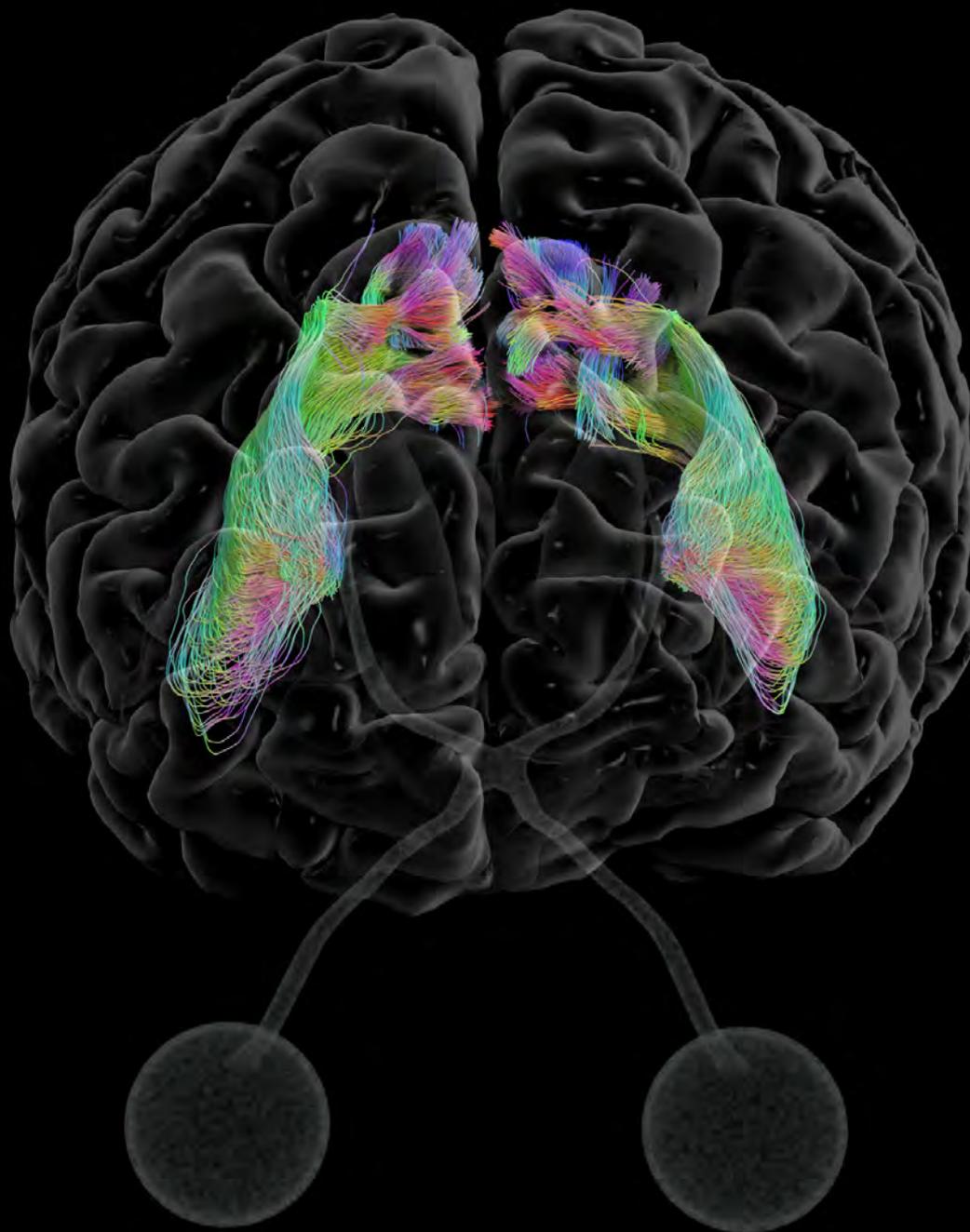


**USC** Roski Eye Institute

Keck Medicine of **USC**



# 2019 ANNUAL REPORT

KECK SCHOOL OF MEDICINE OF USC  
DEPARTMENT OF OPHTHALMOLOGY

# MESSAGE FROM THE CHAIR

The mission of the USC Roski Eye Institute is to provide exceptional clinical care, to train the future leaders in ophthalmology and to develop novel therapies in the fight against blindness. As our team educates tomorrow's medical leaders, we continue to be at the forefront of innovation through the convergence of medicine and science.

In 2019, the USC Department of Ophthalmology ranked #1 among all ophthalmology departments in the country in terms of federal NIH Funding. In research funding held by individual principal investigators, Arthur Toga, PhD; Paul Thompson, PhD; Mahnaz Shahidi, PhD; and Qifa Zhou, PhD, were respectively ranked 1st, 8th, 19th and 37th nationally in terms of NIH funding within ophthalmology departments. The Department has been nationally ranked in *U.S. News & World Report* for 26 consecutive years.

Through an integrative and multidisciplinary approach, our extraordinary dedicated team of clinicians, scientists, staff and trainees strive to provide exceptional patient care through state-of-the-art diagnostic services and innovative treatments. The USC Roski Eye Institute continues to offer treatments not widely available in the community, including management of complex retina, glaucoma, neuro-ophthalmology, and uveitis cases, Prosthetic Replacement of the Ocular Surface (PROSE) scleral lens, corneal cross-linking, and advanced keratoplasties such as Descemet's membrane endothelial keratoplasty (DMEK). In November, we proudly launched our Dry Eye Center of Excellence, one of the first centers to identify ocular surface disease biomarkers through the analysis of tear film.

The USC Ophthalmology Residency Program is nationally ranked in the U.S. by Doximity. With the expansion of our residency, fellowship, and hands-on teaching programs, we continue to strengthen our educational mission. Notably, we are grateful to our exceptional alumni who volunteer their time at LAC+USC Medical Center to mentor the next generation of ophthalmologists.

Eliminating blindness is far from impossible. It is what happens when all of the elements – science, innovation, perseverance, and compassion – come together that breakthroughs are made in service of our patients. We thank you for all of your continued dedication and support of our mission and look forward to the year ahead as we strive to develop new treatments and therapies to preserve, protect and restore vision.



A handwritten signature in black ink that reads "Narsing A. Rao".

**Narsing A. Rao, MD**

Grace and Emery Beardsley  
Professor in Ophthalmology  
Professor and Chair  
USC Department of Ophthalmology  
Keck School of Medicine of USC  
Co-Director, USC Roski Eye Institute



A handwritten signature in black ink that reads "Mark S. Humayun".

**Mark S. Humayun, MD, PhD**

Cornelius J. Pings Chair in Biomedical Sciences  
Co-Director, USC Roski Eye Institute  
Director, USC Ginsburg Institute for  
Biomedical Therapeutics

# YOUR VISION IS OUR MISSION

## PRESERVE

The USC Roski Eye Institute diagnoses, treats and manages the most complex eye conditions, from *in utero* to advanced age.

## PROTECT

The USC Roski Eye Institute leads major research in the diagnosis of eye disease with advanced imaging technology to help prevent blindness.

## RESTORE

The USC Roski Eye Institute integrates and applies emerging technologies to develop new methods to restore sight to the blind.



## SPECIALIZED CARE *for* ADULTS & CHILDREN

The USC Roski Eye Institute treats the full spectrum of eye conditions - from the most common to the most complex.

- CATARACT
- CORNEA & EXTERNAL DISEASES
- GLAUCOMA
- LASER VISION CORRECTION
- LOW VISION REHABILITATION
- NEURO-OPHTHALMOLOGY AND ADULT STRABISMUS
- OCULAR ONCOLOGY
- OCULO-FACIAL PLASTIC SURGERY
- OPHTHALMIC MOLECULAR AND IMMUNOPATHOLOGY
- PEDIATRIC OPHTHALMOLOGY
- SPECIALTY CONTACT LENSES AND PROSE
- UVEITIS AND OCULAR INFLAMMATION
- RETINA, VITREOUS AND MACULAR DISEASES & SURGERY

# USC DEPARTMENT OF OPHTHALMOLOGY

# #1

## IN NIH RESEARCH FUNDING AMONG OPHTHALMOLOGY DEPARTMENTS FY 2018

*\*Source: Blue Ridge Institute for Medical Research*

### Top NIH Principal Investigators



#1

Arthur Toga, PhD



#8

Paul Thompson, PhD



#19

Mahnaz Shahidi, PhD



#37

Qifa Zhou, PhD

Cover image: Portions of the connectome of central vision. Created from MRI diffusion tensor imaging data and tractographic reconstruction. Image by James Stanis, Yonggang Shi and Arthur Toga, Professor of Ophthalmology, Laboratory of Neuro Imaging, USC Stevens Neuroimaging and Informatics Institute.

