UCI Health Gavin Herbert Eye Institute

FALL 2023

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IN THIS ISSUE

MEDICAL MILESTONES

Milestone reached in quest for universal coronavirus vaccine

UC Irvine scientists working on a pan-coronavirus vaccine have demonstrated in pre-clinical studies that combining their broad-based antigen approach with current COVID-19 vaccines gives better protection against illness from repeated infection by many virus variants.

"This is a significant milestone," says virologist and immunologist Lbachir BenMohamed, PhD, a UCI professor and director of the Laboratory of Cellular and Molecular Immunology at the university's Gavin Herbert Eye Institute. The eye-care provider has received four National Institutes of Health (NIH) grants to develop a vaccine to combat all coronaviruses, not just the one that causes COVID-19.

"We now have proof of concept that our novel and innovative vaccine approach offers broader protection against COVID-19 and longer-lasting immunity, even as new strains of the virus develop."

In the nearly four years since SARS-CoV2 (severe acute respiratory syndrome coronavirus 2) first emerged in China in late 2019, the virus has continued mutating. New variants and strains have rendered existing vaccines less effective at preventing illness, confounding public health officials. New York health officials reported that 19% of fully vaccinated people in the state had experienced a breakthrough infection as of May 2023.

National policymakers have been calling on scientists to pursue the kind of research that BenMohamed's team first embarked on in early 2020.

"The continued adverse effects of SARS-CoV-2 on individuals and populations necessitate the urgent development of the next generation of vaccines," wrote the U.S. Food and Drug Administration's Peter Marks, MD, PhD, in the Journal of the American Medical Association in late 2022.

In April, the White House announced Project Next Gen, a $5 billion program to speed development of new coronavirus vaccines and treatments.

Lbachir BenMohamed, PhD

Tapping into natural immunity

Current COVID-19 vaccines target the virus' iconic spike protein, which mutates quickly. But the human immune system also reacts to dozens of other SARS-CoV-2 proteins.

BenMohamed and his team began their quest in early 2020, combing through 14 million genome sequences of animal and human coronaviruses for protein antigens that undergo far fewer mutations as the viruses evolve. They identified 10 such antigens that remain consistent across coronavirus variants, then studied these proteins in blood samples from asymptomatic COVID-19 patients, individuals who contracted the disease but had no symptoms.

"We identified the common antigens that remain highly conserved among different variants and are found to be selectively recognized by the immune system of people with asymptomatic COVID-19 cases," the virologist says. "Because these antigens invoke the protective human immune response and keep people from experiencing any disease symptoms at all, they offer the greatest potential for new vaccines."

Over the last year, he and his team discovered that the T-cell antigens they target not only protect against multiple variants of SARS-CoV-2, their benefit is even greater when added to the current vaccines that target the spike protein. Mice and hamsters treated with a combination of current vaccines and the UCI T-cell antigens were better protected from infection by the Delta strain as well as subsequent infection by the newer Omicron strain, which remains the dominant variant around the globe.

"If we can reduce illness and breakthrough infections, not only will the vaccine save lives, but it also will help stop the virus from spreading, both in humans and animals," says BenMohamed. "To be truly effective, vaccines not only need to protect individuals from getting diseases, but also to protect the population from transmitting the disease from one person to another."

Moving toward clinical trials

The next step is to test their vaccine in a phase 1 clinical trial in humans. Before clinical trials can begin, however, they need to partner with a company to produce the vaccine, which will be based on the established mRNA lipid nanoparticle technology, a process BenMohamed says could take up to 18 months. If the vaccine proves safe, phase 2 and phase 3 trials would follow to validate its safety and efficacy.

The team's research has been supported by a $3.7 million, five-year grant from the National Institute for Allergy and Infectious Diseases (NIAID) and seed funding from the Gavin Herbert Eye Institute. The university has filed three additional patents this year for a total of six related to the project.

To raise capital and ultimately bring a pan-coronavirus vaccine to market, BenMohamed co-founded TechImmune LLC, a partnership with the university, the eye institute and investors. TechImmune has raised an additional $2.5 million, including a $600,000 Small Business Innovation Research grant from the NIH.

