



<sup>44</sup> The future ain't what it used to be," famously opined baseball great Yogi Berra, who recently passed away at the age of 90. Berra shares the year of his birth, 1925, with the launch of the Wilmer Ophthalmological Institute, but we at Wilmer could not disagree more—albeit respectfully—with this view of the future.

We honor our past at Wilmer. In this issue, you will read about two professorships established in the names of past giants within ophthalmology who made lasting contributions to the treatment of eye disease and who were also particularly gifted educators. Samuel Theobald, the first professor of ophthalmology here at Johns Hopkins, invented the lacrimal probe used to treat tearing disordersstill used today-as well as the use of boric acid to treat eye infections. One of his students, Alan Woods, went on to become the director of the Wilmer Eye Institute. Maurice Langham, Wilmer's former research director, was honored by a grateful former student in recognition of Langham's teaching and support, which helped launch the student's career.

From the vantage point of the Wilmer Eye Institute, the future is brighter than ever. In the last decade, Wilmer's research program has doubled, and the work highlighted in this report represents only a scratching of the surface of all the exciting projects going on in our laboratories, clinics and operating rooms. Bert Jun, who over a decade ago brought the thennew lamellar surgery for Fuchs' corneal dystrophy to Wilmer, is working on a genetic cure of this disease that afflicts so many families around the world. Jeremy Nathans discovered the genetics of how we see the beautiful colors around us and has identified the genetic defects that are responsible for debilitating eye diseases. In these discoveries lie the seeds for new therapies to restore visiontherapies being tested in the lab or in patients.

We have worked diligently to serve more patients and serve them better. Over the last decade, the number of patients we care for has quadrupled! Today, our new and returning patients are welcome to request same-day appointments. We are scheduling about 1,000 such same-day visits every month. We are also testing software at Wilmer that will give returning patients the option to use an app to schedule their visits at their convenience without picking up a phone.

#### FROM THE VANTAGE POINT OF THE WILMER EYE INSTITUTE, THE FUTURE IS BRIGHTER THAN EVER.

We face the future with confidence because we are fortunate to have great partners. For example, you will read about one of the largest pharmaceutical companies in the world partnering with Wilmer faculty to speed the process of taking discoveries from Wilmer's laboratories to the clinics where they can help our patients. And you will read about T. Boone Pickens, an icon of business—just as Yogi Berra was an icon of our national pastime—and his decision to fund the early careers of Wilmer's next generation of leading ophthalmologists and scientists.

With more than 150 full-time faculty members at Wilmer and our great partners and supporters, I feel that Mr. Berra was describing Wilmer when he declared: "We have deep depth." All of us are united in an effort to end blindness, a task that—you knew it had to be coming—"ain't over till it's over."

Sincerely,

It ! In Donnell

PETER J. McDONNELL, Director



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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.



# EYE CARE FOR EBOLA SURVIVORS

Though Ebola virus disease proved a devastating killer in West Africa in the summer of 2014, there were many who survived the epidemic. While those lucky few are surely grateful for their good outcomes, surviving the disease has been only the first hurdle to recovery. Among the lessdiscussed impacts of defeating Ebola: a host of lingering health effects, including long-term vision problems.

"People who have had Ebola are losing vision, but we don't know why," says Allen Eghrari, M.D., a cornea specialist at the Wilmer Eye Institute. Eghrari is leading a field study in West Africa to catalog and characterize the eye complications of Ebola.

What is known at this point is that the Ebola virus can linger in the eyes of survivors for months after the disease has passed. One-half or more of these survivors will experience a range of vision complications, from simple blurriness to total blindness.

→ Christopher Brady, left, and Allen Eghrari have teamed up to better understand the eye complications of Ebola.





"We plan to listen to survivor complaints and study their eyes to truly understand the impacts. This would be valuable for future outbreaks and for other survivors," he says.

Eghrari and Wilmer colleague Christopher Brady, M.D., a retina specialist, had begun to study the problem even as the virus was still raging in the fall of 2014. That is when Sheila West, Ph.D., Pharm.D., vice chair for research at Wilmer, suggested Brady and Eghrari talk to Rachel Bishop, M.D., an ophthalmologist at the National Institutes of Health.

It turned out that Bishop was on a similar track. That simple recommendation led to a fruitful collaboration. "We knew right away that combining efforts would give us the best opportunity to understand the disease and help the greatest number of patients," Eghrari says.

Their research is now a part of a wider study into the long-term impacts of Ebola, known as PRE-VAIL—Partnership for Research on Ebola Vaccines in Liberia. PREVAIL is a three-part study sponsored by the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health. Eghrari, Bishop and Brady are working in the third phase, which is looking at the broader spectrum of Ebola aftereffects. "Our part of the PREVAIL study is to look at what parts of the brain and body—particularly the eye—may be involved in post-Ebola syndrome," says Eghrari.

"One of the most complex challenges in epidemiology is how to define a case," Brady explains. "Even if someone is a survivor, it can be hard to prove that Ebola is the cause of his or her eye problem."

A physical problem, like loss of vision, he says, might be a direct effect of the virus or an immune response to the infection, or it might be totally unrelated.

The team has traveled several times to West Africa and, in collaboration with John F. Kennedy Medical Center in Monrovia, begun to work hand in hand with Liberian ophthalmologists to train clinicians on the ground to use new examination equipment. They are also training the country's first ophthalmic photographer to catalog the effects of the disease.

"From a medical science perspective, this mission is a great way to make a difference—to work at the cutting edge of public health while bolstering eye care in an underserved region," Brady says.



"FROM A MEDICAL SCIENCE PERSPECTIVE, THIS MISSION IS A GREAT WAY TO MAKE A DIFFERENCE-TO WORK AT THE CUTTING EDGE OF PUBLIC HEALTH WHILE BOLSTERING EYE CARE IN AN UNDERSERVED REGION."

CHRISTOPHER BRADY, M.D.

