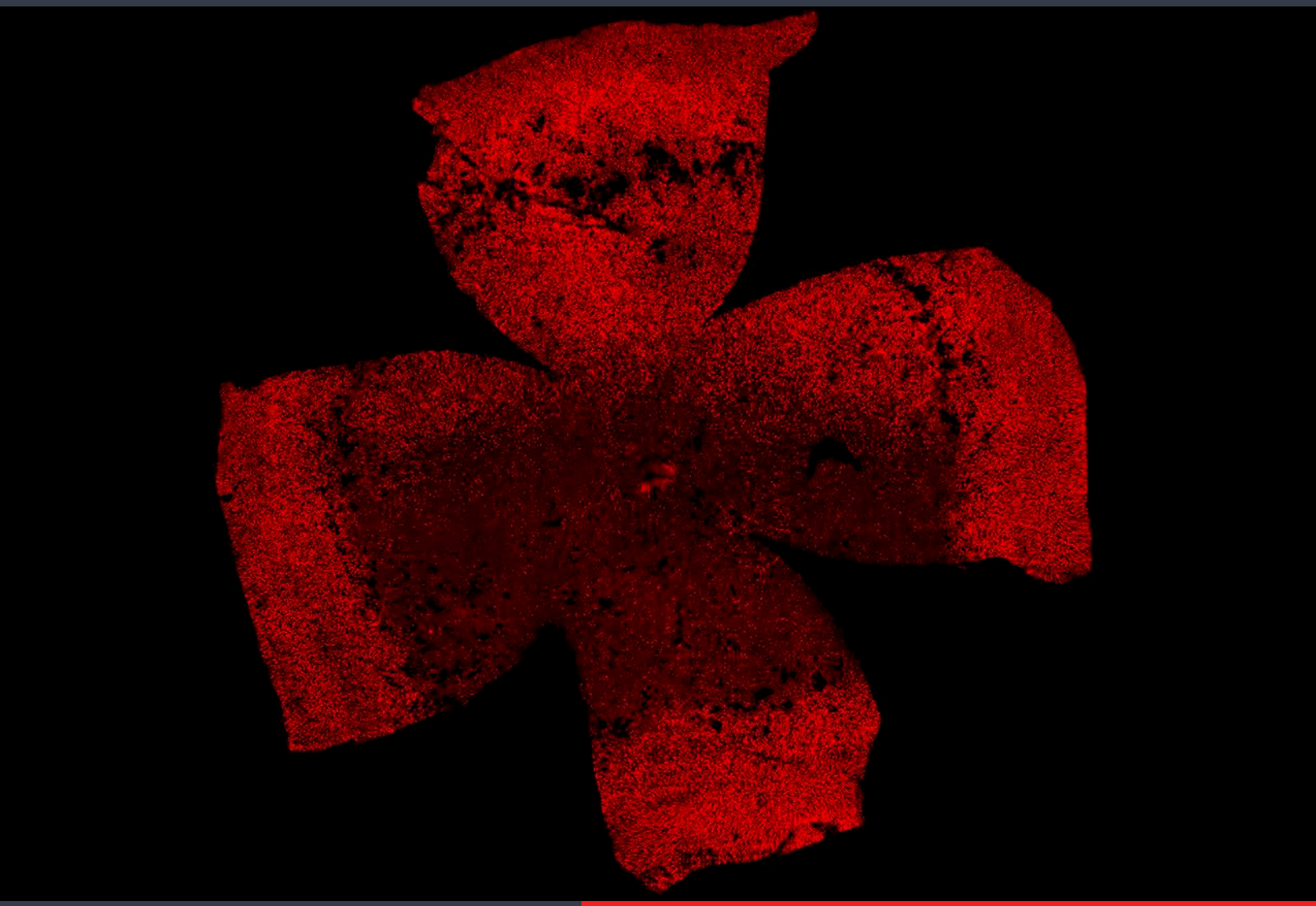
2016 Annual Report

of the IRRF



International Retinal Research Foundation

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www.irrfonline.org

CONTENTS

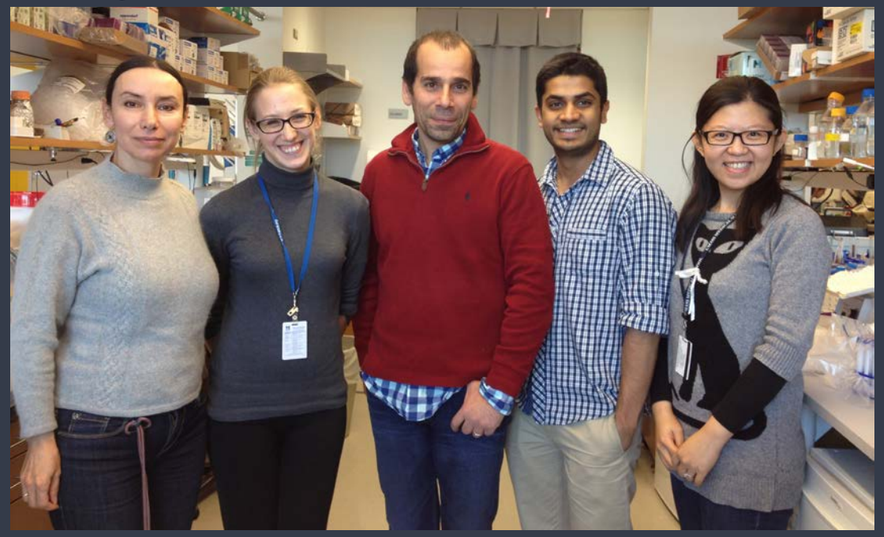
Eivor and Alston Callahan, MD, Endowed Chair in Ophthalmology

The International Retinal Research Foundation (IRRF) has announced plans to endow a Chair in Ophthalmology at the University of Alabama at Birmingham (UAB) to honor its Founder and longtime leader, Dr. Alston Callahan and his wife, Eivor. Along with son, Dr. Michael Callahan, Loris Rich, and Dr. Charles Kelman, Dr. Callahan founded the Birmingham-based Foundation to further research that will someday provide a cure for blinding eye diseases such as macular degeneration. The IRRF is the culmination of his long career in eye healthcare, which began during World War II, when Callahan performed reconstructive eye surgery and became a pioneer in the field of ophthalmic plastic surgery.

Callahan served as the first chairman of the UAB Department of Ophthalmology and in 1963, founded the Eye Foundation Hospital, the first facility in Alabama dedicated to the care and treatment of the eye. UAB purchased the Hospital in 1997 and renamed it the Callahan Eye Foundation Hospital. Today, the Hospital is known around campus as, The Callahan.

The Callahan Chair will also honor his wife, Eivor, who supplied the support and strength that was needed for such accomplishments. The endowed chair will allow UAB to recruit a faculty member who is an expert in retina to pursue his or her research at UAB.

