthia Toth, MD, Joseph A.C. Wadsworth Professor of Ophthalmology, has been appointed Vice Chair for Clinical Research, at Duke University Eye Center in Durham, North Carolina. Dr. Toth specializes in the evaluation and surgical treatment of vitreoretinal diseases in infants, children, and adults, and in novel research resulting in the clinical application of optical coherence tomography (OCT) imaging in surgery and at the bedside.

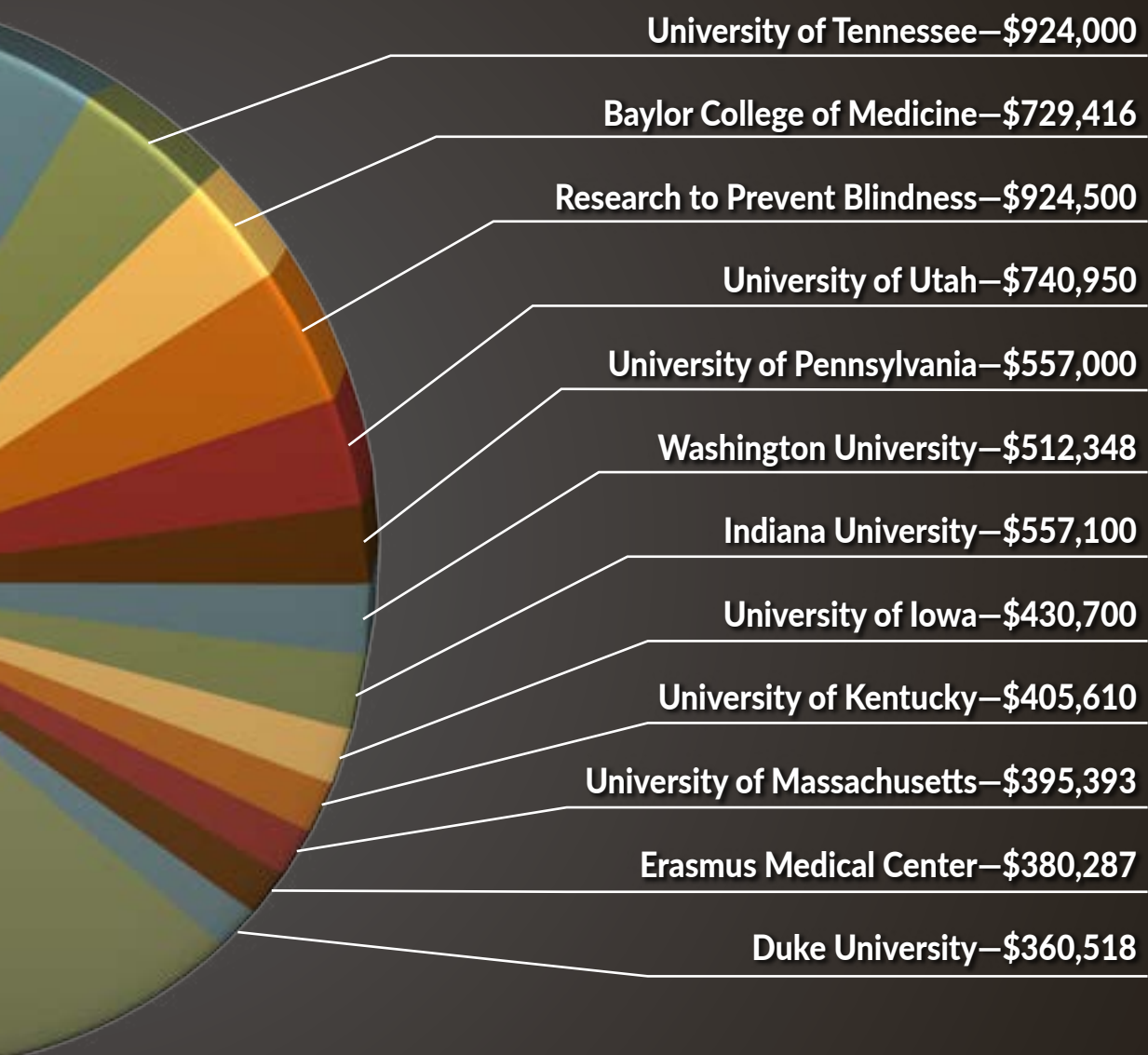
Dr. Toth also served as a URiM (Underrepresented Minority in Medicine) Summer Research Program Mentor at Duke. Duke Eye Center hosted the first URiM Medical Student Summer Mentored Research Program that launched in the summer of 2021 to support and help grow diversity in ophthalmology. This new program aims to catalyze the future of innovation and success of URiM students in ophthalmology