#### THE PREVAIL III PARTNERSHIP AT A GLANCE

- PREVAIL III will take place at various sites in Liberia and is expected to enroll approximately 7,500 people, including 1,500 people of any age who survived Ebola virus disease and 6,000 of their close contacts.
- The research team will follow the Ebola survivors and their close contacts for up to five years, with study visits occurring every six months. At each follow-up visit, participants will undergo a physical exam and additional blood draws to monitor and characterize any changes in Ebola antibody levels and to detect the presence of select medical conditions.
- Using data collected at these site visits, the researchers will calculate the incidence, prevalence and risk factors for various health issues experienced by survivors, such as vision problems, immune system changes, mental disorders, joint pain, diabetes, hypertension and pregnancy complications.
- Close contacts will be used as a control group to assess whether the risks of these conditions are the same or different from those who have not had Ebola virus disease.

SOURCE: National Institutes of Health



## GREAT LEAPS FORWARD FOR FUCHS'

EXPANDING THE TOOLBOX FOR TRANSPLANTATION SURGERY

At the farthest edge of the cornea, deep within the eye, there is a thin layer of cells that helps maintain the cornea's ideal balance of fluid. These cells are known as "pumper" cells for their ability to remove water when necessary to maintain this delicate equilibrium.

When things go awry, however, the pumper cells die, fluid builds, the cornea swells and vision blurs. Eventually, painful blisters appear on the cornea. The disease is known as Fuchs' dystrophy. Often, the only alternative is a corneal transplant.

"For patients, Fuchs' is like looking through wax paper. It's the No. 1 cause of corneal transplants in the U.S. and Europe," says the Wilmer Eye Institute's Albert Jun, M.D., Ph.D., one of the world's leading experts in Fuchs' dystrophy.

← Albert Jun is one of the world's leading experts in Fuchs' dystrophy.



In 2004, Jun was the first surgeon at Wilmer to try a new technique of transplanting just the layer of pumper cells—known as the endothelium—rather than the entire cornea. The technique was extremely delicate and notoriously difficult, requiring the removal of a circle of tissue just one layer of cells thick—a mere 1 one-hundredth of a millimeter.

"That initial technique was so complicated it sort of died a quiet death. Surgeons just stopped doing it," Jun says.

In recent years, however, new techniques and instruments have evolved, transforming the prospects for Fuchs' sufferers.

"These developments have been a great leap forward. We can now remove these fine samples from a donor eye and transplant them in the eye of a Fuchs' patient with minimal physical manipulation of the sample," Jun says.

While Jun is certainly a talented surgeon, he has also earned a comparable reputation as a prolific researcher. His published papers have helped reshape scientific understanding of the genetic antecedents of Fuchs' dystrophy and contributed to the growing toolbox of surgical techniques for transplanting tissues in the eye.

JUN IS NOW ABLE TO CREATE CORNEAL ENDOTHELIUM IN THE LAB THAT IS GENETICALLY IDENTICAL TO THOSE OF A FUCHS' PATIENT. JUN HAS EVEN CREATED A MOUSE MODEL OF THE DISEASE.

"THIS IS A HUGE CONCEPTUAL JUMP THAT WILL SPEED OUR RESEARCH INTO THE CAUSES AND, MORE IMPORTANTLY, THE TREATMENTS FOR FUCHS'."

- ALBERT JUN, M.D., PH.D.

In this regard, the evolution of regenerative medicine has been critical. Jun is now able to create corneal endothelium in the lab that is genetically identical to those of a Fuchs' patient.

Jun has even created a mouse model of the disease. This is more difficult than it might seem. Mice don't normally develop Fuchs'-like diseases. They do not live long enough.

When Jun created the model, however, he discovered something surprising. The disease develops in mice proportional to the mouse's life span. So, even though they live only two years, a 1-year-old, middle-aged mouse will have the cornea of a 50-year-old human.

"This is a huge conceptual jump that will speed our research into the causes and, more importantly, the treatments for Fuchs'," Jun says.

Following this lead to its next logical conclusion, Jun has since used his mouse model to show that drugs can slow the progression of Fuchs', something that had never been demonstrated before.

"It's encouraging. That's the future of our research," Jun explains.

There is one last piece of the puzzle that is critical to Jun's work: philanthropy. The advances he has made simply would not have been possible without the support of people like David Peter Honey, who endowed the Maurice E. Langham, Ph.D., Professorship in Ophthalmology, which Jun now holds.

"Dr. Honey's wonderful gift has been absolutely critical to allow my research to move in the most cutting-edge directions," Jun says.

As for what drives him to do such profound work on a relatively rare eye disease, Jun talks about his personal satisfaction and his place in the world: "I always wanted to be a physician at the cutting edge of care and the kind of scientist who could develop life-changing treatments. I'm incredibly fortunate to be in a career and a university setting that lets me do both."

#### A DONOR'S ROLE

Often, when an established researcher has a new idea or when a young medical researcher is just beginning a new career, the most critical—and most difficult—hurdle is finding the funding that gets a transformative new discovery or technique off the ground.

"Such research into the most promising areas is not yet validated enough to attract funding from more established sources," says Albert Jun, M.D., Ph.D., who is doing breakthrough surgical and basic science research at the Wilmer Eye Institute.

In fact, most of today's remarkable surgical techniques, drug discoveries and fundamental knowledge about the wonders of the visual system — and the many things that can go wrong with it—started as a nascent, unproven idea in the mind of a medical researcher such as Jun. What those ideas lacked were the resources necessary to begin study and to prove that brainstorm to be both scientifically accurate and also helpful for patients.

"That's the all-important role donors play in our work at Wilmer. Philanthropic funding dedicated to a researcher's newest and most innovative ideas allows our research to advance much more quickly," Jun says.

# LEGACY OF ENLIGHTENMENT

#### **CELEBRATING THE SAMUEL THEOBALD PROFESSORSHIP**

When Jeremy Nathans, M.D., Ph.D., was named the inaugural Samuel Theobald Professor at the Wilmer Eye Institute, he knew that the honor was laden with expectation. Theobald was, after all, the first ophthalmologist at Johns Hopkins, an eye specialist long before there was a Wilmer Eye Institute—and Wilmer is hardly a nascent organization.

Theobald served at Johns Hopkins starting in 1889. His retirement in 1925, at age 79, coincided with the founding of the Wilmer Eye Institute. The significance of holding an endowed chair in his name, established by a gift from an anonymous donor, is not lost on Nathans. "This professorship connects us to the many generations of great physicians who have walked these halls. It also is a signifier of the scientific inquiry that is at the core of this great university," Nathans says.