Company president Jeffrey Ulmer, PhD, who has more than 30 years of experience in vaccine research and development with Novartis and GlaxoSmithKline, notes that seven groups of scientists at other research institutions are also working on universal coronavirus vaccines. But he believes the UCI team's approach has distinct advantages because their data show that the immune system of asymptomatic COVID-19 patients selectively recognized their common T-cell antigens and the UCI project aims to confer broad spectrum, long-lasting protective immunity.

The COVID-19 pandemic created the largest global health crisis in a century. Before 2019, previous coronavirus outbreaks caused short-lived public health crises in 2003, 2008, 2012. The disease continues to persist with new variants emerging around the world despite widespread use of current spike-based vaccines.

BenMohamed points out that SARS-CoV-2 is unlikely to be the last coronavirus to cause widespread disease. He hopes that his lab's vaccine approach will make it possible to respond quickly with effective therapies when the need arises.

"Developing the next generation, pre-emptive coronavirus vaccine is about much more than the current pandemic," he says. "Our ultimate goal is to prevent and be better prepared to swiftly respond to future global pandemics."

Tis the season of giving thanks

In this season of giving thanks, we at the Gavin Herbert Eye Institute have much to be grateful for: our patients, donors, clinicians, researchers and the Orange County community, whose continued support keeps us going — and growing.

This fall we mark the 10th anniversary of the opening of the Gavin Herbert Eye Institute. Attendees at our celebratory event on Oct. 17 included our namesake benefactor and eye industry pioneer Gavin Herbert; University of California President Michael V. Drake, MD, an ophthalmologist and former UCI chancellor; current UCI Chancellor Howard Gillman, PhD; and many more visionary donors and university leaders whose generosity and dedication have made the institute a reality. (Read about the celebration on page 11.)

Since the Gavin Herbert Eye Institute opened its doors in 2013, we have expanded rapidly. We have nearly doubled the number of annual patient visits as well as the size of our Department of Ophthalmology faculty, while tripling the number of surgeries performed and the number of graduate students we train. Over the last decade, our research funding from the prestigious National Institutes of Health and the California Institute of Regenerative Medicine has exceeded $89 million. Since 2013, we have raised more than $76 million in philanthropic donations.

As the institute enters its second decade, we continue to grow at a remarkable rate. I'm proud to share that ophthalmology is the leader in attracting new patients to UCI Health, with eye care services making up fully 14% of all new patient visits. We also are the busiest surgical unit within UCI Health, performing 5,000 eye surgeries each year. To better meet that demand, we have added two operating rooms at the institute to our two existing operating suites. We will occupy one of the new facilities immediately, while the fourth will be available to other departments for the time being.

We continue to expand our faculty with the recent hiring of three new ophthalmologists: Andrew Smith, MD; Soroosh Behshad, MD, MPH, and Kapil Mishra, MD, our first ocular oncologist, ensuring that we offer the full spectrum of eye care to our patients across Orange County and Southern California. (Learn more about Dr. Mishra on page 5.)

We also are conducting a national search for a research scientist to join our exciting new program in precision genome editing, which has the potential to permanently reverse inherited causes of blindness. This new program is led by world-renowned vision scientist Krzysztof Palczewski, PhD, director of our internationally regarded Center for Translational Vision Research. In this and other areas, we're actively recruiting both physicians and basic scientists who will enable us to meet the growing needs of our community in this second decade.

Teaching the next generation of ophthalmologists physicians is also a vital part of our mission. We are proud to announce that we are expanding our accredited three-year residency program from nine residents to 12. We also have added three new fellowship programs — uveitis, neuro-ophthalmology and pediatric ophthalmology — to our highly competitive programs in cornea, glaucoma, oculoplastics and retina.

