

OneWilmer

ABOVE: Human stem cells differentiated into retinal ganglion cells (RGCs)

A Dream Team Designed for Collaboration

IN LABS ACROSS THE WORLD, THE BODY OF SCIENTIFIC KNOWLEDGE INCREASES EVERY DAY. BUT AS THIS KNOWLEDGE INCREASES, SO DOES THE TIME IT TAKES TO MASTER IT.

Because researchers have a finite amount of time and attention, to truly leverage both the depth and breadth of today's scientific advances, they need to band together to tackle problems.

Yet, the primary model for medical research is still the single research group, led by a faculty member known as a principal investigator (PI),

who receives a grant from the National Institutes of Health (NIH) to fund his or her lab. The researcher then has discretion as to how much or how little he or she collaborates with others.

The NIH isn't the only game in town, however. Recently, Wilmer ophthalmologist **Don Zack, M.D., Ph.D.**, received generous grants from the Gilbert Family Foundation

(GFF) — established and run by Quicken Loans founder Dan Gilbert and his wife Jennifer — that aim to create a different model. “The grants were given as groups to fund research teams at different institutions to work together. They're not separate grants to each lab,” says Zack. “It's all part of a larger project structurally designed to be a collaboration.”

Continued inside

A Dream Team...

Continued from cover

Part of the structures mandated by the GFF include monthly phone calls and an annual in-person meeting as well as sharing materials such as reagents, cells and animal models; a coordinator provided by the foundation makes sure these processes run smoothly.

The grants, which total \$11 million, fund a “Dream Team” (as the foundation refers to it) whose goal is to preserve and restore vision to individuals suffering from vision loss caused by optic nerve tumors in patients with neurofibromatosis 1 (NF1) — a condition in which tumors can grow within the nervous system and in the skin.

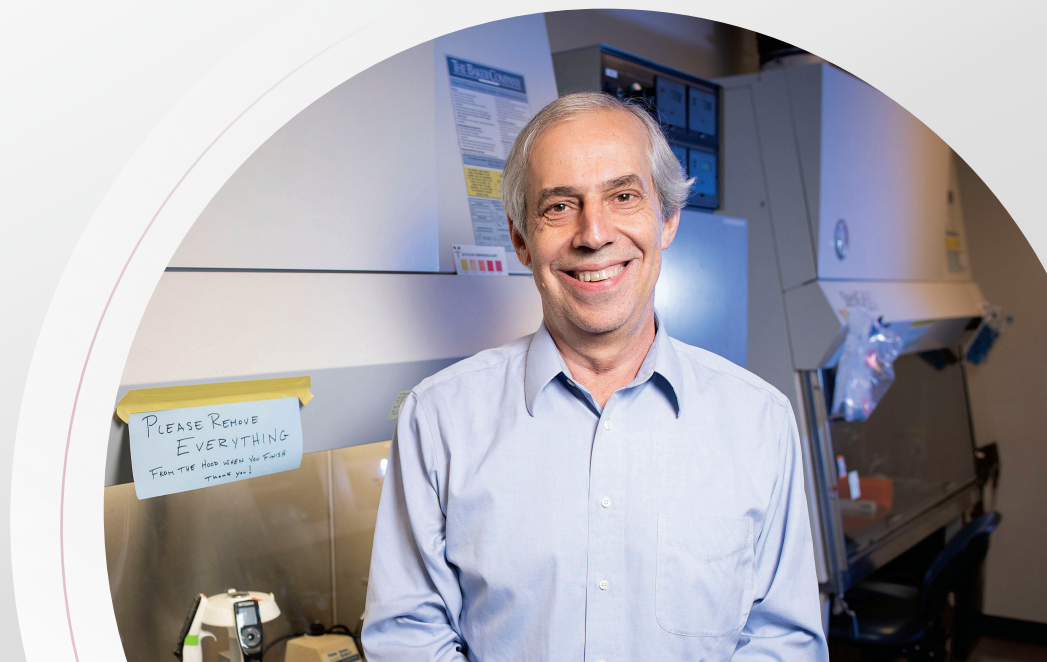
The Dream Team includes 12 experts from the fields of NF1, ophthalmology and neuroscience. The researchers want to “figure out how NF1-associated tumors injure the optic nerve, find ways to reduce the injury, and develop technology to regenerate the optic nerve and restore vision,” says Zack. Their work will likely have implications for other optic nerve diseases such as glaucoma as well.

The initiative is focused on specialized neurons called retinal ganglion cells (RGCs), the cells in the retina that combine to form the optic nerve and transmit visual information from the eye to the brain. An example of how the collaboration works between the researchers involves how these cells are created.

