Imagine being one of the millions of individuals living with some form of corneal disease – blurred vision, trauma, or infections, loss of light sensitivity, blindness. As an adult, losing vision is hard enough. But, for children, it can be harder, negatively impacting their quality of life at a very young age.

So far, the few existing corneal disease treatments are largely effective. However, they don’t work for everyone, leaving a therapy vacuum. There’s a need for new, innovative therapies to reverse or prevent the corneal clouding that robs young children of sight.

That’s where Matt Hirsch, Ph.D., Assistant Professor of Ophthalmology at the University of North Carolina, comes in. With his latest research, he’s using genetics to break down barriers to clear vision, targeting a population that – until now – has had no hope of viewing the world around them. Children born with mucopolysaccharidosis Type 1 (MPS1) face certain blindness without effective intervention.

Together with Joanne Kurtzberg, M.D., chief science officer with the Duke University Medical Center Robertson Clinical and Translational Cell Therapy Program and other colleagues, he’s working to fix their corneas – injecting one small, vital, missing ingredient into the recipe that creates a healthy cornea.

**Children with Corneal Clouding**

Hirsch’s corneal journey began more than two years ago when Kurtzberg asked him to use his genetic therapy expertise to bring sight to children with MPS1, an autosomal recessive disorder affecting 1 in 100,000 children. Without treatment, most of these children will die before age 10. Using allogenic stem cell transplantation, Kurtzberg has alleviated or reversed the skeletal abnormalities, stiffened
joints, cardiac disease, and mental disabilities associated with MPS1. But, the stem cell transplant can’t overcome the mutation – a lack of the IDUA enzyme that breaks down sugar molecules – that causes the corneal clouding preceding blindness.

In these cases, the standard treatment, corneal transplant, won’t work. MPS1 children reject the foreign tissue. So, to tackle this remaining roadblock to improved quality of life, Kurtzberg approached Hirsch, hoping he could identify the avenue for injecting functional IDUA into diseased corneas.

By all indicators, he’s well on his way, using a long-standing genetic therapy in a novel strategy. He’s applying adeno-associated vectors (AAV) to directly deliver the IDUA gene into the cornea.

“Hirsch’s therapy will be the last step in fully correcting MPS1 because it will deliver the gene that’s missing in the eyes,” Kurtzberg said. “The long-term goal with this gene therapy is to provide it to all patients who need it.”

Ideally, she said, the therapy would be administered at roughly the same time as the allogenic stem cell transplant. Usually, recipients are either infants or toddlers under age 2.

Phase 1 safety trials could come as early as 2017 with this new genetic therapy becoming more common in the future. According to Kurtzberg, newborn screening panels will soon check for MPS1, allowing more affected children to be identified shortly after birth. Early detection means more children will get full treatment – and improved outcomes – sooner. Although the therapy’s long-term effects aren’t yet known, Kurtzberg said, the likelihood of any problems with toxicity or adverse reactions is low.

Corneal Clarity: How Injecting Genes Works

AAVs have been around since Hirsch’s post-doctoral advisor Jude Samulski, Ph.D., UNC pharmacology professor, discovered their utility in the early 1980s. But, this is the first time the technique has been applied to treating corneal disease, Hirsch said.

Simply put, Hirsch uses the AAVs to encapsulate IDUA protein. These vectors (AAV-IDUA) are injected into the cornea, the caps break off, and the protein takes hold in the cornea. With IDUA in place, the cornea can break down the sugar molecules that cause corneal clouding and prevent clear sight.

Thanks to the Miracles in Sight network, an organization that collects and distributes corneal tissue to researchers, Hirsch has already tested AAV-IDUA in MPS1-diseased rabbit corneas, injecting 50µL of AAV-IDUA. The dose is up to 10 times the amount needed to reverse the disease, and the corneas showed reduced opacity.

UNC Eye Hosts 2016 Residents’ & Fellows’ Research Day

On June 11, 2016, UNC Eye recognized the accomplishments of graduating residents Veronica Kon Graversen, MD (chief resident), Catherine Reppa, MD, and Cassandra White, MD.

The annual Research Day also featured oral presentations from all UNC Ophthalmology residents and fellows, and the department welcomed special guests like K. Ahmed, MD, FRCSC, and Eydie G. Miller-Ellis, MD as the event’s visiting professors.

