



FOCUS:
CHANGING
THE WAY
THE WORLD
SEES

WILMER EYE INSTITUTE

Sightline Special Edition
Annual Report 2014



BOLD APPROACHES 2014

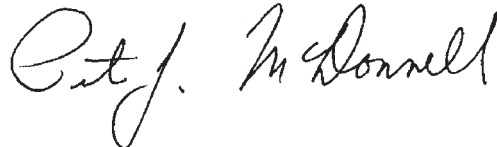


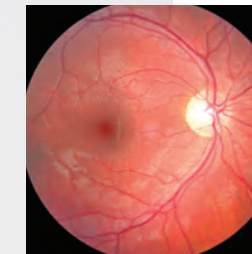
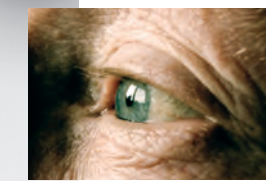
William Holland Wilmer founded the Wilmer Eye Institute at Johns Hopkins on the basis of what was a unique premise in 1925: Housing doctors, patients, students and scientists under one roof would speed discovery and translate more quickly into new clinical treatments to help our patients. Almost 90 years later, the wisdom of his approach has never been more apparent.

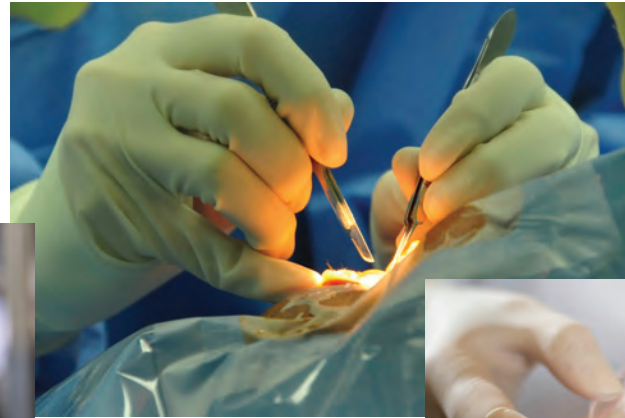
A theme that permeates Wilmer today, as exemplified in the stories you will read in this special issue of *Sightline*, is that teams of physicians, scientists, students, patients and philanthropists working together at our institution can truly “move the needle.” These teams are not just limited to people whose offices reside within the walls of Wilmer—they also include scientists and engineers from other schools at Johns Hopkins (e.g., the schools of education and public health), from other universities and even from companies in other countries. Whether they work with microscopic nanoparticles that may eliminate eyedrops, cells that form a retina in a dish, plastic corneas that make new windows for the eye or children who are not successful readers in our city schools, these teams are uniting to better understand and address the most interesting scientific questions, with the ultimate goal of eliminating the human suffering that comes with vision loss.

A relatively new phenomenon at Wilmer involves faculty members forming companies based upon discoveries in their laboratories that seem to hold great promise to help patients. We now have a handful of nascent enterprises based upon the “intellectual property” developed by our faculty. In addition, working with large, well-established companies may be another mechanism by which faculty can help drive the conversion of their scientific discoveries into products that help people with eye diseases. In the coming months, my expectation is that several such partnerships will be created.

Sadly, the number of Americans with vision loss is increasing. Whatever the proposed explanations—the aging of our population, the epidemic of diabetes—this fact is unacceptable and calls for bold approaches to make dramatic differences while at the same time reducing the costs of medical care. I hope that the exciting projects underway at Wilmer, only some of which we have room to tell you about in these pages, will convince you that Wilmer people are working hard to respond.

Sincerely,

PETER J. McDONNELL, *Director*

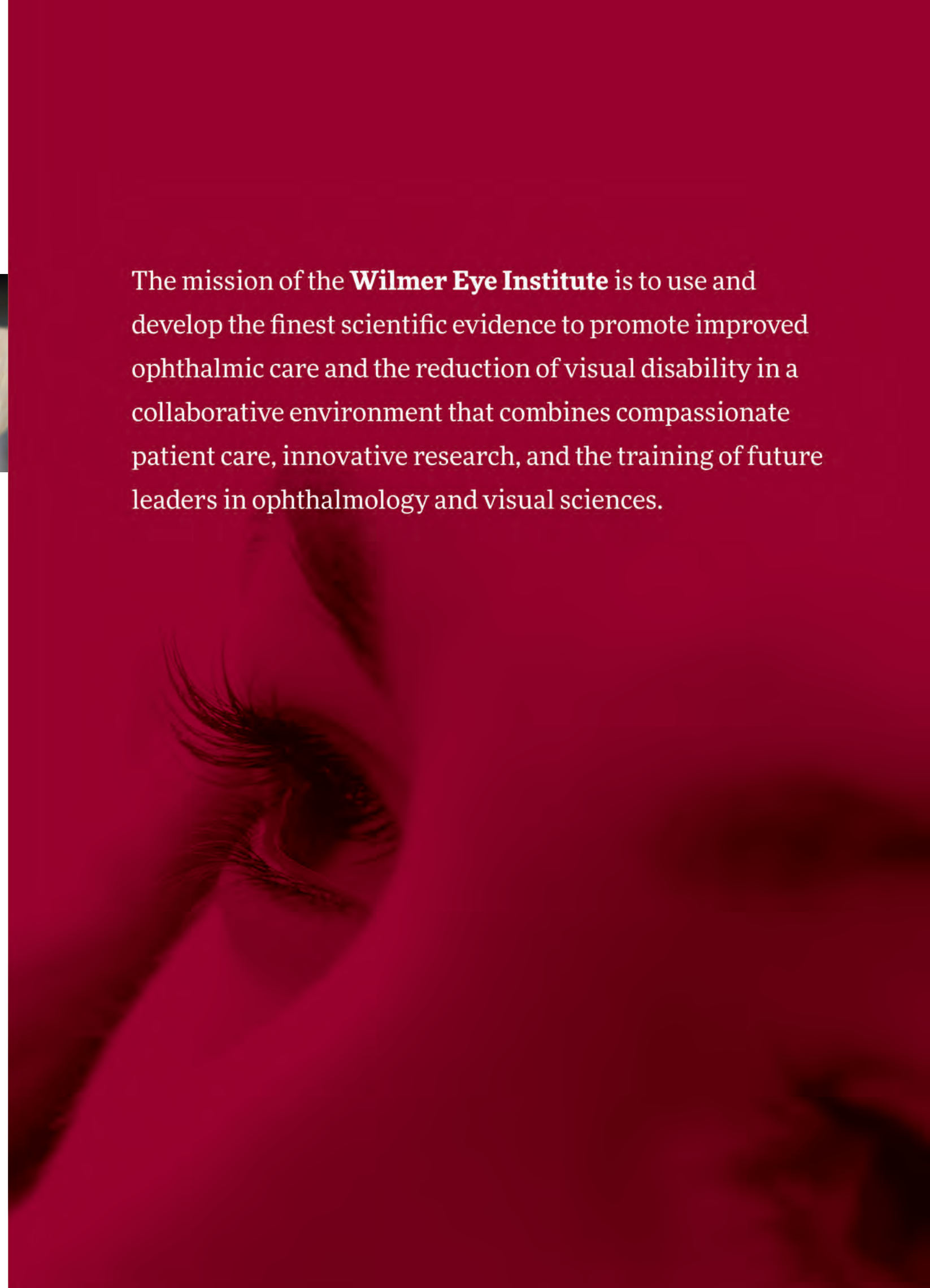
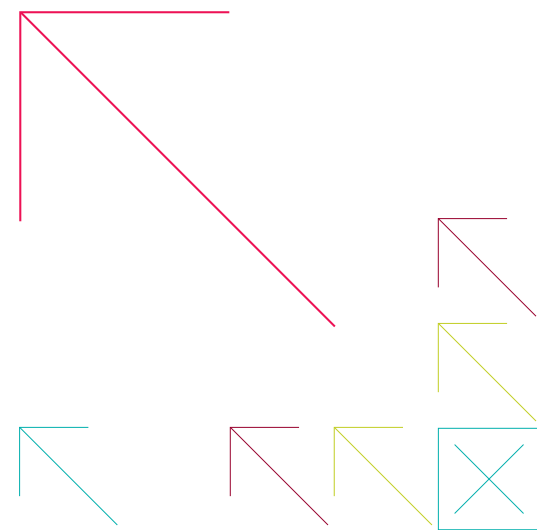




The mission of the **Wilmer Eye Institute** is to use and develop the finest scientific evidence to promote improved ophthalmic care and the reduction of visual disability in a collaborative environment that combines compassionate patient care, innovative research, and the training of future leaders in ophthalmology and visual sciences.