Access the publication ▶



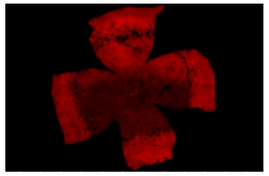
Dr. Claudio Punzo (middle) and his staff. Marina Zieger is pictured far left.

ONCOTARGET

Improved cell metabolism prolongs photoreceptor survival upon retina-pigmented epithelium loss in the sodium iodate induced model of geographic atrophy, Marina Zieger and Claudio Punzo, Department of Ophthalmology and Gene Therapy Center, University of Massachusetts Medical Center, Worcester, MA. This study was conducted with IRRF support.

Age-related macular degeneration (AMD) is characterized by malfunction and loss of retinal-pigmented epithelium (RPE) cells. Because the RPE transfers nutrients from the choriocapillaris to photoreceptor (PR), PRs are affected as well. Geographic atrophy (GA) is an advanced form of AMD characterized by severe vision impairment due to RPE loss over large areas. Currently, there is no treatment to delay the degeneration of nutrient deprived PRs once RPE cells die. Here we show that cell-autonomous activation of the key regulator of cell metabolism, the kinase mammalian target of rapamycin complex 1 (mTOR1), delays PR death in the sodium iodate induced model of RPE atrophy. Consistent with this finding loss of mTORC1 in cones accelerates cone death as cones fail to balance demand with supply. Interestingly, promoting rod survival does not promote cone survival in this model of RPE atrophy as both, rods and cones suffer from a sick and dying RPE. The findings suggest that activation of metabolic genes downstream of mTORC1 can serve as a strategy to prolong PR survival when RPE cells malfunction or die.

