

SHINE *the* LIGHT

FALLING LEAVES

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State-of-the-art research center will be home to leading vision programs

A new structure taking shape across from the Gavin Herbert Eye Institute in Irvine is slated to be one of the largest, most advanced research centers dedicated to basic and translational science and training on the West Coast.

When the Falling Leaves Foundation Medical Innovation Building opens in spring 2025, two pioneering programs dedicated to eradicating blindness will occupy coveted research space.

The 215,000-square-foot facility designed for collaborative “bench to bedside” research was made possible by a generous \$30-million lead gift from Professor Robert Mah and Dr. Adeline Yen Mah’s Falling Leaves Foundation. Twelve of UC Irvine’s high-impact, interdisciplinary research programs were selected to move into the facility based on their potential to transform the face of biomedical research, patient care and public health.

The UCI Center for Translational Vision Research and its new Genome Editing Research Program — both led by

Krzysztof Palczewski, PhD, the Irving H. Leopold Chair in Ophthalmology and Distinguished Professor — will occupy 50,000 square feet.

With leading-edge laboratories, the most advanced scientific equipment and an emphasis on collaboration, Palczewski says this new home will spur innovation among his team’s researchers who are striving to develop sight-preserving technologies and find a cure for blinding diseases.

The need is significant. Glaucoma, severe age-related macular degeneration and diabetic retinopathy are three of the most devastating blinding diseases, affecting 12.4 million people globally. Vision loss has had a significant impact on human productivity and independence, and the costs to treat and care for these patients is an estimated \$139 billion a year in the United States alone.

“The next 10 years will be pivotal in visionary breakthroughs, as our dedicated teams are on the brink of discovering new



Krzysztof Palczewski, PhD

therapies that will revolutionize vision care for patients in our community and across the globe,” says Palczewski. “We will restore hope to the millions of people robbed of their sight or progressing toward blindness, for which virtually no effective treatment options exist today.”

The Center for Translational Vision Research has already gained international acclaim for its efforts in translating basic scientific discoveries into life-changing treatments. Its geneticists, infectious disease specialists and ophthalmology researchers are collaborating on two promising areas of retinal research: gene therapy and noninvasive imaging.

Several vision researchers are using a highly specialized imaging instrument called a two-photon ophthalmoscope, which allows scientists to study real-time disease progression in live cells. Unique to the translational vision center, the imaging device uses a long wavelength infrared laser beam that can penetrate deep into cells without damaging them.

Insights gained from these techniques will help researchers better understand the biological processes occurring throughout various stages of eye diseases, leading to better diagnostic tools and individualized treatments for patients.

The center also is using gene-editing technology to target and repair genetic mutations that cause inherited retinal diseases responsible for blindness experienced by millions of people worldwide. In Palczewski’s lab, researchers already have used gene editing in animal models to restore vision loss caused by retinitis pigmentosa and Leber congenital amaurosis.

UCI vision researchers also are exploring gene-editing therapies for glaucoma, the world’s second-leading cause of irreversible blindness. Multiple genes contribute to the development of glaucoma and researchers have made significant progress in targeting one of these genes, Palczewski says. In animal studies, they have successfully prevented the onset of glaucoma by reducing mutant genes in a critical part of the eye called the trabecular meshwork.

The Genome Editing Research Program will also focus on advancing gene therapies beyond the eye, collaborating with medical researchers who specialize in other inherited diseases.

“Vision science leads the medical disciplines in pioneering gene therapy, and UCI is the global leader in the field of genome editing,” says Palczewski.

“We are committed to advancing the field of genetic therapy by applying the same technology that edits DNA for inherited retinal disease to inherited diseases in any organ in the body by adjusting the means of delivery.”

Palczewski and his colleagues are excited to move into the Falling Leaves Foundation Medical Innovation Building when it opens next year.

“The collaborative environment of this new building will undoubtedly empower our unique expertise in basic and medical genetics,” he says.

“Together, we will pave the way for groundbreaking advancements in gene therapy.”

