Disorders such as age-related macular degeneration and glaucoma progressively eat away at critical structures within the eye, ultimately robbing patients of their vision. By the year 2020, these two illnesses are expected to affect almost 280 million people worldwide. Despite this real and growing public health threat, there is no cure for either affliction. Researchers at UNC Eye are working hard to improve the outlook for patients, inventing methods in the field of regenerative ophthalmology to combat the damage wrought by these progressive diseases.

“Our researchers are focused on translational research, conducting studies with the main goal of developing new therapies,” says Donald L. Budenz, M.D., M.P.H., Kittner Family Distinguished Professor and Chair of Ophthalmology. “The current therapies for age-related macular degeneration and glaucoma do little more than ameliorate the symptoms. In my mind, efforts like stem cell research and gene therapy have the potential to actually cure disease. That desire to bring about cures, combined with the strength of UNC’s existing research program, put us in a position where I think we can truly make a difference.”

UNC Eye is taking a three-pronged approach in its search for cures. Sai Chavala, M.D., is reprogramming stem cells to take the place of retinal cells damaged by age-related macular degeneration. Teresa Borras, Ph.D., is hijacking viruses to deliver genes as therapy for glaucoma. Scott Lawrence, M.D., is making designer nanoparticles that can encapsulate and deliver therapeutics to areas of the eye affected by glaucoma.

“We are addressing the two big causes of irreversible blindness, both here in the United States with macular degeneration and worldwide with glaucoma,” says Dr. Budenz. “There is real clinical relevance and a bench to bedside nature in the translational work we are doing.”

**Stem cells**

Macular degeneration is a common eye condition that causes damage to the macula, a small spot near the center of the retina. Because the disease develops as a person ages, it is often called age-related macular degeneration (AMD). It manifests in two forms: “wet” and “dry”. The wet form is caused by abnormal blood vessels that leak blood and fluid into the macula. The dry form is caused by tiny yellow deposits, called drusen, that cause the macula to deteriorate over time. Though there are several new treatments for wet AMD, there are no FDA-approved treatments for dry AMD.

“Unlike the wet form, dry AMD is more insidious and progresses very slowly,” says Dr. Sai Chavala, an assistant professor of ophthalmology. “We can follow patients over months and years, and we have this huge window of opportunity to intervene with a drug or therapy to halt the progression of the disease.”

With support from a National Eye Institute K08 award, Dr. Chavala is exploring therapies to replace some of the most susceptible cells in dry AMD, specifically a layer of cells in the macula known as retinal pigment epithelium or RPE cells. These cells support the light-sensing neurons of the retina, and without them, the neurons die off, causing irreversible vision loss.

His approach involves taking cells from another part of the eye and reprogramming them into pluripotent stem cells or iPS cells – specialized cells that can give rise to any other cell type -- before inducing them to transform into RPE cells. He has been able to reprogram the cells using only one factor, a major improvement over the four factors initially used in the Nobel Prize-winning work of his predecessor Dr. Shinya Yamanaka.

Clinical trials are already underway testing replacement RPE cells derived from another type of stem cell, called embryonic stem cells. But Dr. Chavala thinks his approach is better, and not just because it circumvents the ethical concerns associated with using cells taken from human embryos.

“iPS cells are immunologically superior to ES cells,” says Dr. Chavala. “Because the replacement cells come from the patient’s own body, there is less chance of rejection. Clinical trials with iPS cells are next, and I am hopeful that this approach can prevent vision loss.”

(continued on page 3)
Chair’s Corner

2013 was certainly an exciting year for UNC Eye, beginning with the opening of the North Carolina Eye Bank Microsurgical Skills Lab and finishing the year with the opening of the New Kittner Eye Center. But we’re just getting started! In this edition of the newsletter, you’ll read about the UNC Laser Vision Center opening in early 2014, our research expansion into the areas of gene therapy and stem cell therapy for eye diseases, and our telemedicine program to prevent blindness from diabetic eye disease.

Refractive error is the most frequent cause of visual impairment world-wide. Traditionally corrected with glasses or contact lenses, refractive errors can also be corrected with lasers. I am pleased that we will be able to offer laser vision correction to the UNC and Triangle Community starting in 2014 with the help of new faculty member Karl Stonecipher, MD, world-renowned expert in refractive surgery, Rich Davis, MD, a cornea subspecialist who developed a successful refractive surgery practice while chairman at the University of South Carolina, and Nisha Mehta, OD, our newest faculty member with 10 years’ experience in optometry and refractive surgery evaluations.

