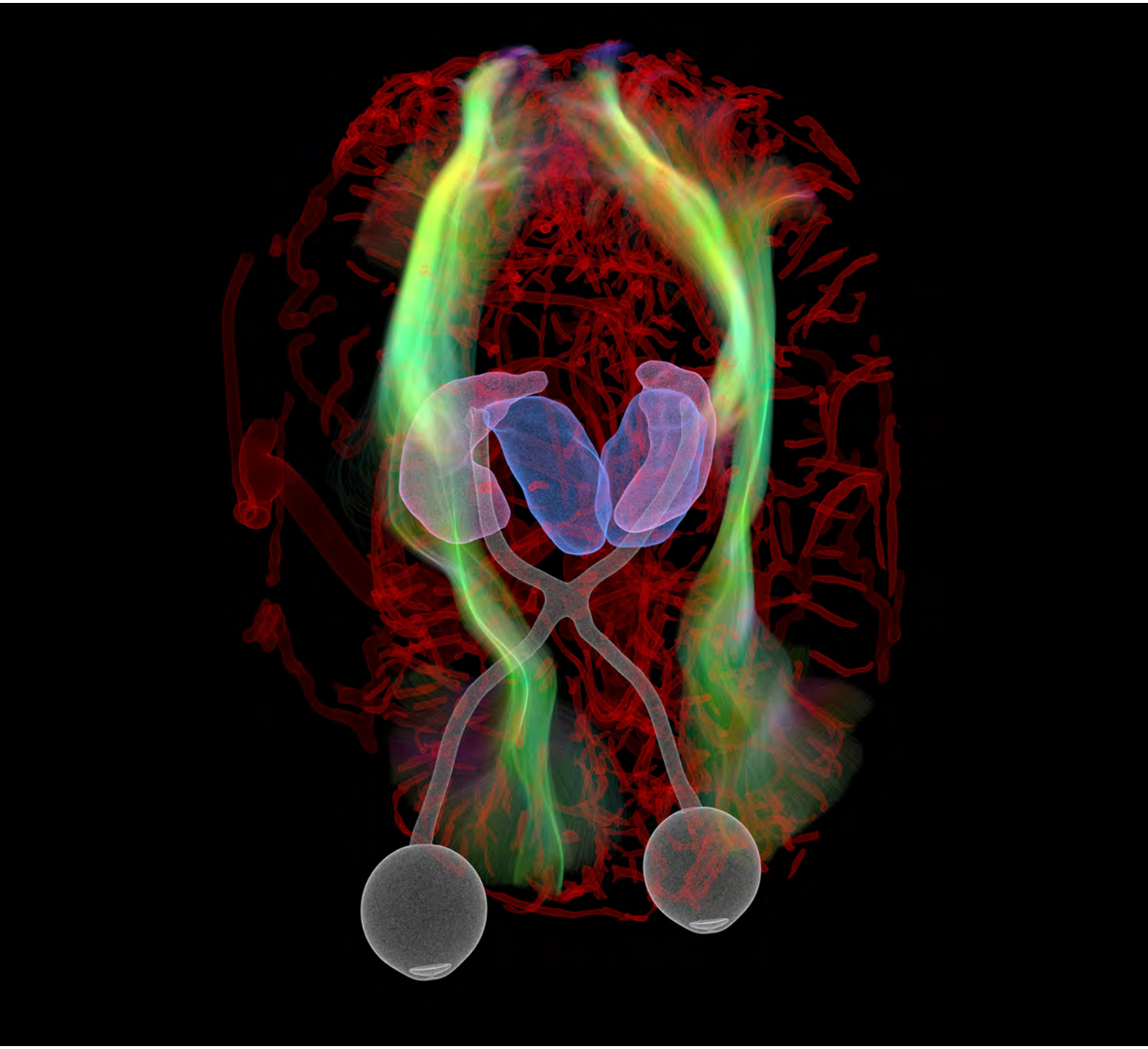
USC Roski Eye Institute

Keck Medicine of USC



2021 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, train the future leaders in ophthalmology, and 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 integration of medicine and science.

In 2021, the USC Department of Ophthalmology ranked #1 among all ophthalmology departments in federal NIH Funding, for the fourth year in a row. The department has been nationally ranked as **one of the top departments** in *U.S. News and World Report* for 28 consecutive years.

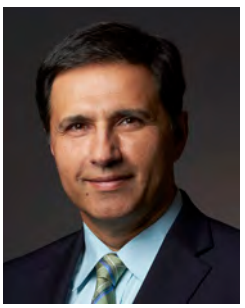
The LAC+USC Ophthalmology Residency Program is nationally ranked in the U.S. by Doximity. With the expansion of our residency, fellowship and hands-on teaching programs, we continue to strengthen our educational mission. We are grateful to our exceptional alumni who volunteer their time at LAC+USC Medical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

The USC Roski Eye Institute continues to offer treatments not widely available in the community, including the management of complex cornea, retina, glaucoma, neuro-ophthalmology, oculoplastic, and uveitis cases. This year, we also launched a new Visual Electrophysiology Unit (VEU) to aid in the detection of inherited retinal diseases.

In FY 20-21, the unexpected COVID-19 pandemic continued to hit the world. The USC Roski Eye Institute experienced clinical productivity loss similar to all other academic eye institutes in the country. However, our visit volume is gradually returning to 90% of pre-COVID volume.

This work could not have been achieved without the extraordinary collaborations of all of the Roski community. 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.

J. Martin Heur, MD, PhD
Professor and Interim Chair
Charles C. Manger III, M.D.
Chair in Corneal Laser Surgery
USC Department of
Ophthalmology
Keck Medicine of USC



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

Narsing A. Rao, MD
Grace and Emery Beardsley
Professor of Ophthalmology
Co-Director,
USC Roski Eye Institute
Keck School of Medicine

YOUR VISION IS OUR MISSION

PRESERVE

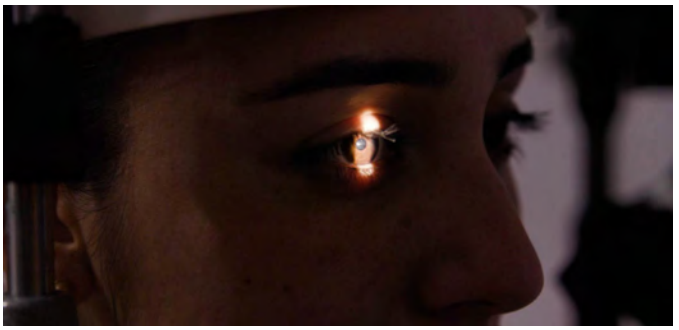
The USC Roski Eye Institute diagnoses, treats and manages the most complex eye conditions, from in utero to advanced age.

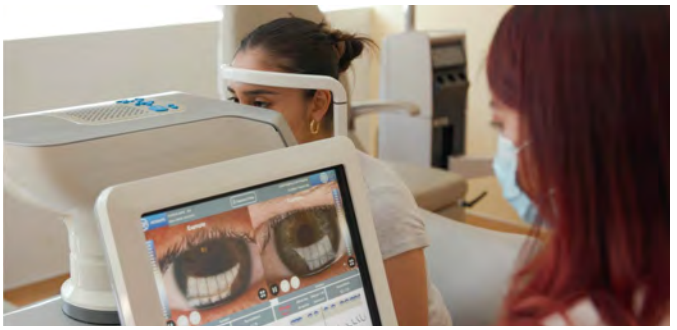
PROTECT

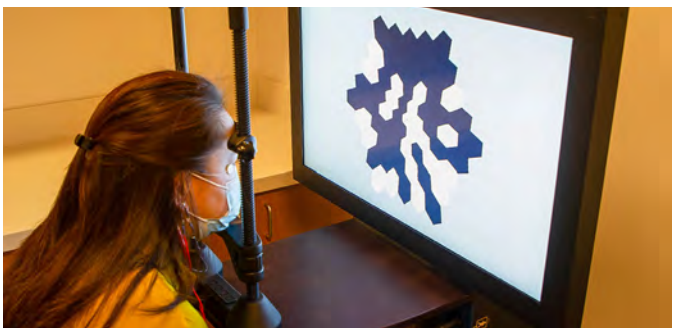
The USC Roski Eye Institute leads major research in the diagnosis of eye diseases with advanced imaging technology to help prevent blindness.