Jeremy Nathans, in the lab. →



Nathans is a molecular biologist and geneticist. He is first and foremost a researcher, intent on revealing the details of nature's mysterious ways.

"The difficulties of doing scientific research are compounded by the uncertainty of not knowing most of the time—whether one is even on the right track. But the rare moments of insight are priceless," Nathans says.

Nathans' research has focused on inherited diseases of the retina. His and other labs across the university and the world have been, piece by piece, cataloging the genetic and biochemical bases of retinal diseases, many of which lead to blindness. Nathans was the first scientist to apply molecular genetics approaches to the visual system. His lab has contributed fundamental discoveries in both basic and clinical vision science. Among his many accomplishments, he isolated the genes coding for the human visual pigments and elucidated the molecular basis of inherited variation in human color vision.

His disease research includes defining the biochemical basis of Stargardt disease and vitelliform macular dystrophy—two early-onset forms of macular degeneration—as well as the rhodopsin mutations responsible for the most common form of retinitis pigmentosa.

"This professorship connects us to the many generations of great physicians who have walked these halls. It also is a signifier of the scientific inquiry that is at the core of this great university."

The eye is a beautiful system. "Stunningly so," Nathans says. He sees it as a marvel of engineering, in which intricate anatomy is elegantly wedded to awe-inspiring function. "I think many research ophthalmologists are motivated both by the beauty of the visual system and the tragedy of vision loss, and are intent upon both a deeper understanding of the visual system and better treatments of eye diseases," Nathans says.

#### -Jeremy Nathans, M.D., Ph.D.

In collaboration with Gerald Jacobs at the University of California, Santa Barbara, he genetically engineered mice to have trichromatic color vision, an experiment that demonstrated the brain's remarkable plasticity in visual processing. Lately, his work has been exploring the all-important blood-brain barrier and blood-retina barrier, specializations in blood vessel structure in the brain and retina that keep toxic substances out of the body's most sensitive tissues. Most importantly, however, throughout his entire 35-year career, Nathans has built a reputation for openness. He is known as a consummate collaborator with other researchers, both at Johns Hopkins and at other universities. Notably, he worked with King-Wai Yau, Ph.D., in the Department of Neuroscience at Johns Hopkins on macular degeneration, and with Michael Repka, M.D., and David Guyton, M.D., at Wilmer to study eye movement disorders.

Likewise, Nathans has been generous in sharing the fruits of his discoveries. The many products of his research—cDNA libraries, antibodies, DNA constructs, cell lines and genetically engineered mice—have been distributed to hundreds of other laboratories without constraint.

"Like many researchers, we are strongly motivated by the hope that our work will help people who are suffering from or at risk for vision loss. Sharing freely accelerates everyone's research and brings us closer to the next breakthrough," Nathans says.

Despite his standing in the biomedical community and the many demands placed upon his time, Nathans can still often be found at his lab bench or teaching medical and graduate students. It is a legacy of enlightenment that has been handed down to him from previous generations, just as Samuel Theobald himself would have wanted it to be.



*† Samuel Theobald* 

#### THE 'GENIUS OF INFINITE PAINS'

Born in Baltimore in 1846, Samuel Theobald earned his M.D. from the University of Maryland at age 22, then went abroad to study ophthalmology and otology before opening a practice in Baltimore in 1871.

In 1874, he established the Eye and Ear Dispensary, and in 1882, he was instrumental in founding the Baltimore Eye, Ear and Throat Charity Hospital.

In 1889, he was appointed as an ophthalmic surgeon at the brand-new Johns Hopkins Hospital. When the university's medical department was established a few years later, Theobald was appointed clinical professor of ophthalmology and otology. In 1910, he became the 14th president of the American Ophthalmological Society.

Theobald stepped down as chair of the department at Johns Hopkins in 1925, when the Wilmer Eye Institute was founded. Following his death in 1930, William Wilmer was effusive in his praise of Theobald: "In his scientific work, he showed the genius of infinite pains; in his ethical relations to his colleagues, he set a high ideal; to his friends, he showed a character full of charm."



# **GOOD KNIGHTS**

#### **GRANTS JUMP-START EARLY-CAREER SCIENTISTS**

The Knights Templar fraternal organization charts its beginnings to the 11th century. Like many fraternal organizations, the Knights pride themselves on good deeds in their communities. One of the pillars of that commitment is the Knights Templar Eye Foundation (KTEF), which seeks to improve vision through research, education and access to care.

The Wilmer Eye Institute began its relationship with KTEF in 1985 when then-director of Wilmer, Alfred Maumenee Jr., created the Knights Templar Foundation Scientific Advisory Committee to screen proposals for research in pediatric ophthalmology. Maumenee was a Knight himself.

KTEF grants are targeted toward researchers in the early stages of their careers. In the 30 years since Maumenee first built the partnership, the resulting grants have helped jump-start the research portfolios of numerous young researchers.

← Randolph S. Disney of the Knights Templar Eye Foundation and Wilmer's Zhenhua Xu, Ph.D., review research progress in the lab.



1 The Knights present Wilmer with a check.

Among the most recent is Laura Asnaghi, Ph.D., M.Sc., a research oncologist who uses her grants to study retinoblastoma, the most common eye cancer in children. If not treated quickly, these cancers can spread and become life-threatening. In particular, she studies the Notch signaling pathway that plays a fundamental role in healthy eye development in the fetus, but later also in the cancer.

"We are trying to identify opportunities for drug interventions on Notch pathways to prevent tumor growth and spread," says Asnaghi. "This research would not have been possible without KTEF, and I'm proud to say my grant was recently renewed for a second year."

Besides Asnaghi, this year's recipients included Zhenhua Xu, Ph.D., whose mentor, Elia Duh, M.D., was also a past KTEF grantee. Duh has since made a name for himself studying the genetic mechanisms of the blindness-inducing abnormal blood vessel growth that occurs in the retinas of premature infants in retinopathy of prematurity.

"When I received my KTEF grant, I had just finished my ophthalmology residency at Wilmer and was starting up my research program. KTEF funding provided me with invaluable initial resources to get my career off the ground. This gave me a tremendous advantage in establishing my lab, and we have published multiple studies relating to retinopathy of prematurity," Duh says. "Dr. Xu is continuing that tradition."