# A New Dry Eye Center of Excellence

Millions of people suffer from the discomfort of dry eye syndrome. From irritation, redness, and sensitivity to light, dry eyes can make everyday life difficult. In August 2019, the USC Roski Eye Institute established the USC Dry Eye Center of Excellence. Here, a team of experts trained in ocular surface disease offer a multidisciplinary, personalized approach to treating specific dry eye causes and symptoms. Some of the treatments include prescription eye medication, broad band light therapy and tear film analysis.

## Treatments offered include:

- Broad Band Light Therapy (BBL)
- LipiView II ocular surface interferometer
- Prescription eye medications
- Punctal occlusion
- Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE) or scleral lens treatment
- Tear film analysis



Above: (1) The Dry Eye Center Team. (2) Dr. J. Martin Heur examines a patient. (3) Dr. Gloria Chiu consults with a patient.



Above: The Dry Eye Center of Excellence Grand Opening Ribbon Cutting. *L to R*: Keck School of Medicine Dean Laura Mosqueda, Center Co-Director Dr. Sarah Hamm-Alvarez, Department of Ophthalmology Chair Dr. Narsing Rao, Keck Medicine of USC CEO Rod Hanners, Center Director Dr. J. Martin Heur.

# International Ophthalmology

## Indochina



In 2009, Professor Narsing Rao met ophthalmology faculty and residents of the teaching hospital in Siem Reap, Cambodia, including Drs. Piseth Kong from Cambodia and Somsiri Sukavatcharintr from Thailand. Through their interactions, it became apparent that the ophthalmic education in Indochina was focused on cataract, diabetic retinopathy, and glaucoma. However, the students were not exposed to other diseases such as Intraocular Infections, Inflammations, and Uveitis, which are common in developing Asian countries. These disorders, if not diagnosed and treated properly, resulted in blindness.

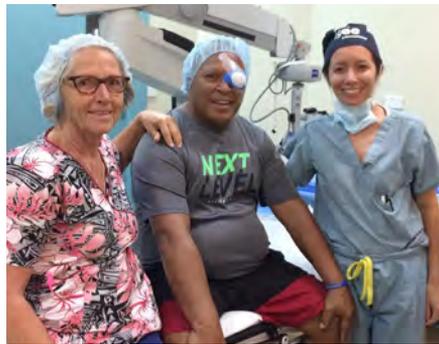
In 2010, the concept of the Indochina Ocular Inflammation and Infection Education Meeting was developed by Professor Rao with Drs. Kong and Sukavatcharintr. The major purpose: to provide current methods of diagnosis and treatment of the ocular inflammations and infections by experts from the USA, Europe, Japan, Thailand, India, Australia and the USC Roski Eye Institute. Moreover, to stimulate research collaboration on ocular inflammatory and immune processes and establish guidelines on the medical management and surgical approaches to the treatment of ocular infections and inflammatory diseases.

In 2012, the first Indochina meeting was organized in Siem Reap by Professor Rao and the Cambodian ophthalmological society. In an effort to educate as many students from the region as possible and compensate for lack of student travel funds, the meeting was planned so that the teachers traveled to the students.

Subsequent meetings have been held annually in Laos, Malaysia, Mongolia, Myanmar, Thailand, Vietnam, and again this year in Siem Reap, Cambodia.

In recent years, several ophthalmologists from Indochina developed an interest in the diagnosis and treatment of infectious uveitis entities. They became speakers and local leaders in the field and in teaching young ophthalmologists. Such change will assure long-term sustainability of the educational mission of the Indochina meetings. This will help with early diagnosis and interventions to prevent or minimize vision loss in patients suffering from uveitis and related intraocular inflammations and infections.

# Fiji



Dr. Grace Richter returned for the third time to the Taveuni Eye Project in rural Fiji this year. She joined other volunteers performing manual small incision cataract surgery (MSICS). MSICS is an ideal form of cataract surgery in developing regions that is highly cost-effective, performed manually without expensive equipment (the only needed electricity being for the operating microscope), yet uses an efficient and specialized surgical technique that can remove very

mature cataracts and creates a self-sealing sutureless wound. The effect of this annual project in Taveuni is numerous blind Fijians being given the gift of sight again. While Fiji has recently initiated a residency program graduating local Fijian ophthalmologists that perform MSICS, the need is still too great and they still rely on international volunteers to reduce the burden of treatable blindness.

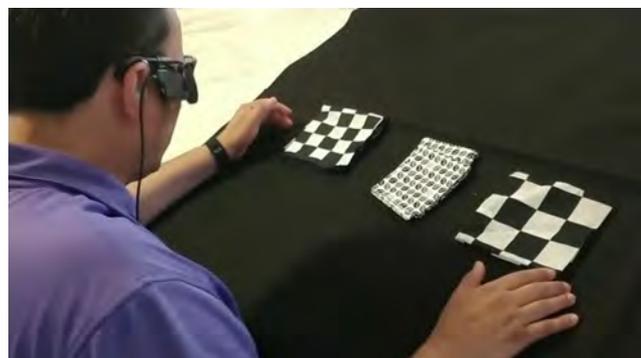
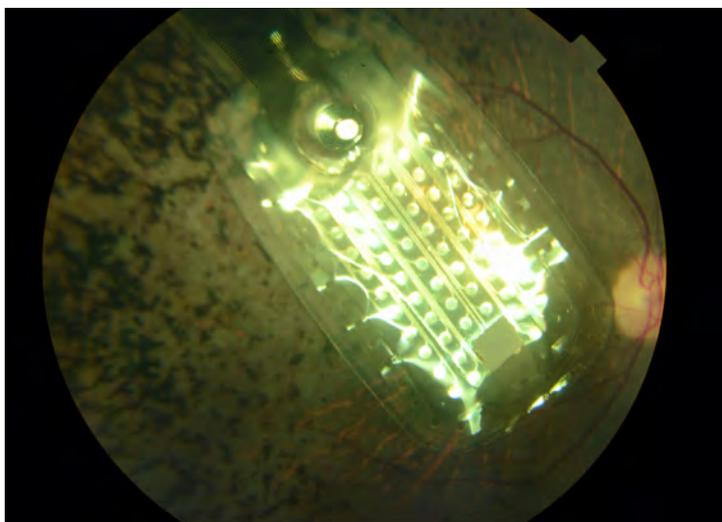
# Armenia



“We love all children equally.” As a faculty member of the USC Roski Eye Institute, Dr. Thomas C. Lee upholds this philosophy for all children who come through the doors of the Vision Center at Children’s Hospital Los Angeles. It doesn’t matter where a child lives, the Vision Center believes every child deserves to see the beauty of the world around them. But their desire isn’t limited to LA, California or even the nation. They also reach out to train doctors half way around the world to care for children in need. In partnership with the Armenian Eye Care Project, the Vision Center has trained ophthalmologists in Armenia to diagnose and treat a devastating form of childhood blindness. As Armenia’s healthcare systems have evolved, the pediatricians have saved premature babies that historically died but now survive with the advent of the latest technology and incubators. However, every new solution creates a new problem. As more premature infants survive, some develop a devastating form of childhood blindness,

Retinopathy of Prematurity (ROP). With no prior experience managing ROP, the eye doctors in Armenia were at a loss on how to diagnose or treat this devastating form of blindness. The Armenian Eye Care Project reached out to the Vision Center to establish a training program that would educate both ophthalmologists and neonatologists about this disease, how to diagnose, and then treat the more severe forms. In addition to annual workshops in the capital city of Yerevan, Dr. Lee and his team have supervised them remotely using a specialized retinal camera that would take images of the babies in Yerevan and then upload them to the Internet, which they could then review remotely. As a result of this partnership, the rate of blindness from ROP has dropped significantly and now the Armenian doctors are training ophthalmologists in the neighboring countries as a way to give back and pay it forward.

# Light After Years of Darkness



*Left: The electrode array part of the Argus that is fixed onto the retina is about 10x5 mm. The edge of the electrode array touches the optic nerve head. Above: Christopher wearing his glasses. With the Argus turned on, he can differentiate different size patterns of a checkerboard.*

Christopher Sanchez was born with Usher Syndrome Type 2, an eye condition that affects the light-sensitive cells in the retina. His eyesight worsened throughout his youth until he went blind at age 27. He spent the next 20 years in darkness.