To read this paper in its entirety, please follow the link:: www.impactjournals.com/oncotarget/index.php?journal=oncotarget&page=article&op=view&path%5B%5D=7330&path%5B%5D=20985



ABOUT THE COVER PHOTO

Retinal flat mount of mouse 4 weeks post sodium iodate injection showing in red surviving cones after loss of retinal-pigmented epithelium. The radial extent of retinal-pigmented epithelium damage can be inferred from the area the dark pigmented epithelium cells cover. Cones are identified by cone arrestin positive signal in red. (See related paper, "Oncotaget" above.)

Claudio Punzo, Ph.D., Assistant Professor, Department of Ophthalmology & Gene Therapy Center, University of Massachusetts Medical School (UMMS)

Dowling-Werblin Symposium: Half a Century of Retina Research; Neural Circuitry, Retinal Disorders and Restoration of Vision

Along with other leading vision research foundations, the International Retinal Research Foundation (IRRF) provided sponsorship for the Dowling-Werblin Symposium that presented highlights of the progress in retinal circuit analysis since 1969, its implications to neural information processing in the brain, its application to retinal dysfunction and diseases, and how it helps to develop prosthesis and other methods to restore vision.

One of the optimal goals of brain research is to understand how neuronal networks respond to signals from the environment, and how individual neurons and synapses process information elicited by natural stimuli of the outside world. The retina is part of the brain as it embryonically derives from the neural tube. It is also the most accessible part of the brain because it is anatomically separate from the rest of the brain and it can be readily stimulated by its natural input – light. Our understanding on anatomical and functional neural circuitry of the retina far exceeds our knowledge of any other parts of the brain, and the tremendous success of functional analysis of retinal circuitry during the past 4-5 decades was inaugurated by the landmark papers in 1969: Organization of Retina of the Mudpuppy, Necturus maculosus I: Synaptic Structure John E. Dowling and Frank S. Werblin, J. Neurophysiology, 32, 315-338, 1969; Organization of Retina of the Mudpuppy, Necturus maculosus, II: Intracellular Recording, Frank S. Werblin and John E. Dowling, J. Neurophysiology, 32, 315-338, 1969. In these papers, Werblin and Dowling made the first complete set of intracellular recordings of light responses from all known types of retinal neuron, and for the first time, defined the receptive field properties of these cells. They discovered the ON-center/OFF surround and OFF-center/ON-surround bipolar cells, which initiate the ON and OFF channels and the center-surround antagonistic receptive fields that are found to be the fundamental units for spatial information processing in retinal ganglion cells, LGN and cortical neurons. They also found that the output synapses of interneurons in the outer and inner retina (horizontal cells and amacrine cells) mediate surround responses of bipolar organizational plan for all vertebrate retinas and has served as the guidebook for retinal network analysis until now.

SupportSight℠ Program

Linking patients, caregivers and families affected by diseases of the retina with the most up-to-date information and knowledge.

Over four days in March 2016, the International Retinal Research Foundation partnered with the EyeSight Foundation of Alabama to bring free SupportSight℠ Seminars on age-related macular degeneration to Huntsville, Birmingham, Montgomery and Mobile, Alabama. These seminars, conducted by the Macula Vision Research Foundation (MVRF), a Pennsylvania based non-profit organization, were open to the public and led by local retina specialists, low vision experts, other healthcare professionals and vision scientists.

Focusing on the latest information on advancements in treatment of AMD, these programs also provided practical strategies to enable the participants to live more comfortably and to maintain their physical and emotional well-being. The MVRF has been providing these seminars for over 15 years to more than 40,000 participants. Overall, 262 individuals attended from Alabama.

Experimental Eye Research

Astrocyte structural reactivity and plasticity in models of retinal detachment, Gabriel Luna, Patrick W. Keeley, Benjamin E. Reese, Kenneth A Linberg, Geoffrey P. Lewis, Steven K. Fisher. Neuroscience Research Institute, University of California, Santa Barbara; Center for Bio-image Informatics, University of California, Santa Barbara. (March 2016)

This study was conducted with IRRF support – Geoffrey Lewis and Steven Fisher.

