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UCI Health C Gavin Herbert Eye Institute

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RESEARCH UPDATE

The Immune System of the Eye

Dr. Pearlman's Research With Neutrophils

Neutrophils are among our very best friends, the first responders of the human body's immune system. They are our most plentiful white blood cells and they rush to the scene of infection to fight off invaders. Their super powers include the ability to move through tissues and reach infections in most areas of the body, including the eye.

Yet at times and in some ways, neutrophils can have a dark side as well, said Dr. Eric Pearlman, professor of ophthalmology at Gavin Herbert Eye Institute (GHEI) and director of UCI's Institute for Immunology. He specializes in research on corneal infections.

"Neutrophils respond to everything," Pearlman said.

"They're the ones who rush in there. Their job is to kill bugs and keep them from disseminating and causing sepsis. They'll release a whole bunch of enzymes that digest the tissue, which is fine in the skin when you have a blister. But it's a problem with the eye."





The immune system response is inflammatory; that's part of how it attacks invaders. But that inflammatory response also causes redness, intense pain and blurred vision.

In order to quell that response in the cornea, ophthalmologists typically prescribe a topical corticosteroid, which can create its own problems after continued use. "Corticosteroids cut off every aspect of the immune system," Pearlman said. With extended use, they also increase intraocular eye pressure, and that can lead to glaucoma.

Pearlman has been working to develop targeted antiinflammatory medications that could be used instead of steroids. These efforts are based on his research on the inflammatory process in the cornea and identifying new targets for therapeutic intervention. He is the co-founder of Alevca Ocular LLC, a company set up to move these novel drugs to market.

In addition, Pearlman has been working on novel pathways for treating fungal infections of the cornea. In developed countries, these infections are often associated with contact lens use. But they also are a sight-robbing scourge in many developing nations, including India. The World Health Organization estimates that 1.8 million people in developing nations are blinded annually from corneal ulcers; in developing nations in

Asia and Africa, up to 65 percent of total corneal ulcers are caused by fungal infection. Effective treatments are lacking.

"Fungal spores penetrate the cornea as a result of trauma to the eye," he said. "The spores will then germinate and hyphae will grow throughout the cornea."

His research, some of which was conducted at the Aravind Eye hospital in southern India, involved developing topical medications to starve the fungus by competing for essential nutrients, including iron and zinc. His work on this has been published and the medication patented.

The National Eye Institute recently renewed Pearlman's grant for research on fungal infections of the cornea. He is the recipient of a second grant for work on bacterial infections of the cornea.



MESSAGE FROM THE CHAIR

We recently hosted the fifth annual Bench to Bedside Symposium, where many researchers presented their exciting work.

This annual meeting focuses on translational research, and is the brainchild of Jack Schoellerman, chairman of the Discovery Eye Foundation, which provides research support to GHEI. This year, the March meeting drew more than 120 researchers and ophthalmologists for a lively day of presentations. Videos of these presentations will be available on our website: www.eye.uci.edu.

It started with a look at UCI's focus on integrative medicine, which has been made possible by the extraordinary \$200-million gift from Susan and Henry Samueli. Dr. Shaista Malik, director of the Susan Samueli Center for Integrative Medicine, spoke about how mindbody states can affect cardiovascular health. I had the honor of speaking about applying rigorous scientific methodology to integrative health, using as an example large National Eye Institute-sponsored studies that demonstrated the benefits of certain nutraceutical supplements in slowing the progression of age-related macular degeneration.

One of the meeting's highlights was the presentation by UC San Diego research star Dr. Napoleone Ferrara, winner of the Lasker-Debakey award for clinical medical

Faculty members

Cataracts, Cornea, External **Disease and Refractive Surgery** Vice Chair, Ophthalmology Faculty Sumit (Sam) Garg, MD Vice Chair, Clinical Ophthalmology Matthew Wade, MD **Cataracts and Glaucoma**

Anand Bhatt, MD Ken Lin, MD, PhD Sameh Mosaed, MD

Comprehensive Ophthalmology Kavita K. Rao, MD

Marjan Farid, MD

Sanjay Kedhar, MD

Rick Hill, MD

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research. Ferrara, who was honored for his discovery of the key molecule responsible for wet macular degeneration, spoke about the process of discovery. His amazing work led to the development of the drugs Avastin and Lucentis, which are used to treat age-related macular degeneration as well as various types of cancer.