Karl Wahlin, Ph.D., is a postdoctoral fellow and specialist in cell and molecular biology. He used his KTEF grant to study how photoreceptors develop and are maintained in the retina to find insight into possible treatments for Leber's congenital amaurosis, the most common inherited retinal dystrophy in children.

Leber's occurs when photoreceptor cells die. Aside from experimental gene therapy, there are currently no treatments or cures for the disease. Thanks in part to his KTEF grant, Wahlin has been able to grow 3-D human eyecups in the lab from skin-derived stem cells to study how photoreceptors grow and survive.

Additionally, in what is known as a "disease-ina-dish" approach, Wahlin is able to genetically engineer the DNA of these lab-grown cells in ways that are identical to mutations found in children with Leber's. From there, he hopes to study how the disease works and, eventually, to pursue potential treatments. "KTEF FUNDING PROVIDED ME WITH INVALUABLE INITIAL RESOURCES TO GET MY CAREER OFF THE GROUND. THIS GAVE ME A TREMENDOUS ADVANTAGE IN ESTABLISHING MY LAB, AND WE HAVE PUBLISHED MULTIPLE STUDIES RELATING TO RETINOPATHY OF PREMATURITY."

- ELIA DUH, M.D.

For Wahlin, the grant from KTEF really meant an all-important vote of confidence.

"Funding is always difficult to obtain. In stem cell funding in general, there's a perception that there's lots of funding, but it's not true," Wahlin says of the importance of his grant, adding: "Layer in that childhood retinal dystrophies are rare, and it gets tougher still. But this work is important, and KTEF saw that promise."

Since his KTEF grant wrapped, Wahlin has since become the only Wilmer researcher to win a prestigious, multiyear K99 Pathways to Independence Award from the National Institutes of Health.

"This was a terrific grant to move this important research forward. The Knights Templar made real what wouldn't have been possible otherwise," says Wahlin.

#### SUPPORTING CRITICAL ADVANCES 'IN PERPETUITY'

A recent gift from the Knights Templar Eye Foundation has established an endowed professorship in ophthalmology at the Wilmer Eye Institute that will make it possible for Wilmer to fulfill a key strategic priority.

"While Wilmer has benefited for decades from [KTEF] support of our research into eye diseases of children, this most recent extraordinary gift could not have come at a better time for the institute," says Wilmer Director Peter J. McDonnell, M.D. "This endowed professorship will support the recruitment of a worldwide leader in the study of neuroophthalmic diseases, and especially the genetic causes for those diseases."

James N. Karnegis, M.D., Ph.D., who chairs the committee on endowed professorships for KTEF, notes that his organization has established endowed professorships "so that critical advances in the diagnosis and treatment of eye diseases can be ensured in perpetuity."

He continues: "The Wilmer Eye Institute is known worldwide to be an outstanding medical institution with the staff, facilities and culture to remain in the forefront of the science of ophthalmology. The prestigious Knights Templar Eye Foundation Professorship in Ophthalmology will further the goals of both organizations. No doubt this endowment partnership will benefit humanity into the limitless future."

# ON THE GENETIC TRAIL OF A KILLER

ADVANCING THE STUDY OF METASTATIC CANCER

Advances in faster, less expensive DNA sequencing in recent years have transformed the field of cancer research. Mary Beth Aronow, M.D., an ocular oncologist at the Wilmer Eye Institute, is using these evolving tools to explore the dynamics of uveal melanoma, the most common form of primary eye cancer in adults. Though just five or six people in 1 million will develop the disease, it is a prime candidate for research for many practical reasons.

"Speaking from a research standpoint, eye tumors provide an exceptional model for studying cancer in humans," Aronow explains. These tumors can be directly visualized inside the eye, making it one of the few cancers that can be observed noninvasively in its natural state.





† Uveal melanoma

"Measuring levels of tumor DNA in the blood can help us detect spread of the cancer earlier. We hope when we implement new treatments, and when we note a change in tumor DNA in the blood, it can tell us whether the therapies are effectively killing tumor cells."

- Charles Eberhart, M.D., Ph.D.

Uveal melanoma spreads at a high rate. Approximately one-half of patients will develop cancer in other organs.

Aronow and her collaborators—including Ben Ho Park, M.D., Ph.D., an oncologist at the Johns Hopkins Kimmel Cancer Center; Charles Eberhart, M.D., Ph.D., a pathologist at Wilmer; and Laura Asnaghi, Ph.D., M.Sc., a research associate in Eberhart's lab—are developing techniques to test blood for bits of mutated DNA that break free and travel through the bloodstream when a cancerous cell dies.

"Uveal melanoma provides a unique opportunity to study cancer behavior in ways we can't with other cancers. Genetic tools only expand our capabilities," says Park, who specializes in genetic approaches to cancer research.

Cancer cells are free to wander the circulatory system to other organs, usually the liver or the lungs, where they can contribute to the development of new tumors—the complex process known as metastasis. Most cancer deaths, in fact, are not caused by the original tumor, but by the spread of the disease to other parts of the body.

The good news is that when uveal melanoma is detected and treated early, patients have a better chance of survival. This knowledge is the driving factor of Aronow's work. "The earlier we can detect these tumors, the better," she says.

The goal is to develop a deeper knowledge of how uveal melanoma develops and behaves, and to look for ways to head off spreading of the disease, which can occur even after the primary tumor is treated. Metastasis of uveal melanoma can take five to 10 years to occur. In scientific terms, mutated DNA in the blood is a biomarker—an indisputable indication of both the presence and the severity of a cancer. To that end, much is known already about the genetics of uveal melanoma. Many of these tumors harbor mutations in either of two genes—GNAQ or GNA11.

"Measuring levels of tumor DNA in the blood can help us detect spread of the cancer earlier. We hope when we implement new treatments, and when we note a change in tumor DNA in the blood, it can tell us whether the therapies are effectively killing tumor cells," says Eberhart.

Among the many advantages of genetic techniques, notes Aronow, is that they are noninvasive. "This testing requires a routine blood sample," she says.

While screening patients for a disease that only affects perhaps five or six people in 1 million probably won't become commonplace, Aronow does foresee the use of genetic techniques with high-risk patients who have had the cancer before, to test for recurrence.