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THINK SMALL

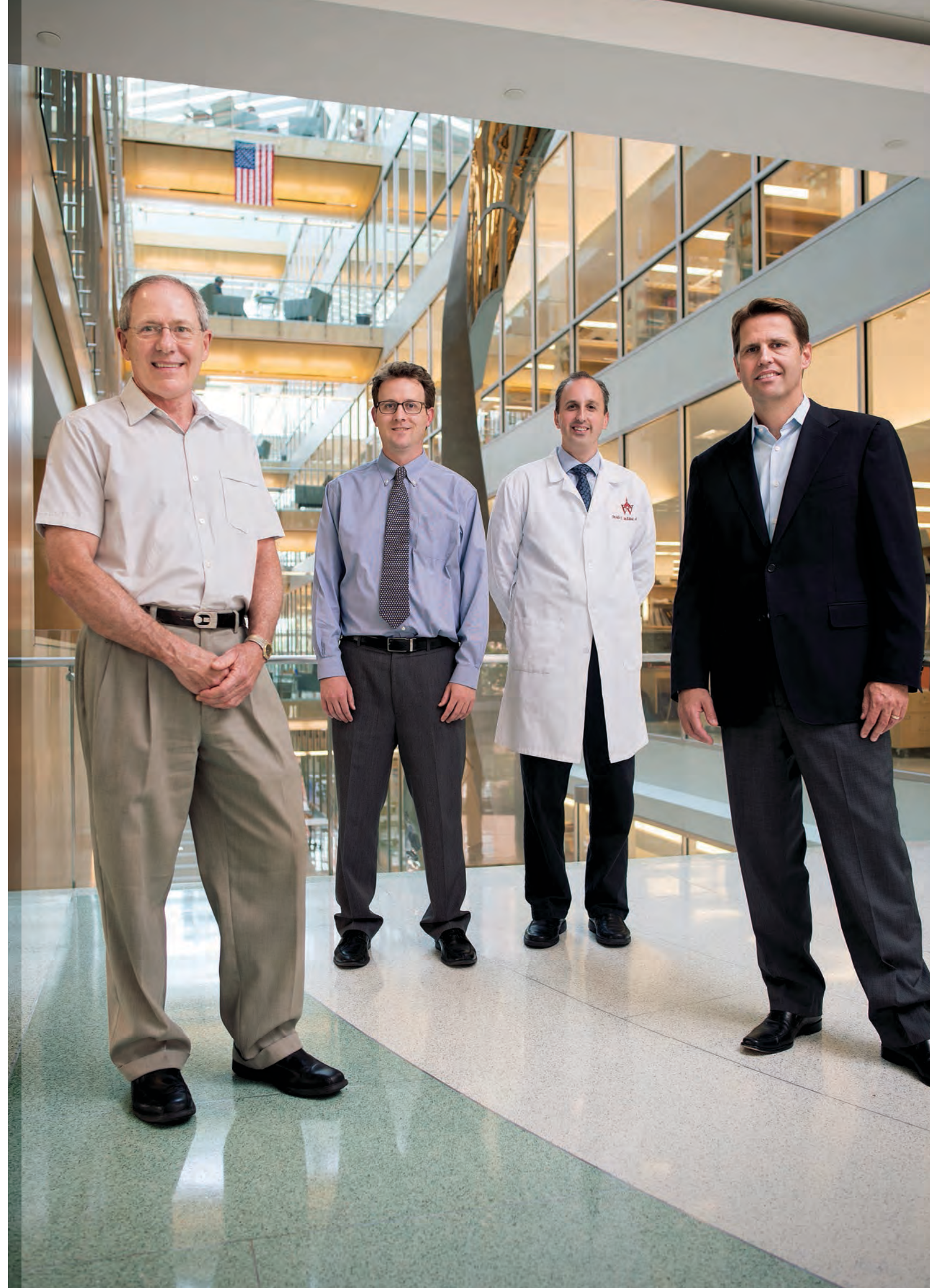
WILMER LEADS NANOMEDICINE REVOLUTION

Pharmaceutically speaking, the delicate and complex tissues of the eye represent one of the most challenging of all human systems. Getting drugs where they need to be—in sufficient quantity and to remain there long enough to be effective—is a monumental challenge.

Toward such goals, several teams at the Wilmer Eye Institute are hot on the trail of

a revolutionary new approach that goes small to solve these very big challenges. The researchers are exploring the fascinating and promising world of nanomedicine to design new ways to deliver drugs in the eye. Nanomedicine is conducted at the scale of single molecules—particles that are less one ten-thousandth the thickness of a human hair.

→LEFT TO RIGHT: Harry Quigley, M.D.; Ian Pitha, M.D., Ph.D.;
Derek Welsbie, M.D., Ph.D.; Justin Hanes, Ph.D.



*“If we can solve these problems,
it will be the single greatest advance
in glaucoma care in a century.
And it’s now within reach.”*

– HARRY QUIGLEY, M.D.

“If we can solve these problems, it will be the single greatest advance in glaucoma care in a century. And it’s now within reach,” says Harry Quigley, M.D., the A. Edward Maumenee Professor of Ophthalmology and director of Wilmer’s Glaucoma Center of Excellence.

For patients suffering from myriad eye diseases, the choices for drug delivery today are limited. Injections into the eye are one option, but they are not for the faint of heart, and the drugs quickly dissipate. The other option is eyedrops.

Drops, however, have their drawbacks. They can’t reach deep into the eye, and chemicals added to them can cause irritation. And then, of course, there is the big downside: the adherence problem, as Quigley calls it. Drops depend on the patients, often elderly and arthritic, to self-administer drugs, sometimes as often as three times a day.

“The drugs never make it into the eye. The patient either forgets or skips them altogether, or they try,

but the drops roll helplessly down the cheek,” Quigley explains.

He and his team are looking to overcome these challenges through the nanomedical delivery of eyedrops. While the drugs they are studying are not new, how the drugs are formulated is. Like the gelatinous capsules that contain larger-scale medications, nanomedicines consist of a biodegradable polymer (plastic) “backbone” that encapsulates the drug molecules. Each molecule of the drug is, in essence, a pill in and of itself. The polymers dissolve slowly, releasing the drug over time.

“The polymers are similar to those used in dissolving sutures—strong but temporary. When they biodegrade, they dissipate into water and carbon dioxide, leaving the drug behind,” says Ian Pitha, M.D., Ph.D., who is working with Quigley on his glaucoma research.

Others at Wilmer working in the same direction include Peter Campochiaro, M.D., the George S.

and Dolores D. Eccles Professor of Ophthalmology and an expert in diseases of the retina, who is investigating a long-lasting therapy for the “wet” form of age-related macular degeneration. In preliminary tests in laboratory animals, Campochiaro showed that a nanoparticle drug was still effective almost four months later.

Likewise, Donald Zack, M.D., Ph.D., and Derek Welsbie, M.D., Ph.D., have had success in nanomedicines. One glaucoma drug they are developing together protects the sensitive optic nerve structures from effectively killing themselves, a process known as apoptosis.

The common thread running throughout these many efforts is Justin Hanes, Ph.D., the Lewis J. Ort Professor of Ophthalmology and director of the Center for Nanomedicine at Wilmer. Hanes is a biomedical engineer and an expert in formulating the various polymers and nanoparticles the ophthalmologists use in their research.

Hanes can imagine a day when macular degeneration patients get injections once a year, perhaps even less frequently, rather than the once-a-month injection that is typical today. And for those now using eyedrops, Quigley is testing an injectable glaucoma nanoparticle dose that sits just under the tissue covering the eye—the conjunctiva—not in the eye itself.