◀ Access this article

Drs. Geoffrey Lewis and Steven Fisher and Gabriel Luna, BA, Research Specialist with the Neuroscience Research Institute.

ABSTRACT:

Although retinal neurodegenerative conditions such as age-related macular degeneration, glaucoma, diabetic retinopathy, retinitis pigmentosa, and retinal detachment have different etiologies and pathological characteristics, they also have many responses in common at the cellular level, including neural and glial remodeling. Structural changes in Müller cells, the large radial glia of the retina in retinal disease and injury have been well described, that of the retinal astrocytes remains less so. Using modern imaging technology to describe the structural remodeling of retinal astrocytes after retinal detachment is the focus of this paper. We present both a review of critical literature as well as novel work focusing on the responses of astrocytes following rhegmatogenous and serous retinal detachment. The mouse presents a convenient model system in which to study astrocyte reactivity since the Müller cell response is muted in comparison to other species thereby allowing better visualization of the astrocytes. We also show data from rat, cat, squirrel, and human retina demonstrating similarities and differences across species. Our data from immunolabeling and dye-filling experiments demonstrate previously undescribed morphological characteristics of normal astrocytes and changes induced by detachment. Astrocytes not only upregulate GFAP, but structurally remodel, becoming increasingly irregular in appearance, and often penetrating deep into neural retina. Understanding these responses, their consequences, and what drives them may prove to be an important component in improving visual outcome in a variety of therapeutic situations. Our data further supports the concept that astrocytes are important players in the retina's overall response to injury and disease.

To access this article:

http://dx.doi.org/10.1016/j.exer.2016.03.027http://dx.doi.org/10.1016/j.exer.2016.03.027

2016 Loris and David Rich Postdoctoral Scholar Recipient

Saumil S. Sethna, PhD

University of Maryland, School of Medicine

Project Title:

CIB2 in the retina: cell types, function and molecular mechanism.

Baltimore, Maryland

Dr. Sethna joined the lab of Zubair M. Ahmed, PhD, in the Department of Otolaryngology – Head & Neck Surgery at the University of Maryland in March 2015, working as a research fellow. The main focus of research in Dr. Ahmed's lab is Usher syndrome, an autosomal recessively inherited disorder characterized by deaf-blindness. In 2012, Dr. Ahmed's lab reported mutation in Cib2 (an encoded calcium-binding regulatory protein that interacts with DNA-dependent protein kinase catalytic subunits and is involved in photoreceptor cell maintenance), causing Usher syndrome type I in humans. Since that time, Dr. Sethna has presented data revealing that Cib2 knockout mice have progressive loss of retinal function, and pathophysiology in the retinal pigment epithelium (RPE), including defects in phagocytosis. From this, Dr. Sethna hypothesized that loss of Cib2 leads to RPE Ca++ (calcium) imbalance that perturbs OS (outer segment) phagocytosis, RPE pathology and PR (photoreceptor) functional defects.

2016 Alston Callahan, MD Postdoctoral Scholar Recipient

Norimitsu Ban, MD

Washington University Department of Ophthalmology

Project Title:

Cholesterol Homeostasis in Age-related Macular Degeneration (AMD).

St. Louis, Missouri

Dr. Ban received his M.D. degree from Keio University School of Medicine, Tokyo, Japan in 2005. He then joined the graduate program at the prestigious Keio University Graduate School of Medicine, Tokyo, and completed his PhD in Cell Biology in 2014. His graduate research has been published in several high-impact peer-reviewed publications including *Experimental Gerontology, Experimental Diabetes Research and the Journal of Neuroscience.* Under the mentorship of Rajendra Apte, PhD, Director of Translational Research at Washington University, Dr. Ban is using his experience to conduct molecular research, as well as translate discoveries into the clinical realm as part of his vitreoretinal practice.

"I have no doubt that Norimitsu will excel as a clinician scientist, who in addition to his clinical expertise, will provide the bridge to translate fundamental discovery from the bench to the bedside," said Dr. Apte.

2016 Charles D. Kelman Postdoctoral Scholar Recipient

Sushil Dubey, PhD
University of Kentucky, Chandler Medical Center

Project Title:
Epigenetic regulation of autophagy by histone deacetylases in retinal pigment epithelium.

