WILMER
Cure Glaucoma
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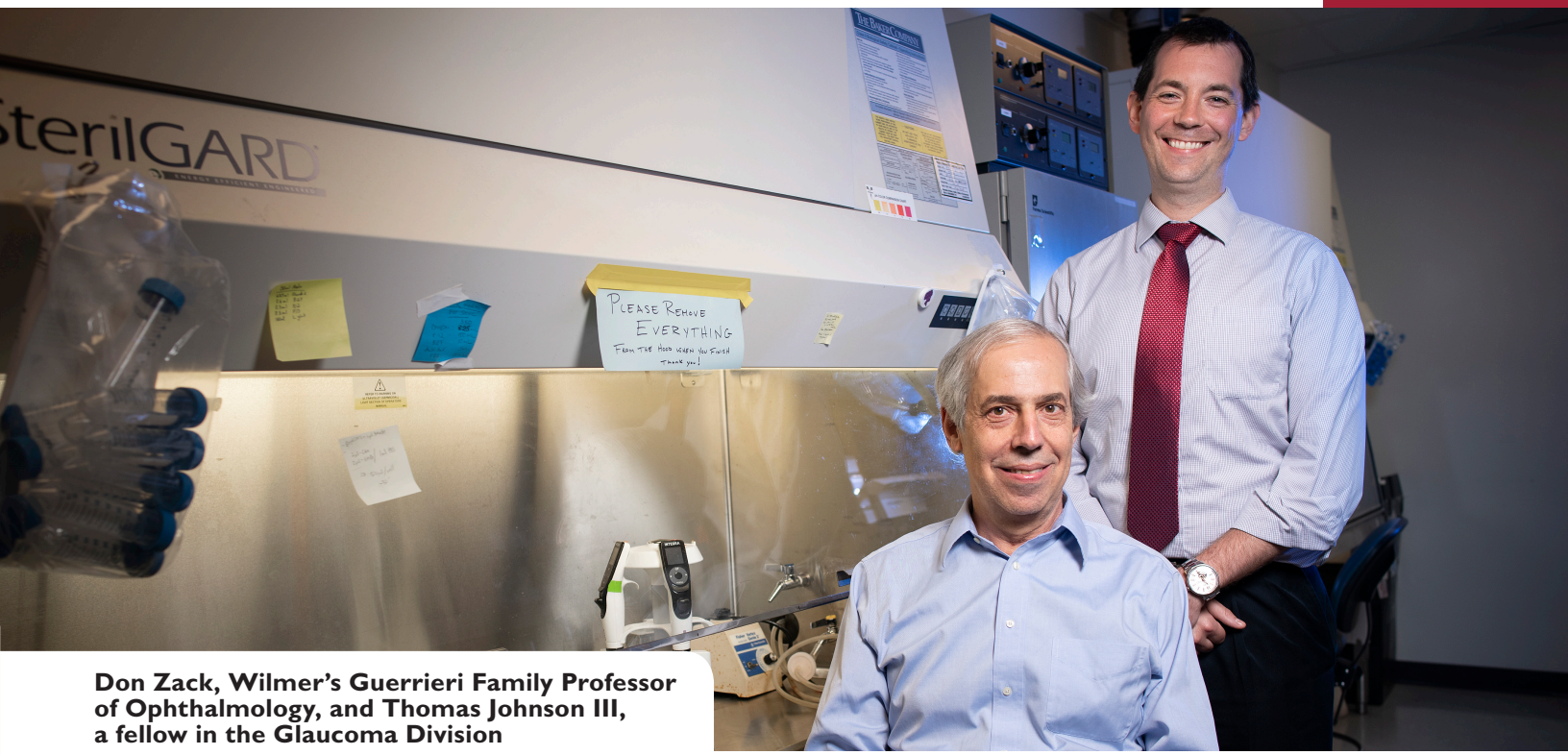

Don Zack, Wilmer's Guerrieri Family Professor of Ophthalmology, and Thomas Johnson III, a fellow in the Glaucoma Division

Unraveling the Optic Nerve

When we "see the light," we are doing more than simply comprehending. Our eyes capture the light and transform it into electrical impulses, which the optic nerve transmits to the brain. The brain then translates those impulses into what we see around us.