“Instead of daily drops, we hope to numb a little spot on the eye and inject the drugs where they’ll last for months. It’s painless and removes the burden of adherence from the patient,” Quigley says. “It is a dramatically better approach.”

LUCKY INDEED

When Saranne Kosberg first experienced glaucoma symptoms, some 20 years ago, she bounced between doctors searching for help. Eventually, she ended up in the care of Harry Quigley, M.D., at the Wilmer Eye Institute.

Now, two decades on, she is still with Quigley and still largely symptom-free.

Not only is Kosberg a patient of Quigley’s, but she and husband, Livingston, are benefactors of his research. The couple has generously funded several areas of research, including nanomedicine. Human trials of these transformative drugs are closer than ever before, but the research is demanding.

“The Kosbergs’ generosity and their impact have been profound,” Quigley says.

“We wanted to encourage cutting-edge research,” Saranne says. “It is remarkable to help develop these revolutionary eye treatments. Dr. Quigley is a great doctor and a great human. We are lucky indeed.”



CLASSROOM INSIGHTS

PIONEERING STUDY AIMS TO IMPROVE READING IN LOW-INCOME COMMUNITIES

The crushing disadvantages of poverty are many and profound. The last burden any impoverished child needs is the inability to read well. And yet, for as many as eight in 10 elementary school students who live in pockets of poverty across the U.S., reading is a tremendous challenge. Exactly why remains a mystery.

“**W**e don’t know if these kids have a fundamental reading problem, such as dyslexia, or whether there is something more basic at play in the form of eye and vision problems—problems that we might correct with early eye screening and intervention,” says Michael Repka, M.D., M.B.A., the David L. Guyton, M.D., and Feduniak Family Professor of Ophthalmology and chief of the Division of Pediatric Ophthalmology and Adult Strabismus at the Wilmer Eye Institute. Toward that goal, Repka is one of three co-directors on a multidisciplinary team of researchers from Wilmer and the Johns Hopkins School of Education who have commenced a first-of-its-kind study in Baltimore City schools. The study will not only search for answers to these vexing questions, but it will also seek solutions to them.

The team hypothesizes that vision problems, including refraction difficulties, eye misalignment, magnification problems, etc.—not a fundamental inability to read—are at the heart of reading deficits

for at least some of the struggling readers in low-income communities. These challenges are relatively easy to overcome. The hope is that in doing so, reading scores will improve.

“We know that kids who fall behind in reading are less likely to succeed in life, but there has never been a study that separates the kids who can’t read from the kids who are struggling to see clearly,” says David Friedman, M.D., Ph.D., M.P.H., director of the Dana Center for Preventive Ophthalmology, the Alfred Sommer Professor of Ophthalmology and one of the study’s co-directors.

Friedman and Repka are world-renowned vision specialists with expertise in public health as well as clinical research and care. Their collaborator is Robert Slavin, Ph.D., director of the Johns Hopkins School of Education’s Center for Research and Reform in Education. Slavin led development of Success for All, a reform strategy now used in more than 1,000 schools nationwide to increase student achievement in high-poverty areas.



“WE KNOW THAT KIDS WHO FALL BEHIND IN READING ARE LESS LIKELY TO SUCCEED IN LIFE, BUT THERE HAS NEVER BEEN A STUDY THAT SEPARATES THE KIDS WHO CAN’T READ FROM THE KIDS WHO ARE STRUGGLING TO SEE CLEARLY.”

DAVID FRIEDMAN, M.D., PH.D., M.P.H.

The present study traces its roots back several years to the day Slavin reached out to Friedman with his idea. In subsequent years, an exhaustive review of the published literature and existing studies revealed a dearth of scientific understanding of the problem.

“To our surprise, no one had ever approached the problem in this way before,” Slavin says. Thus, a study was born.

In the first part of the initiative, the researchers are administering reading tests to about 400 second graders in Baltimore City schools to identify those with reading problems. The children will be given vision and eye testing to determine how many poor readers have eye problems.

In the next stage, the researchers will implement corrective interventions, including distributing glasses and other targeted treatments. These stages will happen relatively early in the year. The children will

then complete their school year as normal. In the spring, the Johns Hopkins researchers will return to test reading scores and compare the kids’ performance against national averages to gauge success.

“This is really an epidemiological study and is pretty aggressive in its plan to identify, intervene and retest all within a single school year. If we’re successful—and we have every reason to believe we will be—the next big step will be to create a system for schools to manage vision problems as a normal part of their reading program nationwide,” Slavin says.

In terms of impact, the potential is great, since correctable vision problems are estimated to affect 5 to 10 percent of low-income children across the country.

“You’re talking about a lot of kids—millions, perhaps. It would have an enormous impact on real lives,” Friedman says.

† Wilmer’s newest recruit, Megan Collins, M.D., will join Repka, left, and Friedman in this project.



† Bob and Diane Levy

THE GIFT OF READING

Bob Levy and his wife, Diane, are philanthropists keenly focused on education.

“We want to support efforts with the potential to solve problems in the long run, not just make them better in the short term,” says Bob, chairman of Chicago-based Harris Associates.

The roots of Bob’s philanthropic connection to the Wilmer Eye Institute can be traced to his late mother, who had been a patient there. That bond, in turn, led him to Wilmer’s David Guyton, M.D., the Zanyvl Krieger Professor of Pediatric Ophthalmology. The Levys played a role in supporting one of Guyton’s inventions—an automated device to improve screening for attention-deficit hyperactivity disorder.

More recently, the Levys turned their support to the work of Friedman, Repka and Slavin.

“The idea that many low-income kids just need some basic help seeing better made a lot of sense to us,” explains Bob. “Giving them the gift of reading might be the single greatest boost to their future potential anyone could possibly provide. We got excited and had to help.” If the study bears fruit, Bob hopes that the approach can one day be replicated to benefit disadvantaged children in his home city of Chicago.



“RETINA IN A DISH”

TRANSFORMING THE STUDY OF EYE DISEASE

M. Valeria Canto-Soler, Ph.D., is holding the future in her hand. In a glass flask filled with clear liquid float several small pieces of pinkish-white human tissue that arc gently with a natural curve, like the crown of a jellyfish. They are tiny retinas, but they are different from any previously known to science. They were grown entirely in the lab from stem cells.

“**W**e have been able to recreate in the lab the developmental process for the formation of the retina almost as it happens in the womb,” says Canto-Soler, director of the Retinal Degenerations Research Center at the Wilmer Eye Institute.

Hailed among a small coterie of the world’s top researchers working in regenerative medicine, Canto-Soler led a team of researchers, including Xiufeng Zhong, Ph.D., who published a groundbreaking paper in June 2014 that thrilled the ophthalmological world by describing a relatively simple process for teasing the retinas to grow.