Christopher's dream was to see his son's face. But for many years, the concept of a cure sounded impossible. However, when Christopher learned of the reputation of the USC Roski Eye Institute, he traveled with his wife from their home in Stockton, CA to Los Angeles, hoping to meet an ophthalmologist who could improve his vision.

He came under the care of Hossein Ameri, MD, PhD, the Director of the USC Retinal Degeneration Center. Through many tests and discussions, Dr. Ameri deemed Christopher a strong candidate for the Argus II – a cutting-edge device invented by Dr. Mark Humayun, Co-Director of the USC Roski Eye Institute that would be surgically implanted into Christopher's eyes.



**Hossein Ameri, MD, PhD**  
Assistant Professor of Clinical Ophthalmology;  
Director, USC Retinal Degeneration Center

“His eye was suitable,” Dr. Ameri said of the decision. “He seemed to be a great candidate in every respect.”

Dr. Ameri made sure Christopher understood what eyesight would be gained. He would not have strong enough vision for driving or recognizing faces, but would be aware of his surroundings.

The surgical team, led by Dr. Ameri, placed a belt around Christopher's eye and inserted an electrode array, the size of a microchip, into his eye and fixed it onto his retina. The video captured by the camera in Christopher's glasses transforms the electrical signals by a small video processing unit that wirelessly communicates with the electronics placed around his eye, allowing Christopher to see.

After surgery, Christopher can see many details he thought he would never see again. He can see the lights on a Christmas tree, the movement of a car, the shine of light hitting metal. Oftentimes, he will touch an object he sees for the first time in twenty years to remember that it is a table or a chair. He can tell when the train he uses to commute approaches the platform, when its doors open, and whether he needs to step up or down from the platform to enter. Most importantly, he can see the shape of his son's face.

“I waited for this surgery for many years,” Christopher said. “My family and I are so amazed and so happy with the level of care and perfect outcome with the results.”

# ACTIVE RESEARCH FUNDING - DECEMBER 2019

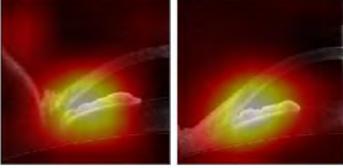
PRINCIPAL INVESTIGATOR	PROJECT	SOURCE
Hossein Ameri, MD, PhD	<i>Evaluating the Efficacy of Lipofectamine-CRISPR-Cas9 in Silencing VEGF-A Gene In Vitro</i>	USC
Jesse Berry, MD	<i>Development of a Surrogate Liquid Biopsy from the Aqueous Humor in Retinoblastoma Eyes</i>	NIH/NCI
David Cobrnik, MD, PhD	<i>Human Specific Signaling Circuitry in Cone Precursor Development</i>	NIH/NEI
David Cobrnik, MD, PhD	<i>Regulation of NCL and RdcVF in Cone Photoreceptor and Retinoblastoma Development</i>	RPB
Kimberly Gokoffski, MD, PhD	<i>Physiologic Electrical Fields Direct Optic Nerve Regeneration</i>	USC
Sarah Hamm-Alvarez, PhD	<i>Protein-polymer Nanomedicine for Sjogren's Syndrome</i>	NIH/NEI
Sarah Hamm-Alvarez, PhD	<i>Microtubule-Based Transport in Lacrimal Gland Function</i>	NIH/NEI
Sarah Hamm-Alvarez, PhD	<i>Expansion of Tear Biomarker Studies in Parkinson's Disease Patient Cohorts</i>	Michael J. Fox Foundation
Mark Humayun, MD, PhD	<i>PRPE-SF, Polarized hESC-derived RPE Soluble Factors, as a Therapy for Early Stage Dry Age-related Macular Degeneration</i>	CIRM
Mark Humayun, MD, PhD	<i>USC Roski Eye K12 Clinician-Vision Scientist Training Program (USC Roski Eye K12)</i>	NIH/NEI
Mark Humayun, MD, PhD	<i>EFRI CEE: Engineered Retinal Epigenomics</i>	NSF
Xuejuan Jiang, PhD	<i>Cumulative Effects of Sickle Cell Trait on the Eye among Older African Americans</i>	NIH/NEI
Xuejuan Jiang, PhD	<i>Intrauterine Exposure to Tobacco Smoke, DNA Methylation, and Vision Disorders in Preschool Children</i>	NIH/NEI
Amir Kashani, MD, PhD	<i>Imaging Cerebral and Retinal Microvasculature in Cerebral Small Vessel Disease</i>	NIH/NINDS
Amir Kashani, MD, PhD	<i>Assessment of Retinal Capillary Density, Morphology and Function in Retinal Vascular Disease Using Novel OCT Angiography Based Metrics</i>	NIH/NEI
Amir Kashani, MD, PhD	<i>Motor, Visual, and Olfactory Changes in Genetic Subtypes of Alzheimer's Disease</i>	NIH/NIA
Amir Kashani, MD, PhD	<i>Functional Imaging in Hypoxic-Ischemic Retinal Disease</i>	NIH/NEI
Gianluca Lazzi, PhD, MBA	<i>Predictive Modeling of Bioelectric Activity on Mammalian Multilayered Neuronal Structures in the Presence of Supraphysiological Electric Fields</i>	NIH/NIBIB
Gianluca Lazzi, PhD, MBA	<i>Connectome-Derived Computational Models of Degenerated Retina for Retinal Prosthetic Design</i>	NIH/NEI
Gianluca Lazzi, PhD, MBA	<i>EAGER: Bioelectronic Color Vision</i>	NSF
Andrew Moshfeghi, MD, MBA	<i>USC Roski Eye Institute - Vitreoretinal Surgery Fellowship Program</i>	Regeneron
Vivek Patel, MD	<i>Human Connectomes for Low Vision, Blindness, and Sight Restoration</i>	NIH/NEI
Narsing Rao, MD	<i>Photoreceptor Oxidative Stress in Uveitis</i>	RPB
Grace Richter, MD, MPH	<i>Defining the Relationships of Retinal Microcirculation with Glaucoma, Systemic Disease, and Ocular Anatomic Factors in African Americans</i>	NIH/NEI
Grace Richter, MD, MPH	<i>Role of Optical Coherence Tomography Angiography in Detecting Retinal Microcirculation Changes after Intraocular Pressure Reduction in Glaucoma</i>	USC
Mahnaz Shahidi, PhD	<i>In Vivo Molecular Imaging of Vascular Disease of the Retina</i>	NIH/NEI
Mahnaz Shahidi, PhD	<i>Imaging of Retinal Oxygenation and Metabolism</i>	NIH/NEI
Mahnaz Shahidi, PhD	<i>Center Core Grant for Vision Research</i>	NIH/NEI
Biju Thomas, PhD	<i>VRC: A Stem Cell-Based Treatment Strategy for Laser-Induced Permanent Retinal Damages</i>	NIH/NEI
Paul Thompson, PhD	<i>Enigma Center for Worldwide Medicine, Imaging &amp; Genomics</i>	NIH/NIBIB
Arthur Toga, PhD	<i>Data Archive for the Brain Initiative (DABI)</i>	NIH/NIMH
Benjamin Xu, MD, PhD	<i>Development and Validation of Quantitative Anterior Segment OCT-based Methods to Evaluate Patients with Primary Angle Closure Disease</i>	NIH/NEI
Sandy Zhang-Nunes, MD	<i>Therapeutic Applications of Ultrasound for the Prevention and Treatment of Dry Eye Disease</i>	USC
Qifa Zhou, PhD	<i>Non-Invasive Ultrasound Stimulated Retinal Prosthesis</i>	NIH/NEI
Qifa Zhou, PhD	<i>High-Resolution Elastographic Assessment of the Optic Nerve Head</i>	NIH/NEI
Qifa Zhou, PhD	<i>High Resolution Elastography of Retina Under Prosthetic Electrical Stimulation</i>	NIH/NEI
Qifa Zhou, PhD	<i>Large Aperture and Wideband Modular Ultrasound Arrays for the Diagnosis of Liver Cancer</i>	NIH/NCI
Siwei Zhou, MD	<i>Vascular Tortuosity at the Optic Nerve Head as a Surrogate Measure for ICP in IHH Using Optical Coherence Tomography Angiography and Optos Optic Nerve Imaging</i>	FFS/NANOS

AGS (American Glaucoma Society) • CIRM (California Institute for Regenerative Medicine) • DoD (Department of Defense) • FFS (Fight for Sight) • NANOS (North American Neuro-Ophthalmology Society) • NCATS (National Center for Advancing Translational Sciences) • NCI (National Cancer Institute) • NEI (National Eye Institute) • NHLBI (National Heart, Lung and Blood Institute) • NIBIB (National Institute of Biomedical Imaging and Bioengineering) • NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases) • NIH (National Institutes of Health) • NIMH (National Institute of Mental Health) • NINDS (National Institute of Neurological Disorders and Stroke) • NSF (National Science Foundation) • RPB (Research to Prevent Blindness)

# MULTIDISCIPLINARY COLLABORATIONS

## Extending Beyond the Department

With a multitude of USC departments, schools and institutions, USC Roski Eye Institute clinicians and researchers continue to advance vision research through dynamic collaborative initiatives.