Lexington, Kentucky

Dr. Dubey attended Madurai Kamaraj University in Madurai, India, where he received a Master in Science degree and later completed a fellowship and received his PhD from Aravind Medical Research Foundation, also in India. Dr. Dubey's current focus is to attain experience in the emerging field of epigenetics, while supporting his interest in ocular biology. He is investigating the epigenetic regulation and transcriptional repression mediated through histone deacetylases in aging retina and age-related macular degeneration (AMD).

The groundwork for the proposed research was laid by identifying the altered expression of histone deacetylases in advanced dry AMD. Dr. Dubey's preliminary data indicates the role of these altered regulators in autophagy in retinal pigment epithelium. He feels his background in the field of ocular genetics and epigenetics, coupled with vast experimental skills, will prove to be an asset for the present research project. The proposed project aims to open translational avenues to advance dry AMD therapeutics while exploring the role of this epigenetic phenomenon in the aging retina.

Strong Partnerships Produce Increased Research Funding

The IRRF continues its support of multi-partner alliances that increase our funding capabilities for young scientists who are developing their independent research projects. New York-based Fight For Sight (FFS), and the IRRF have combined resources to provide two Grants-in-Aid awards — The International Retinal Research Foundation Award — that are offered and administered by FFS. These important funding opportunities allow recipients to compete for larger, multi-year grants from the NIH or other governmental private sources. The IRRF and FFS share a commitment to early-career scientists making this alliance more important than ever. Today's young researchers face many funding challenges and it is imperative they are given every support vehicle available.

The 2016 awardees are Kinga M. Bujakowska, PhD, Harvard Medical School, Massachusetts Eye and Ear; and Yannis M. Paulus, MD, Kellogg Eye Center, University of Michigan.