Message from the chair

This is an era of remarkable era of growth for UCI Health and the UCI School of Medicine. Orange County's only academic health system recently announced the acquisition of four new hospitals and their outpatient medical facilities in Fountain Valley, Lakewood, Los Alamitos and Placentia. In addition, UCI Health — Irvine, a new \$1.3 billion medical campus, opened its first building April 30 at at Jamboree Road and Birch Street.

Across the street from the Gavin Herbert Eye Institute, the Falling Leaves Foundation Medical Innovation Building is taking shape. Both our Center for Translational Vision Research and the Genome Editing Research Program will move into the state-of-the-art research facility, their efforts significantly boosted by generous gifts from Trish O'Donnell, the Clemons Family and an anonymous donor. We are incredibly grateful for their support, as well as for the confidence placed in our team by School of Medicine Dean Michael J. Stamos, MD, and Vice Chancellor of Health Affairs Steve A.N. Goldstein, MD, PhD, who allocated this critical research space to our vision programs.

Several new ophthalmology scientists will be joining these program in the summer. We look forward to sharing information about their exciting vision research in coming months.

We are also proud to announce that the Research to Prevent Blindness (RPB) has renewed its five-year, \$575,000 unrestricted grant to the Department of Ophthalmology. We appreciate the continued support of the nonprofit organization's president, Brian F. Hofland, PhD. We thank the many faculty members who contributed to the grant process, especially Vladimir Kefalov, PhD.

Notably, our department is one of very few nationwide to receive the trifecta of competitive ophthalmology funding: the unrestricted RPB grant, a National Eye Institute P30 Center Core Grant for Vision Research and a National Institutes of Health T32 Training Grant.

Recently, the UC Irvine Academic Senate honored one of our own with its prestigious Distinguished Senior Faculty Research Award. Krzysztof Palczewski, PhD, the Irving H. Leopold Chair of Ophthalmology and Distinguished Professor, was recognized for his groundbreaking research to cure and prevent blindness with precision genome editing. This award is especially meaningful since it is bestowed by colleagues throughout the campus.

Amid all the progress we have seen, I'm saddened to report that the global vision community suffered a profound loss late last year with the passing of M. Cristina Kenney, MD, PhD, a renowned scientist and clinician at the Gavin Herbert Eye Institute. She was a cherished friend, an exceptionally collaborative researcher and a mentor to countless individuals, including our international retina research fellows for the last two decades. We miss her dearly. Read about her legacy in this issue of *Shine the Light* (page 8).

As always, we are grateful to our incredible community of patients, researchers and supporters who inspire our quest to end blindness. We look forward to continuing to share updates with you as these programs flourish and bear fruit.



A handwritten signature in black ink that reads "Baruch Kuppermann".

Baruch D. Kuppermann, MD, PhD

Director, UCI Health Gavin Herbert Eye Institute
Chair, Department of Ophthalmology,
UCI School of Medicine