Applying artificial intelligence to develop a unified platform for automated analysis of anterior segment OCT images

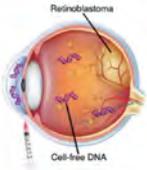
▶ Department of Biomedical Engineering



Brent Liu, PhD



Benjamin Xu, MD, PhD



Development of a Surrogate Liquid Biopsy from the Aqueous Humor in Retinoblastoma Eyes

▶ Department of Biological Sciences



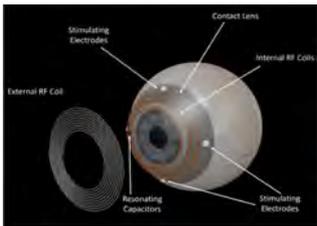
James Hicks, PhD



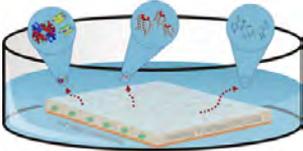
Peter Kuhn, PhD



Jesse Berry, MD



EFRI CEE: Engineered Retinal Epigenomics



PRPE-SF, polarized hESC-derived RPE Soluble Factors, as a Therapy for Early Stage Dry Age-related Macular Degeneration

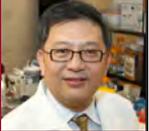
▶ Department of Pathology  
▶ Department of Pharmaceutical Economics and Policy  
▶ Department of Translational Genomics



David Hinton, MD



Dan Hong Zhu, MD, PhD



Stan Louie, PharmD



Bodour Salhia, PhD



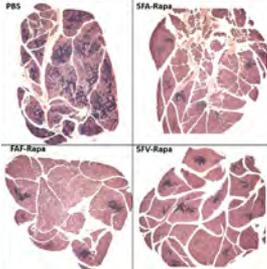
Mark Humayun, MD, PhD



Gianluca Lazzi, PhD, MBA



Expansion of Tear Biomarker Studies in Parkinson's Disease Patient Cohorts



Protein-polymer Nanomedicine for Sjogren's Syndrome

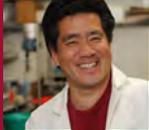
▶ Department of Neurology  
▶ Department of Pharmacology and Pharmaceutical Sciences  
▶ Department of Preventive Medicine



Mark Lew, MD



Wendy Mack, PhD



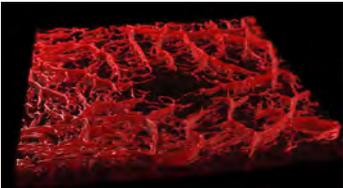
Curtis Okamoto, PhD



J. Andrew MacKay, PhD



Sarah Hamm-Alvarez, PhD



Laboratory of Neuro Imaging Resource (LONIR)

▶ USC Stevens Neuroimaging and Informatics Institute  
▶ Laboratory of Neuroimaging



Arthur Toga, PhD



Paul Thompson, PhD

# Research Progress

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The USC Ophthalmology Department received five new NIH RO1 grants in the 2019 calendar year.

## Recent NIH RO1 Grant recipients include:

**Xuejuan Jiang, PhD**, received a 5-year RO1 grant from the National Eye Institute to investigate biomarkers that relate exposure to maternal smoking during pregnancy to children's vision health and evaluate epigenome as a potential driver of differential susceptibility to pediatric ocular diseases.

**Amir Kashani, MD, PhD**, received a 5-year RO1 grant from the National Eye Institute to develop methods to detect and quantify preclinical changes in retinal capillaries of subjects with diabetes before the onset of diabetic retinopathy, thereby improving our ability to prevent irreversible changes associated with retinal ischemia.

**Gianluca Lazzi, PhD, MBA**, received a 3-year RO1 grant from the National Institute of Biomedical Imaging and Bioengineering to develop a modular,

integrated, multiscale computational modeling framework for the design of safe and effective peripheral neurostimulators. The proposed effort will consist of a) generation of computational models of peripheral nerves; b) development of the computational modules and platform; and c) experimental verification of the results.

**Biju Thomas, PhD**, received a 3-year RO1 grant from the National Eye Institute to study the use of a stem cell derived co-graft transplantation technique to repair permanent damage of the retina caused by a laser.

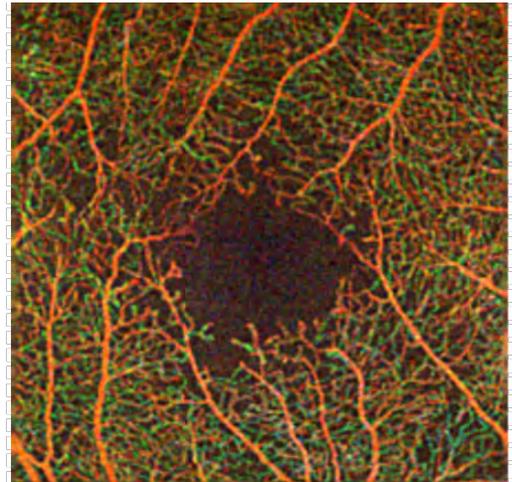
**Qifa Zhou, PhD**, received a 4-year RO1 grant from the National Eye Institute to investigate the biophysical mechanisms of ultrasound stimulation on retinal neurons, and to conduct functional testing of the ultrasound devices developed.



*Figure Legend:* Depth encoded wide field swept source optical coherence tomography (OCTA) of the human retina (PlexElite, Carl Zeiss Meditec Inc) provides high resolution and non-invasive images of the retinal capillaries. OCTA does not require injection of contrast dye into human patients and is therefore much safer and less costly than conventional fluorescein angiography. The technology can identify individual capillaries and detect the earliest changes in blinding retinal vascular diseases like diabetic retinopathy and age-related macular degeneration. Dr. Kashani's lab is leading the implementation of this technology in several ongoing human clinical trials.

# Research

## Detecting Diabetic Eye Disease Before Irreversible Damage Is Done



**Left:** Color fundus photograph of the retina in a diabetic subject cannot reveal capillary level changes that are occurring early in diabetic and vascular diseases. **Right:** Optical Coherence Tomography Angiography images can provide non-invasive, high resolution images of individual capillaries in the same subject showing microscopic vascular damage that is otherwise undetectable.

Diabetes mellitus (DM) and hypertension (HTN) are two common vascular diseases that ultimately lead to compromised blood flow in the retina and vision loss. Current tests for staging these diseases are not effective in detecting the earliest changes in the smallest blood vessels (capillaries) nor in detecting incremental capillary changes (improvement or worsening) in later stages of the disease. Dr. Amir Kashani's group at the USC Roski Eye Institute is implementing novel imaging methods using optical coherence tomography and optical coherence tomography angiography in human subjects to identify novel biomarkers of capillary loss or damage before subjects have vision loss or doctors can see changes in the eye during an examination. These technologies have the potential to improve the diagnosis and management of vascular retinal disease, thus preventing vision loss, decreasing cost and improving the quality of care for patients.

## A Novel Way to Biopsy an Aggressive Childhood Cancer

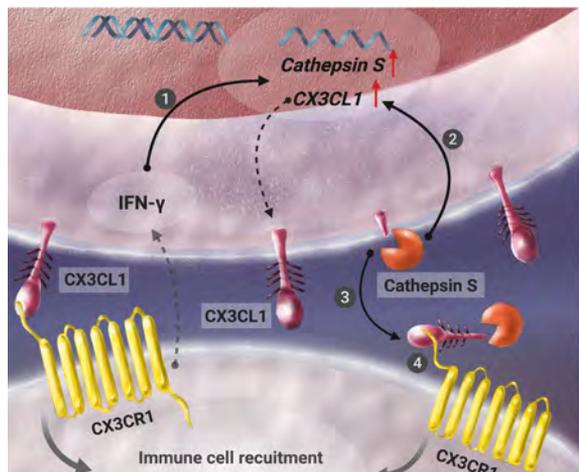
Unlike most cancers, retinoblastoma, a cancer that forms in the eyes of young children, cannot be directly biopsied due to the spread of the cancer outside the eye. To overcome this clinical problem, Dr. Jesse Berry focuses her research on a novel approach to creating a surrogate biopsy -- or liquid biopsy -- to detect RB tumor-specific DNA using the aqueous humor, the clear fluid in front of the eye.