“Another lab generated cells that have the NF1 mutation, either from a patient or using CRISPR-Cas9 editing,” says Zack. “They sent the cells to us, not as RGCs, but as stem cells. We are making those stem cells into retinal ganglion cells.” His lab will study the RGCs with the NF1 mutation and he will send them to other collaborators who will do the same.

Zack is optimistic that this could be a more productive structure for research projects because of its size and the amount of funding. “This is a very directed collaboration. The goal is to help patients with NF1 see again. They picked the groups who they think can work together to achieve this goal,” says Zack. ●

Don Zack »





« Fasika Woreta

Partnering to Restore Sensation

Tears are necessary for a healthy emotional life. They're also necessary for a healthy cornea. When the cornea senses pressure or stimulation, we blink and produce tears that nourish and protect the eye. If a cornea loses sensation (called a neurotrophic cornea), the formation of tears slows down, the tissue begins to dry out, and the cells of the cornea break down — resulting in ulcerations that become infected and scar the tissue. Scarred corneas can lead to impaired vision and even blindness.

Until recently, people with neurotrophic corneas could receive treatment for symptoms but not for the root cause — the lack of sensation itself. “We could only offer lubrication, closing the eyelids and other supportive measures to patients,” says **Fasika Woreta, M.D.**, a cornea specialist at the Wilmer Eye Institute and 2019 Johns Hopkins Physician of the Year.

That changed when Woreta teamed up with **Richard Redett, M.D.**, the interim director of the Department of Plastic and Reconstructive Surgery at Johns Hopkins, to offer a procedure

called corneal neurotization. This surgery involves removing a nerve from the leg, grafting it to a working nerve in the forehead or neck and connecting that nerve graft to the neurotrophic cornea. The working nerve will sprout nerve fibers that eventually grow into the neurotrophic cornea to restore sensation.



Redett (left) is an expert in restoring nerve function to the face and procedures that restore sensation and movement to parts of the body that have lost it. When former colleagues at the Hospital for Sick Children in Canada informed Redett that they had begun performing the corneal neurotization procedure and were getting great results, he decided to introduce the procedure in Baltimore. He could harvest and graft the nerve, but would need an ophthalmologist for the delicate eye surgery required to attach the nerve graft to the cornea.

“[Luckily], we have a long history of collaborating with Wilmer — one of the best ophthalmology hospitals in the country, with thousands of patients and a very

strong corneal service,” says Redett. He approached the chief of Wilmer’s cornea division, **Albert Jun, M.D., Ph.D.**, who recommended Woreta as a potential partner.

Woreta quickly signed on to the idea. “There was no surgery we could offer patients before this procedure,” says Woreta. “The fact that we can restore sensation and improve the health of their cornea is exciting.”

The restored sensation allows tears to bathe the cornea as often as needed, which sustains and preserves it. For some patients, if they have the procedure early enough in the progression of their condition, the scarring will stop, which will halt their vision loss. Other patients, however, may require a corneal transplant because of the damage. In those cases, having a cornea with restored sensation exponentially increases the success rate of a corneal transplant.

A complex procedure such as corneal neurotization can only happen when experts join forces. “One of the great things about working at Hopkins is the ability to collaborate with other surgical specialists. I think it makes us all better surgeons,” Redett says. ●

Wilmer, Bel Air Takes Center Stage



Meghan Berkenstock, M.D., (left) had a problem. An assistant professor of ophthalmology

at Wilmer, Berkenstock had a patient whose optic nerve she needed to see more clearly to determine if his glaucoma was progressing. The obstacle? He had a very long (myopic) eye. The machine used to image his optic nerve, called an optical coherence tomography (OCT) machine, employs light waves to take cross section pictures of the retina and optic nerve. But the light has to travel farther in a myopic eye, making the signal weaker and the scan less reliable.



Berkenstock expressed her frustration to **Melissa Collins, (left)** a certified ophthalmic technician and

photographer who performs imaging in Wilmer's Bel Air clinic. Berkenstock suggested that they place a lens in front of the patient's eye to boost the signal strength of the OCT scan. "Why not use a contact lens?" suggested Collins. All eye clinics have plenty of trial contact lenses. "It was brilliant!" says Berkenstock. "I did the scan without the contact lens and

repeated it with the contact lens, and the signal strength improved."

Because this is Wilmer, the story does not end there. Berkenstock scoured the academic literature to see if there were previous publications on this technique and found there were none.