Our team

Cataracts, cornea, external disease and refractive

Soroosh Behshad, MD, MPH

Marjan Farid, MD

Vice Chair, Diversity, Equity, and Inclusion

Sumit (Sam) Garg, MD

Vice Chair, Clinical Ophthalmology

Sanjay R. Kedhar, MD

Vice Chair, Clinical Research

Olivia Lee, MD

Kailey Marshall, OD

Matthew W. Wade, MD

Comprehensive ophthalmology

Kavita K. Rao, MD

Glaucoma and cataracts

Austin Fox, MD

Ken Y. Lin, MD, PhD

Sameh Mosaed, MD

Vice Chair, Ophthalmology Faculty

Andrew Smith, MD

Low vision

Karen Lin, OD

Nilima Tanna, OT

Neuro-ophthalmology

R. Wade Crow, MD

Lilangi Ediriwickrema, MD

Vivek Patel, MD

Samuel J. Spiegel, MD

Ocular oncology

Kapil Mishra, MD

Oculoplastics

Lilangi Ediriwickrema, MD

Jeremiah Tao, MD

Ophthalmic pathology

Maria Del Valle Estopinal, MD

Optometry

Joseph Bui, OD

Timothy Scott Liegler, OD

Pediatric ophthalmology

Charlotte Gore, MD

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Annabelle Storch, OD

Donny Suh, MD

Kimberly Walker, OD

Research

Lbachir Benmohamed, PhD

Andrew Browne, MD, PhD

James V. Jester, PhD

Tibor Juhasz, PhD

Vladimir Kefalov, PhD

Vice Chair, Research

Timothy Kern, PhD

Philip Kiser, PhD

Henry J. Klassen, MD, PhD

Baruch D. Kuppermann, MD, PhD

Anthony B. Nesburn, MD

Krzysztof Palczewski, PhD

Eric Pearlman, PhD

Magdelene Seiler, PhD

Dorota Skowronska-Krawczyk, PhD

Gulab Zode, PhD

Retina and vitreous

Andrew Browne, MD, PhD

Baruch D. Kuppermann, MD, PhD

Chair, Department of Ophthalmology

Stephanie Y. Lu, MD

Vice Chair, Education

Mitul C. Mehta, MD

Kapil Mishra, MD

Mohammad Riazi, MD

Strabismus

Charlotte Gore, MD

(adults and pediatrics)

Vivek Patel, MD

(adults)

Stephen Prepas, MD

(pediatrics)

Annabelle Storch, OD

(pediatrics)

Donny Suh, MD

(adults and pediatrics)

Kimberly Walker, OD

(pediatrics)

Uveitis

Sanjay R. Kedhar, MD

Olivia Lee, MD

Help for thyroid eye disease



Dr. Lilangi S. Ediriwickrema and Dr. Jeremiah P. Tao

Thyroid eye disease is an autoimmune disease that causes inflammation to tissues around the eyes and can lead to dryness, redness, double vision, trouble closing eyelids completely and a noticeable bulging of the eyes.

“Moderate to severe thyroid eye disease can also be socially stigmatizing, affecting patients beyond their clinical symptoms,” says Lilangi S. Ediriwickrema, MD, a UCI Health ophthalmologist at the Gavin Herbert Eye Institute and an assistant professor in the UCI School of Medicine’s Department of Ophthalmology.

Ediriwickrema, who specializes in oculofacial plastic surgery and neuro-ophthalmology, is part of an interdisciplinary team that treats patients with thyroid eye disease at the UCI Health Gavin Herbert Eye Institute.

While the disease most often affects individuals who are already experiencing an overactive thyroid, it sometimes appears in individuals with low or even normal thyroid levels — especially if they smoke. It’s not unusual for an ophthalmologist to be the first to diagnose a thyroid imbalance when a patient seeks care for dryness, vision problems and eyelid swelling.

At the eye institute, patients diagnosed with thyroid eye disease may be referred to the oculofacial plastic and orbital surgery team led by Jeremiah P. Tao, MD, who specializes in ophthalmic plastic and reconstructive surgery. He and Ediriwickrema work closely with various specialists to determine the best treatment options — including some that preserve vision.

For some patients with thyroid eye disease, prescriptions to treat the inflammation offer relief and the condition may resolve itself. In certain cases, however, surgery is the most effective and efficient treatment.

“It’s important for patients to be seen by specialists who have all the tools in the toolbox to not only monitor but also treat this disease,” explains Tao, professor and director of the department’s fellowship program.

Patients with moderate to severe thyroid eye disease may undergo decompression surgery. In this procedure, Tao or Ediriwickrema create more space around the eye to accommodate the swelling that causes unsightly bulging and, in some cases, vision loss. Typically, this involves removing some bone around the eye.

“Inflammation in the eye socket can cause an assortment of problems,” explains Tao. “Decompression surgery sometimes offers immediate relief and takes pressure off the optic nerve, thereby reducing the risk of permanent vision loss.”

Patients whose thyroid eye disease causes double vision may require strabismus surgery to adjust eye muscles so that the eyes move together again. Patients who have complications from severe dry eye may also need a cornea specialist to help manage their care.

Patients may also undergo oculoplastic surgery with Tao and Ediriwickrema for eyelid retraction or to remove extra tissue and fat that accumulated around the eye as a result of the disease.

Tao and Ediriwickrema are optimistic that new therapeutic options can be found to provide customized multidisciplinary care for thyroid eye disease. With funding from the National Institutes of Health, she is studying how the disease affects blood vessels and other tissue around the eye.