The S. Dace McPherson, Jr. Memorial Lecture was given by Dr. Ahmed and entitled “A New Era in Glaucoma Surgery”. Dr. Ahmed is recognized as being one of the most experienced complex eye surgeons in the world and has trained numerous surgeons in innovative surgical techniques. He holds multiple faculty appointments including an assistant professorship at the University of Toronto and a clinical professorship at the University of Utah.

Dr. Miller-Ellis graduated from UNC Eye in 1989 and is now Professor of Clinical Ophthalmology and Director of the Glaucoma Service at the Scheie Eye Institute at the University of Pennsylvania. She honored us by delivering this year’s David E. Eifrig Distinguished Alumnus Lecture, entitled “The Primary Open Angle African-American Glaucoma Genetics Study”.

(Continued from page 1)
clouding with no negative impacts in less than 24 hours, Hirsch said. The most exciting results to date have come from the partnership with the University of Pennsylvania (UPENN) involving four MPS1 dogs – two post-symptomatic and two pre-symptomatic. UPENN researchers are testing the therapeutic AAV-IDUA against a control vector. After only two weeks of lab testing, all reports indicate AAV-IDUA works extremely well in reducing or eliminating corneal clouding, Hirsch said.

If the therapy works well in dogs, he said, it will likely work well in clinics, and human use could begin without an extensive amount of primate testing.

“These children’s lives are of relatively poor quality without sight,” he said. “No one is saying hold off or slow down. Toxicity isn’t a concern. We just want efficacy. If we get that, there’s nothing holding us back from moving forward.”

In fact, he said, Kurtzberg has already identified more than 70 children who could benefit from AAV-IDUA gene therapy. And, the work could open many doors.

“Hirsch’s work on a rare disorder will serve as a prototype, a demonstration project, a proof-of-concept for more common diseases,” she said. "It's very important to treat these children with rare diseases, but we won’t stop there. This therapy paves the way for treatment of common corneal diseases that affect more people.”

Corneas & Inflammation

Hirsch's work with corneas doesn’t stop there. He's also working with Richard Davis, M.D., UNC Associate Professor of Ophthalmology and cornea specialist, on one of the most pressing problems with corneal care – attacking and reducing corneal opacification due to neovascularization.

“If you can block neovascularization in the disease setting, it would be amazing," Davis said. “You can bypass from the root problem, including corneal transplant rejection, viral and bacterial infection, and hypersensitive reactions. All of these things produce neovascularization that has the potential to cause blindness and visual impairment.”

To combat neovascularization and inflammation, Hirsch targeted human leukocyte antigen-G (HLA-G), a histocompatibility protein that plays a role in whether the body rejects foreign substances. This time, Hirsch tested his genetic therapy by inducing blood vessel growth in rabbits. Using the same AAV model, he substituted HLA-G for IDUA and tested whether the therapeutic vector could slow down or prevent vessel growth in rabbit corneas. Rabbits who received the injection experienced no vessel growth; those who didn’t saw an extensive amount of vascularization.

“This work is very promising. It potentially will change the world of corneal disease,” Davis said. “It’s a huge step forward in the management of corneal blinding disease if it works.” If successful, the AAV model could replace current anti-inflammation treatments, including steroids that can cause an increase in intraocular pressure and glaucoma.

Dry Eye: Next Level Treatment

Alongside his work with Hirsch’s cutting-edge genetic therapy research, Davis concentrates on bringing to his patients the latest developments in alleviating dry eye symptoms that accompany corneal disease. For example, he said, AAV-HLA-G could be a “slam dunk” for also treating dry eye that arises from inflammation.

To further augment what the UNC Kittner Eye Center and the Carolina Eye Research Institute are doing to help patients with dry eye symptoms, the N.C Lions and Lions Club International Foundation contributed more than $100,000 to purchase two state-of-the-art machines that treat light sensitivity, burning or gritty sensations, and discomfort from wind, dryness, or redness.

These funds have been used to purchase the Lipiflow Thermal Pulsation System, equipment that heats the inside and outside of the eye lid to remove any blockages causing dryness, the Lipiview Ocular Surface Interferometer which takes and store pictures of the eyes lipid layers, and an Intense Pulsed Light (IPL), which is a procedure that closes blood vessels and has been shown to reduce inflammation in the eyelid oil glands that cause the most common type of dry eye – evaporative dry eye.