The discovery of tumor DNA in the aqueous humor holds exciting potential for a molecular diagnosis, prognosis and possibly personalized treatment for children with retinoblastoma. This novel liquid biopsy technique has already identified a novel biomarker -- gain of chromosome 6p -- which is associated with an aggressive phenotype. These children are more likely to relapse after treatment and need the eye removed.

This was published in *Molecular Cancer Research*, an *American Association for Cancer Research Journal*. A recent publication in *Ophthalmology* further demonstrated that this biomarker could be isolated from the aqueous humor only, and not the blood.



# Cathepsin S Activity As a Driver of Aqueous Tear Deficiency in Sjögren's Syndrome



Research in the Hamm-Alvarez laboratory has explored the role of the cysteine protease, cathepsin S, in the development of the aqueous-deficient dry associated with the autoimmune disease, Sjögren's syndrome. Cathepsin S is increased in tears and in the tear-producing lacrimal gland, in Sjögren's syndrome. Activity of this protease may play a role in disease development. To test this, the Hamm-Alvarez laboratory recently utilized a murine disease model of tear deficiency in Sjögren's syndrome. They administered a specific inhibitor of cathepsin S in two forms to mice with established tear deficiency: systemically and topically. Administration through either modality suppressed lacrimal gland inflammation and improved tear flow, confirming a role for cathepsin S in disease development.

Cathepsin S is broadly implicated in inflammation. The Hamm-Alvarez laboratory has focused recently on its role in activation of a chemokine, fractalkine, in the lacrimal gland and on the ocular

surface in Sjögren's syndrome. Membrane bound fractalkine can be shed into the extracellular space by cleavage by different proteases, including cathepsin S, an event that increases migration of immune cells containing the fractalkine receptor to the site of cleavage. The Hamm-Alvarez laboratory has found that fractalkine levels are enhanced in tears, cornea and lacrimal glands of the murine model of Sjögren's syndrome. Fractalkine receptor-enriched immune cells are also increased in the lacrimal glands of diseased mice. Cathepsin S may thus contribute to inflammation by increasing local fractalkine in tissues of the ocular surface system, thus signaling to immune cells enriched in fractalkine receptor to migrate to the gland.

# Electrical Fields Direct RGC Axon Regeneration In Vivo

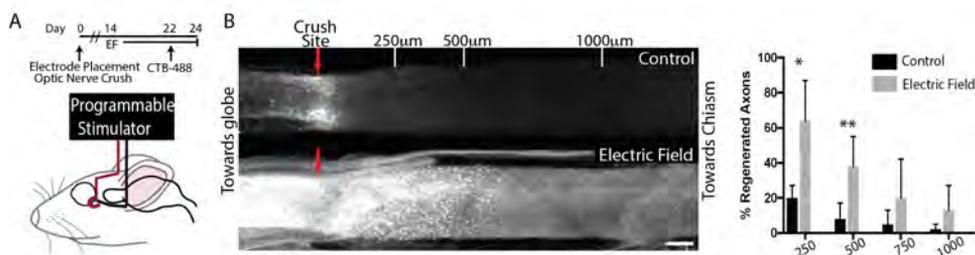
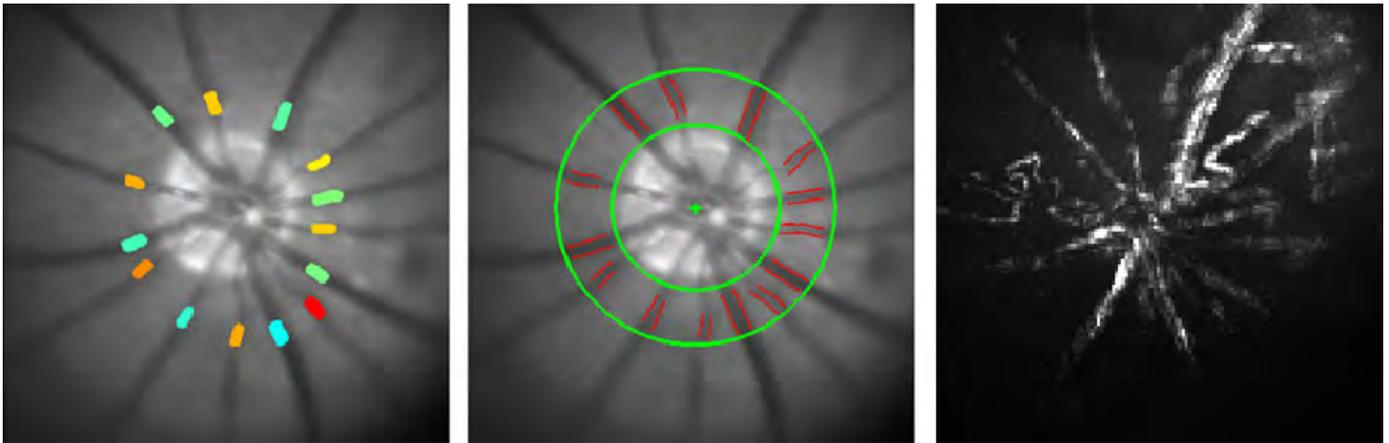


Figure 1: EFs direct RGC axon regeneration in vivo. A) Schematic of experimental timeline. Two weeks after crush injury, optic nerves were stimulated with an electric field for 10 days. Red line: anode, Black line: cathode. Anterograde labeling of regenerating retinal neurons was performed with Cholera ToxinB-Alexa488 (CTB-488). B) Rat optic nerves. Red line: crush site. White dots represent regenerated axons post optic nerve crush. Graph: % of regenerated axons at various distances from crush site (error bars=standard deviation), n=4. 100µm scale bar. \*p < 0.001; \*\* p < 0.05, one-way ANOVA.

It is estimated that 18 million people worldwide are legally blind from glaucoma, a disease that damages the optic nerve, the cable that connects the eye to the brain. Blindness is irreversible because the cells that make up the optic nerve, retinal neurons, have a limited capacity for self-repair and are incapable of regenerating. Although scientists have been able to use stem cells to produce new neurons to replace degenerated cells, when these healthy retinal neurons were injected into rodent eyes, they failed to make new connections with the brain. These experiments demonstrate that the native signals in the eye and optic nerve are unable to direct the growth of transplanted retinal neurons on their own.

Our research group, led by Dr. Kimberly Gokoffski, takes an innovative approach to this problem using electrical stimulation to direct retinal neuron growth. The body has naturally occurring electrical currents and they have been shown to play an important role in directing wound healing and tissue patterning during development. In tissue culture experiments, we have demonstrated that electric fields direct the growth of retinal neurons (Gokoffski et al. IOVS 2019). To test whether electric fields will direct growth of retinal neurons in living animals, we placed electrodes along the optic nerve of rodents whose nerves were previously injured via crush injury (Fig. 1A). Our preliminary data show that 10 days of electric field application directed significantly more regeneration of damaged retinal neurons over control animals (Fig. 1B). These results suggest that electrical fields may be an effective adjuvant for cell-transplantation based strategies, used to direct transplanted retinal neurons to regenerate the optic nerve and restore vision in patients blinded by glaucoma.

# Understanding Retinal Oxygen Dynamics in Retinal Diseases



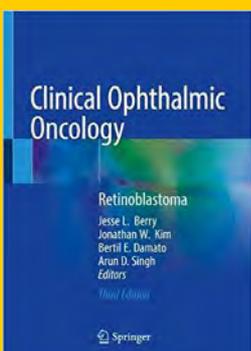
**Left:** Retinal arterial and venous oxygen tension measurements displayed in pseudocolor. **Middle:** Retinal vessel boundaries detected automatically are outlined on a red free image. **Right:** Projection image of fluorescent microspheres circulating in retinal vasculature.

The research program directed by Mahnaz Shahidi, PhD, Professor of Ophthalmology and Biomedical Engineering, targets comprehensive evaluation of retinal vasculature, hemodynamics, and oxygen metabolism in health and disease. Her research team is investigating disease mechanisms in experimental models coupled with conducting clinical research studies.

