

RESEARCH UPDATE

Promising research for macular degeneration

Healthy Mitochondria Protect Against Cell Degeneration

Through two remarkable research collaborations, Gavin Herbert Eye Institute (GHEI) ophthalmology professor M. Cristina Kenney has made promising discoveries in the search for an effective treatment for macular degeneration. Those discoveries may lead scientists to more effective ways to treat Parkinson's and Alzheimer's diseases.

Macular degeneration is caused by deterioration of the retina's central region which gives us our ability to see fine details. Peripheral vision remains intact, but the central image grows increasingly blurred and eventually can be lost altogether. It is not treatable in its "dry" form, which make up 90 percent of cases. Parkinson's disease is a degenerative neurological disorder that can cause muscle rigidity, involuntary movements and many other symptoms. Alzheimer's disease causes the loss of memory and cognitive skills, and eventually physical functions. In all three diseases, cell death plays a critical role.

All three also tend to afflict older people, said Kenney. Her area of research has focused on mitochondria, the part of the cell that produces energy; when the mitochondria don't function properly, cells deteriorate and die.

Malfunctioning mitochondria might be behind macular degeneration, Kenney hypothesized. In order to find out,



her team worked with cultured cells that all had identical nuclei, but had been depleted of their mitochondria. Then mitochondria-rich platelets were obtained from people with macular degeneration; other platelets were from people of the same age with normal vision.

"The reason we use platelets is because they have a lot of mitochondria and no nuclei," Kenney said. The mitochondria from patients' platelets were fused into the cultured cells and, just as hypothesized, the cells with mitochondria from macular degeneration patients began to die, while the others remained healthy.

The next step involved determining whether the faulty mitochondria could be rescued. For this, the team treated the cells with Humanin G, a potent variation of the peptide humanin, which has strong nerve-protecting and cell-protective properties. The Humanin G was obtained in collaboration with Pinchas Cohen, dean of the USC Davis School of Gerontology, who also has a strong interest in the role of mitochondria in age-related diseases.

The results, as Kenney's team reported in the July 2017 journal Cell Death and Disease, were promising. "If we treat them with Humanin G, they don't die," Kenney said.

There's just one problem: "Humanin G is not commercially available, and the likelihood of a company creating and selling it is low" Kenney said. But what about existing, FDA-approved medications that have similar properties and are used for other medical conditions? For this, Kenney's group teamed with Dr. Howard Federoff, Professor of Neurology at UCI. Federoff's group has been particularly interested in the role of malfunctioning mitochondria in Parkinson's disease.

"They screened a number of drugs that are FDAapproved," Kenney said. "Drugs that are going to target the mitochondria and that will increase the amount of PGC-1-Alpha," an important regulator of energy metabolism.

There are 11 such drugs and in collaboration with Federoff's laboratory, her group has tested one of those, called PU-91.

"We found it increases the number of mitochondria," Kenney said. "So we're really super-excited about it. Because these drugs are already FDA-approved, we wouldn't have to go through extensive safety trials because those already have been done."

The funding isn't currently available, but the next step is to test the other drugs, and to try testing them for Parkinson's as well. "Maybe there's something five to 10 times better than PU-91," Kenney said.

MESSAGE FROM THE CHAIR

It's been an extremely busy few months at GHEI. The faculty and leadership have wasted no time in getting started on the implementation of a sweeping strategic plan.

Initially, we have concentrated on hiring clinicians to build our practice into a full-scale vision-care institute that covers not only every subspecialty within ophthalmology, such as retina and cornea specialists, but also sub-subspecialties within those groups.

Dr. Andrew Browne recently joined GHEI from the Cleveland Clinic after completing his training in a world-class retina practice. His clinical interests include medical and surgical diseases of the retina. Browne also brings a strong and innovative research focus to our department. GHEI, of course, is already at the forefront of research on retinitis pigmentosa using work on progenitor cells. Browne's work takes a different path, developing retinal organoids for potential retinal transplants and advanced imaging to assess tissue function.

We are adding personnel in pediatric ophthalmology beginning with Dr. Charlotte Gore, who joins us from Kaiser Permanente in the Washington D.C. area. Gore is interested in researching new treatments for pediatric nystagmus, and she is featured in our clinical Q-and-A in this issue of Shine the Light.