The UNC School of Medicine is a wonderfully collaborative institution and we are partnering with numerous researchers to develop new cures for eye diseases. I say “cures” because I believe we are on the verge of major breakthroughs in gene therapy and stem cell replacement therapy that will cure, rather than ameliorate, major causes of blindness such as age related macular degeneration and glaucoma. The research team that we have assembled is working in the area of Regenerative Ophthalmology. Our hope is that assembling researchers working in the same disciplines (gene and stem cell therapy) for different diseases (glaucoma, retina, and corneal diseases) will result in synergies that will result in cures. We are partnering with Jude Samulski, PhD, world-renowned Director of the UNC Gene Therapy Center and Viral Vector Core, Joe DeSimone, PhD, Director of the UNC Nanomedicine Institute, and many other researchers at UNC. This is a very exciting time for research in eye diseases and partnering with researchers in the UNC community will allow us to make great strides toward our goal of curing and preventing blindness from diseases such as macular degeneration and glaucoma.

Finally, one of the missions of the UNC School of Medicine is to help all the people of the state of North Carolina, not just those in the Triangle. As the state’s only public Department of Ophthalmology, we feel a burden to help people across the state, either by preventing or treating eye diseases. Of course, with a full-time faculty of 20 physicians, there are only so many patients we can help using the traditional model of patient visits to the doctor. Thanks to a health services grant from the Duke Endowment, Dr. Seema Garg is spearheading the first of several telemedicine projects to reach patients in underserved rural areas of North Carolina. Dr. Garg is expanding on her successful research project, which was funded by the NIH, to develop a model to examine ALL diabetics going to their primary care doctors for care using telemedicine. This project will be a model for future health care delivery systems in the United States and abroad where resources are limited and doctors are scarce.

So enjoy this issue of our newsletter. I would encourage you to contact me if you would like to find out more about our efforts and how you might partner with us.

Donald L. Budenz, MD, MPH
Kittner Family Distinguished Professor and Chairman
UNC Eye Care Center
Gene therapy

While Dr. Chavali’s approach employs entire cells to preserve vision, his colleague Dr. Terete Borras is using bits of the cells’ blueprint, DNA, as new treatments for eye disease. Her disease of choice is glaucoma, a progressive disease caused by abnormally high pressure within the eye that damages the optic nerve and can lead to vision loss. Treatments for the disease are short-acting, and only about half of glaucoma patients use the recommended daily doses of eye drops.

“The essentially, we want to use genes as drugs, because they last longer and are more specific,” says Dr. Borras, a professor of ophthalmology with two R01 awards from the National Eye Institute. “On one hand, we are searching for genes that could reduce intraocular pressure, and on the other we are trying to develop viral vectors that could deliver these genes to the tissues affected in glaucoma.”

The target of Dr. Borras’ efforts is the trabecular meshwork, a sponge-like tissue at the base of the cornea responsible for draining fluid out of the eye. If that tissue gets clogged, fluid accumulates and pressure increases in the eye. The trabecular meshwork could get clogged for a number of reasons, including through the build-up of extracellular matrix, a material that helps cells and tissues maintain their structure.

Dr. Borras is using a gene called matrix metalloproteinase 1 (MMP1) that will break up the extracellular matrix, with the potential to open up the trabecular meshwork and relieve the intraocular pressure in patients with glaucoma. She is collaborating with the UNC Gene Therapy Center to develop the best virus to carry that genetic cargo into eye cells. They have selected aden-associated virus or AAV, a virus that has been used safely in a number of gene therapy clinical trials.

To test whether it worked, she used steroids to induce glaucoma in sheep, injected them with the viral vector containing the MMP1 gene, and then measured the intraocular pressure. She found that the pressure was lowered over a period of weeks in the animal models, lending support to her approach. Now she is tweaking her technique, testing different types of AAV and also adding in other pieces of genetic material that could help make a better, smarter form of gene therapy.