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 2020

Top NIH Principal Investigators

#1
Paul Thompson, PhD

#2
Athur Toga, PhD

#26
Mahnaz Shahidi, PhD

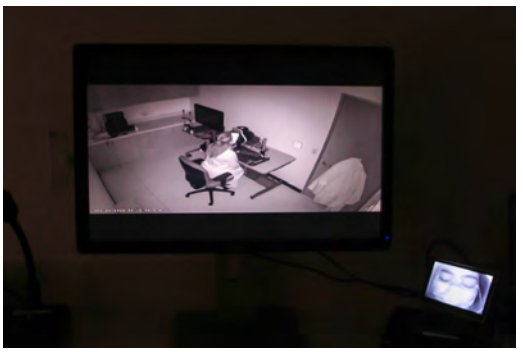
#38
Gianluca Lazzi, PhD, MBA

#43
Qifa Zhou, PhD

#58
Sarah Hamm-Alvarez, PhD

*Source: Blue Ridge Institute for Medical Research

New Visual Electrophysiology Unit



Pictured: A patient undergoes full field ERG, multifocal ERG and automated Goldmann visual field testing in the VEU.

The USC Roski Eye Institute opened its new Visual Electrophysiology Unit (VEU) to community physicians in 2021. Referring ophthalmologists may now directly refer their patients to the VEU for testing.

The VEU features state-of-the-art equipment that aids in the detection of inherited retinal diseases, such as retinitis pigmentosa, as well as optic nerve diseases, and a variety of other eye conditions. Among many advanced pieces of equipment, the VEU includes an ERG machine, which measures retinal function by recording electrical responses of the retina when light is shone into a patient's eye.

"Think of it like an electrocardiogram for the eye," said Dr. Hossein Ameri, Associate Professor of Clinical Ophthalmology, and the Director of the USC Retinal Degeneration Center, who spearheaded the creation of the VEU.

In addition to serving patients and the ophthalmic community, the VEU will service USC Roski Eye Institute's research and academic missions and will create a platform for investigating the pathophysiology of eye diseases. The VEU will also give residents and fellows access to the most modern versions of visual function tests and provide them with the opportunity to learn about advanced diagnostic tools.

Example of tests performed at the VEU include:

- Full field electroretinogram (ffERG), commonly called ERG
- Pattern electroretinogram (pERG)
- Multi-focal electroretinogram (mfERG)
- Flash visual evoked potentials (fVEP)
- Pattern visual evoked potential (pVEP)
- Electro-oculogram (EOG)
- Dark adaptometry
- Pupillometry
- Automated Goldmann visual field, including both kinetic perimetry and static perimetry
- Microperimetry
- Farnsworth Munsell 100 Hue color vision test

The Corneal Correction

How a Specialty Scleral Lens Restored a Patient's Sight

Pictured: Dr. Chiu removing PROSE device from Maria's eye.

Three years ago, an outside clinic diagnosed Maria Contreras with keratoconus, a degenerative eye disease that causes thinning and bulging of the cornea. Maria's deteriorating vision was affecting her daily activities. She was even told by her doctor that she might have to give up her drivers license.

"I knew their treatment wasn't working and I needed to do my own research," Maria said. "There had to be other options for me."

A friend, who'd received treatment for a similar condition at the USC Roski Eye Institute, recommended that Maria schedule a consultation with Dr. Gloria Chiu. Dr. Chiu is an optometrist who focuses on prescribing specialty contact lenses for various eye conditions, including keratoconus.

Dr. Chiu learned that Maria had only been prescribed glasses to correct her vision. "This surprised me because for many keratoconus patients, glasses don't work adequately once the condition becomes more advanced and the eye shape has become distorted. This is when specialty contact lenses or scleral lenses are required to best correct the vision."

Dr. Chiu at first fitted Maria with rigid gas permeable (RGP) contacts, but when Maria experienced dicomfort, Dr. Chiu then presented her with a PROSE treatment option.

"The moment I put them on, I started to cry," Maria said. "I knew this was something amazing."

Although PROSE offered a way to improve her vision, Maria faced another hurdle: her insurance would not cover the scleral devices. Fortunately, Dr. Chiu offered a new solution. In 2011, a former grateful patient of hers helped to establish the PROSE Care Fund, created to provide financial assistance for PROSE treatment to low income patients or to those whose insurance denied coverage.

Weeks later, Maria was approved and fitted with her custom PROSE lenses. "It has been a month now and I am able to drive comfortably and travel outside. I see the colors, details of flowers, people's faces, and how beautiful the world is. I cannot express how grateful I am."

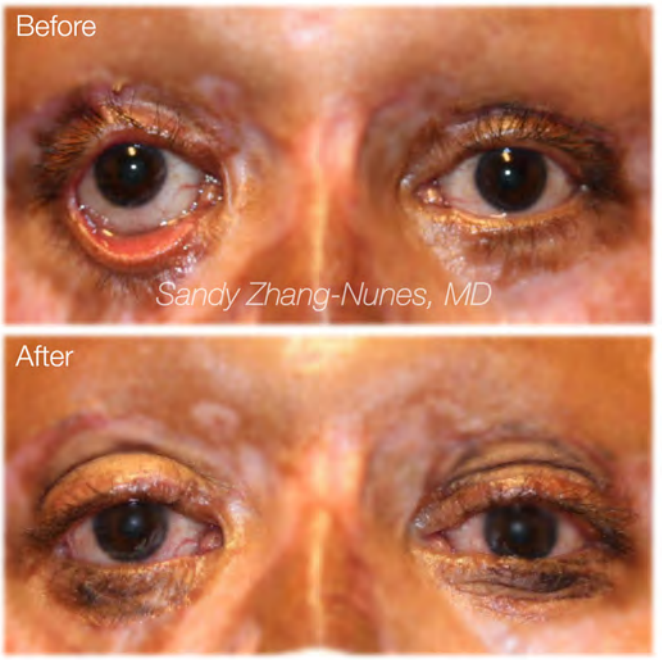
Dr. Chiu will continue to monitor and treat Maria's eyes. Although advanced keratoconus is currently a degenerative eye disease that cannot be reversed, the PROSE lenses have given Maria her life and sight back.

A longer version of this story originally appeared on our website.

Scan the QR code to read the full story:

The Ability to Blink

How Oculoplastics Saved a Burn Victim's Eyelids



Pictured: Bilateral eyelids skin grafting, ectropion, and retraction repair. Four months post-op right eyelids and two months post-op left eyelids

When Joe Cruz had a car accident in Northern California, burn marks left his face so devastated that he lost the ability to blink. He was in constant pain, frequently needed to apply ointment to his eyes, and could only sleep by rolling his eyeballs into the back of his head.

When he consulted with an ophthalmologist in Northern California, the eye doctor recommended eyelid repair surgery. However, because Joe was using Medi-Cal insurance, the doctor would not accept him as a patient. Joe's search for an ophthalmologist who could repair his eyelids led him all the way to Los Angeles, where he discovered Dr. Sandy Zhang-Nunes, the Director of Oculo-Facial Plastics Services at the USC Roski Eye Institute.

"When I first met Joe, he couldn't blink or protect his eyes," Dr. Zhang-Nunes recalls. "Without immediate treatment, he could have lost his eyes."

Dr. Zhang-Nunes repaired Joe's eyelids over the course of two surgeries; one for each eye. In both procedures, she took full thickness skin grafts to surgically reconstruct Joe's eyelids. "Because of the burns, I couldn't take skin from the areas I typically use, such as the other eyelid or behind the ear. The area inside his upper arm was the best skin to match with his eyelids."

Since skin naturally retracts as it heals, Dr. Zhang-Nunes needed to acquire enough extra skin tissue to allow Joe to shut his eyes completely once healed. "We needed to forecast exactly how long the eyelids would be once they healed, to ensure Joe could close his eyes and blink."