However, Aronow notes that above all, if she and her Wilmer-Kimmel collaborators are successful, their techniques could be widely applicable to other, more common cancers. "This research is really about advancing the study of all cancers," Aronow says of the broader promise for her cutting-edge work.

### MISSION: MIDDLE EAST ADDRESSING CHALLENGES UNIQUE TO THE REGION

Keratoconus, a relatively uncommon disease of the cornea in the Western world, appears to be much more common in Saudi Arabia. perhaps due to particular environmental and genetic factors. Other eye health challenges that seem to be present in the region include advanced cataracts and a significant proportion of the Saudi population battling diabetes—a disease that begets vision complications, among its many afflictions.

Despite it all, a single Saudi hospital—the King Khaled Eye Specialist Hospital (KKESH) in the capital, Riyadh—is responsible for serving the eye care needs of almost 29 million Saudis. Since 2010, a collaboration between the Wilmer Eye Institute and KKESH pronounced "KAY-kesh" is helping to address the unique ophthalmological challenges of the Middle East's largest nation.



"A SIMPLE SMARTPHONE CAN PREVENT BLINDNESS. IF KERATOCONUS CAN BE DETECTED EARLY, IT CAN BE STOPPED. IF DISCOVERED TOO LATE, HOWEVER, THE SURGERY REQUIRED TO FIX IT IS VERY COMPLICATED AND CAN ALSO FAIL, LEAVING THE PATIENT BLIND."

#### - WILLIAM MAY, M.D.

"These environmental factors add up to a profound challenge for eye specialists, but the relationship between Wilmer and KKESH is helping to close many of those gaps on multiple fronts," says William May, M.D., an ophthalmologist at Wilmer and among the coterie of Johns Hopkins physicians in Saudi Arabia spreading Wilmer's worldrenowned expertise to this underserved population.

The work of the partnership extends to virtually every aspect of eye care. J. Fernando Arevalo, M.D., a retina specialist at Wilmer, recently completed a four-year tenure in Saudi Arabia. While there, he helped train new residents and fellows, worked to improve the operational efficiency of the hospital to reduce wait times, and established evidence-based treatment protocols for serious conditions, such as inner-eye inflammation and diabetic macular edema.

"Soon, the retina faculty at KKESH will reach 15 doctors—a team comparable in size to the retina division in Baltimore. It's one of the best in the world now," says Arevalo.

In addition to education and treatment, Wilmer is bringing high-tech clinical tools to Saudi Arabia. Among the myriad devices will be a bevy of cellphones.

May and Donald Stone, M.D., also an ophthalmologist at Wilmer, have begun to work with a U.S. software developer to perfect a smartphone app that might allow Saudi parents—and perhaps grandparents too to examine very young children for keratoconus.



"A simple smartphone can prevent blindness. If keratoconus can be detected early, it can be stopped. If discovered too late, however, the surgery required to fix it is very complicated and can also fail, leaving the patient blind," May explains.

Another high-tech tool May and his Wilmer-KKESH colleagues are particularly excited about is a computer-controlled femtosecond laser able to perform highly precise microsurgeries within the eye—a first for the Middle East. It uses an image of the eye to plan and execute extremely fine incisions that are so delicate they can be made to just a single layer of cells. The resulting incisions are self-healing, require no sutures and leave little to no scarring.

Using the femtosecond laser, May and colleagues are able to accomplish feats once thought impossible to improve success rates for corneal transplants and to soften extremely hard cataracts that are causing vision impairment.

Sultan Al-Rashidi, M.D., a cornea fellow at KKESH, earned top honors for his poster presentation on the femtosecond laser at the recent American Society of Cataract and Refractive Surgery annual symposium.

"In Saudi Arabia, patient corneas are often cloudier and the cataracts are harder than we find in the United States. It makes the cataract surgery more difficult, but the femtosecond laser is changing the field," May says.



With their Saudi partner, Saeed Motowa, M.D., the Wilmer surgeons are able to mark a location deep in the cornea of patients with late-diagnosis keratoconus, for instance. Then the surgeons work on a layer of cells immediately adjacent to the innermost part of the cornea—the corneal endothelium.

The surgical distinction between the two layers is critical. If the endothelium can be maintained, it dramatically reduces the prospect of tissue rejection in the transplanted cornea, May says.

So successful are the femtosecond laser surgeries that May thinks they might eventually be automated

entirely, removing human error and allowing such surgeries to transition out of the highly specialized center at KKESH into rural Saudi Arabia, where the need is greatest.

"The partnership with KKESH fits into Wilmer's mission of preventing blindness and disease internationally, as we have done significantly in the past," May asserts. "That's what makes this relationship so special and so important."



#### Bayer HealthCare

and

#### Johns Hopkins University

collaborate to develop new ophthalmic therapies

June 2015

# BAYER AND WILMER: FOUND IN TRANSLATION

**NEW COLLABORATION IS A 'WIN-WIN'** 

In medical research, there are generally considered to be three stages. The first is basic science, which seeks to understand what is happening when disease strikes. Later, of course, there are clinical trials of promising new drugs and therapies with real patients to gauge safety and efficacy. In between, there is translational medicine.

Translational medicine unfolds when researchers take what they know from basic science—how a protein folds, for instance, or how a gene works—and try to devise new ways to inhibit undesirable behaviors through drugs and other therapies.

Last June, The Johns Hopkins University and Bayer HealthCare announced a five-year collaboration to promote translational medicine for debilitating diseases of the eye. Bayer will fund research and offer the services of its ophthalmic scientists to partner in research efforts. The partnership will focus first on retinal diseases, such as macular degeneration, Stargardt disease and retinal vein occlusions, among others, with the possibility to expand to other areas of the eye and perhaps to other parts of the body eventually. The partnership is the largest of its kind in the history of The Johns Hopkins University.

"There is a critical need for new therapies that treat a variety of serious diseases of the eye," says Peter J. McDonnell, M.D., director of the Wilmer Eye Institute and the William Holland Wilmer Professor of Ophthalmology at Johns Hopkins. "Additional research will allow us the opportunity to make significant advances in this area." In the partnership's earliest phases, Wilmer and Bayer researchers will collaborate on investigating new targets and disease mechanisms, drug delivery technologies, and biomarkers for so-called back-of-the-eye diseases that have high unmet medical needs.