“If we are going to use these viral vectors as medicines, then we have to develop them in a way that can be regulated,” says Borras. “It is great to have a vector that lowers intraocular pressure, but it may not be good to have that all the time. With cutting and pasting different sections of DNA together, we could create a gene that will turn on when the pressure is there and then off when there is no pressure. It would be like a thermostat – it would only kick in when it was needed.”

Dr. Budenz, who before becoming chair conducted research in gene therapy and was the first researcher to transfer genes to the trabecular meshwork in live animals, is pleased with the progress that has been made, both in the Borras lab as well as at UNC in general.

“UNC is an exciting place to explore gene therapy for the eye because we have the full spectrum of research expertise, from viral vector engineers, to experts in animal models, to people who can perform clinical trials,” says Budenz.

Nanoparticles

UNC researchers are not putting all their genes into one basket. As an alternative to viral delivery, Dr. Scott Lawrence is designing specialized vessels called nanoparticles that can carry drugs or therapeutic genes into the eye. Like Dr. Borras, his ultimate target is the porous trabecular meshwork affected in glaucoma patients.

Rather than introducing beneficial genes to break up the extracellular matrix in this tissue, Dr. Lawrence is targeting deleterious genes responsible for the build-up of the material. In 2011, he showed that he can inject strands of genetic material called small interfering RNAs into the eye in rat models to silence one offending gene called myocilin.

Now he is using an American Glaucoma Society Young Clinician Scientist Grant and assistance from the UNC Center for Nanomedicine to test different sizes and types of nanoparticles to see which can most effectively protect and transport these genetic soldiers where they need to go. Dr. Lawrence thinks that his findings may ultimately be applied not only to the delivery of genetic material, but to drugs as well.

“The discoveries being made with standard gene therapy through viral vectors may stand alone, or they may be enhanced by nanoparticles that could make it easier for them to get into the cell,” says Dr. Lawrence, an assistant professor of ophthalmology.

Therapies based on nanoparticles and gene therapy could be combined with other work in stem cells and regenerative medicine to create the best possible outcomes for patients with glaucoma and other eye disorders.

“There is a growing emphasis on neuroprotective therapies, so we may be able to deliver growth factors that can strengthen or protect the optic nerve and other sensitive structures in the eye,” said Dr. Lawrence. “It’s possible that one day we will be delivering a single injection to glaucoma patients every few months or once a year that would augment the function of trabecular meshwork while at the same time protecting the optic nerve and retinal ganglion cells. This is an area of active research in regenerative therapy that gives us hope for the future.”
Celebrating Our Donors

October 10th was a special day at the UNC Kittner Eye Center as David Kittner was honored at an Open House celebrating his major support, which includes establishing two of our largest endowments at $1 million each. Many other donors, alumni and friends joined in the celebration as they toured the state of the art new eye care facility located off NC Hwy 54 and Interstate 40.

Generous Donor Gifts Help Fight Blindness

UNC Eye faculty and staff are fortunate to be the beneficiaries of the giving spirit of our patients, alumni and friends through the entire year. As a way of expressing our gratitude, we have placed the names of our donors on our new Kittner Eye Center Wall of Honor, aka “Donor Boards,” prominently located just to the left of the main entry at the new UNC Kittner Eye Center.

The next time you are in the UNC Kittner Eye Center, we invite you to take a look at our list of donors who have made our growth and innovations possible. THANK YOU for making a difference in our program as we provide state of the art Eye Care and Research.

If you are interested in becoming a donor to UNC Eye, please contact Sandy Scarlett, Development Director, at 919-843-1299 or use the enclosed mailer to send in your donation.

Community Low Vision Center Opens in Kittner Eye Center

Through a partnership with A Brighter Path Foundation, UNC Eye recently opened a Community Low Vision Center on the second floor of the new Kittner Eye Center.

The Community Low Vision Center offers compassionate, individualized attention in a holistic approach to rehabilitation for people of all ages with reduced or diminishing vision.

A complete line of low vision and adaptive technologies to improve quality of life are available, helping people with low vision learn to live as independently as possible.

To find out more about the Community Low Vision Center at Kittner Eye Center, call 919-595-8564.

We invite you to join Susan Huntting, of the Samuel and Rebecca Kardon Foundations H&S, and have your name or organization’s name featured on the Kittner Eye Center Wall of Honor.