After waking up from the surgeries, Joe's eyelids were sutured shut for three weeks, which is why only one side was done at a time. As the surgical area healed, the stitches slowly dissolved, allowing Joe's eyelids to reopen.

"My vision and eyesight are now back to normal," Joe said, several months following the procedures. "Though I am very cautious about rubbing or touching them." Joe voiced his gratitude to Dr. Zhang-Nunes for accepting him despite his insurance. "She is probably one of the best doctors in California. I am blessed to have her in my life."

"I appreciated his positive outlook," said Dr. Zhang-Nunes. "He didn't give up and we weren't going to give up on him. We've done our best to help Mr. Cruz see better, look better, and feel better. That's my motto."

When Blindness Attacks

How Research and Cutting-Edge Clinical Techniques Saved a Woman's Sight

Pictured: Dr. Benjamin Xu wih Vanessa.

Vanessa Ho was beginning her Saturday morning when she suddenly felt intense pain and blurry vision in her right eye. She had experienced these symptoms before and knew that if left untreated, the attack would lead to glaucoma and permanent vision loss. She called the USC Roski Eye Institute to reach the ophthalmologist she had recently begun to see, Dr. Benjamin Xu.

Dr. Xu returned her call within minutes and requested that she come into the clinic. Once there, Dr. Xu used a laser peripheral iridotomy to break the acute attack and relieve the pressure buildup. The procedure proved successful. By that evening, Vanessa's eyesight was restored.

While the treatment proved a temporary fix to restore Vanessa's eyesight, she continued to see Dr. Xu and underwent cataract surgery to provide a permenant solution. "Dr. Xu treated me with passion and confidence, from his caring to his knowledge about closed angle glaucoma," Vanessa said.

Dr. Xu also leads an NIH-funded research lab that focuses on improving the care of patients with angle closure glaucoma. "While this is the second most common form of glaucoma, it is the most visually devastating," he said. "It's essential to research this disease because at-risk patients often go unnoticed by their doctors. It's the type of condition that you won't find if you don't look for it."

Dr. Xu's research group is developing new clinical tools to assist ophthalmologists in catching angle closure earlier. The Xu lab combines optical coherence tomography (OCT) with artificial intelligence to develop automated devices for detecting at-risk patients.These devices could one day serve as a replacement for gonioscopy.

The Xu lab is also currently using Big Data to clarify the impact of angle closure glaucoma in the U.S. "There have been few studies on angle closure glaucoma in the U.S. which has led to an underestimation of its impact on patients. Our results suggest that angle closure glaucoma is not only common in Asian-Americans, but Hispanics and African-Americans as well. We're working hard to raise awareness for people who are most vulnerable to the disease."

Dr. Xu collaborates with researchers from around the world to find new solutions to prevent people from developing angle closure glaucoma. "Patient awareness, early detection, and prompt treatment are the best tools we have to save people from angle closure glaucoma and permanent vision loss."

A longer version of this story originally appeared on our website.

Scan the QR code to read the full story:

Celebrating 45 Years of
Preserving, Protecting & Restoring Sight

Pictured (L to R): Awards received by Dr. Haller, Dr. Tsai, and Dr. McLeod.

On Saturday, June 12th, USC Roski Eye Institute faculty, alumni and guests came together to celebrate the department's latest innovations across all subspecialities of ophthalmology, hosted digitally on Zoom for the first time in the symposium's history.

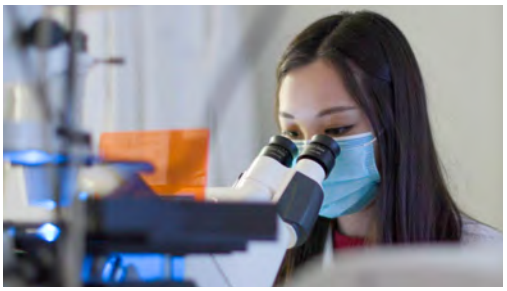
"This symposium has come to serve as a hallmark for our department and I know that this day will be one of knowledge sharing and growth for all of us," said J. Martin Heur, MD, PhD, Interim Chair of the Department of Ophthalmology, in his welcome remarks.

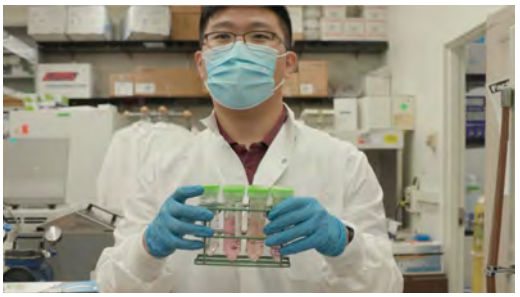
During the symposium, the USC Roski Eye Institute presented three awards:

- Julia Haller, MD, received the 2021 Laureate Award for her groundbreaking research in retinal pharmacology, macular surgery, retinal venous occlusive disease, diabetic retinopathy, age-related macular degeneration, the repair of complicated retinal detachments and health care disparities. The Laureate Award represents the highest honor bestowed on an individual in recognition of their academic achievements in the preservation, protection and restoration of vision.
- Stephen D. McLeod, MD, was recognized as a USC Roski Distinguished Lecturer and presented a lecture entitled, "DSAEK vs DMEK, Thinner or Thinnest?"
- James Tsai, MD, MBA, received the Alumni Award in recognition of his dedicated service and commitment to excellence in resident and fellow education.

Highlighted topics included: Dry AMD; Gene Therapy for Blinding Retinal Diseases; Gene Therapy for AMD; Systemic Health and Dry Eye; an Approach to Evaluating a Swollen Optic Disc; Glaucoma Management; Qualitative and Quantitative OCTA Metrics in Glaucoma; Glaucoma Detention in Telemedicine; an Update on Diabetic Retinopathy; Minimizing Hydroxychloroquine Toxicity; the Role of Digital Health, Telemedicine, and AI in Ophthalmology; Choroidal Melanoma; Retinoblastoma Treatment; and the Intersections of Oculoplastic and Dry Eye.