With the help of Collins and **Denise Ricard, (right)** another ophthalmic



technician at the Bel Air clinic, Berkenstock set out to change that. They designed and executed a study to see if using a contact lens did consistently boost the signal strength of the OCT machine, resulting in better images of the optic nerve in patients with high myopia.

Berkenstock says it was a Bel Air-specific process, from conception to recruiting the patients. The location of the study is important, she says, because it "showcases that our clinics outside of East Baltimore are places where a lot of great things can happen." She, Collins and Ricard found that patients were excited to enroll in a study that could help others and were glad they did not have to drive downtown to do so.

The close collaboration between Berkenstock, Collins and Ricard is unique. While Berkenstock

is accustomed to publishing academic studies, Collins and Ricard are not as familiar with this aspect of medicine.

"It's not something I ever thought I'd be part of," says Ricard, referring to the study.

"It's exciting to be a part of something that's going to possibly help people in the future." Collins too is surprised, yet pleased to be an author on the research paper based on the study.

"I stumbled upon this idea because we were going back and forth about the patient. It was pretty neat just to hear Dr. Berkenstock say, 'Wow. Why hasn't anybody thought of this before? Let's get this moving,'" says Collins. "She wanted to be the first to have it published." And they will be — in the prestigious journal *Ophthalmology Glaucoma*.

"Based on our data, the use of a contact lens statistically improved the signal strength and average nerve fiber layer thickness of the spectral domain OCT scan," says Berkenstock. Because the signal strength and quality of the OCT scans improved, they were able to see a thicker nerve fiber layer than previously noted, which has broad implications for patient treatment—from adjusting the number of drops prescribed to determining the need for surgical interventions. ●

Esen Akpek »

Uncovering a Significant Cause of Dry Eye



Despite affecting more people than rheumatoid arthritis, Sjögren's syndrome is considerably less well known.

While 1.2 million individuals in the U.S. have rheumatoid arthritis, 1.4 million people have a diagnosis of Sjögren's syndrome — 90% of which are women. The two conditions are often compared because both are autoimmune diseases.

Like all autoimmune disorders, Sjögren's syndrome causes the immune system to attack the body. The most common symptoms people with the condition experience are dry mouth and dry eyes. The latter symptom is what brings them into the care of **Esen Akpek, M.D.**, director of the Ocular Surface Disease and Dry Eye Clinic at Wilmer.

Akpek has spent more than a decade examining the prevalence and consequences of the disease. Her interest stemmed directly from her experience with patients. She noticed a lot of her patients presenting with dry eye had fatigue, dry mouth and joint

pains. "I started working them up — sending them to rheumatology, internal medicine, ENT," says Akpek. They found that many of these patients had Sjögren's syndrome.

That eventually led to a paper that predicts the incidence of Sjögren's syndrome among patients with dry eye is much higher than previously thought. "What was known is 90-something percent of patients with Sjögren's have dry eye. But what percentage of dry eye patients have Sjögren's was not known," says Akpek. "In 2009, we showed that 1 in 10 do — that's a very high percentage." Akpek believes the actual number of people with Sjögren's syndrome is closer to 4 million.

Her work also demonstrated that there is a 10-year lag time in the diagnosis of Sjögren's syndrome, which is significant because of the disease's potential complications — from systemic ones such as lymphoma or hepatitis to localized ones such as corneal scarring and blindness.

"Of all the autoimmune diseases, patients with Sjögren's syndrome are the most likely to develop lymphoma over their lifetime," says Akpek. "It's a very important disease."

It is also a disease that requires teamwork. As associate director of the Johns Hopkins Jerome L. Greene Sjögren's Syndrome Center, she partners with doctors throughout the hospital — particularly rheumatologists — to treat patients.

Generally, ophthalmologists do not treat patients with systemic medications, but rheumatologists do. "Sjögren's is a multisystemic, multi-organ system disorder. No one person can handle the entire patient. You need experts in different kinds of fields," says Akpek. "Collaboration is necessary." ●

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AS I SEE IT

***Peter J.
McDonnell,
M.D.***

Dear Friends,

First and foremost, I hope that you are safe and well during this challenging time. While we have moved most of our communications to electronic versions, we were able to produce this newsletter beforehand.

Although the stories about research and patient care do not touch on coronavirus, they do highlight one of our strengths: collaboration. Wilmer was founded on the concept that bringing patient care, research and teaching under one roof would improve all three.

The ability of our faculty and staff to collaborate is what has allowed us to adapt so quickly to the current situation by utilizing telemedicine, postponing non-urgent surgeries and deploying many employees to work from home — all to achieve our primary goal: keeping our patients healthy and safe.

When the time is right, we look forward to seeing you again. Until then, please take care.

Kind Regards,