The Future Word

Ultimately, Hirsch said, his genetic therapy work – and the support garnered for current clinical treatments – are paving the way for UNC to be a leader in corneal gene therapy. The research and patient-oriented care place the University in a position to significantly impact quality of life for many people and to fill in the gaps of caring for cornea disease.

“UNC Ophthalmology has the big vision of developing multiple gene therapy treatments to prevent and cure blindness,” Hirsch said. “Our corneal gene therapy is one of several translational research programs designed to make this vision a reality.”

Telmo Alejandro Llanga, will translate his research knowledge learned as a partner with Dr. Matt Hirsch to his upcoming training in Medical School. An example of Chancellor Folt’s reference to the focus on collaboration among UNC Departments and Schools.
As Chairman of the UNC Department of Ophthalmology it is an honor to provide an annual update to those we serve: our patients, alumni, friends, and donors. Over the last year our department’s dream to establish a collaborative Carolina Eye Research Institute (CERI) has taken another major step forward by the dedication and hard work of our researchers. They have made new discoveries in finding cures for Glaucoma, Retinal and Corneal diseases. Our cover story tells about Matt Hirsch’s incredible success at developing gene therapy for a rare childhood disease called Hunter’s Syndrome, for example.

The infrastructure of CERI will continue to expand over the next several years and will be impacted by the involvement of our supporters. Part of my role as Chairman is to identify individuals, corporations, and foundations who want to engage with us and become a vital part of our discoveries for cures. I would urge you to take time to read about our research in this newsletter as well as the information on our website www.unceye.org. If there is a disease focus that interests you, please let us know by sharing your interest with your physician, who can refer you to the appropriate staff member to assist you.

If you are one of our donors already, thank you again from all of our faculty and patients for sharing your gifts to ensure we can be successful. We view you as our Research Partners and hope many more will join us at any level during the new year ahead. Our Campaign Advisory Board members have personally given their financial support and introduced others to our mission, for which we are very grateful. Also during the year, we have added new clinical faculty to ensure that all services in the field of eye care are available to our patients at the UNC Kittner Eye Center and in our other locations listed in this newsletter. Our former fellows and residents represent us across the country as they serve their local communities and many also send in generous gifts to ensure their alma mater is equipped to carry on their legacies.

Our three-fold mission of patient care, research and education is alive and thriving as a result of a strong faculty, staff and alumni. We send our best wishes to each of you for the new year ahead and I look forward to sharing our continued progress.
A Commitment to Clinical Trials at UNC Kittner Eye Center: Translating Research into Improved Treatments

UNC is internationally known as a research university, and the UNC Kittner Eye Center is proud to participate in that tradition. We are currently recruiting for Dry Eye, Glaucoma, Pediatric, and Retina studies, and we need your help finding these patients. Please contact our Research Manager Sandy Barnhart at sandy_barnhart@med.unc.edu or call 919-843-0076 if you have any patients that meet criteria for the following studies:

**DRY EYE CLINICAL TRIALS**

**Parion P-321-202 Study** (PI: Dr. Davis) Subjects with Mild to Moderate Dry Eye Disease will be randomized between placebo and study drug and followed for 28 days. Total study participation will last approximately 7 weeks.

**GLAUCOMA CLINICAL TRIALS**

**Open Angle Glaucoma or Ocular Hypertension / Alcon Simbrinza24 Study** (PI: Dr. Knight) Subjects with Open Angle Glaucoma or Hypertension will need to be off glaucoma meds (washout) for up to 28 days, and those who meet study criteria after that will be randomized to placebo or study drug and followed for one month, including two 24 hour study visits. Total study participation will last approximately 2 months, including washout.

**Normotensive or Primary Open Angle Glaucoma / NEIGHBORHOOD Study** (PI: Dr. Budenz) Subjects with Normotensive or Open Angle Glaucoma will be asked to give 2 vials of blood and complete a medical history questionnaire for this genetic study. There will be only one study visit.

**RETINA CLINICAL TRIALS**

**Dry Age-Related Geographic Atrophy/Genentech Proxima A** (PI: Dr. Houghton) This study is following the natural history of Advanced Dry Age Related Macular Degeneration AMD (Geographic Atrophy). This is a 4 year observational study with visits every 6 months. Patients must have geographic atrophy in both eyes. Vision must be 20/100 or better with no prior treatment for AMD other than AREDS vitamins.