“The treatment landscape is continually evolving,” says Ediriwickrema. “We hope that in the next 10 to 20 years we can offer patients even more options to manage this disease.”

Thank you to our donors

A heartfelt thank you to our friends, patients, faculty, staff and friends for their incredible generosity. Your contributions have helped us advance our mission to develop innovative technologies to diagnose and treat eye diseases and disorders; implement clinical solutions that give our patients the most advanced medical and surgical eye care available; and support educational programs that prepare the next generation of ophthalmic leaders. (Donors listed contributed \$2,000 or more between July 1, 2023 and April 30, 2024)

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To learn more about how you can support the Gavin Herbert Eye Institute, please contact Nikki Gaitan, nmgaitan@hs.uci.edu or Amber Harness, at aharness@uci.edu



Trish O'Donnell and Dr Krzysztof Palczewski

A gift for future vision

As a trained sociologist, Trish O'Donnell enjoys studying people. At a luncheon held at the Gavin Herbert Eye Institute last year, she noticed Krzysztof Palczewski, PhD, from the moment he stepped onto the terrace.

The renowned vision scientist holds the Irving H. Leopold Chair in Ophthalmology and is a Distinguished Professor at UC Irvine. Palczewski's contributions to vision research and ophthalmology have garnered numerous international awards and he recently was elected to both the U.S. National Academy of Sciences and the National Academy of Medicine. Yet what impressed O'Donnell most during their conversation that day was his charisma and persuasiveness.

"He is so versatile that he can be both an impressive scientist and extremely social," says O'Donnell. "He's not content to merely observe from behind the microscope."

As one of the 20 million Americans experiencing age-related macular degeneration (AMD), O'Donnell was intrigued by Palczewski's ambitious goal of eradicating vision loss and blindness caused by inherited retinal diseases. His research at the UCI Center for Translational

Vision Research and the Genome Editing Research Program focuses on advanced precision tools to edit and repair genes responsible for vision loss from inherited diseases such as glaucoma and AMD.

After touring Palczewski's research lab and meeting some of the scientists on his team, O'Donnell decided to create an endowment to support their work. The Trish and John O'Donnell Family Fund will underwrite vision

continued on page 8

"The confidence Trish O'Donnell has vested in me is truly invaluable. With her generous support, we are positioned to make significant strides in vision research, promising tangible improvements in the lives of countless patients. Her remarkable generosity and her belief in our mission resonate deeply, making her not only a benefactor but a cherished individual whom I am privileged to know."

— Krzysztof Palczewski, PhD

research led by Palczewski in the new Falling Leaves Foundation Medical Innovation Building when it opens next year across from the eye institute in Irvine.

“The eye is the most important instrument for living well,” she explains. “By making this gift to support vision research, I decided this would be a wonderful way to make a major difference in the lives of so many individuals.”

It was Palczewski’s unique blend of scientific acumen and passionate determination to tackle vision problems affecting millions of people around the world that inspired her “leap of faith” to invest in research that could benefit future generations.

“He’s a phenomenal man, putting his heart and soul into this work,” O’Donnell says. “I want him to be able to use his skills to do as much as he can to combat vision loss and blindness.”

M. Cristina Kenney — beloved scientist’s legacy lives on



Dr M. Cristina Kenney

The Gavin Herbert Eye Institute and the international vision research community suffered a profound loss with the passing of renowned scientist and clinician M. Cristina Kenney, MD, PhD, in December 2023.

A beloved colleague in the UCI School of Medicine’s Department of Ophthalmology and a respected contributor to the UCI Center for Translational Vision Research, Kenney was also a cherished mentor to countless scientists and clinicians over her long career. She was 74.

Her pioneering research in age-related macular degeneration (AMD) led to improvements in treatment that patients benefit from today.

Kenney was among the early researchers to explore the potential of mitochondria, the part of cells that produce energy. Using cybrids — a type of hybrid cell created in a lab — she demonstrated the

wide-ranging effects of mitochondrial therapy. Her work led to greater understanding of the biological causes of AMD and better pharmacological treatments. It also opened the door to studying mitochondria’s role in other age-related conditions such as Parkinson’s disease, Alzheimer’s disease, glaucoma and diabetic retinopathy.