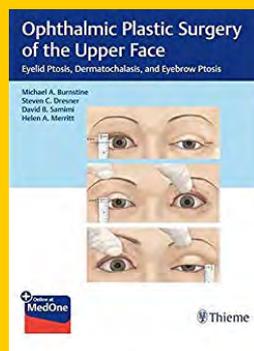
One of her ongoing translational research projects is focused on understanding retinal oxygen dynamics in experimental models of retinal diseases with the use of novel imaging technologies that she has pioneered. Oxygen supplied to the retinal tissue by the vasculature is necessary for cellular metabolism to maintain normal function. Derangements in retinal oxygenation have been implicated in a number of eye diseases, including vascular occlusions, diabetic retinopathy, retinopathy of prematurity, and glaucoma. Her research aims to gain knowledge of impaired oxygen availability and utilization to better understand the pathophysiology of retinal ischemia and thereby advance therapeutic interventions for retinal diseases.

Overall, the findings from her research studies impact the field by broadening knowledge of the pathophysiology of retinal diseases that is necessary for devising interventions for restoration of vision and prevention of vision loss.

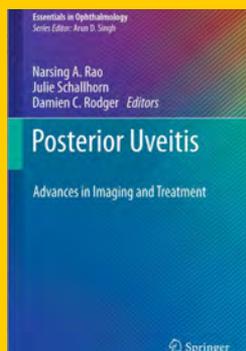
## Book-Length Faculty Publications



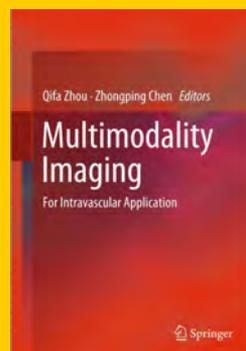
Jesse Berry, MD



Michael Burnstine, MD



Narsing Rao, MD



Qifa Zhou, PhD



Qifa Zhou, PhD

# Giving Back to the Community

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## Teen Innovation Entrepreneurship Program



The USC Roski Eye Institute hosted 25 local high school students in a two week eye health educational program as part of the Teen Innovation Entrepreneurship Summer Program. Faculty in ophthalmology introduced students to various eye conditions and the latest research and technology in eye care, as well as provided guidance for students interested in pursuing careers in ophthalmology.

Students participated in hands-on activities such as cow eye dissections and peer exams with diagnostic equipment. Students also learned about the global impact of ocular conditions and created solutions to help improve eye health in their local communities.

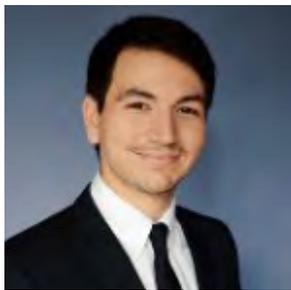
## LA Times Festival of Books Vision Screenings

In April of 2019, the USC Roski Eye Institute offered basic vision screenings and education at the *Los Angeles Times* Festival of Books for the fifth year in a row. Drs. Lernik Torossian, OD; Kent Nguyen, OD; and Jessica Chang, MD; along with staff and volunteers, set up at the Keck Medicine of USC Health Pavilion. Community members of all ages approached the booth with questions and left with a better knowledge of prescription glasses and various eye conditions.



## Medical Student Rotation

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**Medical students on our rotation (L to R):** Gabriel Sanz from University of Puerto Rico School of Medicine, Abinaya Thanappan from Columbia University College of Physicians and Surgeons, and Jessica Hsueh from Case Western Reserve University School of Medicine

The USC Roski Eye Institute offers a special ophthalmology training rotation available to medical students both nationally and internationally. Every year, medical students who have specific sub-specialty interests in ophthalmology are encouraged to apply. Selected medical students rotate three at a time from March through October. The program exposes them to clinical work, OR procedures, as well as other specialties.

The medical student rotation is part of our mission to serve as mentors to the doctors of tomorrow. Several students who participated in rotations have gone on to become residents in our program. Rotations are also available for optometry students. Currently, optometry students at Marshall B. Ketchum University in Fullerton, CA, rotate once a week for 10 weeks in our clinic.

# Education and Training

## RESIDENCY PROGRAM

Each year, hundreds of applicants compete for seven positions. In addition to clinical rotations at the **USC Roski Eye Institute**, training is also provided at **Los Angeles County+USC Medical Center (LAC+USC)**, **Children's Hospital Los Angeles (CHLA)**, and the **VA Downtown Los Angeles Medical Center**. With a total of 21 residents, we have positioned ourselves as one of the largest programs in the Western U.S.

## PROGRAM LEADERSHIP



**Narsing Rao, MD**  
*Professor and Chairman*



**Charles Flowers Jr., MD**  
*Program Director*



**Brandon Wong, MD**  
*Associate Program Director*



**Malvin Anders, MD**  
*Chief of Ophthalmology,  
LAC+USC Medical Center*

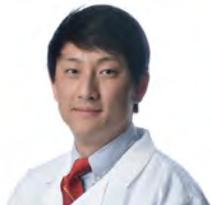
- Our residency program maintains its large volume of clinical material, consistently excellent hands-on training and high research output within the resident body. Our residents have been in the top 5% of programs nationwide for the past seven consecutive years in total ophthalmologic surgeries and procedures performed.
- Our residency continues to maintain one of the highest Accreditation Council of Graduate Medical Council (ACGME) resident survey results across all post-graduate programs at LAC+USC Medical Center.
- Our AUPO-compliant fellowship programs continue to thrive, with fellows from across the nation choosing our institute to further their subspecialty training.
- Our faculty are very involved in medical student education through lectures, workshops, hands-on teaching in the clinic and OR, and mentoring research projects. There is also a thriving ophthalmology student interest group that engages in several community outreach activities each year with faculty guidance, led by Dr. Jessica Chang, Director of Medical Student Education.



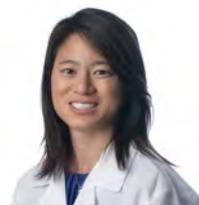
## 2019-2020 Graduating Residents



**Jennifer Danesh, MD**  
UCLA  
Los Angeles, CA



**Yong (Andy) Han, MD**  
Yale  
New Haven, CT



**Tiffany Ho, MD,  
Co-Chief**  
USC  
Los Angeles, CA



**Hadi Kaakour, MD, MS**  
University of Miami  
Miami, FL



**Ravi Shah, MD,  
Co-Chief**  
Baylor College of Medicine  
Houston, TX



**Jing (Meghan) Shan,  
MD, PhD**  
Harvard  
Cambridge, MA



**Younging Zhang, MD**  
USC  
Los Angeles, CA

## 2019-2020 Graduating Fellows



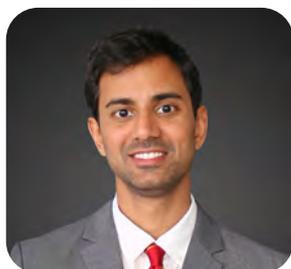
**Walid Abdallah, MD, PhD**  
Surgical Retina  
Zagazig Faculty of Medicine  
Zagazig, Egypt



**Justin Dredge, MD**  
Glaucoma  
SUNY - Stony Brook  
Stony Brook, NY



**Eric Hamill, MD**  
Oculoplastics  
Baylor College of Medicine  
Houston, TX



**Sagar Patel, MD**  
Surgical Retina  
UT Southwestern  
Dallas, TX



**Kristina Voss, MD**  
Cornea  
University of Arizona  
Tucson, AZ



**Siwei Zhou, MD**  
Neuro-Ophthalmology  
University of Pittsburgh  
Pittsburgh, PA

# Grand Rounds Case Study

## “SOMETHING SEEMS DIFFERENT”

### CHALLENGING EYE CARE



**Hong-Uyen Hua, MD**  
PGY-3 ophthalmology resident



**Andrew Moshfeghi, MD, MBA**

Associate Professor of Clinical Ophthalmology,  
Director of Clinical Trials  
Director of the Vitreoretinal Surgery Fellowship Program and  
Director of the Medical Retina Fellowship Program

#### HISTORY

- Chief complaint: sudden blurry vision
- 51 yo M with recently diagnosed acute promyelocytic leukemia complains of sudden blurry vision.
- Review of systems:
- No past ocular history, surgical history of open reduction internal fixation of the right leg in 1989, no pertinent family history
- Medications: ATRA (All Trans Retinoic Acid) – started 2 weeks prior to presentation, Idarubicin, Arsenic trioxide, Vancomycin for neutropenic fever