ACTIVE RESEARCH FUNDING - DECEMBER 2021





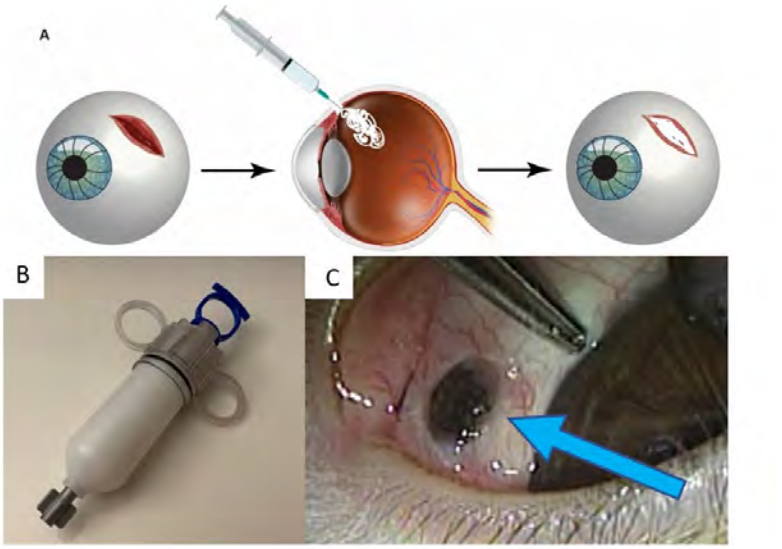
PRINCIPAL INVESTIGATOR	PROJECT	SOURCE
Jesse Berry, MD	Harnessing the Power of Data to Save Lives: Building the Retinoblastoma Data Commons	Children's Cancer Research Fund
Jesse Berry, MD	The Aqueous Humor Liquid Biopsy for Retinoblastoma: Evaluating Heterogeneity	Hyundai Hope On Wheels
Jesse Berry, MD	Comparing Blood to Aqueous Humor as a Liquid Biopsy for Retinoblastoma	CHECT
Jesse Berry, MD	Development of a Surrogate Liquid Biopsy from the Aqueous Humor in Retinoblastoma Eyes	NIH/NCI
Mark Borchert, MD	Validation of a Method of Functional Vision Assessment for Cortical Visual Impairment	Private Foundation Donor
Mark Borchert, MD	Developing Evidence-Based Criteria for Initiating Treatment for NF1-OPG	CTF
Melinda Chang, MD	Eye Tracking and Teller Acuity for Visual Assessment in Children with Cortical Visual Impairment (CVI)	BCC
Melinda Chang, MD	Validation of Eye Tracking in Children with Cortical/cerebral Visual Impairment (CVI) and Correlation with Neuropsychological Testing	TSRI
David Cobrinik, MD, PhD	Successive Responses to Oncogenic Aberrations in Retinoblastoma Genesis.	NIH/NCI
David Cobrinik, MD, PhD	Trans-cytoplasmic Transport of Repetitive Element DNAs	TSRI
David Cobrinik, MD, PhD	Repetitive Element DNAs in Bladder and Breast Cancer Liquid Biopsies	USC
David Cobrinik, MD, PhD, and Aaron Nagiel, MD, PhD	Predictive Medicine Inherited Retinal Dystrophy Gene Correction Program	KTEF
Kimberly Gokoffski, MD, PhD	Measurement of Vascular Tortuosity in IIH by OCTA and Optos	FFS/NANOS
Kimberly Gokoffski, MD, PhD	Electric Fields Collaborate with Cdc42 to Direct Optic Nerve Regeneration	BrightFocus Foundation
Kimberly Gokoffski, MD, PhD	In vivo Application of Electrical Fields Directs Retinal Ganglion Cell Axon Regeneration	NIH/NEI
Kimberly Gokoffski, MD, PhD	Electric Fields Collaborate with Rac1 to Direct Optic Nerve Regeneration	Baxter Foundation
Kimberly Gokoffski, MD, PhD	Novel, Large-Field Gradient, Electrical Stimulator to Accelerate Peripheral Nerve Regeneration into Split Thickness, Skin Graft Donor Sites	USC
Kimberly Gokoffski, MD, PhD	Bioengineered Neuro-Modulation for Neuroprotection and Neuro-regeneration	USC
J. Martin Heur, MD, PhD	Enhanced Preservation of Donor Corneas	OneLegacy
Sarah Hamm-Alvarez, PhD	Protein-polymer Nanomedicine for Sjogren's Syndrome	NIH/NEI
Sarah Hamm-Alvarez, PhD	Development of a Novel Tear-based Biomarker Assay for Diagnosis of Parkinson's Disease Using RT-QuIC	NIH/NIA
Sarah Hamm-Alvarez, PhD	Defining the Interplay of Interferon-gamma and Cathepsin S in Age-related Dry Eye	NIH/NEI
Sarah Hamm-Alvarez, PhD	Microtubule-Based Transport in Lacrimal Gland Function	NIH/NEI
Sarah Hamm-Alvarez, PhD	Characterization Of Recombinant Protein Expression In Hek293 T Cells	OysterPoint Pharma
Mark Humayun, MD, PhD	USC Roski Eye K12 Clinician-Vision Scientist Training Program (USC Roski Eye K12)	NIH/NEI
Mark Humayun, MD, PhD	PRPE-SF, polarized hESC-derived RPE Soluble Factors, as a Therapy for Early Stage Dry Age-related Macular Degeneration	CIRM
Mark Humayun, MD, PhD	EFRI CEE: Engineered Retinal Epigenomics	NSF
Mark Humayun, MD, PhD	EAGER: Engineered Nano-scale Barrier to Prevent Viral Infections	NSF
Xuejuan Jiang, PhD	Intrauterine Exposure to Tobacco Smoke, DNA Methylation, and Vision Disorders in Preschool Children	NIH/NEI
Xuejuan Jiang, PhD	Validation of Imaging and Blood-based Small Vessel VCID Biomarkers in Multiethnic Population	NIH/NINDS

Gianluca Lazzi, PhD, MBA	Predictive Modeling of Bioelectric Activity on Mammalian Multilayered Neuronal Structures in the Presence of Supraphysiological Electric Fields	NIH/NIBIB
Gianluca Lazzi, PhD, MBA	CRCNS: US-Spain Research Proposal: Computational Modeling of PNS Stimulation	NIH/NIBIB
Gianluca Lazzi, PhD, MBA; Mark Humayun, MD, PhD (Co-PI); Kimberly Gokoffski, MD, PhD (Co-PI)	GCR: Reprogramming Biological Neural Networks with Field-Based Engineered Systems	NSF
Juan Carlos Martinez, MD	Motor, Visual, and Olfactory Changes in Genetic Subtypes of Alzheimer's Disease	NIH/NIA
Aaron Nagiel, MD, PhD	Role of Non-canonical Wnt Signaling in the Developing Human Photoreceptor-bipolar Cell Synapse	RPB
Aaron Nagiel, MD, PhD	Hippo Pathway Inhibition for the Treatment of Geographic Atrophy	Thome Memorial Foundation
Aaron Nagiel, MD, PhD	Development and Maintenance of the Human Photoreceptor-Bipolar Cell Synapse	NIH/NEI
Aaron Nagiel, MD, PhD	Development and Maintenance of the Photoreceptor-Bipolar Cell Synapse in Human Retinal Organoids	TSRI
Narsing Rao, MD	Research to Prevent Blindness Unrestricted Grant	RPB
Grace Richter, MD, MPH	Defining the Relationships of Retinal Microcirculation with Glaucoma, Systemic Disease, and Ocular Anatomic Factors in African Americans	NIH/NEI
Mahnaz Shahidi, PhD	Imaging of Retinal Oxygenation and Metabolism	NIH/NEI
Mahnaz Shahidi, PhD	Center Core Grant for Vision Research	NIH/NEI
Mahnaz Shahidi, PhD	Imaging of Retinal Oxygen Metabolism in Diabetic Retinopathy	NIH/NEI
Mahnaz Shahidi, PhD	Retinal Vessel Features as a Marker of Idiopathic Intracranial Hypertension Treatment Response: A Secondary Analysis of the Idiopathic Intracranial Hypertension Treatment Trial	NIH/NEI
Mahnaz Shahidi, PhD	Two-photon Imaging of Oxygen and Blood Flow in Retinal and Cerebral Vasculature	NIH/NINDS
Noelle Stiles, PhD	Restoring Sight to the Blind: Neural Imaging with Retinal Prostheses	NIH/NEI
Biju Thomas, PhD	VRC: A Stem Cell-Based Treatment Strategy for Laser-Induced Permanent Retinal Damages	NIH/NEI
Biju Thomas, PhD	Integration and Functionality of Retinal Organoid Transplants	NIH/NEI
Brian Toy, MD	Health Disparities in the Development, Persistence, and Progression of Uveitis and Ocular Inflammation in the United States	NIH/NEI
John Whalen, PhD	Thermoreponsive Reversible Adhesive for Temporary Intervention of Ocular Trauma - II	DoD
John Whalen, PhD	Reversibly Adhesive Hydrogel for Temporary Treatment of Traumatic Open Globe Injury in Austere Environments	DoD
Brandon Wong, MD	Development of an Integrated Teleglaucoma Care Program for a Safety-Net Health System	AGS
Benjamin Xu, MD, PhD	Development and Validation of Quantitative Anterior Segment OCT-based Methods to Evaluate Patients with Primary Angle Closure Disease	NIH/NEI
Benjamin Xu, MD, PhD	Anatomical Mechanisms for Development and Progression of Primary Angle Closure Disease: A Cross-Sectional and Longitudinal Analysis	AGS
Benjamin Xu, MD, PhD	Development of Quantitative OCT-based Methods to Detect and Evaluate Biometric Risk Factors for Primary Angle Closure Disease	FFS
Benjamin Xu, MD, PhD	Treatment Patterns and Clinical Outcomes in Newly-Diagnosed Cases of Angle Closure With and Without Glaucoma: A Cross-sectional and Longitudinal Analysis	AGS
Liya Xu, PhD	Single Particle Analysis of Extracellular Vesicles in the Aqueous Humor of Retinoblastoma Eyes: Moving Towards an Integrated Liquid Biopsy	KTEF
Qifa Zhou, PhD	Combined OCT/US/PAT System for Intravascular Imaging	NIH/NHLBI
Qifa Zhou, PhD	Large Aperture and Wideband Modular Ultrasound Arrays for the Diagnosis of Liver Cancer	NIH/NCI
Qifa Zhou, PhD	High-resolution Elastographic Assessment of the Optic Nerve Head	NIH/NEI
Qifa Zhou, PhD	Non-invasive Ultrasound Stimulated Retinal Prosthesis	NIH/NEI
Qifa Zhou, PhD	Phase Resolved ARF Optical Coherence Elastography for Intravascular Imaging	NIH/NHLBI
Qifa Zhou, PhD	Biomechanical Mapping of the Optic Nerve Head and Peripapillary Sclera Using High Frequency Ultrasonic Elastography	NIH/NEI
Qifa Zhou, PhD	Super Resolution Ultrasound Blood Flow Imaging of the Posterior Eye for Glaucoma	USC

