DMEK: Corneal Transplant Surgery Comes of Age

The development of corneal transplant procedures has a long and notable history – from the pioneering efforts of Columbia University’s Ramon Castroviejo in the mid-20th century, to the first successful posterior lamellar keratoplasty by Charles Tillet in 1956, to the development of deep lamellar endothelial keratoplasty (DLEK) by Dr. Mark Terry in 1999.

“Drs. Mark Terry and Gerrit Melles developed the predecessors to Descemet Stripping Automated Endothelial Keratoplasty [DSAEK], which has been the standard of care for treating corneal endothelial disease in the U.S. since about 2012,” says Christopher S. Sales, MD, MPH, a corneal transplant surgeon at NewYork-Presbyterian/Weill Cornell Medical Center. “DSAEK is a partial-thickness, suture-less approach to keratoplasty. It revolutionized corneal transplant surgery by eliminating all of the problems associated with full-thickness, sutured grafts.”

Dr. Sales specializes in lamellar, or selective corneal transplant surgery, including the most advanced form of endothelial keratoplasty, Descemet membrane endothelial keratoplasty (DMEK). “DSEAK restores endothelial function at the expense of adding a redundant layer of corneal stroma to the recipient’s cornea. DMEK, on the other hand, restores normal endothelial function but preserves normal corneal anatomy,” explains Dr. Sales, who completed his fellowship training in corneal transplant surgery and

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Glaucoma:
Accelerating Genetic Discoveries for Clinical Applications

“Glaucoma is a very complex disease of aging, increasing in prevalence with each decade of life,” says Jeffrey M. Liebmann, MD, Director of the Glaucoma Service and Vice Chair for the Department of Ophthalmology at NewYork-Presbyterian/Columbia University Irving Medical Center. “While there are known inherited disorders – many in the field of retinal disease – with glaucoma, we have genetic information that accounts for disease in perhaps 5 to 10 percent of individuals. It is still a wide open area for discovery.”

With the support of a major award from The Brown Foundation, Dr. Liebmann and his team of clinicians and ophthalmic researchers have launched the Brown Glaucoma Genetics Initiative, a continuum of investigative and therapeutic projects focused on the discovery of novel genes, with the aim of developing treatments for specific subtypes of the disease. “For the past two years, we’ve been building our genetics discovery program, bringing in the requisite specialists to help us advance from the science of genetics to the development of clinical therapies,” says Dr. Liebmann.

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DMEK: Corneal Transplant Surgery Comes of Age (continued from page 1)

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anterior segment reconstruction under Drs. Mark Terry and Michael Straiko at the Devers Eye Institute in Portland, Oregon in 2015. “Patients who know about DMEK ask for it because it provides rapid visual recovery, frequently to 20/20 within a few weeks after surgery, and ‘high-definition’ quality of vision. I like DMEK because my patients are happy and the risk of rejection is <1 percent, so there are almost never steroid-associated comorbidities.”

“The thickness of the tissue transplanted with DMEK is only 5 to 10 microns, which is much less than with other procedures,” continues Dr. Sales. “With penetrating keratoplasty, surgeons transplant 550 microns of full thickness corneal stroma. In DSAEK, less tissue transplanted, the lower the antigenic burden, the lower the rejection rate.”

Expanding Indications for Endothelial Keratoplasty

DMEK’s superb clinical outcomes have widened the indications for corneal transplant surgery. “With penetrating keratoplasty, patients would have to wait until they were debilitated by their vision because of the procedure’s significant morbidity,” says Dr. Sales. “With DSAEK, and especially now with DMEK, patients can have surgery much earlier. I perform DMEK on a wide range of pathology, from patients complaining of glare caused by moderate Fuchs dystrophy, to patients unable to see more than hand motions from bullous keratopathy after glaucoma surgery. A few years ago, I operated on a 97-year-old retired physician with advanced Fuchs dystrophy, who came to me from Vermont. After we did her DMEK, she was able to leave assisted living because she could finally read her mail again.”

Dr. Sales and George J. Florakis, MD, an ophthalmologist at NewYork-Presbyterian/Columbia University Irving Medical Center, are among the few surgeons performing DMEK in the Tri-state area, with patients coming to see them from all parts of the country.

“Today, there are somewhere between 8,000 to 10,000 DMEK procedures performed annually in the U.S. It was probably half that a year ago, and half that number the year before,” says Dr. Sales. “But while DMEK has been available since 2006, its adoption by corneal transplant surgeons has been even slower than DSAEK because the skill set needed for DMEK is highly specialized. Now that we have DMEK, we want to make it available to more patients by giving surgeons what they need to adopt the procedure. My academic research aims to democratize DMEK by developing technology that de-skills the procedure and facilitates skills transfer to my colleagues.”

Dr. Sales has developed simulation technology for DMEK that mimics the pressure and volume dynamics of the human anterior chamber during DMEK, which he uses to teach the procedure to surgeons in the U.S. and abroad (see sidebar). Dr. Sales is also collaborating with biomedical engineers on Cornell’s Ithaca campus to develop novel approaches to keratoplasty with support from Weill Cornell’s Daedalus Fund for Innovation.

Reference Article


For More Information

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Advances in Ophthalmology

Genetics: An Ophthalmic Subspecialty

In 2017, the Department welcomed Irene H. Maumenee, MD, one of the world’s leading experts in genetic eye diseases and regarded as the founder of genetics as an ophthalmic subspecialty in the United States. Dr. Maumenee has devoted her career to the understanding of genetic eye diseases, illuminating the etiologies of rare hereditary ophthalmic disorders, as well as more common diseases, such as open-angle glaucoma and age-related macular degeneration.