The optic nerve, however, is not a singular entity. Its many components include more than 1 million fibers (axons) from retinal ganglion cells (RGCs)—specialized neurons that have cell bodies in the retina and that project axons into the brain as part of the optic nerve. These cells play a key role in the development of glaucoma—damage to and death of RGCs cause the vision loss that occurs in glaucoma.

"Retinal ganglion cells are the telephone cables. No telephone cable, I talk to you, you don't hear me," says **Don Zack, M.D., Ph.D.**, director of Wilmer's Stem Cell Ocular Regenerative Medicine (STORM) Center. "The eye is still seeing, but the brain doesn't know it in glaucoma."

Because humans cannot regenerate their RGCs (unlike frogs and some fish), the vision loss caused by glaucomatous optic nerve damage is, currently, irreversible.

So, when Zack and other Wilmer researchers were able to create and purify RGCs using stem cells "in a dish"—meaning in the lab—it was a big deal. The accomplishment yielded two advantages. "We can now study human retinal ganglion cells, whereas before you had to study mouse cells or rat cells, which are great, but we want to treat humans and not mice," says Zack.

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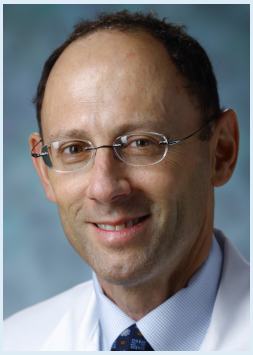


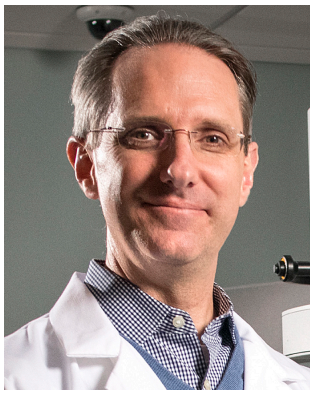
Henry Jampel, M.D., M.H.S., Wilmer's Odd Fellows Professor of Ophthalmology, has been appointed the inaugural editor-in-chief of the newly launched journal *Ophthalmology Glaucoma (OG)*. *OG* is the official journal of the American Glaucoma Society and a member of the American Academy of Ophthalmology family of journals. The journal will release its first issue in summer 2018, and then publish issues every other month. Jampel will employ the 15 years of experience he gained as the deputy editor-in-chief of the journal *Ophthalmology* to helm *OG*, which aims to become the journal of choice for high quality glaucoma-focused science.

Wilmer's Epic Journey

Quirky is not a word often used to describe a software company, but that's the one **Michael Boland, M.D., Ph.D.**, chose to describe Epic, the creators of Johns Hopkins' electronic health record (EHR) system. "It is a reference to classical poetry where an epic poem is someone's complete life story," says Boland, a glaucoma specialist and Wilmer's director of information technology.

Within Epic, many specialties have a product customized to their needs. The obstetrics product is called Stork, the cardiology product—Cupid. "Kaleidoscope is the ophthalmology product, and that comes from the Beatles song 'Lucy in the Sky with Diamonds,' which contains the lyric 'the girl with kaleidoscope eyes,'" says Boland.

Quirky indeed. But also transformative for patient care. "Now everything we do is in one place. If you're a patient seen anywhere in Johns Hopkins—any hospital, any clinic—all of your records are now part of one record system," says Boland.

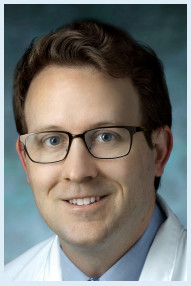


Epic provides several advantages to patients and health care professionals alike. For Wilmer patients, a central location for records means that patients can be seen at one Wilmer location and their information will be available at all locations. Thus, patients are not tied to one particular Wilmer clinic. In addition, through a feature called MyChart, patients can see the notes from their appointments and they can securely email their doctors.

For his part, Boland cites how much easier it is to find information. "You can tell what's going on with a patient without having to go back through a paper chart," he says. "We can then spend more time discussing whatever is going on with the patient that day."