Among GHEI's many shining stars to speak were Dr. Henry Klassen, who explained his research using human progenitor cells in the treatment of retinitis pigmentosa, which has had remarkable early success; Dr. Sanjay Kedhar, who discussed the connection between the gut microbiome and uveitis; and Dr. Andrew Browne, who spoke about his research using stem cells to make retinal organoids.

Overall, it was an exhilarating day of scientific and medical dialogue, thanks to the wonderful program organized by GHEI's Dr. Cristina Kenney. It was a reminder of how GHEI and UC Irvine are at the cutting edge of work to develop new treatments for devastating eye diseases.



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

Neuro-ophthalmology Chantal Boisvert, MD R. Wade Crow, MD

Oculoplastics Jeremiah Tao, MD

Ophthalmic Pathology Donald S. Minckler, MD

Optometry

Kathleen Dang, OD Timothy Scott Liegler, OD Kailey Marshall, OD Poonam Varsani, OD

Pediatric Ophthalmology

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Retina and Vitreous

Andrew Browne, MD, PhD Baruch D. Kuppermann, MD, PhD Chair, Department of Ophthalmology Stephanie Lu, MD Mitul Mehta, MD Mohamed Riazi, MD

Uveitis Sanjay Kedhar, MD

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Eric Pearlman, PhD Jing Yang, MD, PhD

CLINICAL HIGHLIGHT



A Family Tradition of Giving

Some things run in the family of Cristina Kenney and Anthony Nesburn. Ophthalmology, for one. Both are top-level researchers at UCI Health's Gavin Herbert Eye Institute (GHEI). The couple's daughter is an ophthalmologist. So was Nesburn's father.

Giving is also a family tradition. "My family is philanthropic, and did a lot of gift-giving," Nesburn said. "It's something you sort of learn and you pass on to your kids." His mother funded a writing contest for school children. Later, with the financial support of grateful patients, Nesburn and his family helped start the Discovery Eye Foundation to fund basic eye research. Both he and Kenney are actively involved with the foundation.

Kenney's father was also a physician who gave his time and talents to many good causes in New Mexico, where she grew up. "My parents were among those who founded the Santa Fe Chamber Music Festival." she said.

Unsurprisingly, then, Dr. Kenney and Dr. Nesburn are

regular donors to GHEI. Joining other community supporters, they have contributed to many important programs, including the GHEI Capital Campaign, the Roger F. Steinert Endowed Chair, and the 20/20 Society annual fund which supports research. Lately, Kenney and Nesburn have been planning to create a lectureship to draw topflight speakers to GHEI.

"One of the great things you can do is to donate money to support research," said Nesburn, GHEI's vice chair for basic research, whose work includes efforts to develop a vaccine against ocular herpes. "Research is always scrambling to find money."

Kenney, a professor of ophthalmology at GHEI, thinks it's important to walk her talk as a researcher. "If you're part of it, you should be supporting it yourself," said Kenney, whose work focuses on the role of faulty mitochondria in the development of macular degeneration. "How can you ask others to give if you don't believe in it and do it yourself?"



Dr. Rick Hill

Q&A with an Ophthalmologist – Dr. Rick Hill

Unlike most ophthalmologists joining Gavin Herbert Eye Institute (GHEI), Rick Hill isn't a newcomer to Orange County or to UC Irvine. He was an associate professor at the medical school who left in 2005 to open a private practice locally and to conduct research in his area of specialization: glaucoma.

Q: How long have you been practicing in Orange **County?**

A. Since 1990

Q. And what led you to return to UCI?

A. My private practice grew and left me with little time for research. By donating my practice to UCI and joining GHEI, my patients could be seen by some of the top-notch specialists in the country at a top facility. I can still see some of those patients at GHEI, be with my patients, friends and colleagues, as well as have time to continue my research.

Q. What has been the focus of your research?

A. We need glaucoma surgeries that have lower morbidity, are minimally invasive and afford patients rapid vision recovery. To address these problems, I developed a series of implants called iStents. These stents allow fluid to bypass resistance in the trabecular meshwork or access other drainage pathways in order to lower eye pressure.

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Q: What are you working on these days?