Each research project will be evaluated by Bayer and funded individually. Grant proposals are already being written, and projects will start in the second half of 2015. Should any commercial drugs flow out of the partnership, Bayer would have the first option to license any resulting intellectual property from Johns Hopkins.

WILMER AND BAYER RESEARCHERS WILL COLLABORATE ON INVESTIGATING NEW TARGETS AND DISEASE MECHANISMS, DRUG DELIVERY TECHNOLOGIES, AND BIOMARKERS FOR SO-CALLED BACK-OF-THE-EYE DISEASES THAT HAVE HIGH UNMET MEDICAL NEEDS.

"We're going beyond exploring the mysteries of nature and trying to discover and speed innovative treatments from the lab to the clinic. In the end, this is about helping patients," says David Greenwald, Ph.D., a director of corporate relations for Johns Hopkins Technology Ventures and alliance manager of the Bayer alliance.

"Bayer is strongly committed to further expanding its research efforts in the area of retinal diseases," says Andreas Busch, head of global drug discovery and member of the Executive Committee of Bayer HealthCare. "The Wilmer Eye Institute's deep understanding of eye disease biology and patient care and Bayer's expertise in drug discovery and development in ophthalmology complement each other perfectly." Greenwald notes that the relationship draws upon the significant expertise of Johns Hopkins' many divisions.

"The strength of Johns Hopkins' contribution to this partnership is our ability to collaborate beyond Wilmer to bring in specialists from oncology, computer science, engineering and others to create broadly interdisciplinary teams to pursue truly cutting-edge research," he says.

Ultimately, there is even an opportunity for philanthropists to get involved, potentially matching private donations with the resources of Bayer to extend the partnership's reach even further.

"No matter how you look at it, the relationship between the Wilmer Eye Institute and Bayer is a win-win for all parties involved: Bayer, Johns Hopkins and patients," Greenwald says.



*t* Representatives of Wilmer Eye Institute, Bayer Pharmaceuticals and the Office of the President for Johns Hopkins University gather to celebrate the kick-off of the collaboration.

# EXTENDING WILMER'S REACH

SATELLITE PROGRAM SEES MARKED GROWTH

No. Tar V

Over the past 12 years, Wilmer's patient volume has quadrupled, largely due to the demographic "tidal wave" of aging baby boomers. "At Johns Hopkins, only geriatrics sees a higher percentage of Medicare patients than does Wilmer," says Wilmer Director Peter J. McDonnell, M.D., who notes that the vast majority of eye disease—cataracts, macular degeneration, glaucoma—is age-related.

The continued growth of Wilmer's satellite locations has made it possible for Johns Hopkins to keep up with this burgeoning patient volume. The Green Spring Station location, for example, handles 37,000 outpatient visits per year, and the Bel Air office last year handled more than 33,500 outpatient visits.

The Green Spring Station satellite location handles 37,000 outpatient visits per year.  $\rightarrow$ 





† Christina R. Prescott, M.D., Ph.D., at the Ambulatory Surgical Center at the Bel Air satellite location

"At Wilmer in the past, some patients might have had to wait three months or longer for an appointment downtown at the Johns Hopkins Hospital campus," says McDonnell. "We are now doing more than 1,000 same-day appointments each month—and our satellites are a key part of that."

When patients or referring physicians call Wilmer, staffers in the Wilmer call center use a sophisticated software system to check the availability of physicians at every satellite location. Thus, a caller might be told: "Our doctors at location X are all booked up, but we can get you in right away today at location Y, and location Y might actually be even closer to your home."

"Our patients love that," says McDonnell.

Convenience is also an important factor. Some patients find it intimidating to drive downtown and deal with city traffic and parking, McDonnell says. "These patients really treasure the ability to have much of their eye care done close to home."

As evidence of overall patient satisfaction, McDonnell points to two honors bestowed in 2015: Wilmer's Bel Air and Columbia offices were selected as the Best of 2014 in eye care in *Harford Magazine* and *Howard Magazine*, respectively.

Wilmer's satellite locations are also making it possible for Johns Hopkins to extend the reach of clinical trials to patients who previously have found it difficult to gain access to these studies of cutting-edge therapies. The Frederick office, for example, has established a community-based clinical trials program to investigate new treatments for retinal disease. And physicians at Green Spring Station are actively exploring retina patterns of care and the use of femtosecond laser-assisted cataract surgery.

McDonnell says that Wilmer's satellites are also playing an increasingly important role in medical training. "Here at The Johns Hopkins Hospital, we tend to see very complicated cases, but that's not the case for most ophthalmology practices outside of hospitals, where many of our alumni will work. Those practices see patients with earlier-stage problems, i.e., less severe disease, than we typically see at the East Baltimore campus.

"With the satellites, our medical students, residents and fellows can now be exposed to that type of environment during training," says McDonnell. He points to Green Spring Station and Johns Hopkins Bayview Medical Center as two key training locations.

Looking to the future, McDonnell says Wilmer's satellite locations will continue their crucial role. "We have essentially outgrown our historic facilities here on the East Baltimore campus," he says. "The growth of our satellites gives us the space to hire brilliant new doctors and will be key to ensuring prompt access for any patient or referring doctor who needs our help."



"The growth of our satellites gives us the space to hire brilliant new doctors and will be key to ensuring prompt access for any patient or referring doctor who needs our help."

-Peter J. McDonnell, M.D.

# ATTACKING UVEITIS ON ALL FRONTS

**RAISING THE PROFILE OF BIRDSHOT CHORIORETINITIS** 

As both a researcher and a clinician, Jennifer Thorne, M.D., Ph.D., is exploring the many facets of uveitis, a family of inflammatory eye conditions, to learn more about what causes the conditions, how they progress and, most importantly, how to counteract them through drugs and other therapies.

Thorne researches the clinical and visual outcomes of inflammatory eye diseases, exploring the best imaging techniques by which to monitor the diseases and looking into the immunologic roots of the disease. "And, of course, we are delving into ways to treat the inflammation by assessing various treatment options," Thorne says.