Yannis M. Paulus, MD
University of Michigan, Kellogg Eye Center

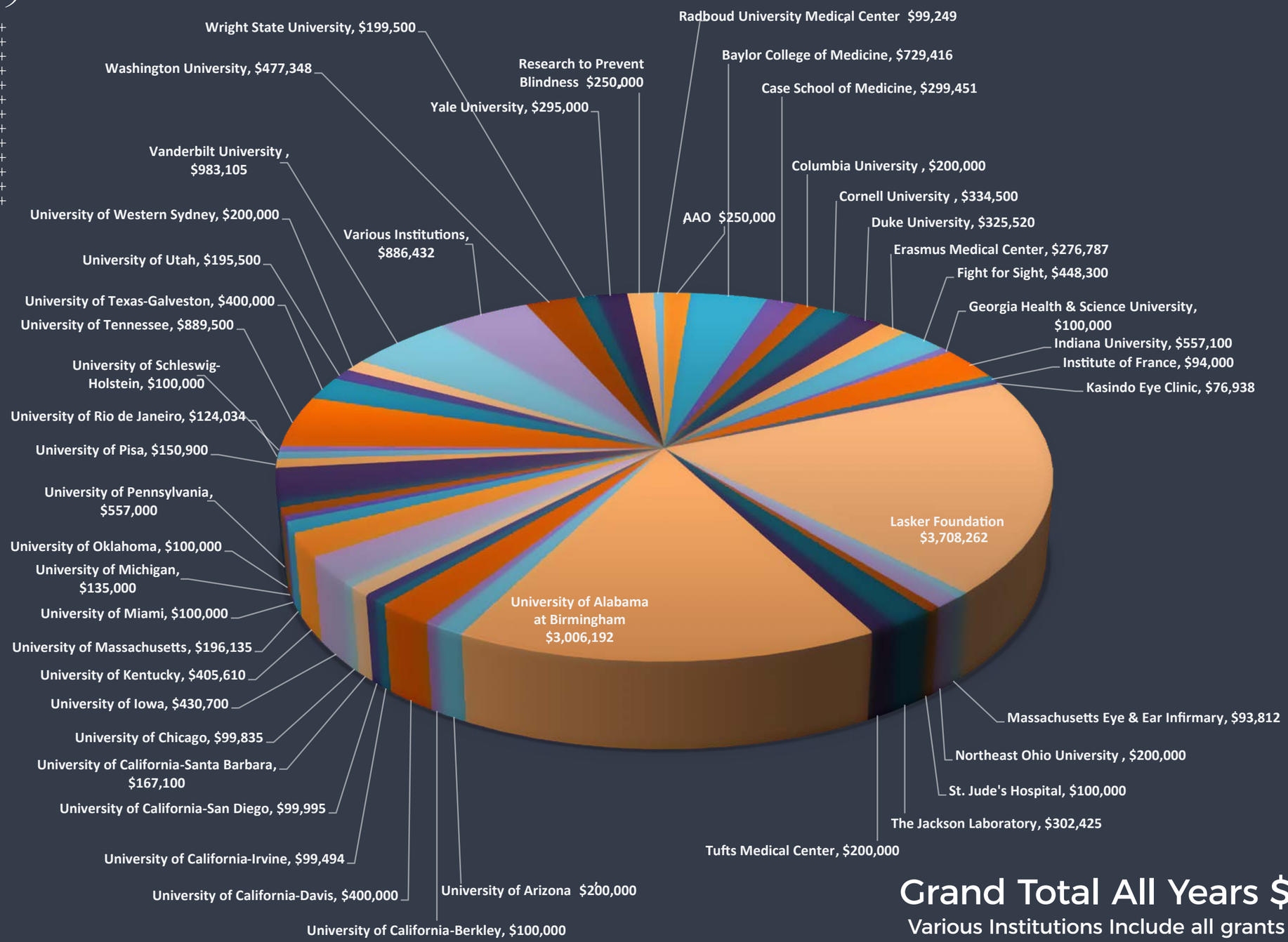
Dr. Paulus graduated from Stanford University School of Medicine in 2009, followed by an Internship at Memorial Sloan-Kettering Cancer Center, 2010; Ophthalmology residency at Stanford University School of Medicine, 2013; and a vitreoretinal surgical fellowship at Wilmer Eye Institute, Johns Hopkins University in 2015. Dr. Paulus's clinical practice specializes in retina and uveitis, with research interests in the development of novel retinal imaging systems and therapeutic techniques and technologies, including photoacoustic imaging, molecular imaging, restorative retinal laser therapy, and surgical techniques. The goal of his research is to allow physicians in real time to determine cellular markers for earlier diagnosis, improved treatment monitoring and more individualized precision medicine tailored to each patient's unique molecular markers.

Kinga M. Bujakowska, PhD
Harvard Medical School, Massachusetts Eye and Ear

After earning her PhD in Molecular Genetics, University College London, Dr. Bujakowska continued her training with a postgraduate diploma, Research Transfer and Biomedical Innovation, at the University of Paris VI, France. Dr. Bujakowska's research focuses on the genetics of inherited retinal degenerations (IRDs). In the past, her research has focused on the disease mechanism of a dominant form of retinitis pigmentosa (RP), caused by mutations in the splicing factor gene PRPF31. During her postdoctoral fellowships at the Institute de la Vision in Paris and Massachusetts Eye and Ear, she contributed to the discovery and characterization of five new disease genes, and discovered that mutations in IFT172 lead to isolated RP and Bardet Biedl syndrome. She has also participated in the development of genetic testing of patients with IRDs.

Dr. Bujakowska is currently working to discover further genetic causes of IRDs, and plans to develop tools to study the functional implications of mutations in the new candidate disease genes and participate in the development of therapies for these diseases.

The International Retinal Research Foundation Grants 1998 – Present



Grand Total All Years $18,019,054

Various Institutions Include all grants less than $75,000

UAB Connections

No one disputes the importance of scientific research into the causes and cures of the diseases that plague our society, however in focusing on these aspects of the problem, the needs of those who are afflicted are sometimes overlooked. During 2016, the IRRF supported a unique program that provides an urgently needed service not traditionally offered to patients with vision diseases.

UAB Connections (University of Alabama at Birmingham), is an expert-led health-education support group for patients with various eye conditions, including retinal specific diseases. Through this clinical service, UAB Connections helps patients and their families beyond medical and surgical treatment by providing skills to help them cope with the ongoing challenges of living with a vision impairment. The support group meets monthly at the Callahan Eye Hospital to hear from experts in the fields of Ophthalmology, low vision and rehabilitation during a structured discussion-based presentation. Additionally, patients, as well as their families, are engaged through monthly activities within the community that promote recreational and social interaction to prevent isolation, depression and withdrawal following vision loss.