A. In the past, medical and surgical glaucoma therapies treated only the symptoms, not the cause of the disease. These therapies also led to red eyes and surgical complications. I have a thought about what the primary defect is in open angle glaucoma and we are currently validating that theory and hope to produce a new family of medications. In addition, I will also be working on an entirely new, physiologically based approach to micro-invasive glaucoma surgeries (MIGS). My patients and I are looking forward to joining GHEI and being part of its future.

PATIENT SPOTLIGHT

Medical Mission to Nepal



Performing eye surgery in a remote village of Nepal required finding a table big enough to work as an operating surface, and rolling out sleeping bags on the floor for a night's rest.

And that was the easy part.

Getting to the village required the team of doctors to make a long trek in a four-wheel-drive vehicle, followed by two days of backpacking through challenging terrain on treacherous trails, with eyeglasses, surgical equipment and other supplies stowed in their backpacks and on the backs of mules.

"There's no road into this area," said UCI Health ophthalmologist Dr. Sanjay Kedhar. "It was probably only 15 to 20 miles of hiking, but with constant elevation changes."

Kedhar, an associate professor of ophthalmology at the Gavin Herbert Eye Institute and a cornea specialist, would spend three days there, mostly performing cataract surgery.

There was a place for the doctors to spread out their sleeping bags at night. There also was a room for surgery — but no operating table.

"We had to scour the town searching for a suitable table," Kedhar said. "There was just one; we found it at a restaurant and they let us use it for the few days we were there." Patients walked into town from surrounding villages in order to be treated. Over three days, the doctors screened 800 patients and performed surgery on 71 of them. The mission also provided food for the patients and places for them to stay.

"We work with the local monastery so the monks actually go out into the villages to let the community know there will be an eye camp," Kedhar said. Elementary schools bring their students. Many of the patients needed reading glasses, which were provided for free. Others received antibiotics or other eye medications.

Though the Nepalese patients are unfamiliar with surgery, they tend to be less nervous about it than many Americans, Kedhar said. They get no medications to help them relax before surgery, just local anesthetic injections around the eye. Afterward, they leave with bandages that remain on for a day.

As stoic as they were, once the bandages were removed, some of the patients reacted with clear astonishment and joy. One man began to dance and wanted the doctors to dance with him.

Another patient was carried into the village by her son-in-law.

"She had had very bad cataracts in both eyes for the past three years," he said. Her son-in-law carried her everywhere because they lived in a mountain area where the terrain is uneven and walking without seeing is difficult. When her bandages were taken off, she was looking around, looking at the colors of everything. The day after her surgery, she was able to walk out of the village on her own.

"The son-in-law was probably happier than she was."

To see a video of the mission, go to https://vimeo.com/256732590.

Stanley Rosen

Corneal Stem Cell Transplant Restores Quality of Life.



Eye surgery could not give Stanley Rosen more time, but it restored his quality of life. For this, his wife is profoundly grateful to his GHEI ophthalmologist, Dr. Marjan Farid.

Rosen had struggled with visual impairment for many years, said Glenda Rosen of Laguna Woods. Eventually, those problems developed into a condition in which the surface of the eye could not produce new cells to repair damaged tissue, Farid said. The scarring and haziness of the cornea cost him his sight. Glenda Rosen and her husband would go on regular nature walks, where the trees where labeled with interesting information. Unable to see, Glenda would read these descriptions to Stanley.

Although Stanley Rosen, a retired attorney, was battling brain cancer, he still proceeded with a corneal stem cell transplant with Farid. She is one of a handful of ophthalmologists who can perform the difficult procedure. It worked, and among the happiest moments of Rosen's last six months were the times that he and his wife would take their favorite walk, and he could see the trees clearly and read the signs himself until he died in late 2012.

When his wife needed cataract surgery, she asked Farid to perform the procedure. "My eyesight is 20/20 now," she said.

And then, when Stanley Rosen's son required eye surgery, Farid once again made things right. Phillip Rosen, who has a developmental disability, was very nervous about the procedure. "Dr. Farid's bedside manner was wonderful, particularly the moment when she was about to wheel him in," Glenda Rosen recalled. "She smiled at him and said, 'You look just like your father.' That was a priceless way to make Phillip feel he was in the right place with the right person."

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Thank you to our donors

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12th Annual Colloquium

Gavin Herbert Eye Institute To register: www.ghei.uci.edu October 12 and 13, 2018

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

Regaining Your Eyesight: Considering Surgery to Get Rid of Your Glasses or Contacts?

Matthew Wade, MD Mon., Nov. 5, 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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