#### EXAM FINDINGS

- BCVA: count fingers at 3 feet OU
- Pupils round and reactive, no rAPD
- IOP 10 OD, 11 OS
- Brightness sense 50% OD, no red desaturation, color plates 1/8 OU
- Extraocular movements full
- Anterior segment exam unremarkable without signs of inflammation

#### DIFFERENTIAL DIAGNOSIS

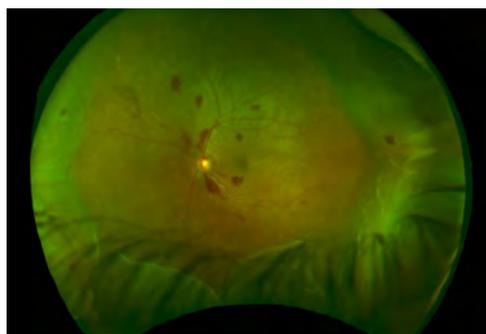
- Neoplastic (e.g. Leukemic infiltration)
- Medication induced
- Inflammatory (e.g. Vovt-Kayanagi-Harada disease)
- Infectious
- Vascular (e.g. Malignant hypertension)
- Surgical (e.g. Intraocular surgery)
- Idiopathic (e.g. Uveal effusion syndrome)

#### DIAGNOSIS

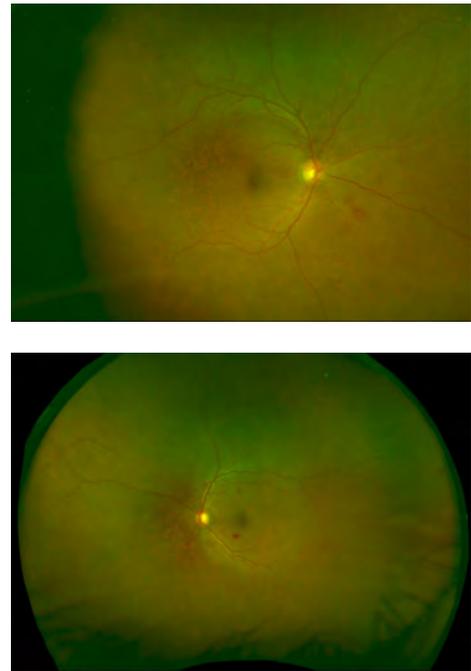
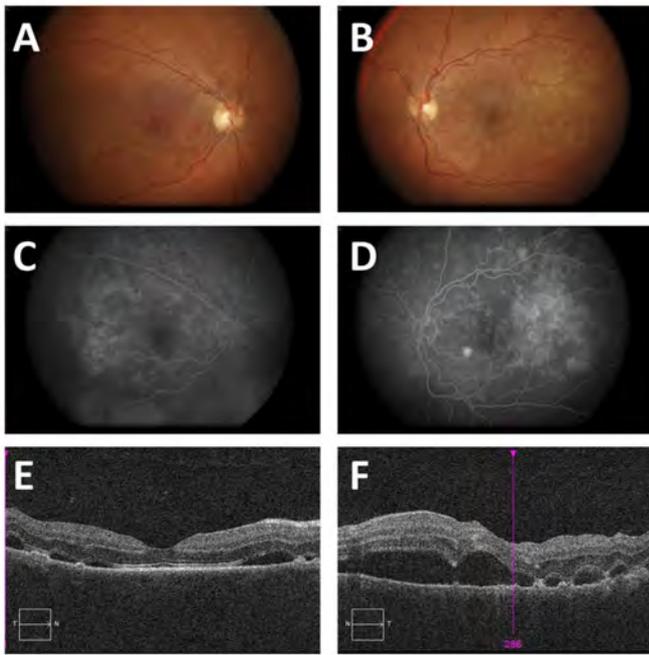
- The first reported case of bilateral choroidal effusions due to differentiation syndrome - a complication of all trans retinoic acid and arsenic trioxide
- Leukemic retinopathy

#### PATHOPHYSIOLOGY

- Differentiation syndrome occurs in the setting of induction therapy for acute promyelocytic leukemia with all trans retinoic acid (ATRA) and arsenic trioxide (ATO).
- Acute promyelocytic leukemia manifests with leukemic blast cell morphology, coagulopathy, and



*Above:* Colored Optos fundus photos of the right eye and left eye respectively, four days from presentation, demonstrate peripheral choroidal effusion with areas of stippled subretinal fluid in the macula, areas of scattered white-centered intraretinal hemorrhages, and hypopigmented mottling in the posterior pole.



Above: From the *American Journal of Ophthalmology Case Reports*, this is a 35 yo F with APL, started on ATRA who developed hypotension, tachycardia and developed acute renal impairment, peripheral edema and weight gain. (A, B) Fundus photographs showing multifocal, pale yellow lesions concentrated at the posterior poles. (C, D) Mid-phase fluorescein angiogram images show areas of early choroidal hyperfluorescence corresponding to the yellow retinal lesions with late leakage of fluid into the subretinal space (E, F) Optical coherence tomography demonstrates multiple small discrete areas of retinal pigment epithelial elevation adherent to the thickened outer retina with widespread multifocal areas of sub-retinal fluid. (Photos/*Am Journal of Ophthalmology Case Reports*).\*

Colored fundus photo of the right eye (above) and left eye (below) 6 weeks from presentation after brief cessation of ATRA and brief course of IV dexamethasone. ATRA had been restarted without complication. Fundus photos demonstrate resolution of the choroidal effusion and subretinal fluid with residual areas of stippled hypopigmentation in the macula. There are few residual white-centered intraretinal hemorrhages—improving signs of leukemic retinopathy.

- chromosome translocation t(15:17).
- Mainstay of induction therapy is ATRA and ATO
- Differentiation syndrome occurs in ~25% of patients receiving ATRA/ATO
- Our patient demonstrates, to our knowledge, the first case of bilateral choroidal effusions as an ophthalmic manifestation of differentiation syndrome

### TREATMENT

- Patient was started on dexamethasone 10 mg IV BID 2 hours later
- ATRA was held, arsenic trioxide was continued

### PROGNOSIS AND FUTURE DIRECTIONS

- Vision improved from count fingers to 20/70 and 20/50 in 4 days after treatment for differentiation syndrome
- 2 weeks later, choroidal effusions and subretinal resolved, with improving leukemic retinopathy
- 8 months later, patient is doing well on ATRA and ATO therapy with vision returning to 20/20 OU

### REFERENCES

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# TRAINING *the* NEXT GENERATION *at* LAC+USC

Residents at LAC+USC Medical Center engage in a rich learning environment seeing everything from trauma to complex neurological conditions involving the eye to common eye ailments, including diabetic retinopathy, cataracts, and glaucoma. They simultaneously manage the complex inpatient and emergency consult service for ophthalmology as well as run the busiest outpatient clinic in the hospital. Between 250-350 patients are seen in the ophthalmology clinic daily with 8-10 surgeries also being performed daily. Our residents come out of their three year residency with supreme experience and extraordinary skills prepared for any job or fellowship they desire.