AGS (American Glaucoma Society) • BCC (Blind Children's Center) • CIRM (California Institute for Regenerative Medicine) • CHECT (Childhood Eye Cancer Trust) • CTF (Children's Tumor Foundation) • DoD (Department of Defense) • FFS (Fight for Sight) • KTEF (Knights Templar Eye Foundation) • NANOS (North American Neuro-Ophthalmology Society) • NEI (National Eye Institute) • NHLBI (National Heart, Lung and Blood Institute) • NIA (National Institute on Aging) • NIBIB (National Institute of Biomedical Imaging and Bioengineering) • NINDS (National Institute of Neurological Disorders and Stroke) • NSF (National Science Foundation) • OneLegacy (OneLegacy Foundation) • NCI (National Cancer Institute) • RPB (Research to Prevent Blindness) • TSRI (The Saban Research Institute) • USC (University of Southern California)

Research Progress

Smart Materials for Temporary Intervention of Ocular Trauma



From Concept to Prototype. (A) Schematic detailing how the disposable applicator that can control temperature is used to deploy the reversible hydrogel adhesive to temporarily seal a penetrating injury of the eye using limited resources. **(B)** Photograph of the first manufactured prototype applicator. **(C)** Rabbit eye with hydrogel sealant effectively applied (arrow) to close a puncture for 48hrs.

The Department of Defense's (DoD) military medical system has seen a steady increase in combat-related ocular injuries that peaked above 10% in the Middle East conflicts due to IED use by enemy combatants. Penetrating injuries cause the internal fluids of the eye's hollow structure to expel, which, if not treated quickly, can lead to retinal detachment, infection and permanent vision loss. With a desire to keep ocular surgeons and other medical specialists away from the front line, DoD has sought to identify novel techniques for temporarily stabilizing eye trauma in remote field settings. Currently, when casualties cannot be seen by a specialist immediately, the standard of care is to affix a rigid shield over the eye sockets to provide a basic protection. This program seeks to develop simple-to-use reversible interventions to temporarily stabilize injured eyes in situations where patients cannot be seen right away by a specialist, to help minimize the risk of visual acuity loss or vision loss.

Led by Jack Whalen, PhD, this program seeks to leverage latest materials science discoveries to develop a novel approach to temporarily stabilize or "seal" these types of wounds. In one program, a temperature sensitive hydrogel "adhesive" material is being developed that, when cooled near freezing temperature, absorbs water and thus behaves like a viscous fluid, e.g. toothpaste. But when heated to body temperature the hydrogel expels water becoming a semisolid, tacky adhesive, e.g. chewing gum. Funded since 2014 and recently awarded a new 2-year grant from DoD, Dr. Whalen and his team are: 1) developing a complete pathway to product manufacturing, 2) performing tests of the new adhesive in *in vitro* and *in vivo* models to secure FDA approval to begin clinical safety testing and 3) designing a first-in-man clinical study, as well as identifying a clinical site to potentially start human testing in 2024.

Electric Fields Direct Full Length Optic Nerve Regeneration and Partial Restoration of Visual Function In Vivo

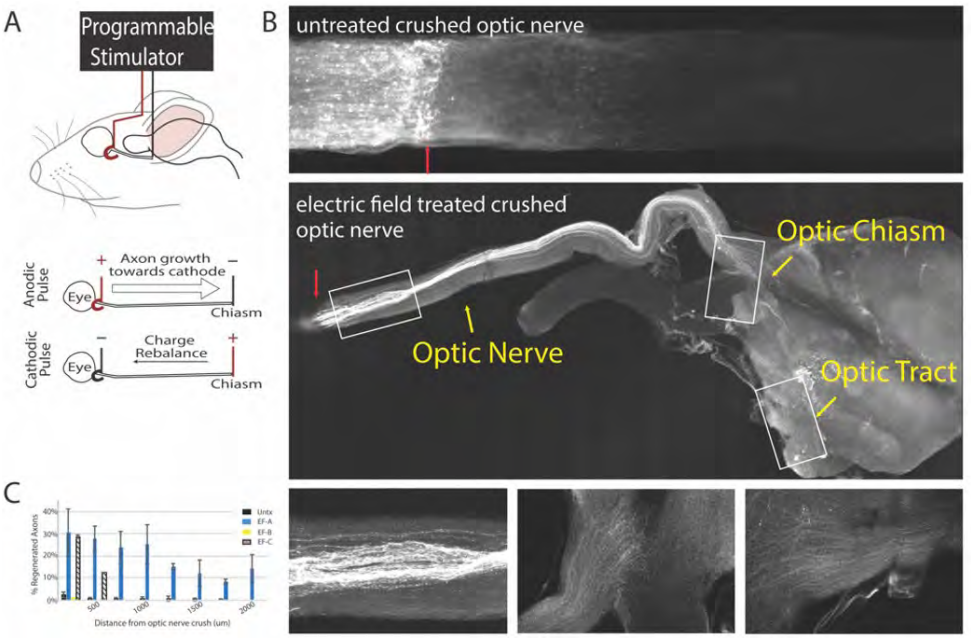
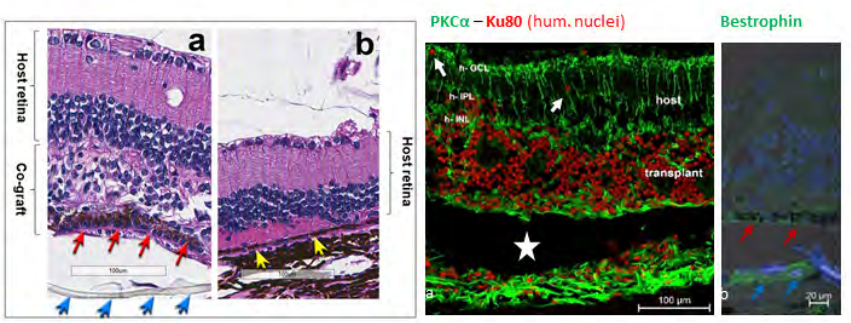


Figure 1: EFs direct full length optic nerve regeneration after crush injury. (A) Schematic of experimental set up. (B) No regenerating axons (white) seen crossing the crush site (red arrow) in untreated rats while EF treated rats demonstrated full length regeneration through the optic chiasm and tract. (C) % of regenerated axons at various distances from crush site relative to pre-crush labeling (error bars=SD), Untx = untreated.

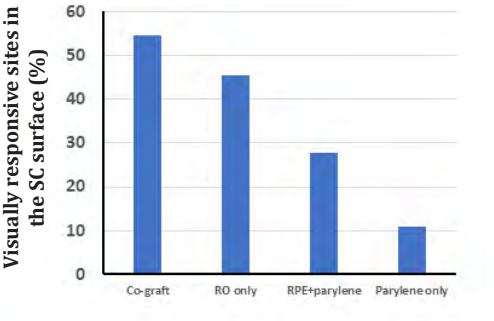
Over 60 million people worldwide are blinded by chronic neuro-degenerative diseases like glaucoma, a condition that leads to selective atrophy of the neurons—retinal ganglion cells (RGCs)—whose axons make up the optic nerve. Restoration of vision in these patients requires development of therapies that will help injured RGCs repair themselves. To date, no therapy exists that can regenerate the optic nerve. The approach we propose to take to address this clinical need is to use electric fields (EFs) to promote RGC survival and direct RGC axon regeneration. The premise for this approach is based on previous findings that 1) immediate application of EFs after optic nerve injury increased RGC survival 1.5-fold over controls and 2) EFs directed regeneration of RGC axons in tissue culture experiments.