Cynthia Toth, MD

The International Retinal Research Foundation Grants 1998 – Present





Grand Total All Years \$25,845,935

Various Institutions Include all grants of \$300,000 or less

THE IRRF BOARD OF DIRECTORS



MICHAEL A. CALLAHAN, MD,

has served as President since 2004 and gives generously of his time. Since 1998, Dr. Callahan has held a faculty position as Professor of Ophthalmology in the Department of Ophthalmology at the University of Alabama at Birmingham (UAB), and teaches the intricate surgical procedures of phacoemulsification and intraocular lens insertion. In addition, Dr. Callahan lectures on ophthalmic plastic surgery. Dr. Callahan is also very involved in providing ophthalmic care in the U.S. and countries worldwide, where medical care is not readily available.



JOHN S. PARKER, MD,

serves as Vice President while devoting himself to private ophthalmology practice and teaching responsibilities in the UAB Department of Ophthalmology where he trains ophthalmology residents and donates time and expertise caring for indigent patients. Dr. Parker has served as Director of the Corneal Service and as Director of the Residency Training Program in the UAB Department of Ophthalmology.



V. HUGO MARX, III,

serves as Treasurer and has been a member of the IRRF Board since 2004. Mr. Marx operates several corporations, which represent various industries, including health care, investment banking and venture capital. Through his numerous businesses, Mr. Marx has provided charitable donations as medical supplies, food and support items used in multiple, extreme emergency situations in and outside the U.S.



PAUL S. STERNBERG, JR., MD,

serves as Director of Research Funding for the Foundation in addition to his many other responsibilities at Vanderbilt University in Nashville, Tennessee, where he is Associate Dean for Clinical Affairs and Assistant Vice Chancellor for Adult Health Affairs at the Vanderbilt School of Medicine. He also serves as professor and chairman of the Department of Ophthalmology and the Vanderbilt Eye Institute. With a special interest in age-related macular degeneration, Dr. Sternberg oversees a cell biology and biochemistry laboratory that carries out studies into the causes of the disease.



CYNTHIA A. TOTH, MD

was invited to join the IRRF Board of Directors in 2019 and assists in grant-funding determinations. Dr. Toth is a professor of ophthalmology at Duke Eye Center in Durham, North Carolina. She is the Joseph A.C. Wadsworth Distinguished Professor of Ophthalmology, Vice Chair of Clinical Research and is a professor of biomedical engineering. Dr. Toth specializes in the evaluation and surgical treatment of vitreoretinal disease in infants, children and adults, and in novel research resulting in the clinical application of optical coherence tomography (OCT) imaging in surgery and at the bedside. Her clinical interests and skills include the surgical treatment of macular diseases (as macular hole, epiretinal membrane and vitreomacular traction), retinal detachment, proliferative diabetic retinopathy, proliferative vitreoretinopathy (PVR), and retinopathy of prematurity (ROP).



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Today's scientists play a crucial role in the universal struggle against debilitating eye diseases, but financial funding is needed to facilitate and sustain their efforts. As of year-end 2021, the IRRF had granted more than \$25 million in support of scientific investigations targeting all structures of the human eye, with emphasis on finding the causes, prevention and cure of degenerative diseases. If you would like to help with this challenge, please send your tax deductible contribution to:

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