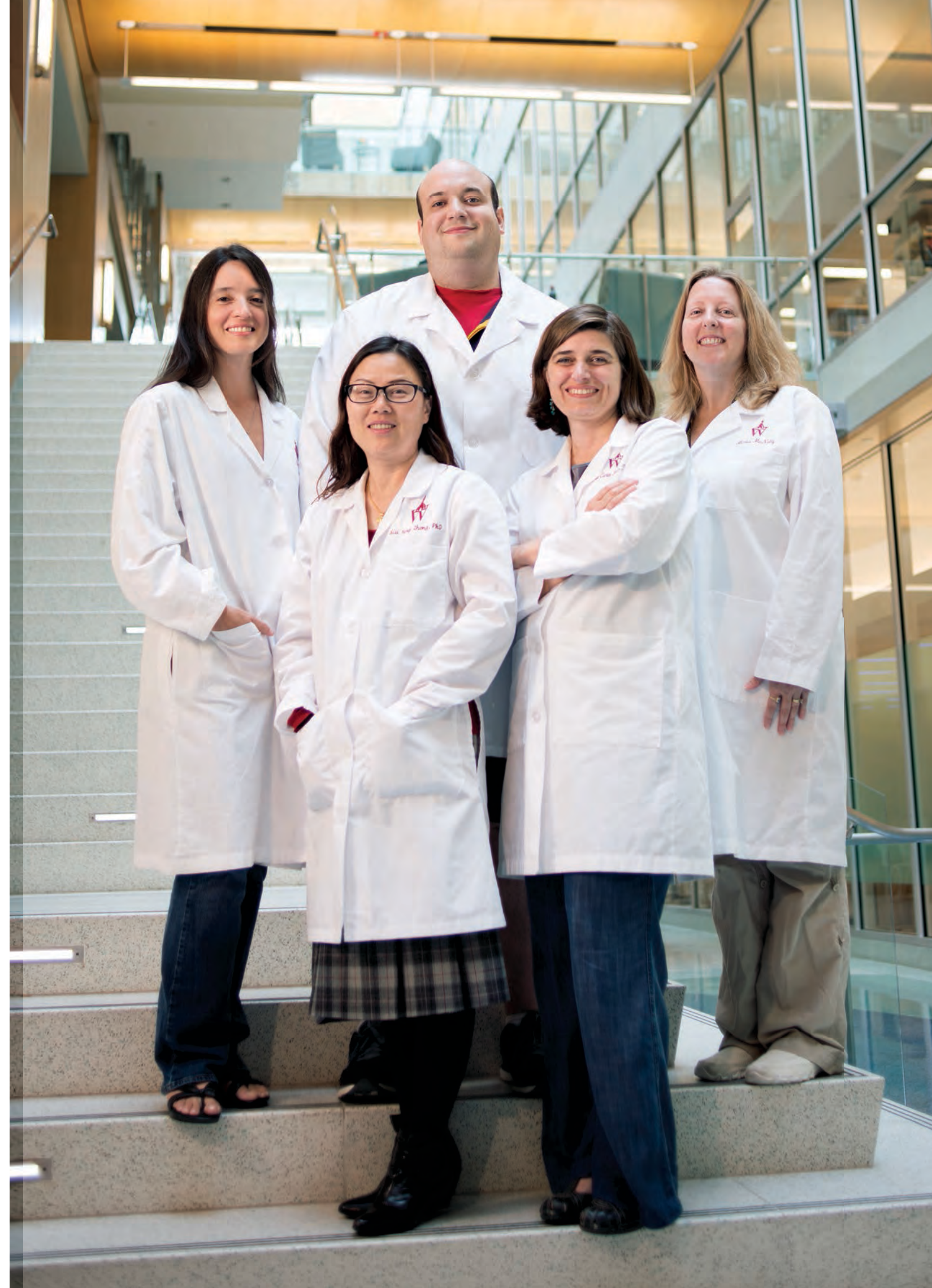
“Though just 1 millimeter in diameter, these retinal ‘cups,’ as we are calling them, resemble very much the curvature of the human eye, and they contain all the many types of retinal cells arranged exactly as they would be in the eye,” Canto-Soler says.

In these tissues, scientists eventually hope to gain a better understanding of how the eye works and to potentially re-create diseased tissues to better understand what goes wrong, then test new drugs and therapies.

Such specimens might allow researchers to replicate a patient’s specific disease or abnormality for study in the lab.

Some have described the approach as a “disease in a dish,” potentially allowing doctors to try any number of therapeutic approaches to find what is likely to work in a particular patient and to do so at a previously unimaginable pace. If an approach isn’t effective or some side effect arises, the researcher could simply begin anew on a freshly created sample from the patient.

— BACK ROW, LEFT TO RIGHT: *Maria Natalia Vergara, Ph.D.*;
Christian Gutierrez, M.S.; *Minda McNally, M.S.*
FRONT ROW, LEFT TO RIGHT: *Xiufeng Zhong, Ph.D.*;
M. Valeria Canto-Soler, Ph.D.





“Anything we can do to speed and improve study is a great boost for the field and to the patients who await better treatments,” Canto-Soler says.

While others have achieved limited retinal regeneration from stem cells, Canto-Soler and her team were the first to achieve advanced tissues that actually contain all the major cell types of the retina and that duplicate the retina’s layered structure and its gently arcing, cuplike shape.

What’s more, the photoreceptors in Canto-Soler’s study demonstrate a level of maturation not seen in regenerative studies before. The receptors are sensitive to light. (Though not so mature that they are yet capable of sending signals to the brain, once they reach full maturity, they may yet achieve that milestone.)

Perhaps most exciting of all Canto-Soler’s advances, however, is the process her lab has developed to regenerate the tissues. Earlier studies had to employ complex applications of various biochemicals to coax the tissues through development. Canto-Soler’s method is actually much closer to what occurs in the womb and is essentially self-regulating.

“We have established a simple and efficient process. These tissues grow freely, in suspension, almost by themselves, as if they just know what they need to do,” Canto-Soler says.

In combination, these Wilmer advances—the ability to regenerate complex, mature retinal tissues and the easily replicable process by which to do it—hold the even greater promise that retinas grown in the lab might someday be transplanted into people suffering from diseases and injury in order to restore sight.

“That day is a long way off,” Canto-Soler says.

“Even though our cells are photosensitive, we still don’t know if they are capable of transmitting the signal to other retinal cells and eventually generating all the information necessary for the formation of a visual image. And then, of course, there are years of clinical study that would be needed for transplant to happen,” she says.

“But this study does bring us one step closer to that possibility.”

“THOUGH JUST 1 MILLIMETER IN DIAMETER, THESE RETINAL ‘CUPS,’ AS WE ARE CALLING THEM, RESEMBLE VERY MUCH THE CURVATURE OF THE HUMAN EYE, AND THEY CONTAIN ALL THE MANY TYPES OF RETINAL CELLS ARRANGED EXACTLY AS THEY WOULD BE IN THE EYE.”

M. VALERIA CANTO-SOLER, PH.D.

REGENERATIVE MEDICINE AT WILMER

M. Valeria Canto-Soler is not alone in using stem cells and regenerative medicine to explore eye disease. The following are a few of the basic scientists spearheading the Stem Cell and Ocular Regenerative Medicine Center at Wilmer. Their clinical collaborators span every disease area and division at the Wilmer Eye Institute.

- **JENNIFER ELISSEEFF, PH.D.**, the Jules and Doris Stein Research to Prevent Blindness Professor and director of the Translational Tissue Engineering Center, is using regeneration to help repair eye injuries in the cornea with new bioadhesives and membranes.
- **DONALD ZACK, M.D., PH.D.**, the Guerrieri Family Professor of Ophthalmology in the Center for Genetic Engineering and Molecular Ophthalmology, is using stem cells to grow diseased retinal pigment epithelial cells and has begun screening thousands of small molecules for efficacy against the specific genetic mutation the cells share.
- **GERARD LUTTY, PH.D.**, the G. Edward and G. Britton Durell Professor of Ophthalmology, is working to regenerate certain capillary cells that he will inject into the eye in hopes of restoring blood flow to diseased areas of the retina.
- **SAMUEL YIU, M.D., PH.D.**, is using stem cells to regenerate tear glands to replace the nonfunctioning glands in patients with severe dry eye disease.

3-D MODELING

IMPROVING RESULTS OF ORBITAL SURGERY

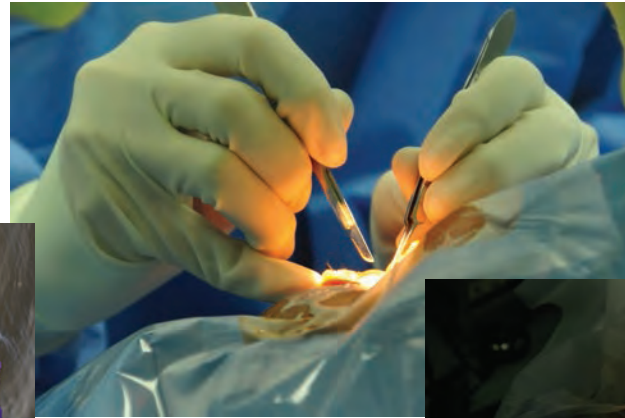
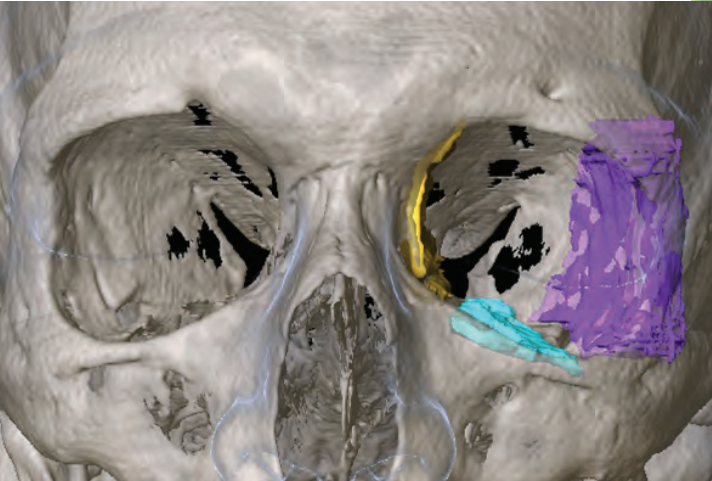
Michael Grant, M.D., Ph.D., is a reconstructive eye surgeon who sees surgery differently than most other doctors. It's not that he views the practice of surgery differently. It's that Michael Grant literally sees things differently than most.