Leveraging the expertise of neuro-ophthalmologists, cell biologists, electrophysiologists and electrical engineers, a team lead by Dr. Kimberly Gokoffski has collected compelling preliminary data demonstrating that EF application may be an effective therapeutic modality to direct optic nerve regeneration in living animals. Her group's studies indicate that treatment with electric fields initiated one week after crush injury 1) directed 3-fold more RGC survival over untreated controls, 2) directed full length optic nerve regeneration, and 3) restored partial electrophysiologic function to the superior colliculus of adult rats after crush injury—something never observed in untreated controls.

Tissue Engineering Technique to Repair Irreversible Retinal Damages



Co-graft technique to repair severely degenerated retina. Histology data showing reconstruction of a severely damaged rat retina.

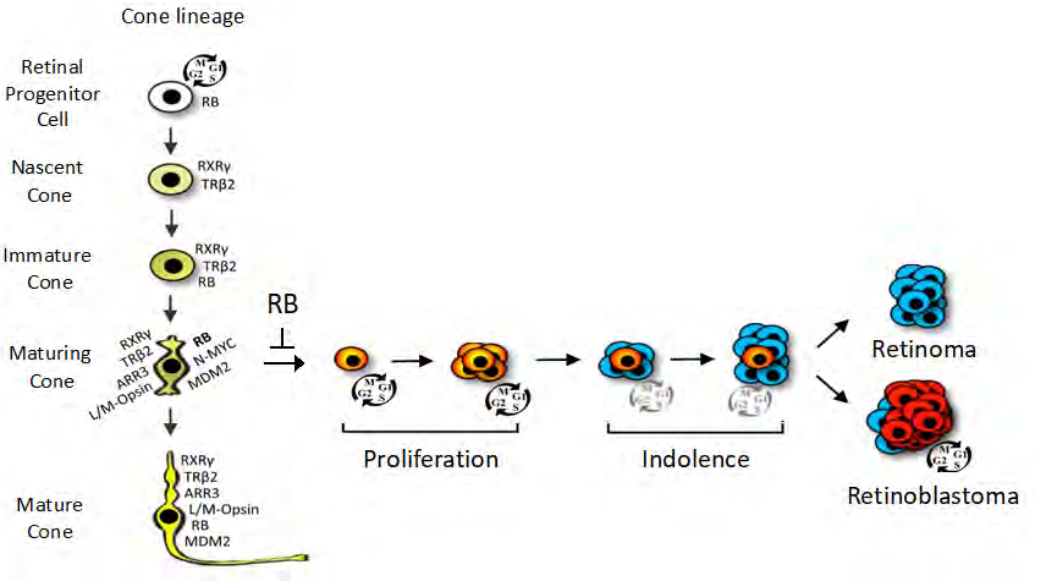


Co-graft technique to repair retinal laser injuries. Co-graft implanted rats showed better visual functional improvement based on MEA recording.

End-stage age-related macular degeneration (AMD) and retinitis pigmentosa (RP) are two major retinal degenerative diseases that result in irreversible vision loss. Permanent eye damage can occur in battlefields due to laser beams or any high-intensity light. In most of these disease conditions, both the light sensitive photoreceptors and its supporting cells (retinal pigment epithelium) can be damaged. Currently there are no therapies for advanced stages of retinal diseases and permanent retinal injuries where cell replacement remains as a major hope.

The broad scope of the retinal transplant research in the laboratory of Dr. Biju Thomas at the USC Roski Eye Institute is to develop novel tissue engineering strategies to repair severely damaged retina. His laboratory uses stem cell-derived retina organoid sheets as an easy and reliable source for photoreceptor replacement. It contains almost all the retinal cell types found in a developing retina. With the support of funding from the National Eye Institute, Thomas's laboratory has demonstrated successful application of a "total retina patch" consisting of retina organoid sheets and retinal pigment epithelium (RPE) cells. Retina organoids and polarized RPE cells (cultured on a biocompatible substrate) were made into a co-graft using alginate as a bio-adhesive. *In vivo* transplantation experiments were conducted in retinal degenerate rats and rats with laser-induced retinal damages. Structural reconstruction of the severely damaged retina was demonstrated based on long-term survival of the co-grafts in the rat subretinal space and the integration of the grafts with the host retina. Visual functional improvements in co-graft implanted rats were demonstrated by electrophysiological mapping of the brain visual center (superior colliculus) using a novel multi-electrode (MEA) array recording system. Dr. Thomas's future research is planned to better understand host-transplant integrations to improve the visual functional benefits with the goal of translating this strategy into a therapy for curing blindness.

Finding the Origin of Retinoblastoma Tumors



Pictured: The Cobrinik lab has found that retinoblastomas develop from RB1-mutated maturing cone precursors that initially proliferate, then enter a prolonged indolent state that leads to senescent retinoma lesions and retinoblastoma tumors. Reference for the figure: Singh et al., 2018, Proc. Natl. Acad. Sci. 115: E9391.

Whereas the genetic basis of retinoblastoma was related to the retinoblastoma gene (RB1) more than 50 years ago, and the cell cycle role of the pRB protein was discovered about 25 years ago, the reason why RB1 mutations specifically cause retinal cancers has been an enduring mystery. With a team of outstanding colleagues, Dr. David Cobrinik sought to understand this tropism by identifying the cell type in which the pRB tumor suppressor operates and defining the characteristics that sensitize to pRB loss.

With Dr. Thomas C. Lee, the team found that pRB is especially highly expressed in the cone precursors of the developing retina. With postdoctoral fellow Xiaoliang Xu, they found that cone precursors also highly express oncoproteins, such as MDM2 and N-MYC, which enable the cone precursors to proliferate and form tumors in response to pRB loss, thus identifying the retinoblastoma cell of origin. At the Vision Center at Children's Hospital Los Angeles, postdoctoral fellow Hardeep Singh showed that only the maturing cone precursors proliferate, reflecting their increased MDM2 and N-MYC expression during cone outer segment genesis. In ongoing work, doctoral student Dominic Shayler is documenting cone precursor gene expression that sensitizes to pRB loss, while doctoral student Sijia Wang and postdoctoral fellow Sunhye Lee are deciphering the early gene expression and cell cycle changes that mediate retinoblastoma initiation.

Dr. Singh's work also revealed that proliferating pRB-deficient cone precursors enter an indolent state resembling senescent retinoma lesions while a few escape, months later, to form retinoblastoma masses. This indolence state may characterize pre-malignant lesions in the retinae of neonates who are destined to develop retinoblastoma. Doctoral student Jinlun Bai aims to understand how the proliferating cone precursors enter indolence and how they escape to form retinoblastoma masses, whereas doctoral student Kevin Stachelek has defined "progression" changes that may enable increasingly more aggressive cancerous growth. These studies aim to enable new approaches to prevent and improve treatment of retinoblastoma in genetically predisposed children.

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

J. Martin Heur, MD, PhD
Professor and Interim Chair

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 encounters, 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 eight 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.