You may have noticed new construction underway next door to the us. We are especially excited about this 200,000-square-foot medical research building, which will include state-of-the-science laboratory facilities thanks to a $30 million lead gift from the Falling Leaves Foundation, established by UCLA professor emeritus Robert A. Mah and Dr. Adeline Yen Mah. Our Center for Translational Vision Research is among the top candidates to occupy what is expected to be one of the largest, most advanced research facilities in the West. Space in the new building would relieve some of our scientists' current lab constraints and spur more collaborative research endeavors. To that end, our donors have once more proven most generous, almost immediately giving $3 million toward a $20 million campaign to support ophthalmology lab space in the Falling Leaves Foundation Medical Innovation Building.

None of our achievements over the last decade would have been possible without the loyal support of our philanthropic community and UCI leadership, and we are deeply grateful to them. Above all, we are indebted to the patients we serve, the people who make our clinical and research efforts worthwhile each and every day.

My sincere thanks,

Baruch D. Kuppermann, MD, PhD

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

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Specialist in rare eye cancers joins UCI Health

Kapil Mishra, MD, is like a missing puzzle piece. The new UCI Health ophthalmologist's expertise in certain cancers of the eye was the last ophthalmic subspecialty needed at the Gavin Herbert Eye Institute. Until now.

Eye cancer may be quite rare — about five cases per million people annually — but Mishra is currently the only ocular oncologist practicing in Orange and Riverside Counties, which means hundreds of patients in the region may need his services each year.

Returning to UCI Health as a physician is a homecoming for Mishra, who completed a residency in internal medicine at the UCI School of Medicine. Growing up in the Inland Empire, he'd always viewed UCI as a beacon of healthcare excellence.

"Anytime anyone needed complex or higher level coordination of a multidisciplinary disease, they'd be referred to UCI Health," he remembers. "My impression was that UCI was a cutting-edge place offering high-acuity care, and that was welcomed by the community, not only in Orange County but beyond."

After earning his medical degree from Icahn School of Medicine at Mount Sinai in New York City, Mishra was excited to complete his residency at UCI Health. He went on to complete a second residency, in ophthalmology, at Johns Hopkins University in Baltimore, Md., followed by a fellowship in vitreoretinal surgery — surgery on the retina and the fluid-filled spaces inside the eye at Stanford University in Palo Alto.

This training makes Mishra uniquely equipped to help patients dealing with a variety of retina diseases, including uveal melanoma, or skin cancer in the eye. He also is the first UCI Health physician who can treat the condition surgically by implanting a small radioactive plaque in the retina, which targets the tumor for several days before it is removed. He also works with patients whose cancer has spread to their eyes from other parts of the body. Such metastatic cancers can cause a variety of vision problems, with treatment options ranging from radioactive plaques to lasers.

Eye sight can also be affected by radiation and chemotherapy used to combat other types of cancers. Mishra collaborates with a patient's cancer care team to determine whether the vision changes are a result of toxicity of the treatment or an inflammatory reaction and help manage those side effects.

Not all eye tumors are cancerous. Mishra also treats benign hemangiomas and other non-malignant growths in the back

of the eye that can cause vision problems. Ultimately, ruling out a potentially life-threatening eye cancer, and providing a patient with an accurate diagnosis and proper treatment, is a top priority for both Mishra and his patients.

Mishra expects to stay busy working with the institute's ocular oncology team, which includes cornea specialist Olivia Lee, MD, who operates on tumors on the eye surface, as well as oculoplastics specialist Jeremiah Tao, MD, and Lilangi Ediriwickrema, MD, who deal with tumors on the bony outer structure of the eye called the orbit. He is excited to be working with a multidisciplinary UCI Health team to serve patients with complicated cases.

"Patients are often scared and may have been referred multiple times before I see them," Mishra says. "I have the opportunity to develop a significant relationship with ocular oncology patients as we address what can be a very complex disease pathology, involving all parts of the eye.

In addition to seeing patients at the eye institute, Mishra is dedicated to improving vision health globally, particularly in underfunded regions of the world. Through partnership with India's Aravind Eye Hospital in Tamil Nadu, he is developing a device that would manually break apart cataracts because traditional cataract procedures involve ultrasound, a technology not widely available. He is also collaborating with researchers from other institutions to develop a telehealth option to screen patients in Ghana for sickle cell retinopathy.