“We're using advanced three-dimensional imaging and pre-operative computer assisted planning to help us

make surgeries safer, more predictable and, ultimately, more successful for patients,” says Grant, who directs the Wilmer Eye Institute's Ocular and Orbital Trauma Center.

Grant is among a handful of surgeons around the world using today's remarkable computer technology to craft exact-scale patient models to improve surgical outcomes in orbital surgery.





“The eye is an incredibly complex, confined environment where you have the delicate eye, of course, and nerves—two of which are attached to the eye—muscle and bone, all in very close proximity. It’s a technically demanding environment,” he says. “Being able to see things in three dimensions is a great advantage.”

Whether he is correcting general reconstructive problems, congenital malformations or traumatic injuries, Grant’s orbital reconstruction efforts often involve manipulating the bones of the eye socket—structures that are hidden from view. The traditional practice has been to handle what is, by every measure, a three-dimensional problem in just two dimensions, by using flat images for planning.

While 2-D imaging certainly helps doctors peer through the soft tissues to understand and plan bone reconstruction, this approach is limiting. Like playing golf with one eye closed, the surgeons are handicapped from the start.

“Not a lot of sophisticated planning was possible, but we can now operate within a millimeter of accuracy and assess our success while still in the operating room,” Grant says.

He begins by taking a series of preoperative CT scans of the patient and feeding the data into sophisticated computer algorithms that produce an exact-scale model of the patient. In essence, he is creating a virtual patient.

Sometimes those models exist on a computer screen. After planning his surgery in his office, he downloads the imagery to a USB memory stick, takes it into the operating room and, using advanced technologies developed by a company in Germany, projects his plans directly onto the face of the patient.

Like a surgical GPS, these maps guide his every incision in real time. Then, before he wraps up, Grant can compare his plan against the results, all while still in the operating room. If necessary, he can adapt on the spot, reducing the need for follow-up surgeries.

“We can now operate within a millimeter of accuracy and assess our success while still in the operating room.”

—MICHAEL GRANT, M.D., PH.D.

In other instances, Grant prints out life-size, exact-scale plastic models using a 3-D printer. By surgically manipulating the models, he can get a much better feel for what he needs to do in the operating room.

In one example, Grant explains how he used plastic, 3-D printed models as his surgical patient, cutting and manipulating the plastic “bones” of the virtual patient’s left eye socket to model how he wanted to reconstruct that patient’s damaged right eye socket. In the operating room, the surgery then became like solving a jigsaw puzzle, with Grant cutting and shaping the pieces of real bone to match those he created in his models.

“This is definitely the next generation of surgical planning and another example of the Wilmer Eye Institute’s leadership,” Grant says. “Wilmer has always been at the cutting edge, always looking for ways to use technology to take on the most difficult clinical problems in new ways.”



MISSION COMPLETE

By the time Steven Talley retired from the military in 2012, his Graves’ disease had progressed to the point that his doctors at Walter Reed Hospital said his was the worst case they had ever seen. They referred him to the Wilmer Eye Institute.

“My eyes were in really bad shape,” says Talley, who was referred to Michael Grant for orbital surgery.

Grant used his advanced imaging techniques to explain to Talley exactly what was happening and what he was going to do to relieve the pressure. “The pictures were really very helpful in my understanding. I could see my optic nerve was stretched tight across my eye. It really was a worst-case scenario,” he says.

After the surgery, Talley was pleased by the results, but it was the reaction of his family that provided the first clue to his dramatic transformation.

“They said, ‘You don’t even look like the same person,’” Talley recalls. “It’s almost miraculous, what he’s done. It’s mission complete.”

ARTIFICIAL CORNEAS

A GLIMMER OF HOPE THROUGH THE CLOUD

In 2008, an arterial stroke cost Harriet Koppe the use of her left eye. Luckily, her right eye, troubled as it was by glaucoma and extreme dry eye, was still functional. Two years later, however, a simple impulse—a lone rub of the eye—scratched her good cornea.

“My eyelashes are hard and brittle and turned inward by the eyedrops I use for glaucoma. I scratched my cornea with my own eyelash,” Koppe says. The scratch eventually turned into a perforation.

That’s when Koppe came to the Wilmer Eye Institute’s Esen Akpek, M.D., the Bendann Family Professor of Ophthalmology and one of the world’s foremost eye surgeons specializing in the use of artificial corneas. Akpek performed several patching surgeries on Koppe’s cornea, but by the time her cornea was patched, it was completely opaque and had grown numerous blood vessels, stealing her sight.



“Dr. Akpek said that I would reject a human cornea transplant, but there was another option”—an artificial cornea, Koppe recalls. “The choice wasn’t very difficult.”

For many who look out at the world through clouded corneas, transplants represent the hope of restored vision. While most of those surgeries are successful, a small portion will fail due to reasons ranging from tissue rejection and diseases such as dry eye to the physical failure of the eye into which the transplant is sewn.

“Artificial corneas made of modern plastics have become the solution of last resort for patients for whom human transplants are no longer viable and whose only alternative is total blindness,” says Akpek, who directs the Ocular Surface Disease and Dry Eye Clinic at Wilmer.

Akpek replaces the corneas with clear cylinders of biologically inert plastic that are immune to rejection, clouding and other risks that affect human tissues. In the last decade, Akpek and her colleagues have performed more than 150 of these transplants. She first began transplanting artificial corneas in 2004, when the technology was still in its infancy. At that time, only 100 or so transplants of artificial corneas had ever been done.

The results are often dramatic and immediate. In one study of

transplants of artificial corneas in 15 patients, only one failed to gain vision. For another patient in the study, vision improved to 20/60, and the transplant was still stable more than seven years later. Koppe’s sight has returned to roughly 20/80, good enough that she can read her own typewritten notes without glasses.

“Historically, artificial corneas were a last resort, but the technology has improved considerably, and results like these are changing the field. We suggest artificial corneas should be the primary procedure for certain patients for whom human transplants are no longer an option,” Akpek says.

Until 2006, implantation had only been performed in adults. But that’s changing. Akpek was on a team that performed the world’s first transplant of artificial corneas in two infants, who are still faring well, though they require frequent visits to the doctor for monitoring.

“We think that artificial corneas could restore sight in certain, very specific children with complex diseases who are at high risk for transplant failure,” Akpek says.

Ultimately, however, the team’s impact has been felt most profoundly at the individual level, in many nameless patients whose eyesight has been restored due to the skill of Akpek’s team at Wilmer.

“One day after my surgery, Dr. Akpek took the bandage off,” Koppe recounts. “I went from literal darkness to looking out my window and seeing a flower. It was almost like being born again.”

“That’s the greatest reward,” says Akpek.



“One day after my surgery, Dr. Akpek took the bandage off,” Koppe recounts. “I went from literal darkness to looking out my window and seeing a flower. It was almost like being born again.”



† Shameema Sikder, M.D.

A NEW WAY TO TRAIN EYE SURGEONS

Currently under construction and slated to open in spring 2015, the Wilmer Eye Institute’s Center of Excellence in Surgical Innovation and Education will represent a fundamentally new way to train eye surgeons.