Kenney was such an inspirational leader that many researchers stayed with her lab for years, even decades — including a few who followed her from Cedars Sinai Medical Center when she joined UC Irvine in 2002.

She welcomed everyone into her lab, including undergraduates, medical students, international ophthalmology fellows and scholars from other departments. For example, when Kevin Schneider was researching obesity for his doctorate in pathology, he needed expertise on mitochondria. Not only did Kenney offer insights and advice, she also let him use her lab equipment and offered guidance on his experiments. After receiving his PhD in 2016, he joined her lab as a post-doctoral scholar, expanding his research into other avenues related to mitochondria’s role in aging and disease.

Kenney not only allowed undergraduate students to participate in research, she also recognized them as co-authors on published papers, which would significantly boost their prospects of securing a highly competitive ophthalmology residency after medical school.

Cycling again after complex cataract surgery

Just before Thanksgiving 2023, Eugene Diaz went to his ophthalmologist in his hometown of Corona for what he thought would be a routine cataract surgery. But when the eye doctor had trouble removing the cataract, he stopped the surgery and referred the accountant to the UCI Health Gavin Herbert Eye Institute.

Diaz spent the holiday weekend fearing he would lose his eyesight and his livelihood. The cloudy vision in his left eye already made it nearly impossible to work on his computer. The avid cyclist, a veteran of 200-mile double-century rides, was no longer able to ride his bike. His loss of depth perception made even simple tasks like going down a staircase challenging. After the incomplete surgery, his vision problems got worse.

"It felt like a nightmare," he says.

Once he arrived at the eye institute in Irvine, Diaz knew he was in good hands. He had the most thorough eye exam of his life, including an ultrasound of the back of his eye, cornea mapping and measurements for new intraocular lenses. Then he met Dr. Soroosh Behshad.

"I was a little scared and not sure what to expect," says Diaz. "But after he spoke to me for the first few minutes, I felt comfortable and ready."

Behshad showed Diaz the new images taken of his eye and explained exactly what was causing his vision problems. He then described step-by-step what the patient could expect during and after the surgery. Diaz was surprised and relieved when his procedure was scheduled for a few days later.

He was further put at ease when Behshad explained that the Gavin Herbert Eye Institute has a full range of subspecialists experienced in the most complicated cases. If Behshad couldn't remove Diaz' cataract with an anterior approach, a retina specialist would be on hand to help remove it with a posterior approach, ensuring the surgery would be successful this time.

Four months later, Diaz is fully recovered with 20/20 vision in his left eye. He's back to work and, best of all, back on his bike and getting in shape to pedal the long



Eugene Diaz and Dr. Soroosh Behshad

distances he enjoys most. Since he works in Irvine, he plans to continue getting his vision care at the eye institute.

Mindful of his own experience, Diaz advises people to get routine eye check-ups. He points out that his cataract had been developing long before his vision got so bad he had to seek help.

"Don't take your eyes for granted," he says. "You really need to have your eyes checked, or you won't know if you have something wrong until you can't see."



Dr. Andrew Browne and Dr. Ken Lin

Leveraging AI for better eye care

Artificial intelligence has taken the world by storm in recent years as AI-generated images, videos and text have triggered Hollywood strikes and influenced school policies and political campaigns. AI also holds great promise for improving healthcare.

The physician-scientists at the UCI Health Gavin Herbert Eye Institute are using existing AI tools to treat patients and they also are developing AI-powered innovations to advance vision care in the future.

“People tend to think AI is a post-pandemic novelty, but in reality it has already transformed various aspects of medical diagnostics,” says Ken Y. Lin, MD, PhD, a specialist in glaucoma and cataract surgery at the eye institute. “Aspects of AI have been quietly running in the background to ensure greater accuracy and efficiency in care delivery.”

For example, Lin notes that no two patients taking vision field tests experience the exact same series of flashing lights in their periphery. Thanks to AI, the machine is able to adapt the eye exam based on each person’s first few responses.

Lin, an associate professor in the UCI School of Medicine’s Department of Ophthalmology and the UCI Henry Samueli School of Engineering, describes new ways in which AI is changing vision care at the eye institute and around the world.