Community Low Vision Center

We invite you to join Susan Huntting, of the Samuel and Rebecca Kardon Foundations H&S, and have your name or organization’s name featured on the Kittner Eye Center Wall of Honor.

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Laser Vision Correction Services added in 2014

UNC Laser Vision Center, located inside the Kittner Eye Center, will open in early 2014. Patients will be provided the most up to date refractive surgery procedures, including LASIK, PRK, and IntraLase. Introducing our LASIK staff:

Karl Stonecipher, MD is a highly experienced, board-certified ophthalmologist who has performed more than 50,000 LASIK procedures. He has published more than 100 book chapters, abstracts, and articles and regularly lectures nationally and internationally on the subjects of refractive and corneal surgery. He is currently involved in FDA trials for the Study of Cornea, Cataract, and Refractive Surgery.

Richard Davis, MD brings over 16 years of experience providing vision correction, including his days pioneering LASIK at the University of South Carolina dating back to 1997, having earned designation as a Bausch & Lomb “Center of Excellence.”

Nisha Mehta, OD, FAAO joins UNC Eye as a new faculty member, focused on comprehensive optometry, contact lens, and refractive surgery. Patients will see Dr. Mehta for their evaluation appointments to determine if LASIK is the right vision correction option for them. Dr. Mehta joins UNC Eye after serving as an Associate at Washington Eye Center, in Washington, NC since 2011.

Telemedicine’s Role in Preventing Diabetes-Related Blindness

BY MARLA VACEK BROADFOOT, PH.D.

The leading cause of blindness in working-age Americans is diabetic retinopathy, a complication of elevated blood sugar that damages the tiny blood vessels of the retina. Vision loss is not inevitable, and can actually be prevented if retinopathy is caught early and treated with laser surgery or medical therapy. Yet, on average, less than half of diabetic patients in the United States undergo the annual eye exams needed to diagnose this common form of blindness. Long travel distances, copays, cultural and language barriers, and lack of patient education and awareness of the importance of regular eye exams can all keep patients from being evaluated by an eye care provider.

Seema Garg, M.D., Ph.D. thinks harnessing technology may be key to overcoming many of these barriers. With a two-year, $400,000 grant from the Duke Endowment, she is placing sophisticated cameras for capturing retinal photographs in four clinics throughout rural parts of North Carolina. Dr. Garg has already partnered with the Mountain, Eastern, Southern Regional, and Greensboro Area Health Education Centers (AHECs) where they are setting up the necessary infrastructure for the project.

"Telemedicine has the potential to be a very powerful tool for preventing blindness," says Dr. Garg, an Associate Professor in the Department of Ophthalmology. "I hope that our effort will have an impact on the quality of life of patients at risk of diabetic retinopathy by improving patient education and awareness as well as increasing evaluation rates."

Unfortunately, most patients are asymptomatic when the disease is in its earliest and most treatable stages. In other words, patients could be losing their eyesight without even realizing it. The only way to know if this damage from diabetes has begun is with a retinal exam.

With Dr. Garg's approach, patients do not have to make a separate trip to an eye care provider's office to get their retinas evaluated, but can have retinal photographs taken during their regularly scheduled visits to the primary care clinic. The digital retinal photographs will then be securely and privately transported over the internet to Dr. Garg, who will interpret the image. If she finds vascular lesions, hemorrhages, or any other characteristics of retinopathy she will report them and suggest a management plan to the primary care physician, who will share the results with the patient.

"Patient education is a big component of our program." "It will be interesting to see if their understanding of the disease will motivate them to follow up with their ophthalmologist when necessary and take better care of their diabetes," says Dr. Garg.

In 2011, Dr. Garg collaborated with the UNC departments of endocrinology, internal medicine and family medicine to bring telemedicine to diabetic patients. In one year, this technology resulted in an increase in evaluation rates for diabetic retinopathy from 32% to 71% in the family medicine clinic, results she and her team published in the JAMA Archives of Internal Medicine. With her Duke Endowment grant, Dr. Garg aspires to improve evaluation rates at the participating AHEC clinics across the state to demonstrate wider implementation of this technology.