One such activity funded by IRRF, and in part by the UAB Vision Sciences Research Center (VSRC), is 'Dinner in the Dark,' a dining experience at Rojo Restaurant that offers enhanced sensitivity and understanding toward those with impaired vision. In a controlled setting via simulation goggles, UAB ophthalmologists and optometrists, residents, and technicians, along with friends and families of the Connections member group, briefly experienced what it is like to live with a vision impairment. Sandra Blackwood, IRRF Executive Director, and Charlotte Bowers, IRRF Director of Operations, attended the event to get a firsthand understanding for how an everyday activity as eating can become a challenge. "It was very intimidating and a little scary at first," remarked Blackwood. "Until you become more confident, you are totally at the mercy of someone else, and that can be hard to accept."

Another aim of UAB Connections, is to provide community education outreach efforts on retinal and other eye diseases. Education efforts are conducted to inform UAB residents/doctoral students, physicians, technicians, community leaders and the general public on what it is like to live with a vision impairment and how to adapt.

For more information on UAB Connections, contact Molly Cox at mollycox@uabmc.edu or (205) 488-0778.

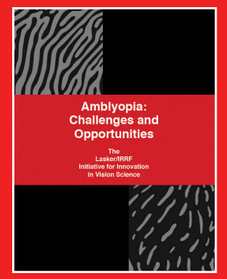
1 *Yoga instructor, Caitlin Justice, facilitated an adapted yoga class for the Connections members and their guests. Exercises included chair stretches, as well as modified sitting and standing poses. The health benefits of physical activity and the value of engaging regular, low-impact exercises to increase overall well-being were explained.*

2 *UAB Connections and the Campus Recreation Center partnered to offer two Beep Kickball tournaments. Sighted students, low vision Veterans, and UAB Connections support group members participated in an adapted game of kickball, in which the ball contains a beeper and the kicker and team members are blindfolded to simulate total blindness.*

3 *MAKEbhm hosted Connections group members to their ceramic studio for a hands-on clay throwing and pottery painting class. Group members were able to create their own piece of pottery under the direction of the studio owner. Raised patterns on the pre-fired cups served as a wonderful tactile guide for those who were painting and the pottery wheel allowed group members to try their hand at a novel craft.*

4 *Support group members tested out their abilities during a group painting class at Sips 'n Strokes. Each individual was allowed to choose from a variety of designs and then received guidanace from the instructor about how to choose contrasting colors and use bold outlines to make the painting more aesthetically pleasing to visually impaired viewers.*

5 *S. Blackwood, IRRF; Bernard Dib, MD, UAB ophthalmology resident; Molly Cox, UAB Connections Facilitator.*



2016 Lasker Awards

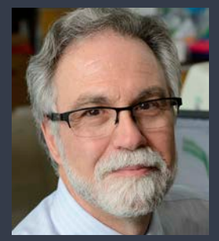
September 2016

The Albert and Mary Lasker Awards continue to be an integral component of the IRRF's collaboration with the Albert and Mary Lasker Foundation. These Awards provide support to outstanding scientists in the medical field by recognizing the contributions made through major advances in the understanding, diagnosis, treatment and prevention of human disease. Along with this support, the two Foundations have established the Lasker/IRRF Initiative for Innovation in Vision Science. For more information about the Awards Program, and to learn about the Lasker/IRRF Initiative for Innovation in Visions Science, please go to: www.laskerfoundation.org.

The 2016 Albert Lasker Basic Medical Research Award honored three physician-scientists for their discovery of the pathway by which cells from human and most animals sense and adapt to changes in oxygen availability – a process essential for survival.

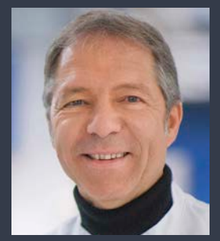
William G. Kaelin Jr.
Dana-Farber Cancer Institute, Harvard Medical School

Peter J. Ratcliffe
University of Oxford, Francis Crick Institute



Gregg L. Semenza
Johns Hopkins University, School of Medicine

The 2016 Lasker-DeBakey Clinical Medical Research Award was presented to Ralf F. W. Bartenschlager, Charles M. Rice and Michael J. Sofia for developing a system to study the replication of the virus that causes hepatitis C and used this system to revolutionize the treatment of this chronic, often lethal disease.