**Wet AMD/ Allergan CEDAR Study** (PI: Dr. Houghton) This is a two year study comparing ranibizumab (Lucentis) with a new study drug for treatment of wet AMD. Patients will be followed monthly for two years, and must not have had any previous treatment for wet AMD. Vision must be between 20/40 and 20/320.

**Diabetic Retinopathy Clinical Research Network (DRCR)** (PI: Dr. Garg) DRCR W: Intravitreous Anti-VEGF Treatment for Prevention of Vision Threatening Diabetic Retinopathy in Eyes at High Risk. This is a 4 year study looking at patients with Severe Non-Proliferative Diabetic Retinopathy (Severe NPDR). Patients will be randomized to either study drug or sham injections to see if study drug injections help to prevent worsening of NPDR. Participants will have best-corrected vision of 20/25 or better and not have any active diabetic macular edema, or any treatment for diabetic macular edema within the past year (including laser and injections).
For those patients whose eye diseases cannot be restored fully through medical or surgical care, there is a valuable resource on the second floor not far from the main entrance of the Kittner Eye Center. Each day Lynn Shields, who herself has limited vision, is waiting for patients to stop in or arrive for a scheduled appointment. UNC Eye is glad Lynn was there when Kim Harley needed help. Not long ago Kim Harley went from having excellent eyesight to being totally blind. In her 40s with much of life ahead of her, she was searching for ways to cope with the fact that what had happened could not be reversed. Where could she get information to help her live a full life? That is when she met Lynn Shields and found out that UNC Kittner Eye Center cares beyond those they can treat medically.

When she left her visit with the Low Vision Community Services at the Kittner Eye Center, she knew there were people who cared and resources that could help. She learned about the NC Division of Services for the Blind, The Library for the Blind and the Physically Handicapped, Helping Hands in Durham and several other agencies. Help us reach those with low vision who can benefit from this special service at the Kittner Eye Center.

To make an appointment call (984) 974-2058. Hours 8:00am to 5:00pm Monday - Friday.

UNC Eye: Reaching New Heights Through the UNC Campaign

UNC Department of Ophthalmology under the leadership of Chairman, Dr. Donald Budenz and the department’s Campaign Advisory Board members is positioned well to reach new heights in fundraising for eye research and other priorities of the department. All donations made to the department will be counted in the overall university wide campaign.

Carol Folt, Chancellor of the University of North Carolina at Chapel Hill, recently noted the tremendous success and growth of research being done at UNC with an emphasis on collaborations and boldness of the researchers. Progress in advancing education, research and patient care cannot occur without taking risks and having patience.

Eye research faculty meet those same standards daily as they explore the promise of gene therapy and stem cell research that can restore sight. It takes patience and focus along with significant amount of federal, corporate and philanthropic funding. The UNC campaign will provide UNC Eye with a platform to promote the need for private support in order to maximize the talent already in place and to recruit and retain researchers.

During this important campaign for UNC Eye there will be annual updates and highlights of our progress. Plan now to be a part of our journey of discoveries that can lead to new treatments and cures for the various blinding eye diseases.

A Decade of Progress and Innovation: UNC Ophthalmic Genetics Clinic

For the past decade, the UNC Department of Ophthalmology has been offering a unique collaborative Ophthalmic Genetics clinic. Dr. Seema Garg, Associate Professor of Ophthalmology and a medical retina specialist, and Kristy Lee, Associate Professor of Genetics and certified genetics counselor, together see patients with complex hereditary eye diseases. Over the last decade, more than 300 patients have been evaluated in the UNC Ophthalmic Genetics clinic, with diagnoses such as retinitis pigmentosa, Stargardt’s disease, cone dystrophy, and choroideremia, just to name a few.

Patients seen in this monthly clinic are offered a complete ophthalmic examination, ancillary testing such as Goldmann Visual Field testing (GVF), spectral-domain optical coherence tomography (OCT), autofluorescence (AF), full-field and multifocal electroretinography (ERG) as well as a comprehensive consultation with our genetics counselor, Kristy Lee, who obtains a family pedigree and then offers genetic counseling, and an array of genetic testing options.