Mishra's research projects are focused on leveraging big data to improve outcomes in vitreoretinal surgery and ocular oncology. Right now, he says, retinal research and innovations are flourishing, which benefits patients at UCI Health and around the world.

"There have been so many recent discoveries for retina diseases, where before there were few options," Mishra says. "It's exciting to be able to offer novel treatments for diseases that millions of people have."

Thank you to our donors

We are grateful to all our donors and would like to highlight those who have made contributions of $5,000 or more in support of our research, educational and community programs from July 1, 2022–Sept. 1, 2023.

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To learn more about how you can support the Gavin Herbert Eye Institute, please contact Amber Harness, director of development, at aharness@uci.edu

The Herberts

Philanthropists reflect on the eye institute they helped build

Nearly two-thirds of people over age 65 experience vision problems such as cataracts, glaucoma or age-related macular degeneration. Gavin and Ninetta Herbert are no exception. They both see ophthalmologists at the eye institute that bears his name.

In the 10 years since the Gavin Herbert Eye Institute opened its doors, it has flourished, treating 75,000 patients this year and delivering nearly 5,000 eye surgeries in the state-of-the-art building on the university campus in Irvine. The Herberts say the care they receive is top-notch.

"The thing I'm most proud of about the eye institute is the reputation it has developed in the community," says Gavin Herbert. "The feedback I get continually about the eye institute from people I meet is very, very positive. It's really quite impressive, everything the whole team is doing."

A longtime vision

Seen by many as the father of Orange County's thriving ophthalmic industry, Gavin Herbert co-founded the pharmaceutical company Allergan and brought it to Irvine in 1966, just as the University of California opened a new campus on land that had been part of the historic Irvine Ranch.

He helped recruit internationally renowned glaucoma researcher Irving Leopold, MD, as founding chair of the UCI School of Medicine's Department of Ophthalmology, bringing instant prestige to the fledgling program. In the 1970s, Herbert and Leopold talked about creating an institute focused on eye research, but the idea lay dormant until the mid-2000s, when dozens of ophthalmic startups sprouted in Orange County.

It was then that Herbert protégé Jim Mazzo — who worked at Allergan for two decades before taking the helm of Advanced Medical Optics — rallied the community to fund a world-class eye institute in Irvine. Corporations and local philanthropists generously donated $40 million toward the effort, including a $10 million naming gift from Herbert's mother, Josephine Gleis.

Gleis had her own connection to the eye institute: She was treated for macular degeneration by Baruch Kuppermann, MD, PhD, now chair of the ophthalmology department and director of the eye institute.

"Certainly a key to the success of the eye institute was the original vision and leadership of Dr. Roger Steinert, and then Barry Kuppermann stepped in and has also done a wonderful job," says Gavin Herbert. "We've been very fortunate to have two terrific leaders to move this project ahead."

Serendipity

Since the opening of the eye institute in 2013, Gavin and Ninetta Herbert have continued to support UCI's excellence in ophthalmology by funding two endowed chairs: the Irving H. Leopold Chair and the Roger F. Steinert, MD, Endowed Chair.

They have also made major gifts to support retina research and vaccine development, the latter of which is of particular interest to Gavin Herbert for its parallels to the development of Allergan's most famous product, Botox.

Initially developed as a highly effective treatment for blepharospasm, or twitchy eyelids, Botox now is used to treat dozens of conditions, ranging from migraines to cerebral palsy, although it is best known for its cosmetic applications.

He sees a similarly happy accident in a vaccine being developed by ophthalmology professor Lbachir BenMohamed, director of the eye institute's Laboratory of Cellular and Molecular Immunology.

BenMohamed's work on a vaccine for a different virus is now a promising prospect for a pan-coronavirus vaccine — one that could stand up to the continually evolving variants of the virus that causes COVID-19, as well as many other coronaviruses.

"That a vaccine to save us from future coronavirus pandemics may emerge from an ophthalmic lab is true serendipity," Herbert says.

Next generation

While Gavin Herbert focuses on research breakthroughs, Ninetta Herbert's heart is with saving the vision of the next generation.