The most valuable feature of Epic is also what inspired the system's name. "It's easier to get a complete picture of the person when you have all the information in one place," says Boland. "During the time of paper charts, each clinic had its own separate records, so the EHR now helps all of us make better decisions for our patients because we are better informed." ■

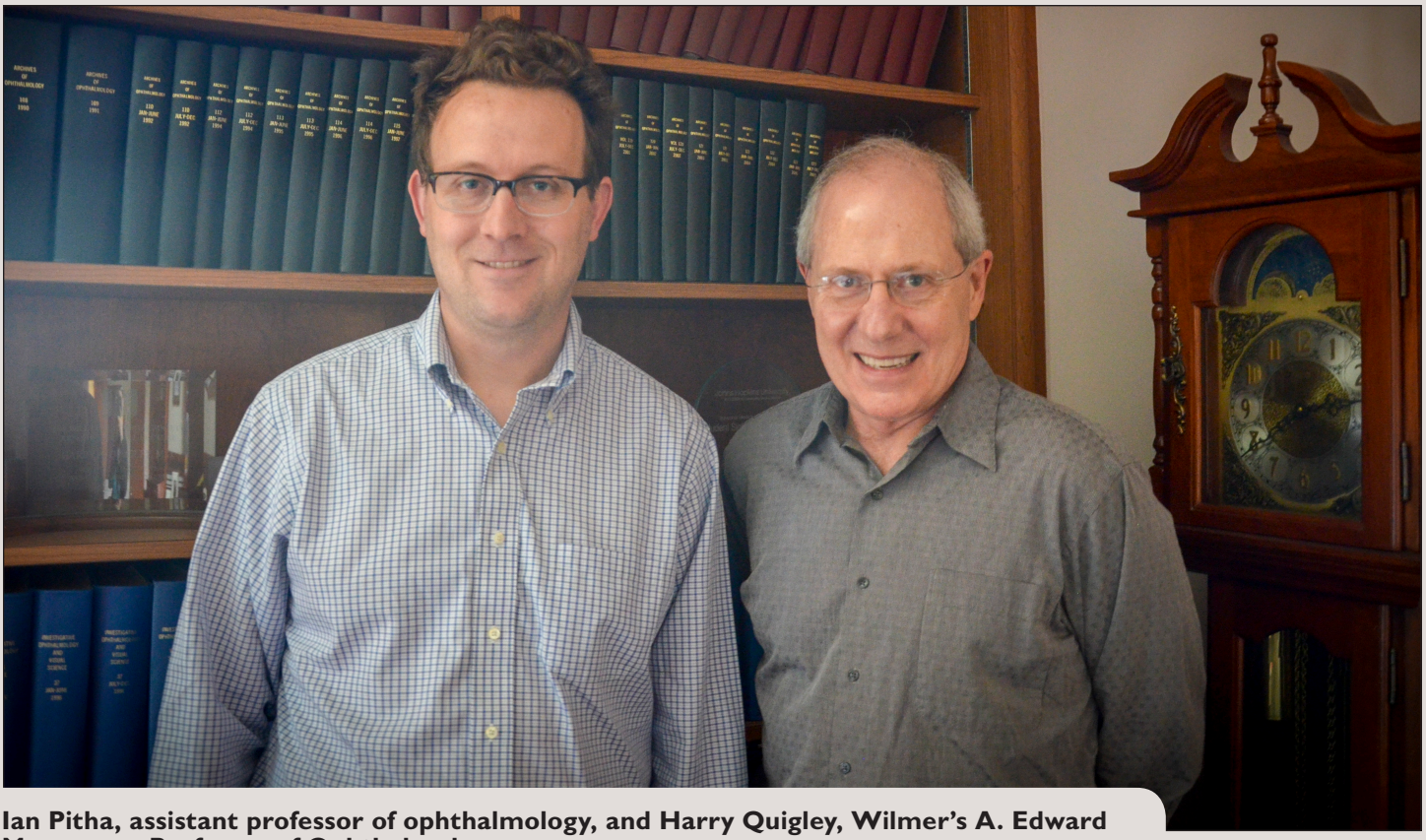
Chief of the Glaucoma Division Pradeep Ramulu, M.D., Ph.D., is pleased to share that two junior faculty members are currently supported by K awards, which are grants given by the National Institutes of Health to sponsor mentored training of researchers with high aptitude. "These grants are prestigious, competitive, and set one up for a future research career," says Ramulu.