Her work has been greatly aided by the financial support of Meredith Cross, a top Washington lawyer, who began to suffer from birdshot chorioretinitis, an extremely rare, noninfectious form of uveitis, in 2012. Cross turned to Thorne for help. Over the course of her treatment, Thorne has been there every step of the way.





THES WALL RECOUNTER THE GENERALTY OF THOSE WHO HAVE FUNDED ENDORED TROPESSMENNER OF THE WEINER EXE INSTITUTE

"When you have a rare disease (see sidebar), you want to know that your doctor is a true expert in your disease and that she cares. At Wilmer, you find people like Dr. Thorne, who have that all-important combination of compassion and expertise that lets you know everything is going to be all right," Cross says.

Thorne's care has helped Cross retain her vision. To help make sure that Thorne is able to continue her birdshot research, devote even more time and resources to it, and raise the profile of birdshot at Wilmer, in 2013, Cross established the Jennifer E. Thorne, M.D., Ph.D., Birdshot Research and Endowed Research Funds, with an initial funding commitment of \$1.25 million.

Recently, Cross and her family went further and endowed a professorship in ophthalmology at Wilmer. Thorne was named as the inaugural Cross Family Professor of Ophthalmology in April 2015. This level of support will have a significant impact on Thorne's ability to undertake her research priorities and is a gift that will continue to make a difference into the future, notes Wilmer Director Peter J. McDonnell, M.D., who adds that Wilmer is very fortunate to have the Cross family as an active partner. "I hope that by raising the profile of birdshot and supporting Dr. Thorne's research, there will be help for people like me forever," says Cross. To her mind, the endowed professorship means there will always be funding for birdshot research. "That means a lot to my family," Cross says.

Thorne is deploying the funds in wide-ranging efforts. In but one research vector, Thorne is analyzing the different ways to monitor for progression of birdshot, in an effort to catch any worsening of this devastating disease at the earliest possible moment so that therapy may be adjusted to prevent damage to the eye and resultant visual loss. The birdshot research funds allowed Thorne to hire a research fellow during the first year of the program to assist in her studies and to increase her collaborative efforts with other birdshot experts in the U.S. and internationally.

Through her philanthropy, Cross believes that she is furthering her own treatment while helping all those with birdshot and other forms of uveitis. She has been able to demonstrate the importance of Thorne's birdshot research to more than 50 other donors, each of whom has made donations to the Birdshot Research Fund, totaling close to \$300,000 to date.



† Meredith Cross and Jennifer Thorne, M.D., Ph.D.

"AT WILMER, YOU FIND PEOPLE LIKE DR. THORNE, WHO HAVE THAT ALL-IMPORTANT COMBINATION OF COMPASSION AND EXPERTISE THAT LETS YOU KNOW EVERYTHING IS GOING TO BE ALL RIGHT."

- MEREDITH CROSS

#### BIRDSHOT IN THE CROSSHAIRS

Telltale spots on the retina give birdshot chorioretinitis its colorful name, but those spots are anything but colorful to patients who suffer from the disease.

"Birdshot symptoms often start insidiously but can be very distracting to patients. There's no pain, but patients may experience floaters, flickering lights, vibrating vision, loss of contrast sensitivity, problems with night vision or other visual difficulties," says Wilmer's Jennifer Thorne.

Birdshot symptoms typically strike in middle age, and birdshot afflicts women slightly more than men. Both eyes are affected. Inflammation can be seen in the choroid, retinal blood vessels and vitreous. The birdshot "spots" are required for disease diagnosis. The majority of patients are positive for the HLA-A29 gene.

"The spots radiate out from the optic nerve in a scattershot pattern, hence the descriptive name birdshot," says Thorne. "The disease has a slow but chronic course, and if it's not treated, birdshot can lead to loss of peripheral vision and, ultimately, central vision."

## SUPPORTING THE BEST IN THE BUSINESS

At the age of 78, T. Boone Pickens eagled No. 11 at Augusta National Golf Club. Not bad for a guy whose macular degeneration had caused him to see double. "I adjust to things pretty well," Pickens explains.

He's had some help adjusting. Ever since he brought his dad to Wilmer with age-related macular degeneration (AMD) some 30 years ago and was then diagnosed with the disease himself, the Texas energy billionaire has flown from Dallas to Baltimore for monthly treatments. Now 87, Pickens still reads, drives and goes to the office every day, on the way to fulfilling a prediction Neil Bressler, now chief of the Retina Division, made when he first diagnosed Pickens' AMD. "Am I going to have eyesight to the finish line?" Pickens remembers asking. "Bressler said: 'I think so.""

That wasn't the case for his father, who was already legally blind when Pickens bumped into fellow native Oklahoman Walter Stark while hunting ducks in Louisiana. It was Stark who connected the father and son with Wilmer. Pickens credits the newer treatments developed in the interim with preserving his own vision. In 2007, wanting to ensure that research into treatments for AMD and other eye diseases continued to advance, Pickens committed \$20 million from his estate to Wilmer to establish the Pickens Scholars program. His gift will allow the institute to attract young researchers from around the globe to explore novel and innovative approaches in four-year stints and will bring Pickens' total support of Wilmer to more than \$28 million, including a named professorship now held by Stark. "At Wilmer, you're dealing with the best professionals in the business," Pickens says.

Pickens, who intends for most of his estate to go to charity one day, is no stranger to philanthropy, having already given away more than \$1 billion. "I want to see the money used for a good purpose with good results," he says.

To hear more from Pickens, watch "*The Visionary T. Boone Pickens*" on rising.jhu.edu/Pickens.



"At Wilmer, you're dealing with the best professionals in the business."

-T. BOONE PICKENS



#### LOYAL COMMITMENT, LASTING LEGACY

A gift through your estate plan can augment your current giving to Wilmer, support our future needs and even establish an endowed fund to honor a loved one. You may also designate Wilmer as a beneficiary of a retirement account or life insurance policy. Gifts such as these cost nothing during your lifetime and allow you to modify your plans if your needs change.

A life income gift is another way to support Wilmer's future. Life income gifts provide an immediate income tax deduction for the value of your gift, plus annual income to you and/or others for life or for a term of years, with the remainder interest used to benefit Wilmer. Popular options include charitable gift annuities and charitable remainder unitrusts, and they may be established during your lifetime or through your estate.