"It is necessary to put the infrastructure in place, including the retinal camera, the cost of which is not trivial. But it really pays in comparison to the costs that will be incurred if we don’t detect retinopathy early," says Garg. "The cost of treating advanced retinopathy as well as the personal and societal costs of blindness are just astounding. When you put it in that perspective, the costs of the infrastructure for telemedicine are an excellent investment."
In Memoriam:
David Eifrig, MD - First Chair of UNC Department of Ophthalmology

David Eric Eifrig, MD, the first Chair of the Department of Ophthalmology at UNC Chapel Hill, passed away peacefully on October 9, 2013 at the age of 78. He was born in Oak Park, Illinois and graduated from Carleton College in 1956.

Dr. Eifrig attended medical school at The Johns Hopkins University in Baltimore, Maryland from 1956-1967. He was a Lieutenant in the U.S. Navy and served in the Medical Corps from 1962-64. His retina fellowship was served in Los Angeles at The Jules Stein Eye Institute from 1967-68.

He began practicing ophthalmology in 1968 in Lexington, Kentucky. He later moved his family to Minnesota and practiced there from 1970 to 1977, becoming Associate Professor. He moved to Chapel Hill, North Carolina in 1977 where he founded the UNC School of Medicine’s Department of Ophthalmology. He was the chairman of the department from then until his retirement in 2000.

Dr. Eifrig was well loved as an academic and clinician at UNC. He was best known for his love of and caring for patients, especially those of lesser means. He served on multiple medical missions, donating his time and money to programs in Africa, Costa Rica, Jamaica, and Saudi Arabia. During one trip to Jamaica, he stood for nearly 14 hours without a break to treat patients who had waited for days to see him and his team. By the end of the day, most nurses and residents serving with him were too tired to stand.

He is survived by his wife of 34 years, Kathryn C. Eifrig and his four children: David E. Eifrig Jr., Elizabeth Ann Hietala, Catherine Marie Eifrig, and Charles William Gustav Eifrig.

Faculty News

Cabrera Receives Funding from North Carolina Lions to Train Visiting Ophthalmologists

When Michelle Cabrera, MD, a pediatric ophthalmologist at UNC Eye, traveled to Gansu Province, China in 2012 to speak at a scientific conference at the Second Hospital of Lanzhou University, she learned about the prevalence of retinopathy of prematurity, the most common cause of childhood blindness in China. While at the conference, Dr. Cabrera met several local ophthalmologists who were eager to learn how to treat this deadly disease, although they were never provided the training and opportunity to do so.

Enter the North Carolina Lions and Lions Clubs, International. Through a grant from the Lions, Dr. Cabrera was able to develop and execute a three-month training program at UNC Chapel Hill for two Chinese ophthalmologists, Dr. Becky Wang and Dr. Jasmine Yi. Through their training with Dr. Cabrera and Dr. Nik Ulrich, Drs. Wang and Yi will be able to help give the gift of sight to over 2,000 babies back in their homeland.

Dutton Delivers Spinoza Chair Lecture in Amsterdam

When Jonathan J. Dutton, MD, PhD, F.A.C.S., stood before his audience at the Academic Medical Center of the University of Amsterdam this past spring, he unfolded before them the stunning 50-million-year evolution of the human orbit – the cavity, the eye, and everything that serves visual function. As recipient of the 2013 Spinoza Chair Visiting Professorship – an honor whose holders include some of the world’s leading physicians – this was his main lecture during his month-long visit.

“The anatomy of the orbit is unique in higher primates, and the structure of the human orbit is only paralleled in chimpanzees, gorillas and orangutans. No other vertebrate animal has the unique anatomy of the human orbit,” Dr. Dutton explains.

“Early on, primates differentiated themselves from other mammals by how they used their eyes. They were active at night, and they lived in the trees, and they needed certain visual adaptations to take advantage of that environment. So the eye had a lot of different changes going on, and the orbit basically had to adapt to serve visual function. That made it unique.”

The topic was a natural choice for Dr. Dutton. He not only is UNC Eye’s departmental vice chair and medical director of the Ophthalmology Ambulatory Care Clinics. He also holds a PhD in evolutionary biology and vertebrate paleontology from Harvard University.