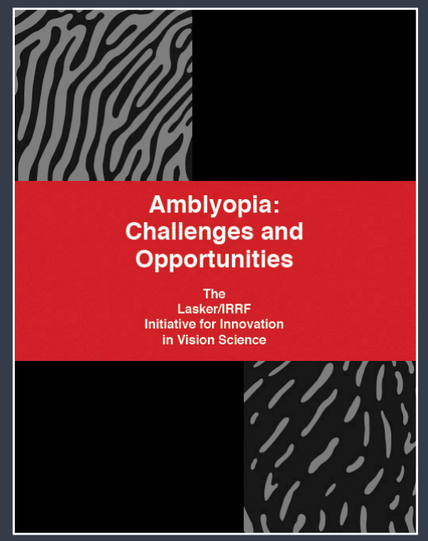
Ralf F. W. Bartenschlager
Heidelberg University

Charles M. Rice
Rockefeller University

Michael J. Sofia
Arbutus Biopharma

2016 Lasker-Koshland Award for Special Achievement in Medical Science honored Bruce M. Alberts for his fundamental discoveries in DNA replication and protein biochemistry; for visionary leadership in directing national and international scientific organizations to better people's lives; and for passionate dedication to improving education in science and mathematics..

Bruce M. Alberts
University of California, San Francisco



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The Lasker/IRRF Initiative for Innovation in Vision Science Amblyopia:

Challenges and Opportunities

The Lasker/IRRF Initiative for Innovation in Vision Science is a ten-year collaboration, launched in July 2008, between the Albert and Mary Lasker Foundation (Lasker) and the International Retinal Research Foundation (IRRF). The Initiative was designed to identify knowledge gaps in vision research and propose innovative strategies to accelerate the discovery of sight-saving treatments and methods to prevent diseases of the eye, especially retinal degenerative diseases, using novel scientific, engineering and technological approaches.

In late 2014, the Initiative's Joint Advisory Board decided that recent scientific advances provided a compelling opportunity to examine the scientific challenges in the field of amblyopia and to propose new approaches and novel treatments for this condition. Amblyopia is a disorder that results in varying degrees of monocular, or occasionally binocular, vision impairment, mainly in children; if not successfully treated, it can lead to permanent vision impairment for life. Its etiology and a precise definition have long defied science's best efforts, but we do know that risk factors for amblyopia include strabismus (crossed eyes), anisometropia (asymmetric eye focus), and deprivation (lens or lid defects). Amblyopia affects 1 – 3% of the population, though estimates vary widely because diagnostic and screening tools may not always be sufficiently comprehensive or available to all populations. How and when to treat amblyopia remains an ongoing challenge, and even whether innovative technologies can restore improved visual function in patients who were not treated when young remains an open question.

International Retinal Research Foundatic

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., M.D.,
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. Dr. Sternberg 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.

Larry A. Donoso, M.D., PhD., J.D.,
serves as Director of Research Education and heads up the Scholar Award program at the Foundation. Dr. Donoso has over four decades of bench and clinical research experience, which adds an important component to the combined talents of the IRRF Board of Directors. Holding degrees in chemistry, experimental biology, biochemistry/biology, medicine, and law, allowed Dr. Donoso to serve as Scientific Director when the Foundation was newly formed and has been a steadfast member of the board for 15 years.

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The IRRF 2016 ANNUAL REPORT

Sandra Blackwood, Editor
Photos: Sandra Blackwood
Larry Donoso, MD, PhD
Design: Robert T. Weathers

Become a benefactor

How You Can Help...

Today's scientists play a crucial role in the universal struggle against debilitating eye diseases, but they need financial funding to facilitate and sustain their efforts. Since 1998, the IRRF has granted more than $18 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:

The International Retinal Research Foundation, Inc.
Attn.: Sandra Blackwood, MPA, Executive Director
1720 University Boulevard
Birmingham, AL 35233

www.irrfonline.org