USC Roski Eye Institute
Keck Medicine of USC

LAC+USC
HEALTHCARE NETWORK

Children's Hospital
LOS ANGELES
We Treat Kids Better

2021-2022 Graduating Residents

Andrew Clark, MD, PhD

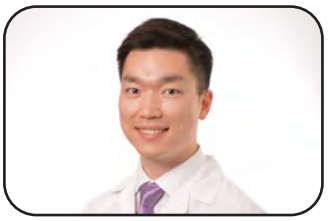
Medical School
USC
Los Angeles, CA

Retina Fellowship
USC Roski Eye Institute
Los Angeles, CA

Joseph Juliano, MD, Co-Chief

Medical School
USC
Los Angeles, CA

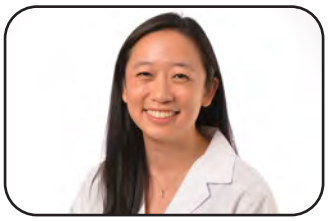
Retina Fellowship
Beaumont Hospital
Royal Oak, MI



Daniel Park, MD

Medical School
University of Pittsburgh
Pittsburgh, PA

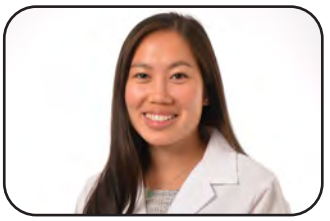
Glaucoma Fellowship
NYU Langone Health
New York, NY



Alice Shen, MD

Medical School
University of Pennsylvania
Philadelphia, PA

Cornea Fellowship
Stanford University
Stanford, CA



Cindi Yim, MD

Medical School
Icahn School of Medicine
New York, NY

Cornea Fellowship
USC Roski Eye Institute
Los Angeles, CA

Leonid Zukin, MD, Co-Chief

Medical School
University of Colorado
Aurora, CO

Cornea Fellowship
Massachusetts Eye and Ear Infirmary
Boston, MA

2021-2022 Graduating Fellows

Linden Doss, MD
Oculoplastics
New York Medical College
Valhalla, NY

Ekjyot Gill, MD
Cornea
SUNY Downstate
Medical Center
Brooklyn, NY

Yong (Andy) Han, MD
Surgical Retina
USC
Los Angeles, CA

Douglas Matsunaga, MD
Surgical Retina
Wills Eye Hospital
Philadelphia, PA

Van Nguyen, MD
Glaucoma
University of Missouri
Columbia, MO

Cameron Pole, MD
Surgical Retina
UCLA
Los Angeles, CA

Grand Rounds Case Study

"It's Not ALL in the Story"

CHALLENGING EYE CARE

Alomi Parikh, MD, MBA
PGY-2 Ophthalmology Resident

Kimberly Gokoffski, MD, PhD
Assistant Professor of Clinical Ophthalmology

HISTORY

- 50-year-old man with a history of leukemia in remission presented with sudden complete vision loss four days after blunt trauma with fists to the right eye

EXAM FINDINGS

- Visual acuity was NLP OD and 20/20-1 OS
- Intraocular pressures were normal
- Pupillary exam was significant for a sluggishly reactive pupil and a relative APD on the right
- Extraocular movements were globally restricted, -3, on the right and full on the left
- Slit lamp examination showed minimal upper and lower eyelid edema with boggy conjunctiva on the right and was otherwise normal
- Dilated fundus exam (Figure 1) showed rare vitreous snow balls, a pale fundus with a cherry red spot in the macula, flame hemorrhages and preretinal hemorrhages, and 360-degree disc edema with a lumpy, infiltrated-appearing nerve

Figure 1 (below): Optos photo of the right eye showing a pale fundus with hemorrhages and an edematous and infiltrated appearing optic nerve.

IMAGING

- OCT macula (Figure 2) showed hyperreflectivity and swelling of the inner segments, relative hyporeflectivity of the outer segments, and subretinal fluid at the fovea

Figure 2 (below): OCT macula of the right eye.

- Fluorescein angiogram (Figure 3) showed choroidal flush with a defect in flow throughout the arterial system
- MRI orbits showed enhancement of the entire length of the optic nerve sheath sparing the nerve body (Figure 4)

Although the presentation was concerning for traumatic optic neuropathy, the appearance of this patient's optic nerve and MRI findings suggested an infiltrative optic neuropathy.

DIFFERENTIAL DIAGNOSIS: INFILTRATIVE OPTIC NEUROPATHY

- Inflammatory etiologies: IgG4 disease, sarcoid, idiopathic orbital inflammatory syndrome, vasculitis
- Neoplastic etiologies: leukemia, lymphoma
- Infectious etiologies: syphilis, TB, fungus
- Since this patient had a prior

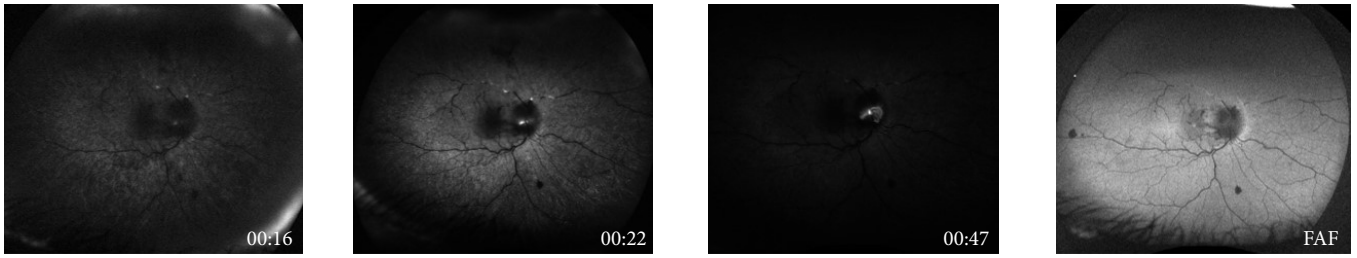


Figure 3 (above): Fluorescein angiogram images and fundus autofluorescence. At 16 seconds there is choroidal flush with a filling defect in the arterial system. At 22 seconds the arteries have still failed to fill. At 47 seconds some of the tributaries near the optic nerve head fill; overall there is minimal filling of any vasculature. The FAF shows hyperautofluorescent areas within the vasculature which are confined to the veins.

history of treated leukemia, leukemic optic neuropathy was high on our differential

LABS AND PATHOLOGY

- Labwork revealed a mild normocytic anemia and was otherwise within normal limits
- CSF cytology was negative for malignancy
- Peripheral smear showed anemia
- Vitreous biopsy was pursued which showed no malignant cells
- After this biopsy the BCR-ABL fusion transcript was detected at an elevated level in the blood and confirmed leukemia recurrence

LEUKEMIC OPTIC NEUROPATHY

- Occurs due to the direct infiltration of leukocytes into the optic nerve or nerve sheath, and can be seen even in cases of systemic remission as the optic nerve is a site of poor penetration of chemotherapeutic agents
- Management is with intrathecal chemotherapy and orbital radiation; adjunctive steroid treatment can be used in some cases

RETINAL VASCULAR OCCLUSION IN LEUKEMIC OPTIC NEUROPATHY

- Several prior case studies demonstrate CRAO, CRVO, or both accompanying leukemic optic neuropathy
- Underlying mechanisms include increased serum viscosity, mechanical compression of the vessel walls by the infiltrated nerve, and infiltration of the vessel walls themselves
- Ocular involvement can be the sole sign of relapse
- Testing can be negative; multiple lumbar punctures are often needed to detect malignant cells and in some cases optic nerve biopsy has been pursued

RETINAL VASCULAR OCCLUSION AFTER TRAUMA

- Trauma can also lead to CRAO or CRVO; in the literature there are numerous cases of delayed vision loss up to 7-10 days after the initial injury
- Based on the history alone, one could have attributed this patient's vision loss to trauma; however the appearance of the optic nerve suggested a diffuse inflammatory process and led to his diagnosis of an ALL relapse – highlighting the value in the ophthalmologic exam

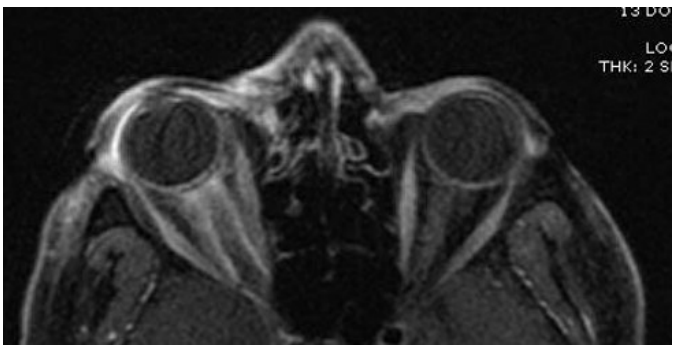


Figure 4 (above): Axial T1 post contrast fat suppressed MRI orbits showing optic nerve sheath enhancement.