"The greatest gift in the world is vision," she says.

As a founding member of the Visionaires, she helps lead a group of community members who support the institute's Eye Mobile for Children. This ophthalmology office on wheels visits local schools and has provided free vision screenings to more than 20,000 children across Orange County.

"Many places don't test children's eyes anymore, even though we know it's critically important," says Ninetta Herbert. "We have to help screen children, because if certain vision problems aren't identified before the age of six, it's harder to treat them."

Through the Eye Mobile for Children, the Visionaires hope to reach more children whose future may be permanently affected without early intervention.

The Herberts also hope to engage a younger generation of local leaders, including parents who may not yet be experiencing the vision problems common with aging, but who care about the eyesight and health of their children and the entire community.

They hope the new generation will champion eye care excellence in Orange County, ensuring that UCI continues its trajectory as one of the world's leading centers for eye care and groundbreaking research. Already, the couple is laying the groundwork for future success by helping to raise funds to build a collaborative ophthalmology research space in the Falling Leaves Foundation Medical Innovation Building, which is under construction next to the eye institute.

"The community has been wonderful about supporting the eye institute over the years," says Gavin Herbert. "We look forward to their participation in exciting new projects, as well."

Q&A: New horizons for glaucoma research

Preeminent glaucoma scientist Gulab S. Zode, PhD, recently joined the UCI School of Medicine's Department of Ophthalmology and its Center for Translational Vision Research. His current projects are supported by several prestigious grants from the National Institutes of Health and the Alcon Research Institute. He recently shared what drew him to UCI and its vision research center.

Q. What brought you to the Department of Ophthalmology?
The quality of work coming from the department and its reputation for ocular research were highly attractive for me. The department has exciting basic and translational research programs with world-renowned faculty like Krzysztof Palczewski, PhD, and others. Also, although the department is very strong in retina research, they did not have any scientists dedicated to the particular aspect of glaucoma that I study.

Q. What is the focus of your glaucoma research?
My research aims to understand intraocular pressure regulation and its relationship to glaucoma. Intraocular pressure, which is elevated in glaucoma patients, is created by aqueous humor dynamics. Aqueous humor is a transparent fluid that provides nutrition to eye tissues. It gets filtered through a specialized structure known as trabecular meshwork. When a patient has glaucoma, their trabecular meshwork blocks the aqueous humor from flowing out normally, which increases pressure in the eye. Yet none of the current treatments for glaucoma target the trabecular meshwork.

My research focus is explaining why trabecular meshwork outflow is blocked in patients with glaucoma, then targeting these pathologies for treatment. In particular, we are studying how a mutation in a glaucoma gene called myocilin can cause damage to the trabecular meshwork. We have discovered that mutant myocilin is misfolded and it accumulates abnormally in trabecular meshwork cells, which results in elevated intraocular pressure and glaucoma. We are now studying cellular processes, including autophagy, which can degrade and remove the abnormal proteins from the eye and cure glaucoma.

Q. What led you to study glaucoma?
I come from a small village in India and I didn't have a lot of choice in subjects when I first came to the United States for graduate school. As a postdoctoral student at the University of Iowa, I ended up working with a clinician who was doing ocular research. He would bring patients to talk with us, including many people who were blind. I began to see his perspective, what motivated him — he always worked to benefit the patient. Around that time, we discovered a treatment for juvenile-onset glaucoma and I saw an opportunity to do translational research that could really help people.

Q. With 3 million Americans suffering from glaucoma, what potential therapies offer the most promise?
There are two exciting translational science projects I'm working on. One is a small molecule approach and the other is gene editing. In both, we are targeting the gene myocilin, which affects trabecular meshwork and therefore eye pressure. It is one of the known causes of inherited types of glaucoma. With the small molecule approach, we're working on developing a chemical that can easily travel through cells to treat the myocilin and delivered with an eye drop. With gene editing, we would correct the mutation at the cellular DNA level, eliminating the disease permanently. That is what also attracted me to UCI: I'm able to work directly with glaucoma clinicians to develop treatments for these patients.