Both our retina and pediatric practices will be expanded further with the arrival this spring of Dr. Mohammed Riazi Esfahani, formerly of Tehran University of Medical Sciences. He is a world-recognized pediatric retina surgeon with a special interest in retinopathy of prematurity.

This is just the start. A search committee is actively seeking a new glaucoma specialist. Committees are being formed to recruit clinicians in additional sub-subspecialties, including a neuro-ophthalmologist, an oculoplastic surgeon and an ocular oncologist. In our next issue, I'll have news about other aspects of our exciting strategic plan, including efforts to recruit world class researchers to expand the already impressive group of basic and translational scientists at GHEI.



Krevich Verfrunan

Baruch D. Kuppermann, MD, PhD Director, Gavin Herbert Eye Institute Chair, Department of Ophthalmology

Faculty members

Cataracts, Cornea, External Disease and Refractive Surgery

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Cataracts and Glaucoma Sameh Mosaed, MD Anand Bhatt, MD

Comprehensive Ophthalmology Kavita K. Rao, MD

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DONOR PROFILE



A donor and partner in corneal health

SightLife Surgical's donation to help create the Roger Steinert, MD, Endowed Chair in Ophthalmology at UC Irvine is only its most recent act in a long history of generosity toward GHEI and worldwide vision care. Monty Montoya, president and CEO of the eye bank company, has had a close relationship with the institute that dates back to 2005, when he started working with Steinert and cornea specialist Dr. Marjan Farid on laser technology to improve corneal transplants.

The company operates an eye bank at GHEI, its only bank in an academic partnership. Along with its nonprofit donor arm called SightLife, the company aims to wipe out corneal blindness worldwide by the year 2040. One project involves culturing endothelial cells from a single donated cornea for use in treating up to 100 patients. Its success in early trials in Japan? "One hundred percent," Montoya said.

Last year, SightLife Surgical sponsored Farid on a medical mission to train cornea surgeons in India. It also sent corneal tissue with Dr. Matthew Wade on his medical

mission to Armenia. Farid said the company also has been instrumental in helping to set up cornea banks in India and to create a culture of tissue donation there, with the goal of establishing a self-sustaining cornea program in that country.

"They did a lot of work and vastly increased the amount of good, available corneal tissue," she said.

When Montoya was approached about a possible contribution to the Steinert endowed lectureship, he felt it was a natural moment to commemorate his longtime colleague, who died last year after serving as GHEI's founding director, with a \$10,000 donation from SightLife Surgical.

"The creation of the endowed lectureship gave us an opportunity to provide tangible recognition of the partnership we have with GHEI and its brilliant people," Montoya said. "It was an opportunity to honor Roger Steinert and all he contributed to SightLife and to corneal medicine."



Charlotte Gore, MD

Welcoming a specialist in pediatric ophthalmology

When people think about eye issues that are serious enough to require an ophthalmologist, they usually have adults in mind. But Dr. Charlotte Gore, a pediatric ophthalmologist newly arrived to GHEI from the Washington D.C. area, provides another view of the field.

Q: How is pediatric ophthalmology different?

A. Kids' eye problems are different. Children most often get eye misalignments called strabismus. Another common problem is amblyopia, when one eye doesn't see as well as the other.

We often can correct strabismus with eyeglasses, but a small percentage of children will need surgery to tighten or loosen certain eye muscles and restore balance.

Q. Misalignment is something parents can see in their children, but what about amblyopia? How is it discovered?

A. Parents usually seek help when their child fails a vision screening. Amblyopia is most commonly caused by the fact that one eye needs glasses but the other doesn't. If one eye has blurry vision, the brain will decide to "see" using only the clear eye. If left untreated, the weak eye will forever be "forgotten."

We use glasses and a part-time patch on the good eye so that the weak eye catches up. The connections between the brain and that weak eye will strengthen and the improvement will last a lifetime.

Q. Cataracts and glaucoma certainly aren't something we associate with children, and yet children can get them. How does that happen?

A. When these conditions show up in kids, they are often congenital. Glaucoma will cause children's eyes to grow abnormally large because of increased eye pressure. Cataracts will cause the child to have significant vision loss.

Often surgery is needed to correct these problems. The greatest thing about treatment for kids is that you can actually reverse the damage caused by glaucoma or cataracts, restore vision and provide them with potential for good vision for many years ahead.