Helping patients see

A surgeon who works primarily with patients affected by glaucoma and cataracts, Lin also has studied deep machine learning and worked on developing new devices to better treat glaucoma. He’s always looking

for opportunities to use AI tools to help his patients. Recently, he noticed that many patients were having trouble identifying their eye drops, which come in small bottles with even smaller print.

“The irony is that the people who need eye drops the most are those who have the most problem identifying the medications in the first place,” Lin says.

That inspired him to develop an AI-powered smartphone app using the phone’s camera to recognize and tell patients which eye medicine they are holding. The UCEye Bottle Identifier app, available for download at Google Play, is now being used by eye institute patients. Lin is developing a new version to incorporate instructions on how and when to use each of type of prescription drops.

Easier 3D imaging

Eye institute researchers are also developing AI programs to get more from diagnostic tools. Retina specialist Dr. Andrew Browne, who has a PhD in electrical and computer engineering, is developing AI-powered tools to help generate 3D models of patients’ eyes with basic ultrasound equipment. Modeling the eye’s anatomy now requires an MRI or CT scan, equipment not typically found in an ophthalmologist’s office. These scans can be time consuming and expensive for patients.

Browne’s device, currently under patent review, uses a motorized system to take images of the ocular anatomy, then introduces AI-augmented tools that can reconstruct 3D models of the eye. With this device, physicians can better monitor retinal and other conditions, such as thyroid eye disease, optic neuritis, intracranial hypertension and pathological myopia.

Assisting surgeons

Browne and Lin are also leveraging AI technology for medical tools that patients may never see but will help surgeons provide the best possible treatment.

Browne has helped develop an AI-powered process to recreate full-color images from photos taken under infrared light, which is invisible to the human eye. Potential applications for the technology could help surgeons operating in low-light conditions.

Lin has developed an AI tool to help eye surgeons see the eye’s trabecular meshwork — a spongy tissue targeted in most minimally invasive glaucoma surgeries. The meshwork is difficult to discern even under a surgical microscope.

“It’s similar to assisted driving,” explains Lin. “The AI tells you where the trabecular meshwork is, but the surgeon still has to make the decisions.”

Browne is also collaborating with computer scientists to develop AI-augmented surgery models that could improve outcomes for patients undergoing eye surgery.

By using videos of eye surgeries, along with data on the results of each procedure, AI can find patterns and nuances that lead to the best surgical outcomes, something that can be difficult for individual surgeons to discern in an unbiased way.

“If we want to learn the definitive impact of more subtle actions that surgeons take during an operation, then we need objective tools to analyze the data from thousands and thousands of surgeries,” he explains.

Both Lin and Browne say AI will inevitably play an increasingly important and beneficial role in ophthalmology.

“AI is going to enhance doctors’ ability to rapidly detect problems and changes in our patients’ eyes,” Browne says.

“We will examine what the technology highlights for us, confirm whether we agree with it and that will allow us to make decisions much more quickly and efficiently. Ultimately, that’s going to be very important for physicians trying to give patients the best possible care.”

UCI Health Gavin Herbert Eye Institute

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Pediatrics July 23, 2024

Sedentary time, screen time, and exercise in kids: navigating kids' habits in the digital age
Donny Suh, MD
Shlomit Radom-Aizik, PhD
(UCI PERC)

Diabetes Aug. 6, 2024

Diabetic risk factors and how they can affect your eyes
Andrew Browne, MD, PhD
Qin Yang, MD
(UCI Diabetes Center)

Cataracts and glaucoma Sept. 3, 2024

What glaucoma patients need to know before cataract surgery
Sameh Mosaed, MD
Andrew Smith, MD

AMD and stem-cell therapy Oct. 1, 2024

Age-related macular degeneration: vision changes and the role of stem-cell therapy
Henry Klassen, MD, PhD
Baruch Kupfermann, MD, PhD

Dry eyes Nov. 5, 2024

What is dry eye and how is it treated?
Soroosh Behshad, MD, MPH

Low vision Dec. 3, 2024

Improve your quality of life while living with low vision
Karen Lin, OD
Nilima Tanna, OT

LASIK Surgery Seminars 6:30–7:30 p.m.

Sept. 5, 2024
Oct. 3, 2024
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