“We’re creating a new teaching approach that breaks out of the master-student model to be more effective at a faster pace,” says Shameema Sikder, M.D., who directs the new center. “We’re interested in improving education for young surgeons, but also in bringing in surgeons who are already in clinical practice to improve their skills.”

The center will have three components. The first will be a knowledge-sharing aspect, where surgeons-in-training can learn from each other in a highly collaborative environment meant to encourage innovation. The second component will include sophisticated 3-D simulators, where residents can hone their skills without the pressures of the operating room. Third, the center will include a state-of-the-art, six-station wet lab, where tomorrow’s surgeons can gain hands-on experience.

“Though this is strictly an ophthalmological center now, the lessons we’re learning might just as easily be applied to other medical disciplines—from ear, nose and throat to plastic surgery,” Sikder says.

DEFYING GRAVITY

NEW CLINICAL TRIALS TAKE ON GRAVES' DISEASE

At the Wilmer Eye Institute's new Bethesda location, doctors are taking a multidisciplinary approach to one of the most vexing challenges in ophthalmology: thyroid eye disease, also known as Graves' disease. They are bringing Wilmer's renowned care to the densely populated Washington metropolitan area, expanding access to clinical trials as never before.

With Graves' disease, the body's immune system inappropriately attacks the thyroid gland and makes it produce outsized amounts of thyroid hormone. Unfortunately, those same antibodies also attack other parts of the body, especially the eyes. The resulting inflammation causes the eyes to bulge and damages muscle and orbital structures, leading to severe eye misalignment and double vision.

"Most people know someone with Graves' disease," says Prem Subramanian, M.D., Ph.D., director of the Thyroid Eye Disease Center at Wilmer's Bethesda office. "It can attack anyone at any time, healthy and unhealthy alike. It crosses all sorts of lines, but unfortunately, treatments for it are not very good at this time."

Against this backdrop, Subramanian and the multiskilled thyroid eye disease team are embarking

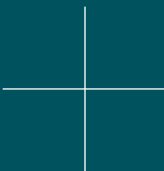
on a first-of-its-kind clinical study to explore an array of new drugs, surgical approaches and technological therapies to fight this crippling disease.

In addition to Subramanian, who studies the neurological roots of eye disease and is a specialist in orbital diseases and eye misalignment known as strabismus, the team includes Nick Mahoney, M.D., a reconstructive eye surgeon, and Shameema Sikder, M.D., a cornea specialist and the medical director of Wilmer's Bethesda location.

"The Bethesda location extends our reach into the Washington metro area, which can benefit from our comprehensive approach to thyroid eye disease. What's more, the facility was designed to encourage multispecialty care in a single location with easy access to endocrine and other specialists who are just a floor away," Subramanian says.



→ LEFT TO RIGHT: Nick Mahoney, M.D.; Prem Subramanian, M.D., Ph.D.; Shameema Sikder, M.D.



A FIGHTING CHANCE

Colin Williams' sister noticed his Graves' disease before he did, suggesting he see a doctor about his eyes "that didn't look right," as she told him. That's when the cascade of symptoms began. Eventually, Williams would experience occasional double vision and pain almost beyond description.

"Sometimes, it felt like my eyes were going to fall out of their sockets. Other times, it was like someone was punching me in the eye," Williams says, describing the symptoms that brought him to Nick Mahoney.

Since taking on Williams as a patient, Mahoney and his Wilmer partners have been relentless, trying various new drops, creams and radioactive iodine treatments to reduce the inflammation and, most recently, removing Williams' thyroid—the root cause of his woes. "Dr. Mahoney and the whole team at Wilmer have been great," Williams says. "At Wilmer, I know I have a fighting chance against this disease."

The team is looking to improve clinical options for patients along a number of therapeutic trajectories, including investigating existing drugs that are already on the market and more aggressive therapies, such as radiation and chemotherapy.

In one example, the team is now looking at the drug Celebrex, normally used to treat arthritis, another autoimmune disease. The theory is that Celebrex might work well to reduce inflammation in the eye sockets and ocular muscles that cause bulging and misalignment.

"We're not developing new drugs—a humongous task—but instead are testing those already at our disposal to see if we can find drugs that work better for those with Graves," says Subramanian.

Another area of particular interest to the team is surgery. In this regard, Subramanian and Mahoney are collaborating with a group of German scientists who are using advanced 3-D imaging techniques and computer algorithms to help ophthalmologists predict surgical outcomes and improve upon existing practices. On the computer, surgeons can remove bone and fat from the eye socket to relieve pressure and reduce bulging without risk.

"Unfortunately, the surgical results don't always turn out exactly as we would hope," Subramanian says. "With the models, the surgeons can gain insight into the effects of given surgical choices on the patient, all before doing the actual surgery."

The team will explore low-dose radiation therapy that has been shown to destroy inflamed tissues in the eyes and whether certain chemotherapy drugs are efficacious.

"Because of their well-known risks and side effects, these therapies can be controversial. Some studies have shown promise, but others have contradicted those findings. We plan to clarify with certainty whether they are effective or not," Subramanian says.

While his study is certainly ambitious, Subramanian is upbeat about its promise, and he remains absolute about one thing: the quality of his colleagues at Wilmer.

"I can't think of anywhere else where you have this breadth and depth of expertise, talent and experience not just in eye diseases, but also in engineering and drug development," he says. "You can always find the right people who have the knowledge of a particular cell type or drug, someone with the skills to develop computer models. It's all right here in one place."

"WE'RE NOT DEVELOPING NEW DRUGS—A HUMONGOUS TASK—BUT INSTEAD ARE TESTING THOSE ALREADY AT OUR DISPOSAL TO SEE IF WE CAN FIND DRUGS THAT WORK BETTER FOR THOSE WITH GRAVES'."

PREM SUBRAMANIAN, M.D., PH.D.

TACKLING LOW VISION

LIONS CLUB AND WILMER UNITE

The history of the Lions Clubs' service to the vision-impaired is a long and storied one. It dates to the 1920s, when Helen Keller challenged the Lions to become the "knights of the blind." Since then, the Lions have been irreplaceable in their aid, starting numerous innovative and impactful initiatives ranging from leader dog training programs and eye banks to pressing for white cane laws across the nation.

“You don't join the Lions unless you are interested in service, and for the Lions, that service is focused on the blind,” says Robert Massof, Ph.D., director of the Lions Vision Research and Rehabilitation Center at the Wilmer Eye Institute at Johns Hopkins.

The Lions Low Vision Center is one of the many programs that Lions in the Maryland, District of Columbia and Delaware region—known to the Lions as Multiple District 22—have supported through tireless service and generous philanthropy.

Recently, that relationship took a new and unparalleled turn with a program designed to provide direct service to some 5,000 underserved people in the region with low vision. Known as

the Lions Low Vision Rehabilitation Network—and aptly dubbed LOVRNET—the program will address a troubling dearth of options amid growing demand for low vision rehabilitation. Other funders include the Reader's Digest Partners for Sight Foundation.

“Low vision is not any one condition, but rather a broad term describing any vision loss that cannot be reversed by glasses, medication or surgery,” says Judith Goldstein, O.D., chief of low vision and rehabilitation at the Lions Vision Center. “It is one of the major areas of research and treatment at Wilmer. LOVRNET will deliver novel solutions at an unprecedented scale to address what has been largely an unmet need for many patients.”

→ LEFT TO RIGHT: Robert Massof, Ph.D.; Judith Goldstein, O.D.;
James Deremeik, RT, CLVT





LOVRNET calls upon the grassroots reach of local Lions Clubs and leverages funding to train and provide professional consultative support to rehabilitation teams, creates a unified support network for patients, matches patients to medical and service providers, and improves the quality of care through continuous professional education for health care providers. Organizers expect the regional LOVRNET initiative to serve as a model for a nationwide rollout.

“The response by the Lions across the board has been overwhelming. The direct service component of LOVRNET has been enthusiastic to the point where they are in many ways ahead of us in ramping up the program’s efforts. The Lions have just been tremendous,” says James Deremeik, education and rehabilitation program manager at Wilmer and director of LOVRNET.