Individuals who make a gift through their estate plan or a life income gift are recognized in the Johns Hopkins Legacy Society. To learn more about these and other creative ways to support Wilmer, visit rising.jhu.edu/giftplanning, or contact the Office of Gift Planning at 410-516-7954, 800-548-1268 or giftplanning@jhu.edu.

## 2015 EVENTS

#### DEDICATION OF THE CROSS FAMILY PROFESSORSHIP AND WILMER'S BOARD OF GOVERNORS MEETING

#### APRIL 16, 2015

The dedication of the Cross Family Professorship was an eventful day for Wilmer's Board of Governors and guests—especially since Meredith Cross, a member of the Board of Governors, contributes to the Wilmer Eye Institute in several capacities. We greatly appreciate the ongoing support of the Board of Governors, a key component to Wilmer's success. Jennifer E. Thorne, M.D., Ph.D., was the inaugural recipient of the endowed professorship.



t Wilmer Director Peter J. McDonnell, M.D., presenting the inaugural Cross Family Professor, Jennifer E. Thorne, M.D., Ph.D., with the professorship crystal.



† Mr. John Cross, Dr. Peter J. McDonnell, Dr. Jennifer E. Thorne, and Mrs. Meredith Cross



t The Wilmer Board of Governors Spring Meeting

#### THE 74TH WILMER RESIDENTS ASSOCIATION CLINICAL MEETING JUNE 19, 2015

Wilmer faculty, residents, alumni and special guests gathered for a full day of scientific presentations. Highlighting this year's presentations were Dr. Megan Collins, who gave this year's Susruta Lecture in medical ethics, and representatives from the classes of 1975, 1992 and 1995. The Class of 1975 was gracious enough to make a class gift to support the Center of Excellence in Ophthalmic Surgical Education and Training.



t Albert S. Jun, M.D., Ph.D., Maurice E. Langham Professor of Ophthalmology, presents Megan Collins, M.D., with a plaque to thank her for presenting the Susruta Lecture, an annual lecture on medical ethics given during the Wilmer residents clinical meeting. This lecture is generously sponsored by V.K. Raju, M.D., F.R.C.S.



† Wilmer residents class of 1975. From left to right: Harry A. Quigley, M.D.; John Christiansen, M.D.; Neil R. Miller, M.D.; W. Jackson Illiff, M.D.



† Alumni guest speakers: Tamara Fountain, M.D.; Peter J. McDonnell, M.D.; Dante Pieramici, M.D.; Dean Elliott, M.D.

#### DEDICATION OF THE SAMUEL THEOBALD PROFESSORSHIP JUNE 29, 2015

An anonymous donor made this professorship possible, thus giving the Wilmer Eye Institute the opportunity to honor the first clinical professor of ophthalmology and otology, Samuel Theobald. Jeremy Nathans, M.D., Ph.D., is the inaugural recipient of this endowed professorship, the 38th established at Wilmer.



t Ms. Joanne Nathans, Wilmer Board of Governors Chair Dr. Sanford D. Greenberg, Dr. Peter J. McDonnell and the Samuel Theobald Professor, Dr. Jeremy Nathans



† Dr. Jeremy Nathans and his wife, Dr. Thanh Huynh, with Dr. Peter J. McDonnell, unveiling the Samuel Theobald professorship plaque.

#### DEDICATION OF MAURICE E. LANGHAM, PH.D., PROFESSORSHIP AND WILMER LEGACY SOCIETY LUNCHEON

#### SEPTEMBER 11, 2015

This endowed professorship was made possible by a bequest of former Wilmer resident, David Peter Honey, in honor of Langham. Honey stated that Langham's support and recommendation early in his career were pivotal to his path and success. Albert S. Jun, M.D., Ph.D., was named the inaugural recipient. The dedication was a part of the annual Legacy Society Luncheon, which was highlighted by an address by Wilmer's Director Emeritus, Morton F. Goldberg, M.D.

#### WILMER BOARD OF GOVERNORS MEETING

#### **OCTOBER 15, 2015**

The Board of Governors held its fall meeting on October 15th. Highlights included presentations by Wilmer's newest endowed professorship recipients, Jeremy Nathans, M.D., Ph.D., and Albert S. Jun, M.D., Ph.D., followed by a tour of the laboratory of M. Valerie Canto-Soler, Ph.D., where guests learned about the science behind the "retina in a dish."



† Dean Paul Rothman , Provost Robert Lieberman, Albert S. Jun, M.D., Ph.D., and Wilmer Director Peter J. McDonnell, M.D.





t LEFT: Jun with his immediate family
t RIGHT: Director Emeritus of Wilmer Eye Institute,
Morton Goldberg, M.D., delivering the Legacy Society talk



t Board members (right to left) Dr. and Mrs. Sandy Greenberg and Mrs. Ellen Patz, and supporter Marc Summerlin, hear about the development of the "retina in a dish."



† The sixth floor conference room of the Robert H. and Clarice Smith Building was the fitting location for the Board of Governors dinner following the meeting.

#### SAVE THE DATE: THE 75TH WRA CLINICAL MEETING JUNE 10, 2016



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#### JOIN US IN OUR QUEST FOR DISCOVERY

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. For the past nine decades, our efforts have been made possible by the financial support of our generous donors.

Your investment in the Wilmer Eye Institute makes it possible for our physicians to offer unrivaled patient care to you and to countless others who may find their sight threatened by illness or injury. We invite you to partner with the Wilmer Eye Institute on our quest of discovery and to help us find the next treatment or cure.

For information on how to join us in our mission to end blindness and life altering eye diseases please contact:

WILMER DEVELOPMENT OFFICE, 410.955.2020, wildev@jhmi.edu

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The scientists and staff of the Wilmer Eye Institute at Johns Hopkins gratefully acknowledge our partners in philanthropy listed here. The generosity of these friends supports a tradition of collaboration and far-reaching investigation as, together, we pursue the complex challenges of eye diseases. While our space here is limited, our thankfulness is not. Although gifts of any amount are gratefully received, only gifts, pledges and pledge payments totaling more than \$250 in the fiscal year ending June 30, 2015, could be listed in this report. If any donor was accidentally missed, or if you prefer to remain anonymous, please contact the Development Office at 410-955-2020.

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