Ian Pitha, M.D., Ph.D., assistant professor of ophthalmology, has a K08 grant, also referred to as a Mentored Clinical Scientist Research Career Development Award, to explore alternative strategies for drug delivery to the eye.

Amanda Bicket, M.D., assistant professor of ophthalmology, has a KL2 grant, also referred to as a Mentored Career Development Award, to incorporate patient-important outcomes into the evaluation of glaucoma therapies, with a focus on minimally invasive glaucoma surgery (MIGS) approaches.

Looking into the **Wall of the Eye**



Ian Pitha, assistant professor of ophthalmology, and Harry Quigley, Wilmer's A. Edward Maumenee Professor of Ophthalmology

Researchers at Wilmer have identified a new line of attack in the fight against glaucoma. "If you think of the eye as a ball, about three-quarters of it is the sclera—the white part," says **Harry Quigley, M.D.** Also referred to as the wall of the eye, the sclera—and how it deals with eye pressure—could hold the key to a new way to treat glaucoma.

"At one time, the sclera was considered a piece of shoe leather, not really actively alive or responsive," says Quigley, Wilmer's A. Edward Maumenee Professor of Ophthalmology. Several decades ago, though, Quigley's mentor—and Wilmer Director Emeritus—**Edward Maumenee, M.D.**, pointed out a specific mechanical defect in the optic nerve head, which emerges from the sclera, of patients with glaucoma. At this location, the tissue seemed to "blow out and form a pit," says Quigley. Maumenee told Quigley the path to figuring out glaucoma could involve understanding why that defect happened, which Quigley set out to do.

He discovered that the sclera, far from a piece of shoe leather merely protecting the retina, serves another important purpose. "It determines the effect of the eye pressure on nerve cells that leave the back of the eye and go to the brain," says Quigley. "We found that some people have inherently weaker areas of the optic nerve head and sclera, and that's where glaucoma goes after their vision first."

Quigley then embarked on experiments to alter the sclera in order to see how that affected the development of glaucoma. One experiment involved treating a mouse eye with a drug to make the sclera stronger. Unexpectedly, making the sclera stronger and stiffer actually made the glaucoma damage worse.

In 2016, he tried a different strategy, giving mice with induced glaucoma a blood pressure medication, called losartan, which altered the behavior of the cells in

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Letter from the Chief–**Pradeep Ramulu, M.D., Ph.D.**

Thank you for taking the time to read about the Glaucoma Division of the Wilmer Eye Institute. If you have interacted with one or more of us, I hope you would agree that we prioritize giving you the best possible medical care with the respect and dignity you deserve.

Seeing us in the office, you may not realize that our faculty also spends countless hours outside of the clinic working on new treatments and solutions for glaucoma. In these pages, you will read about the myriad ways we are working toward these goals. Some ongoing projects include

implementing new computer systems to handle your data, researching protection of the optic nerve from damage by modifying the sclera (the white connective tissue of the eye), working to enhance your personal safety by preventing falls, and investigating how we can regenerate the optic nerve. So extensive is the work of our faculty that we even had to save some of the latest achievements of Dr. Craven and Dr. Friedman for our next issue. We are always eager to share details about our ongoing and future projects with those who have a greater interest, so feel free to reach out if you are moved or motivated by what you read herein.

Wall of the Eye *continued from previous page*

the sclera. "We found that altering those cells' behavior with losartan protected the eye against damage to the nerve cells leaving the back of the eye," says Quigley. "And it did so by blocking negative effects of eye pressure transmitted through the sclera to the nerves that were going out the back of the eye." These results proved for the first time that altering the sclera by affecting the cells that live in it could protect a patient from glaucoma. Quigley calls this new strategy "scleral neuroprotection."

Quigley's research team now includes **Ian Pitha, M.D., Ph.D.**, a clinician-scientist who is studying the behavior of scleral cells, called fibroblasts. Prior researchers approached the sclera only from an engineering perspective. "If you're looking at it like an engineer would, you'd say this is a material, how does the material change?" says Pitha. "What I'm trying to say is, this is a material, and it changes, and we've appreciated those changes, but the things that are probably governing that are the cells within the tissue." Using this knowledge, he can lay the foundation for fine-tuning the delivery of drug molecules to these fibroblasts.