“It is innovative and far-reaching programs like LOVRNET that get the Lions Clubs excited,” says Ted Ladd, chairman of the Lions Vision Research Foundation, which has raised much of the funding for the pilot program.

The relationship between Wilmer and the Lions Clubs began in the late 1980s through the encouragement of Arnall Patz, M.D. As then-director of the Wilmer Eye Institute and as a practicing physician, his transformative ideas and work saved countless individuals from blindness. His contributions continue to improve the lives of millions.

Together, Patz and the Lions created the Lions Vision Center at Wilmer, a multidisciplinary team of doctors and rehabilitative specialists collaborating to restore and improve day-to-day functions—including reading, driving, shopping and other important activities—lost to visual impairment.

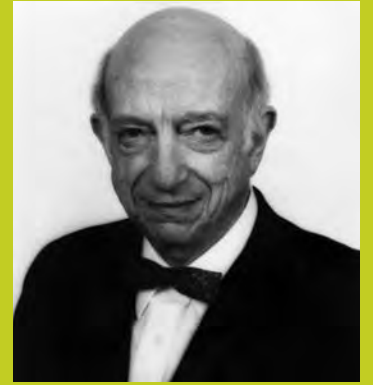
Vision rehabilitation at the Lions Vision Center focuses on the person and his or her individual daily needs, not only on treating the disorder. While low vision services are not a cure, visual ability can be improved, sometimes dramatically, in certain patients.

“LOVRNET will deliver novel solutions at an unprecedented scale to address what has been largely an unmet need for many patients.”

—JUDITH GOLDSTEIN, O.D.

When Patz died in 2010, many who had known, worked with or been treated by him, including the Lions, rallied to endow the Arnall Patz Distinguished Professorship in Ophthalmology, which will benefit the Lions Vision Center, at the behest of Patz’s widow, Ellen, and their children. In this effort, like so many others at Wilmer, the Lions of Multiple District 22 were once again instrumental. With their help, the Patz Professorship’s total recently surpassed the full funding level of \$2.875 million (see sidebar), providing the Lions Vision Center the firm financial footing to better serve patients, educate trainees and conduct research on low vision.

“Helen Keller told Patz years ago: ‘If you want to get anything done, call the Lions,’” recalls Ladd. “Since then, the Lions and Wilmer have been tightly connected. We’re proud of our connection with Dr. Patz’s legacy and the work we and Wilmer have done together for all people with low vision.”



† Arnall Patz

A FITTING TRIBUTE TO A MENTOR

As a doctor, researcher and teacher, Arnall Patz’ legacy cast a wide shadow across all who came in contact with him, not least Lawrence Singerman, M.D., and Richard Shugarman, M.D., two men who as students were fortunate enough to have Patz as a mentor.

“Arnall Patz was the most inspirational man I ever met. As much as I learned about the retina, I might have learned more about dealing with people from him,” Singerman says.

“He was a role model who changed my career and my life. This professorship seemed an enduring tribute to him,” says Shugarman.

While their decision to co-chair the fundraising committee for the Arnall Patz Distinguished Fellowship may have been easy, the challenges of the role were not. The job began amid the difficult financial crisis of 2008, recalls Singerman. More than 200 donors contributed to the professorship.

“The force of Arnall’s personality ultimately made that job easier than it might otherwise have been,” Shugarman says. “Dr. Patz just embodied everything a physician should be.”

PROGSTAR

A NEW PARADIGM IN THE STUDY OF STARGARDT DISEASE

One of clinical ophthalmology's leading researchers, Hendrik Scholl, M.D., director of visual neurophysiology and of the Retinal Degeneration Clinic, plays a critical role in designing studies to ensure tomorrow's breakthroughs are both effective and safe before they come to market.

Scholl was recruited to the Wilmer Eye Institute from Germany to lead several groundbreaking studies. Most recently, he set his sights on Stargardt disease, a debilitating and degenerative disease that begins in childhood, by leading a \$4.8 million study known as ProgStar. The project is a collaboration between Wilmer and the Foundation Fighting Blindness.

"Stargardt is a fascinating disease for study, first because it starts in childhood, but also from a medical standpoint," says Scholl, the Dr. Frieda Derdeyn Bambas Professor of Ophthalmology. "Stargardt's molecular biology is extremely well understood, and we have gene, medical and stem cell therapies in early clinical trials now. I'm not aware of another disease where you have those approaches in clinical stages of development."

The challenge from the clinical researcher's standpoint is that Stargardt is a very slow-progressing disease with complex effects that cause the rate of progression to vary from patient to patient.

Symptoms of Stargardt usually begin early on with difficulty reading and spots (visual field defects) in the center of vision. Telltale yellowish flecks in the macula—the heart of the retina where fine details are registered—confirm diagnosis. The yellow flecks are lipofuscin, a normal byproduct of cell function that usually accumulates only slightly. But due to a genetic defect in Stargardt, there is increased accumulation over time. The prognosis is a slow progression to permanent blindness.

Stargardt is so slow-growing, however, that it can take 20 years or more to conduct a single clinical trial to ascertain the efficacy of an intervention using standard methods.

"PROGSTAR IS ALTERING THESE TIME FRAMES. IT'S A VERY IMPORTANT EFFORT TO SHOW INDUSTRY THAT IF WE TAKE A MEASURED APPROACH TO A CLINICAL TRIAL, WE CAN SHOW RESULTS IN JUST ONE TO TWO YEARS, NOT ONE TO TWO DECADES."

HENDRIK SCHOLL, M.D.



† The ProgStar team

“Few pharmaceutical companies have that sort of patience, but ProgStar is altering these time frames,” Scholl says. “It’s a very important effort to show industry that if we take a measured approach to a clinical trial, we can show results in just one to two years, not one to two decades.”

The patient variability in Stargardt complicates the selection of patients for study and has fostered a debate as to how best to measure the success of clinical trials.

ProgStar, therefore, is actually two studies in one. The first half is a retrospective study of up to 250 patients that looks back at clinical exam results and retinal images collected between 2008 and 2014 to

evaluate how Stargardt progresses. The second aspect is a prospective study that will track up to 250 other patients every six months for a two-year period. The patients in the studies, both children and adults, will be recruited from nine clinical centers across the U.S. and Europe.

ProgStar is not a clinical trial of a single new therapy. Instead, it will employ advances in retinal imaging and in tools for measuring visual fields and acuity to accelerate evaluation of how existing therapies are performing. Among its many goals, ProgStar will explore and accelerate the study of new drugs informed by advances in genetic science.

1

In 1907, Karl Stargardt, a German ophthalmologist, first identified the juvenile macular degenerative disease that bears his name. Stargardt is a genetic abnormality that affects the production of a protein that helps remove lipofuscin, a waste chemical, from the retina. As the yellowy lipofuscin builds over time, eyesight degenerates.



STARGARDT FACTS

2

Though it progresses slowly at first, the degeneration eventually accelerates. In some cases, a person can go from a relatively moderate case to virtual blindness in a matter of months. There is no cure or treatment for Stargardt.



3

Though occurring in just one in 10,000 children, Stargardt nonetheless affects some 30,000 Americans, and many thousands more worldwide. Symptoms usually begin between the ages of 6 and 20.

“In Stargardt research, there’s nothing quite like ProgStar,” Scholl says. “No one in the world has built the patient cohort we have, and the Wilmer Eye Institute has amassed an unprecedented database of information on the disease that this study will surely enhance. ProgStar will lead to better studies of treatments and increase our chances of success against the disease.”

FILLED WITH HOPE

Though Karen Morris is just 45 years old, when she prepares to go to dinner at a restaurant with dim lighting, her get-ready routine now includes a quick trip online to peruse the menu and choose what she will be eating ahead of time. Morris suffers from Stargardt disease, a slow-progressing eye disease that makes it very hard for her to read in low-light situations and may one day leave her blind.

“I hope that day won’t come,” she says. “I have four children, and I hope to watch them grow, see their weddings and their children.”

Morris lives in Cincinnati and travels to Baltimore twice a year to visit Wilmer’s Hendrick Scholl, one of the world’s leading experts in the disease. She’s also enrolled in ProgStar, the first-of-its-kind study Scholl is leading to bring a small measure of hope to those suffering from Stargardt.