REFERENCES

- M.C. Kincaid, R. Green. Ocular and orbital involvement in leukemia. *Surv Ophthalmol*, 27 (1983), pp. 211-232.
- Myers KA, Nikolic A, Romanchuk K, et al. Optic neuropathy in the context of leukemia or lymphoma: diagnostic approach to a neuro-oncologic emergency. *Neurooncol Pract*. 2017;4(1):60–66.
- Currie J. N., Lessell S., Lessell I. M., Weiss J. S., Albert D. M., Benson E. M. Optic Neuropathy in Chronic Lymphocytic Leukemia. *JAMA Ophthalmology*. 1988;106(5):654–660
- Lenk, L., Alsadeq, A. & Schewe, D.M. Involvement of the central nervous system in acute lymphoblastic leukemia: opinions on molecular mechanisms and clinical implications based on recent data. *Cancer Metastasis Rev* 39, 173–187 (2020).
- Zvorničanin J, Kuhn F, Halilbašić M, Mušanović Z. Central retinal artery occlusion and traumatic optic neuropathy following blunt ocular trauma. *Int J Ophthalmol*. 2018 May 18;11(5):893-897.
- De La Porte VM, Lammens M, Dekeyzer S, Van Lint M. Combined Central Retinal Arterial and Venous Occlusions due to Leukemic Infiltration. *Retin Cases Brief Rep*. 2021 Sep 19.

Donor Spotlight

Michele and Dennis Slivinski

Michele and Dennis describe, in their words, their decision to make philanthropic donations to research conducted by Mark Humayun, MD, PhD, that will use stem cell therapy to regenerate the macula:

Michele and I acquired an interest in stem cell therapeutics when Michele was considering a stem cell procedure on her shoulder rotator cuff, which had deteriorated causing pain and restricted range of motion. We discovered that stem cells have the capacity to develop into many of the adult cells of the body with the potential to regenerate human tissue and organs.

Although we were advised that our medical insurance would not cover the expense as it was deemed experimental, we chose to assume the cost rather than elect traditional orthopedic surgery. Michele was pleased with the success. Her pain was relieved, and her range of motion increased.

Our process of philanthropy began with us identifying activities that showed promise for productive and beneficial outcomes. As we investigated projects to support, we learned of Dr. Humayun's work at Keck Medicine of USC using stem cell therapy to regenerate the macula that atrophies with age, causing serious vision loss, often blindness. Dr. Humayun described to us his procedure to implant stem cells onto the damaged area of the eye to facilitate regeneration. After his presentation, Michele and I wondered if Dr. Humayun could do for macular degeneration what Michele's stem cell procedure did for her rotator cuff.

We ultimately decided that it would be a worthy legacy and a very productive use of material resources if we could participate in and further the development of a process that one day may enable many to recover their vision or at least reverse the degeneration. Our gift supporting Dr. Humayun's work could set in motion a process that would substantially improve the lives of many over many generations. In this context we thought of my mother, Gabriella, who experienced vision loss probably due to macular degeneration. It would be an honor if our contribution could save others from her situation.

Once we decided on the project, USC Staff assisted with the development of the method to implement our support of Dr. Humayun's work. Our short-term objective is to fund the current research in the laboratory with gifts in our lifetime. Our long-term objective is to endow a permanent Chair devoted primarily to perfecting a cure for macular degeneration.

Our lives to date did have some influence on our philanthropy decision. Michele devoted a substantial part of her career as a surgical technician, assisting in surgeries including open heart and eye surgery. She experienced several situations when developments in medical procedures had positive outcomes. I have a Ph.D. in philosophy from Vanderbilt University and a J.D. from the USC Gould School of Law. My philosophy inquiry included reflection on bioethics, logic, the scientific method, and the proper allocation of resources.

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.

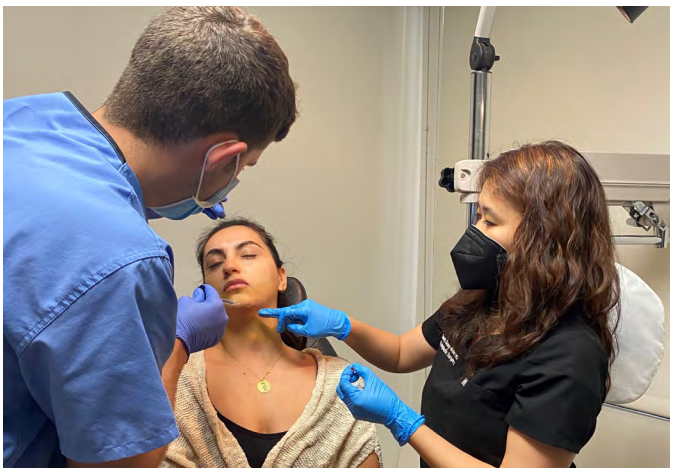
ALUMNI BY THE NUMBERS

68 **VOLUNTARY FACULTY**

15 **DEPARTMENT CHAIRS**

286 **RESIDENTS TRAINED**

311 **FELLOWS TRAINED**



Notable Accolades & Achievements

Jesse Berry, MD
Elected to ARVO Annual Meeting Committee for Anatomy and Pathology/Oncology
Keynote Graduation Speaker, University of Florida Department of Ophthalmology
WIO Recognition of Service Award, Women in Ophthalmology

Cheryl Craft, PhD
Distinguished Honoree, ARVO Foundation

Kimberly Gokoffski, MD, PhD
Fellowship Award, Donald E. and Delia B. Baxter Foundation
Research on Engineering Medicine for Cancer Award, Ming Hsieh Institute (MHI)
Strategic Directions for Research Award (SDRA), USC Office of Research Initiatives & Facilities

J. Martin Heur, MD, PhD
Elected to ARVO Annual Meeting Committee for Cornea

Mark Humayun, MD, PhD
Charles L. Schepens, MD/AAO Award and Lectureship, Retina Research Foundation
USC Stevens Center for Innovation Commercialization Award

Narsing Rao, MD
2021 Lecturer, C. Stephen and Frances Foster Lecture on Uveitis and Immunology
Dr. Venkataswamy Oration Award, Aravind Eye Care System

Brandon Wong, MD
Mentoring for the Advancement of Physician Scientists (MAPS), American Glaucoma Society (AGS)

Benjamin Xu, MD, PhD
2021-2022 IRIS Registry Initiative Award, American Glaucoma Society

Sandy Zhang-Nunes, MD
WIO Educators Award, Women in Ophthalmology

Mark Borchert, MD;
Linda Lam MD, MBA;
Brian Toy, MD;
and Benjamin Xu, MD, PhD;
Top Doctors 2021, *Pasadena Magazine*

Thomas C. Lee, MD
Grace Richter, MD, MPH
Top Doctors of 2021, *Los Angeles Business Journal*

Gloria Chiu, OD, FAAO, FSLS;
Narsing Rao, MD;
and Benjamin Xu, MD, PhD;
American's Best Eye Doctors for 2021, *Newsweek*

Annual Report Cover Image: This volumetric rendering shows the visual system fiber bundles, eyes, optic tract, and vascular system of the brain. Also visible, with reduced opacity, are the inferior fronto-occipital fiber bundles, inferior longitudinal fasciculus, the hippocampus and the thalamus.
Image credits: Laboratory of Neuro Imaging, USC Stevens Neuroimaging and Informatics Institute. Visualization by Jim Stanis and Arthur W. Toga, data from Ryan Cabeen, Yonggang Shi, Samantha Ma, and Danny "JJ" Wang..

USC DEPARTMENT OF OPHTHALMOLOGY

#1

IN NIH RESEARCH FUNDING

AMONG OPHTHALMOLOGY DEPARTMENTS

FY 2020

*Source: Blue Ridge Institute for Medical Research

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PEER-REVIEWED PUBLICATIONS

BEST HOSPITALS U.S.News & WORLD REPORT OPHTHALMOLOGY 2021-22

#13

HOSPITAL FOR OPHTHALMOLOGY IN THE NATION

USC Roski Eye Institute

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
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