A painter's sight preserved

Alert ophthalmologist spots stroke symptoms, saving patient's vision

The way Mary McKay Schaffer sees it, her ophthalmologist not only saved her vision, she saved her life.

Schaffer arrived at the Gavin Herbert Eye Institute in November 2020 for a routine visit with Dr. Sameh Mosaed. A few years earlier, Mosaed had performed surgeries to treat cataracts in both of Schaffer's eyes, as well as mild glaucoma. The procedures restored her vision and she no longer needed glasses. But she still visited Mosaed several times a year for checkups.

An avid painter, Schaffer relies on her sight to choose and mix acrylic paints in search of the perfect colors to bring to life her richly textured portraits of musicians with their instruments, chefs in kitchens and women deep in contemplation.

"Painting is the most natural thing I have ever done," Schaffer says. Although she always loved drawing and painting, she took a 40-year hiatus to work as a special education teacher, then as a booking agent for professional speakers. Today, the 76-year-old Dana Point resident draws inspiration for her paintings from her childhood in North Carolina, a decade of living in Hawaii and now her life in Southern California.

During a visit to the eye institute in fall 2020 for routine tests, Mosaed also checked Schaffer's field of vision. She looked intensely at her patient and said calmly, "Go to the ER right now. You are having a stroke."

Shocked at the idea of any vision problems, Schaffer had her husband drive her directly to the ER. An MRI revealed she was having an acute ischemic stroke that was affecting her right occipital lobe — the part of the brain responsible for vision, including spatial and color recognition so vital for her painting.

At a follow-up visit with Mosaed, the patient recalled a strange moment weeks earlier. While walking with her husband around Dana Point Harbor she didn't recognize a building she'd been strolling past for years. Mosaed's test that fateful day revealed why Schaffer was missing half the field of vision in each eye — a telltale symptom of a stroke.

"I had no visible signs of stroke or disabling characteristics or complaints," she recalls. "But in her calm and professional manner, Dr. Mosaed told me to go straight to the ER. No drama. That's right up there with the best advice I've ever had."

Schaffer stayed in the hospital two days for treatment to dissolve a blood clot in her brain that was causing the stroke. Her doctors were delighted to find no lasting effects to her speech or gait. Astonishingly, her eyesight had returned to 20/20 vision.

"This is extremely unusual to have reversal of vision loss in these types of cases," says Mosaed. "It proves that she was treated before permanent damage was done to the brain. There is a very short window of time before the loss is permanent, typically within a few hours."

Now during her still-routine visits to the eye institute, Schaffer enjoys telling the medical staff that Mosaed saved her life and watching for the look of surprise to cross their faces before sharing the whole story. With each recounting, she reaffirms her gratitude and great fortune to have had an appointment the day she was having a stroke — and that her physician was Mosaed.

"In comparing her with any doctor I have seen, or any doctor who has ever provided me with surgery or advice, Dr. Mosaed ranks No. 1."

An evening under the stars

Celebrating our 10th anniversary

On Oct. 17, 2023, the UCI Health Gavin Herbert Eye Institute celebrated its 10th anniversary with esteemed benefactors Gavin and Ninetta Herbert, as well as UC and UCI leaders President Michael V. Drake, Chancellor Howard Gillman, Provost Hal Stern, Vice Chancellor Steven Goldstein, Dean Michael Stamos and UCI Health CEO Chad Lefteris. Many founding and current supporters also attended to celebrate this momentous occasion. Guests gathered for a reception and dinner on the Mazzo Terrace, where the evening program included remarks from Gavin Herbert and April Steinert.

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Ocular surface tumors, periocular malignancies and more
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Feb. 6, 2024
What causes red eyes and how we treat them
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March 5, 2024
What is keratoconus?
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The importance of annual eye exams; new lens technology
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Cataracts
May 7, 2024
Latest technology in cataract surgery
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Headaches
June 4, 2024
Ophthalmologic evaluation of headaches–a neurologist's perspective
Sam Spiegel, MD
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July 23, 2024
Sedentary time, screen time and exercise in kids: navigating health habits for the digital generation
Shlomit Radom-Aizik, PhD
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