As Director of Ophthalmic Genetics for Jonas Children’s Vision Care at Columbia, Dr. Maumenee is developing a clinical eye genetics service to bring the technology in genetics fully into clinical care. “With Columbia’s focus on precision ophthalmology, as well as resources like the Institute for Genomic Medicine, we have a unique opportunity to make a real difference in understanding and treating genetic blinding diseases,” she says. “Many of these diseases remain undiagnosed or improperly identified, since even the best labs can only identify the genetic causes of about 75 percent of them. That gap has to be filled.”

A Major Research Platform

Columbia has a long history of pioneering work in glaucoma research, including the development in 1996 of the ground-breaking drug Xalatan®, which is still used worldwide. Now, with an impressive roster of researchers focused on various aspects of genetics and with a number of studies planned or in progress from mouse models to clinical trials, the Department plans on taking glaucoma research to another transformative level.

The Therapeutic Potential of Vitamin B3  Noted geneticist and glaucoma researcher, Simon John, PhD, a Howard Hughes Medical Investigator at The Jackson Laboratory in Bar Harbor, Maine, will join the Department of Ophthalmology in Fall 2019. A pioneer in the use of mice for glaucoma studies, Dr. John pursues research to identify new genes, pathways, and aberrant processes that lead to high intraocular pressure and glaucoma. He and his research team recently demonstrated that vitamin B3 potently prevents glaucoma in a mouse model and will be establishing a clinical trial as part of the Brown Glaucoma Genetics Initiative at Columbia to further evaluate the efficacy of vitamin B3 and the role of metabolism in glaucoma.

The pilot study will enroll approximately 60 patients with primary open-angle glaucoma, half of whom will receive vitamin B3 and half of whom will receive a placebo. Over the course of the trial, participants will undergo multiple visual field tests to assess the effectiveness of the treatment. If successful, it would be the first proven vitamin therapy for glaucoma.

Megan Soucy, genetic counselor, and Dr. Jeffrey M. Liebmann

A Pressing Need: Pigmentary Glaucoma  “Pigmentary glaucoma can be very aggressive, leading to vision loss during a person’s most productive years,” notes Dr. Liebmann. “It is urgent that we develop a better understanding of this disease.”

Some 200 individuals with pigmentary glaucoma are being recruited for genetic analysis, under the direction of Rando L. Allikmets, PhD. “If they have affected family members, we will ask them to come in as well,” says Dr. Liebmann. “We hope to identify the relevant gene involved with the disease and derive a treatment aimed at disease-causing defects in that gene – possibly gene therapy or another novel treatment.”

A Promising Genetic Target: Exfoliation Syndrome  Five to 10 percent of people over age 50 will develop exfoliation syndrome. Its ocular manifestations involve all of the structures of the anterior segment, as well as conjunctiva and orbital structures. Konstantin Petrukhin, PhD, has been developing a screening process for small molecules that can modulate LOXL1, one of the genes associated with exfoliation syndrome. Building on Dr. Petrukhin’s work, the Brown Initiative will provide support for harvesting discarded cells from glaucoma surgery to generate exfoliation material in the laboratory. These specimens will be used to assess disease response to novel targeted treatments.

Improving Drug Delivery  Columbia researchers are pursuing sustained-release drug delivery for the treatment of glaucoma, which allows for a single application of a drug to last for a prolonged period of time. “Like in all of medicine, we have good drugs, but the patients don’t always take them,” says Dr. Liebmann. “Instead of eye drops, we could give somebody an injection to lower their pressure that lasts a year. This could have a huge benefit for patients with glaucoma.”

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Glaucoma: Accelerating Genetic Discoveries for Clinical Applications  (continued from page 3)

A Clinical Ophthalamic Genetics Program
Complementing the Department’s robust research endeavors is a comprehensive clinical ophthalmic genetics program. “Once we identify a patient during clinical care, or a patient is referred to us because of a potential inherited disorder, we present the patient’s history and clinical findings to our genetics review group to determine whether or not the patient might benefit from genetic testing,” explains Dr. Liebmann.

Megan Soucy, MS, CGC, a genetic counselor, meets with the patient and family once before testing and again after testing to explain the results. “Genetic mutations are very complicated and can affect multiple parts of the body,” says Ms. Soucy. “Genetic testing can force a lot of people to deal with challenging issues. These test results do not just affect one person; they affect the whole family. But if you can identify the underlying cause, then you can treat the person and also identify who may be at risk in the family for developing these diseases or disorders.”

Ms. Soucy presents all the information to the patient and their family in digestible pieces and also tries to manage their expectations. “We might be sequencing everything in the genome, but there’s a risk that the test report may come back negative,” she says. “That’s where the research comes in. Our investigators use that data to see if perhaps we can identify a novel mutation that can explain the cause of the disease.”

“The first year of the buildup of our genetics program was the acquisition of key components: the people, the funding, and the processes that are required to make it work,” says Dr. Liebmann. “We’ve now expanded our program to serve as a resource. Ours is the only facility of its kind for ophthalmology in New York.”

Indeed, the Department is hosting Precision Ophthalmology 2020: Applying Genetics to Eye Care Today on December 6, 2019, at Columbia University, the first-ever conference focused on the role of genetics in ophthalmology. “We will present cases that describe how the physician made the decision of which type of genetic testing to order and how to interpret the results to form a diagnosis,” says Dr. Liebmann, who is also working to establish an ophthalmic genetics fellowship at Columbia. “There are only six individuals trained in human genetics and ophthalmology in the country.”

Dr. Liebmann and his team are optimistic that genetics will provide potential answers to a number of devastating ophthalmic diseases. “The two things that people fear the most in life, healthwise, are cancer and blindness,” he says. “It just makes us more motivated every day.”