“I just can’t say enough how lucky I feel to be in Dr. Scholl’s care,” Morris says. “And, being in ProgStar, I know that I’m providing others with Stargardt the same hope I have. Studies like this really do matter.”

EVENTS

WILMER CENTER OF EXCELLENCE IN SURGICAL INNOVATION AND EDUCATION LUNCHEON IN HILTON HEAD

MAY 9, 2014

David Leighton, longtime supporter of the Wilmer Eye Institute at The Johns Hopkins University, in honor of the care his late wife, Helen, hosted a luncheon at his Hilton Head Island home. Peter McDonnell, director of the Wilmer Eye Institute, and Shameema Sikder, director of Wilmer's Center of Excellence in Surgical Innovation and Education, discussed the innovative research taking place at Wilmer, specifically with surgical innovations and the education of future ophthalmologists.

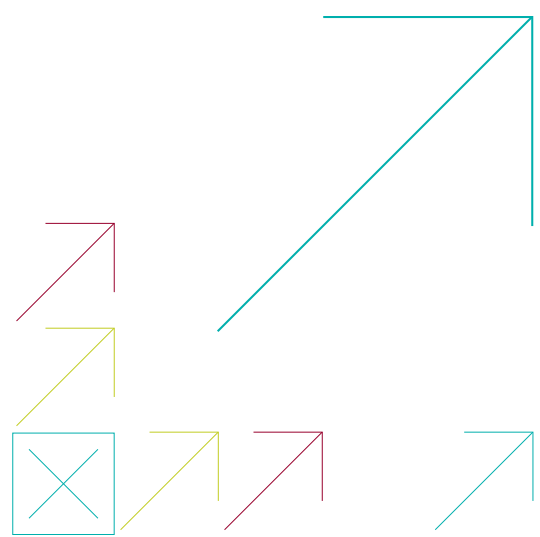
During the luncheon, a special award was given to Sandra Forsythe, member of the Wilmer Board of Governors. Forsythe received the Aida de Acosta Root Breckinridge award for her tireless advocacy for the blind and visually impaired.



↑ Shameema Sikder presents David Leighton with a reproduction of Wilmer's Sightline magazine that highlighted "it takes a community to move an institution forward."



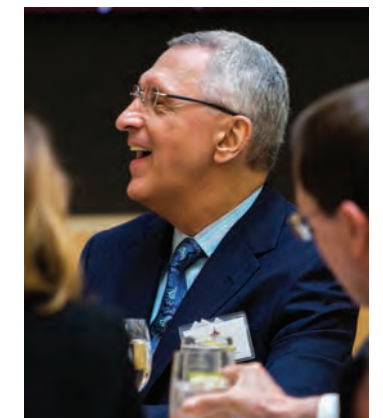
↑ Peter McDonnell presents Sandra Forsythe with the Breckinridge Award.



↑ Lance Bendann, William Wood, Robert Welch and his wife Betty and Claire Jensen, enjoy the celebrations.



↑ Peter McDonnell presents Esen Akpek with the Bendann Family Professorship crystal.



↑ Chairman of Wilmer's Board of Governors, Sanford Greenberg

The Wilmer Board of Governors prepare for their spring meeting. →



DEDICATION OF THE BENDANN FAMILY PROFESSORSHIP, WILMER LEGACY SOCIETY LUNCHEON AND WILMER BOARD OF GOVERNORS MEETING **MAY 19, 2014**

The dedication of the Bendann Family Professorship in Ophthalmology and installation of Esen Akpek as the inaugural professor, and Wilmer's Annual Legacy Society luncheon took place in the T. Boone Pickens atrium in the Robert H. and Clarice Smith Building. These celebrations were followed by the Wilmer Eye Institute's Board of Governors spring meeting.



† Albert Suk Jun presents the Neil R. Miller, M.D., Teaching Award to Richard Kolker.

THE 73RD WILMER RESIDENTS ASSOCIATION CLINICAL MEETING

JUNE 13, 2014

Wilmer faculty, residents, alumni and special guests gathered for a full day of scientific presentations. During the meeting, Wilmer celebrated the lives of Stephen Ryan and Ronald Smith. To quote Morton F. Goldberg, M.D., the Joseph E. Green Professor of Ophthalmology and Director Emeritus of the Wilmer Eye Institute, "Here at Wilmer, they will never be forgotten."

This year's meeting also highlighted presentations by the class of 1974. Wilmer is grateful for their class gift in support of the Center for Surgical Innovation and Education.



— Peter McDonnell, center, with the Wilmer Residence class of 1974. From left to right: Frederick Elsas, William Wood, Thomas Harbin, Jr. and Robert Liss

SAVE THE DATE: THE 74TH WRA CLINICAL MEETING
JUNE 19, 2015



PATIENTS CAME FROM EVERY U.S. STATE AND 84 COUNTRIES

197,576 TOTAL PATIENT VISITS

154
TOTAL CLINICAL FACULTY MEMBERS

FY 14 (7/13-6/14)
BY THE NUMBERS

THE ONLY EYE TRAUMA CENTER IN MARYLAND

DESIGNATED BY THE MARYLAND INSTITUTE FOR EMERGENCY MEDICAL SERVICES SYSTEMS

12,259 SURGERIES

60% AT THE JOHNS HOPKINS HOSPITAL

40% AT FIVE OTHER LOCATIONS

60% AT THE JOHNS HOPKINS HOSPITAL
40% AT FIVE OTHER LOCATIONS

9 LOCATIONS
THE JOHNS HOPKINS HOSPITAL AND EIGHT SATELLITE LOCATIONS

ODENTON / GREEN SPRING STATION / BEL AIR
JH BAYVIEW / JH HOSPITAL / COLUMBIA
FREDERICK / WHITE MARSH / BETHESDA

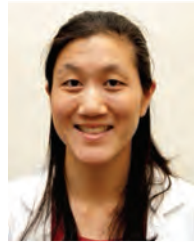
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WILMER RESIDENTS 2014-2015

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Connie Chen

3RD YEAR



Sumayya Ahmad



Jessica Chang



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Farhan Merali



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2ND YEAR



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Craig See



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1ST YEAR



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Jefferson Doyle



Suzanne
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Nazlee Zebardast

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As chief resident of the Wilmer Eye Institute, Morton Goldberg was trained in so many novel and sophisticated techniques that he went straight into retinal surgery when he left, having no need for a fellowship.

And so began a nearly lifelong relationship with Wilmer, the place that Goldberg, the Joseph E. Green Professor of Macular Degeneration and Other Retinal Diseases, considers the finest eye institute in the world. It started the first day of his residency in 1963, when the night nurses took the “new kid” under their wings and helped him find his way with their kindness and skill. Two years later, there was the introduction to his future wife, Myrna, by a teacher’s daughter. For two decades, Morton Goldberg served as ophthalmology chairman at the University of Illinois College of Medicine. Following his return from Illinois in 1989, he spent 14 productive years as Wilmer’s director.

“Wilmer is one of those few institutions where it’s worth devoting your entire professional energy,” Morton says. “There’s a wonderful family feeling that everyone is doing the best possible job to the best of their professional ability.”

When the Johns Hopkins Legacy Society was founded in 2012, the Goldbergs knew right away they wanted to be involved. The Legacy Society honors individuals who make a bequest commitment or life-income gift to any area of Johns Hopkins. Their bequest will support the research and professional travel of the faculty member holding the Morton F. Goldberg Professorship at Wilmer, areas that Morton says are increasingly difficult to finance.

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Wilmer’s strength lies in its tradition of excellence, says Morton, from role models like world-renowned ophthalmologist A. Edward Maumenee and father of neuro-ophthalmology Frank Walsh—who set the bar at the superlative level that continues today—to education that attracts the nation’s top candidates, trains them in the best principles and practices, and catapults them into leadership positions around the globe. His bequest, Morton says, is his contribution to the traditions that mean so much to him.

For information about the Johns Hopkins Legacy Society, contact the Office of Gift Planning at 410-516-7954 or 800-548-1268, email giftplanning@jhu.edu, or visit rising.jhu.edu/giftplanning.





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