In both disciplines, he is an explorer. He has pioneered research in orbital reconstruction, and he has a particular interest in intraocular malignancies. In Amsterdam, in addition to lecturing, Dr. Dutton gave a course to honors medical students in thyroid eye disease and reconstructive surgery. Sharing his knowledge, in fact, has taken him to 60 countries around the globe. “I think the most fun you can get out of learning something and trying to understand it is to simplify it in a way that makes it understandable to other people. That’s what makes it fun,” he says.
Where are they now?
2013 Senior Residents

Former Chief Resident, Kevin Gertsch, MD is currently a Pediatric Ophthalmology Fellow at the University of Iowa.

James Wrzosek, MD, MA is currently in private practice at Raleigh Eye Center in Raleigh, NC.

Jonathan Zoghby, MD is currently a Glaucoma Fellow at the University of Alabama at Birmingham.

New Faculty & Staff

Meet our newest Research Faculty

Three new basic science researchers joined UNC Eye in Fall 2012 with a focus on ocular gene therapy.

Steven Gray, PhD earned his PhD from Vanderbilt University in 2006. He is engineering a virus called AAV to develop novel next-generation tools for retinal gene transfer, to make gene transfer to the eye safer and more effective for a wide range of eye diseases. Dr. Gray’s laboratory is focused on gene therapy, which has garnered considerable excitement after the dramatic benefits seen following treatment of patients with Leber Congenital Amaurosis (LCA), an inherited form of blindness.

Josh Grieger, PhD earned his PhD from UNC Chapel Hill in 2005. Dr. Grieger’s laboratory is focused on designing optimal therapeutic gene expression cassettes for viral gene therapy applications related to various ocular genetic diseases. He is also working to develop safe and efficient Adeno-associated virus manufacturing methods for Phase I and II gene therapy clinical trials.

Matthew Hirsch, PhD earned his PhD from West Virginia University in 2005. Dr. Hirsch’s research is focused on emerging technologies using DNA endonucleases to genetically engineer human and mouse chromosomes. His lab optimizes adeno-associated vector technology for gene editing and oversized gene transfer. Dr. Hirsch’s current applications of these technologies are towards the treatment of muscular, corneal and retinal diseases.

Welcome UNC Eye’s Newest Residents

Veronica Kon-Graverson
Medical School: Catholic University of Santiago de Guayaquil
Internship: UNC Hospitals, Department of Surgery – Chapel Hill, NC

Catherine Reppa
Medical School: University of Texas Health Science Center at San Antonio
Internship: University of Pittsburgh Medical Center, Transition Year Program – Pittsburgh, PA

Cassandra White
Medical School: University of Texas Health Science Center at San Antonio
Internship: Providence Sacred Heart Medical Center & Children’s Hospital, Transition Year Program – Spokane, WA

Welcome UNC Eye’s New Fellows

O’Rease J. Knight, MD
Glaucoma Fellow
Clinical Instructor
Residency: Case Western Reserve University
Medical School: University of Miami Miller School of Medicine
Undergrad: University of Miami; Biology and Religious Studies

Brett Pariseau, MD
Plastics Fellow
Clinical Instructor
Residency & Internship: University of Wisconsin
Medical School: Stanford University
Undergrad: University of Utah; Electrical Engineering

Chelsea Lefebvre, MD
Cornea Fellow
Clinical Instructor
Residency: New York Medical College
Medical School: Duke University
Undergrad: Duke University, Biology
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Directions to UNC
Kittner Eye Center

From West (Greensboro area):
• Drive east on Interstate 40 and take exit 273 for U.S. Highway 54 West.
• Turn right onto Highway 54 West.
• Turn right onto Huntingridge Rd at the second stoplight.
• Take an immediate right onto Nelson Highway.
• The Carolina Crossing building is two blocks up on the left.

From East (Raleigh area):
• Drive west on Interstate 40 and take exit 273A for U.S. Highway 54 West.
• Turn right onto Huntingridge Rd at the third stoplight.
• Take an immediate right onto Nelson Highway.
• The Carolina Crossing building is two blocks up on the left.

Directions from South (Pittsboro area):
• Drive north on U.S. Highway 15-501.
• Bear right on to U.S. Highway 54 east/15-501 north (towards Durham).
• Take the exit for U.S. Highway 54 East (also known as Raleigh Road).
• Before reaching Interstate 40 and Farrington Rd, turn left on Huntingridge Rd at the stoplight.
• Take immediate right onto Nelson Highway.
• The Carolina Crossing building is two blocks up on the left.