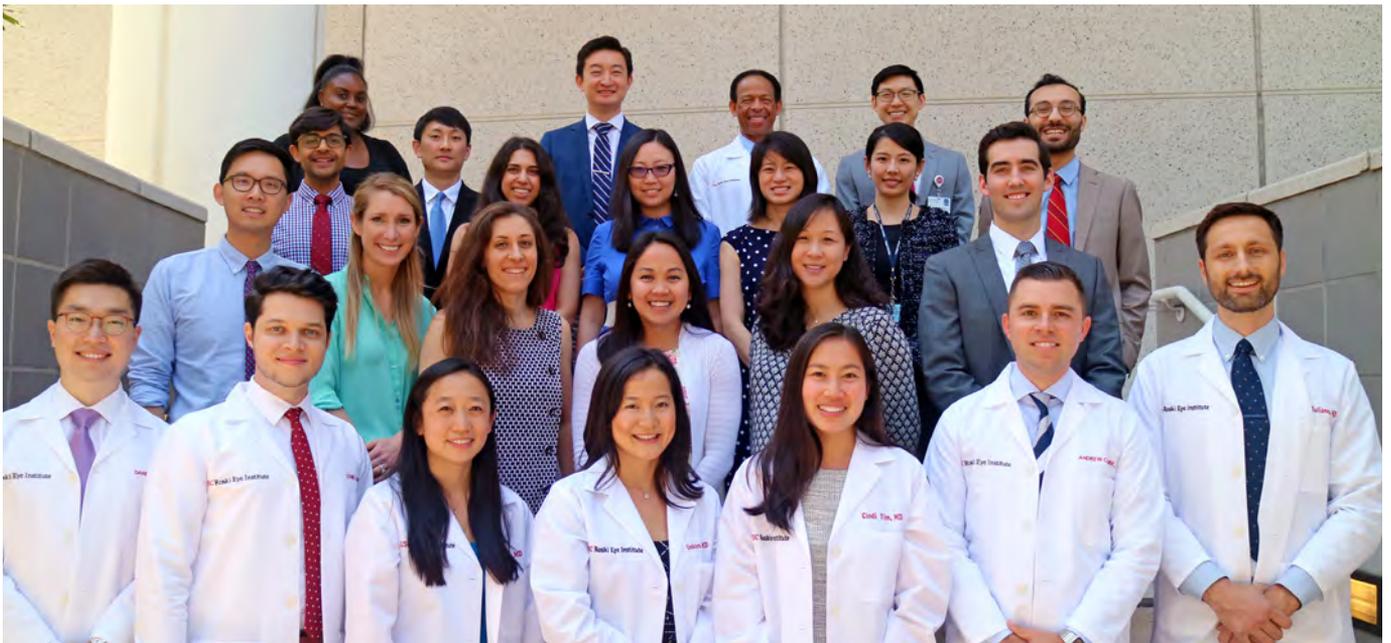
**LAC+USC**  
HEALTHCARE NETWORK

**FY 2018-2019**

**38.5K** Outpatients

**1.9K** Surgeries

**6** Ophthalmic subspecialties



# LAC+USC Ophthalmology Emeritus & Alumni Pay it Forward

## ALUMNI BY THE NUMBERS

**50** VOLUNTARY FACULTY

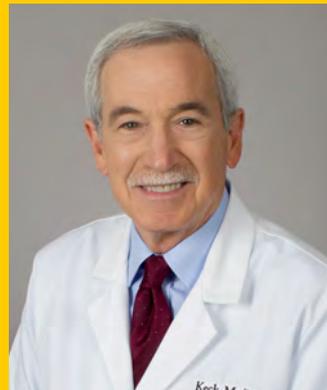
**16** DEPARTMENT CHAIRS

**272** RESIDENTS TRAINED

**300** FELLOWS TRAINED

*"It continues to be an honor and a privilege to participate in the training of residents and fellows."*

- Ronald Green, MD  
Professor Emeritus



*"Proud to support USC ophthalmology as a former resident, chief resident and faculty member."*

- Lawrence Chong, MD

*"USC residents, you are the best and you are the future. It is a pleasure helping you in the OR for the past 30 years."*

- Garlan Lo, MD



*"It's gratifying to share my training and experience with the talented Roski residents in the operating room today."*

- Paul Urrea, MD

*"Training at LAC+USC gives an incredible scope of learning that prepares our residents to be mentors and trusted doctors to our patients and colleagues."*

- W. Lee Wan, MD



# Celebrating 44 Years of PRESERVING, PROTECTING & RESTORING SIGHT



**2019 Laureate Award  
Dr. Paul A. Sieving**

Honored for his groundbreaking research and development of genetic treatments for retinal diseases

On Friday, June 15th, USC Roski Eye Institute faculty, staff, residents and fellows came together to celebrate the **department's latest innovations across all subspecialties of ophthalmology**, hosted at the Health Sciences Campus.

Highlighted topics included: advance retinal implants, the role of OCTA in clinical glaucoma, iridocorneal angle assessment methods, updates on electrical fields for neuro-regeneration, prism use in general and speciality clinics, gene therapy for leber congenital amaurosis, the role of vision in the assessment of concussion, and uveitis epidemiology.



**USC Roski Distinguished Lecturer Awardee  
Dr. Robert N. Weinreb**

for his lecture entitled "Smart Ophthalmology"

This year's speakers included several USC and CHLA ophthalmology faculty, including David Boyer, MD; Jessica Chang, MD; Melinda Chang, MD; Pravin Dugel, MD; Charles Flowers, Jr., MD, FACS; Kimberly Gokoffski, MD, PhD; J. Martin Heur, MD, PhD; Mark Humayun, MD, PhD; Michael Javaheri, MD; Thomas Lee, MD; Alfred Marrone, MD; Aaron Nagiel, MD, PhD; Vivek Patel, MD FRCSC; Grace Richter, MD, MPH; James Salz, MD; Lernik Torossian, OD, FAAO; Brian C. Toy, MD; Benjamin Xu, MD, PhD, and many others.



# Visit from Dr. Brian Hofland President of Research to Prevent Blindness



*Pictured L to R:*  
Dr. Brian F. Hofland,  
Dean Laura Mosqueda,  
and Dr. Narsing Rao

In December 2019, Brian F. Hofland, PhD, President of Research to Prevent Blindness (RPB), visited the USC Roski Eye Institute. Dr. Hofland toured several labs to view ongoing research and met with multiple faculty on the USC Health Sciences Campus. During the visit, he evaluated our research facilities, current NIH funding, mentorship of junior faculty, and the medical school Dean's support of department research.

RPB awarded Narsing Rao, MD, Professor and Chair, USC Department of Ophthalmology with a Research to Prevent Blindness unrestricted grant in 2018. The grant was renewed this past July.

"I enjoyed the visit and learned a lot," said Dr. Hofland. "I was gratified to see the Department building towards strong success on so many levels."

## Notable Accolades & Achievements

### **Jesse Berry, MD**

AAO 2019 Secretariat Award, American Academy of Ophthalmology  
AAO Achievement Award, American Academy of Ophthalmology  
Hope on Wheels Scholar, Hyundai  
Merit Award, The Saban Research Institute

### **Cheryl Craft, PhD**

2019 ARCS Light Recipient

### **Sarah Hamm-Alvarez, PhD**

Member, Bioengineering of Neuroscience, Vision and Low Vision Technologies Study Section

### **Mark Humayun, MD, PhD**

Medal for Innovations in Healthcare Technology, Institute of Electrical and Electronics Engineers (IEEE)

### **Gianluca Lazzi, PhD, MBA**

Fellow, National Academy of Inventors (NAI)

### **Aaron Nagiel, MD, PhD**

Baxter Foundation Awardee

### **Lernik Torossian, OD, FAAO**

California Young Optometrist of the Year Award, California Optometric Association

### **Benjamin Xu, MD, PhD**

Mentoring for Advancement of Physician-Scientists (MAPS) Award, American Glaucoma Society

### **Sandy Zhang-Nunes, MD**

Leadership Award, 2019 Los Angeles Multi-Specialty Cosmetic Academy

### **Qifa Zhou, PhD**

2019 Institute of Electrical and Electronics Engineers Ultrasonics, Ferroelectrics and Frequency Control Society (UFFC IEEE) Fellow

USC DEPARTMENT OF OPHTHALMOLOGY

#1

IN NIH RESEARCH FUNDING  
AMONG OPHTHALMOLOGY DEPARTMENTS

FY 2018

*\*Source: Blue Ridge Institute for Medical Research*



#11

HOSPITAL FOR OPHTHALMOLOGY  
IN THE NATION  
USC Roski Eye Institute

226  
PEER-REVIEWED  
PUBLICATIONS



#16

HOSPITAL IN THE NATION  
Keck Hospital of USC

The USC Roski Eye Institute and LAC+USC Medical Center see patients at the following locations:

**Keck School of Medicine of USC  
Department of Ophthalmology  
USC Roski Eye Institute**

1450 San Pablo Street, 4th Floor  
Los Angeles, CA 90033

(323) 442-6335

**USC Roski Eye Institute - Arcadia**

65 N. First Avenue, Suite 101  
Arcadia, CA 91006

(626) 446-2122

**USC Roski Eye Institute - Pasadena**

625 S. Fair Oaks Avenue, Suite 400  
Pasadena, CA 91105

(323) 442-6335

**USC Roski Eye Institute - USC Village**

835 W. Jefferson Boulevard, Suite 1720  
Los Angeles, CA 90089

(833) USC-EYES

**Children's Hospital Los Angeles**

**The Vision Center**

4650 Sunset Boulevard  
Los Angeles, CA 90027

(323) 660-2450

eye.keckmedicine.org  
#usceye

**USC Roski Eye Institute**  
Keck Medicine of USC



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Give the gift of sight today

eye.keckmedicine.org/giving/

For more information, please contact  
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Senior Director of Development  
(323) 442-5396  
Silviya.Aleksiyenko@med.usc.edu