Genetic testing is crucial in many cases: 1) to confirm the diagnosis, 2) to help determine prognosis, and 3) with the promise of therapies on the horizon, to determine the molecular diagnosis in order to enroll into therapeutic clinical trials. Kristy Lee is also President for the local chapter of the Foundation for Fighting Blindness and thus, can provide numerous resources for further research and social support, critical components of the care of these patients. Our collaborative clinic participated in the clinical trial NCGENES, in which 80 of our patients were offered whole exome sequencing under the auspices of the grant.

UNC Ophthalmic Genetics clinic is accepting new patients. To make an appointment, call Irene Baron at (919) 966-5295.
UNC Eye Welcomes Four New Clinical Faculty Members

Kian Eftekhari, MD
Med School: University of Pennsylvania, Philadelphia, PA
Residency: Scheie Eye Institute, University of Pennsylvania, Philadelphia, PA
Fellowship: ASOPRS, Oculoplastic Fellowship, Center for Facial Appearance, Salt Lake City, UT

Sarah Grace, MD
Specialties: Pediatric Eye Diseases and Management Surgical and Medical Management of Pediatric and Adult Strabismus, Amblyopia, Retinopathy of Prematurity, Pediatric Cataracts, Ocular Motility Disorders, Congenital Nasolacrimal Duct Obstruction Phtosis.
Med School: University of Oklahoma Health Sciences Center, College of Medicine
Residency: Bascom Palmer Eye Institute, University of Miami, Miami, Florida
Fellowship: Bascom Palmer Eye Institute, University of Miami, Miami, Florida

Kathryn Whitfield, MD
Specialties: Pediatric Eye Diseases and Management, Amblyopia and Strabismus, Optic Nerve Abnormalities of Childhood
Med School: University of South Dakota, School of Medicine, Vermillion, South Dakota
Residency: University of Colorado, Denver, Colorado
Fellowship: Vanderbilt University, Nashville, Tennessee

Introducing the UNC Eye Resident Class of 2019

Chris Hwang, MD
Undergrad: North Carolina State University
Major: BS 2007 in Biomedical Engineering
Internship: Santa Clara Valley Medical Center, San Jose, CA
Outside Interests: Sports, music, dance, outdoor activities

Lee Moore, MD
Undergrad: University of Mississippi
Major: BA 2011 in Biology
Internship: UNC Hospitals Internal Medicine
Outside Interests: Athletics, hunting, skiing

Lauren Rushing, MD
Undergrad: Louisiana State University
Major: BS 2010 Biology
Med School: University of Texas - Houston (2015)
Internship: University of Texas - Houston
Outside Interests: Running, backpacking, traveling

Michael Taggart, MD
Undergrad: Brigham Young University - Idaho
Major: BS 2009 in Microbiology
Internship: University of Utah/Duke Neuropsychology
Outside Interests: Distance running, golf, soccer, carpentry and wood carving, playing with my kids, mystery novels, hiking

Meet our UNC Eye Fellows

Nicholas Farber, MD
Vitreoretinal Fellow
Residency: SUNY Downstate Medical Center
Internship: North Shore-Long Island Jewish Medical Center
Med School: University of Virginia School of Medicine

Lamise Rajjoub, MD
Oculoplastic Fellow
Residency: The George Washington University Hospital
Internship: George Washington University/Inova Fairfax Hospital
Med School: The George Washington University School of Medicine

Julie Skaggs, MD
Miracles in Sight Cornea and External Eye Disease Fellow
Fellowship: University of Michigan, Pediatric Ophthalmology
Residency: University of Arkansas
Internship: University of Arkansas
Med School: University of Arizona

Randall Stein
Glaucoma Fellow
Residency: Tulane University Dept. of Ophthalmology
Internship: Abington Memorial Hospital
Med School: Tulane University School of Medicine
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Directions to UNC Kittner Eye Center

From West (Greensboro area):
• Drive east on I-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 I-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

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 I-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

From North on 15-501:
• Drive south on US-501 S
• Keep right at the fork to continue on US-15 S / US-501 S, follow signs for US-70 BUS / Hillsborough Rd / Chapel Hill
• Keep right to stay on US-15 S / US-501 S
• Turn left onto I-40 E ramp to Raleigh / RDU Airport then merge onto I-40 E
• Take exit 273 for NN Highway 54 West
• Turn right onto Huntingridge Rd at the stop light
• Take an immediate right onto Nelson Highway
• The Kittner Eye Center is two blocks up on the left