Rejuvenating the spirit with a medical mission

The nation of Armenia has a unique problem when it comes to corneal transplant: There isn't even the beginning of an eye-tissue bank in the country, or any plans to create one. All the corneas for transplant must come from overseas, and each one is treasured.

"Armenia has a large backlog of patients who need corneal transplants," said Dr. Matthew Wade, a cataract and corneal specialist at GHEI.



So when Wade traveled on his medical mission to the Armenian capital of Yerevan, he took two precious things with him: a supply of donated corneas from the SightLife eye bank at GHEI, and the ability to teach an eye surgeon how to make the most of whatever corneas come her way.

Dr. Anna Hovakimyan, head of the cornea department at the Malayan Eye Hospital in Yerevan, is a renowned ophthalmologist in her country, Wade said. After her week of training last summer with Wade and Dr. John Hovanesian, she now knows how to perform the delicate task of cornea splitting, which can allow one cornea to help two patients.

"The practice of splitting a cornea into parts has been employed in the U.S. for the last few years," Wade said. "The front portion of a cornea, or stroma, is largely structural while the back layer, the endothelium, consists of a layer of cells that keeps the corneal structure clear. One patient may have a corneal scar in the structural stromal portion of the cornea, but normal endothelium. Another patient may have normal structural function but abnormal endothelium. By splitting the cornea into two layers, both of these patients can be treated with a single cornea." The doctors performed their medical mission through the Armenian Eye Care Project. Among the patients Wade saw was a young girl who was born with corneal blindness. The surgical team was able to give her vision for the first time.

Wade found it satisfying to know that his work in Yerevan will now allow a doctor to successfully treat many more patients. His first medical mission had such a profound effect on him that Wade has already planned his next one, to Jamaica in April.



"After that trip, my soul was rejuvenated in terms of what we can do for people. I went there for other people but it ended up being a gift to me as well."



Mourning the loss of a great friend

A longtime friend and supporter of the Gavin Herbert Eye Institute died in January.



Josephine Herbert Gleis, mother of GHEI's founder Gavin Herbert Jr., lived a long and extraordinary life. She was 105 years old when she died in her Linda Isle home in Newport Beach.

In 2007, Gleis and her son provided the \$10 million naming gift to UCI to build GHEI. That set off a wave of donations from local vision companies and individual benefactors who raised the rest of the money to build the institute.

Gleis also funded research into macular degeneration, a retinal affliction that is the third leading cause of blindness. Gleis suffered vision loss from macular degeneration, and in part because of her donations, GHEI now is a leader in research into this eye ailment.

"She was an amazing person," said Dr. Baruch D. Kuppermann, director of GHEI. "Her commitment to eradicating potentially blinding disease was unwavering. Nothing would give the Gavin Herbert Eye Institute faculty greater pleasure than making her legacy one of supporting the people and research that make preventable blindness a thing of the past."

In recognition of this generous woman's devotion to eye health, her family has suggested that instead of flowers, people honor her through memorial donations in her name to support GHEI ophthalmology research. These can be made by mail to: UCI Foundation, FBO: GHEI, Attn: Janice Briggs; 850 Health Sciences Road, Irvine, CA 92697-4375. They can also be made online at eye.uci.edu/donate

Gleis leaves a legacy that is helping people regain their vision now through clinical care at GHEI, and will continue to help them through research into new treatments for eye disease.

Thank you to our donors

Gifts of \$50,000 and above received since July 1, 2017, to the general fund of the Gavin Herbert Eye Institute:

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Gifts of \$10,000 and above to the proposed Roger F. Steinert, MD, Endowed Chair in Ophthalmology:

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\$3,625,500 of the \$5,000,000 goal has been raised to date. To make a donation to this Endowed Chair, contact Janice Briggs, executive director of development, at 949-824-0091 or jbriggs@uci.edu

Gifts of \$25,000 and above received since July 1, 2017, for research:

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Free, informational seminar to learn about LASIK surgery and whether you might be a candidate. April 19, 2018 | 6:30 p.m.

Community Lecture Oculoplastics

Eyelid and Facial Skin Cancers: Treatments in Oculoplastic Surgery Jeremiah Tao, MD May 14, 2018 | 7 p.m.

Irritated Eyes:

Getting the Red Out: Controlling Eye Irritation Marjan Farid, MD Kavita Rao, MD Sept. 17, 2018 | 7 p.m.

You can watch community lectures online at: http://www.eye.uci.edu/videos.html

Make an appointment

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