Scleral neuroprotection is a shift away from the current treatment for glaucoma, which focuses on reducing pressure in the eye. In this new world, says Quigley, "We could treat somebody and say, 'Your eye doesn't care what your pressure is because we can change the scleral response to the pressure.'" As any patient with glaucoma knows, that is saying something. ■

Unraveling *continued from page 1*

The second advantage will be farther down the road—the development of stem cell transplantation-based therapies for glaucoma, a task that has captured the imagination of **Thomas Johnson III, M.D., Ph.D.**, a fellow in Wilmer's Glaucoma Division. Johnson's research involves manipulating the behavior of the human RGCs that Zack creates. Johnson does this in retinal explants—retinas removed from eyes, placed on a dish and kept in a culture that "feeds" them, which keeps the cells of the retinas alive so researchers can experiment on them with the human RGCs. Developing methods to control RGC activities after transplantation is a necessary next step to create a successful therapy for patients.

Johnson explains that the transplantation process will involve more than merely injecting RGCs into a patient's eye. "From there the cells are going to need to migrate into the part of the retina that is missing the RGCs we want to replace," says Johnson. "They're going to need to integrate into the patient's tissue and then create synapses with upstream neurons." The implanted RGCs must make those connections in an organized manner to ensure they can clearly receive signals and transmit them to the brain.

"Our ultimate goal would be to regenerate the optic nerve so that patients who have been robbed of their vision by diseases like glaucoma might be able to see again," concludes Johnson. ■

Fixes for Patients' Fear of Falling

Falls resulted in more than $50 billion in health care costs in 2015, according to a study published in the *Journal of the American Geriatrics Society* in March 2018. As the population ages and develops more diseases that contribute to falls, the cost—emotionally and financially—will only increase. How to prevent falls, though, does not have a single answer. "You can always stop falls by telling people to walk less, but that's an unhealthy way to prevent falls," says **Pradeep Ramulu, M.D., Ph.D.**, chief of the Glaucoma Division. "The only healthy way to prevent falls is to make people fall less when they walk."

The desire to learn how, when and where their patients fell led Ramulu and **David Friedman, M.D., Ph.D., M.P.H.**, director of Wilmer's Dana Center for Preventive Ophthalmology and a glaucoma specialist, to launch the Falls in Glaucoma Study, or FIGS, in 2014. "One of the major risk factors for falls is having poor vision, especially having a visual field loss, which happens with glaucoma," says Ramulu.

Although other studies have examined falls, investigators running those studies measured the frequency of falls over time in order to determine whether a factor such as having glaucoma increased one's likelihood of falling. Measuring falls in this fashion, though, does not capture the behavior of people who have curtailed their movement because they fear falling.

In FIGS, Ramulu, Friedman and their team chose a new tack—they analyzed falls per steps taken. The study involved 250 people, each of whom wore an accelerometer for one week every year for three years. In addition, each participant wore a GPS tracker for one week a year. Throughout the three-year period of the study, participants also kept a diary in which they recorded when they fell.

David Friedman, Alfred Sommer Professor of Ophthalmology

Now that FIGS is wrapping up, their team has findings to share. "One revealing result is that the things that make people more likely to fall per unit of time are not the same things that make them more likely to fall per step they take. For example, poor vision we found increased your likelihood that you would fall per step, but not over time," says Ramulu.

The FIGS team

In addition, their team found that, contrary to expectations, most falls occurred at home. "Every step you take at home is twice as likely to result in a fall as a step you take away from home," says Ramulu. The implications of this information are significant because changing a person's home is easier than changing his or her behavior.

"If we're trying to prevent falls, then why not go after the low-hanging fruit, which is controlling the environment?" says Ramulu. He envisions the next step as launching a study to see where in the home falls occur, which could provide solid data to guide interventions—such as recommendations for the placement of furniture or the percentage of floor space that clutter should occupy before safety becomes an issue.

Ramulu points out that building standards and codes that govern construction already exist. He would like to extend those to the setup of the home. "If you could make concrete recommendations, which were then taken up by people who made apartments for seniors, all of a sudden you could have a very broad impact," he says. "It's not going to fix everything. But even if it decreases a very large number by 5 percent, that would be amazing." ■

WILMER Cure Glaucoma

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