CASEY EYE *Institute*
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A SEMI-ANNUAL NEWSLETTER

Photo courtesy of Jeffrey Farrell

A Disco in the Sky

Casey patient JoDee Hambright can see stars for the first time thanks to gene therapy

Just months after receiving gene therapy surgery at OHSU Casey Eye Institute, JoDee Hambright wrote her doctors to say, "I am ecstatic to report that my night vision has improved drastically. I was able to see stars with my naked eye for the first time!"

Hambright was one of the first 14 patients to receive the groundbreaking gene therapy Luxturna at Casey—one of only six sites in the U.S. qualified to offer this vision-saving treatment.


JoDee Hambright

Finding M&M'S

Hambright's vision problems started early. When she was an infant, her parents noticed she wasn't making eye contact. Later, when she started walking, she couldn't adapt to dark lighting. "My parents put M&M's on the floor, to test my vision," said Hambright.

She was eventually diagnosed with a defect in the RPE gene, an extremely rare condition which produces the specialized proteins needed for full vision. RPE gene mutations cause night blindness, loss of vision clarity and impaired dark adaptation. Many with the condition lose their sight completely, as adults.

Hambright's family and teachers in Colorado were very supportive. She always had extra lighting and magnification in the classroom—but school was always a struggle. Hambright remembers not being able to read the whiteboard or recognize friends in the hallways.

By the time she arrived at college, Hambright's vision was starting to deteriorate. She could only read on the computer or with backlighting. One afternoon, she crashed into a pole while riding her bike. She had started grappling with the reality that she would eventually lose her vision.

Against all odds

And then a news article changed everything: it described a new drug recently approved by the FDA for treating her condition: Luxturna.

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"When I read the article I realized, this is just like me," said Hambright.

To qualify for Luxturna, she needed to confirm that she had RPE65 mutations in both eyes and enough remaining cells in her retina to respond to treatment. She was in luck: The tests were positive. "The odds were astronomical," she said.

Hambright also had to spend some time adjusting to this new possibility. "I had already been working to accept the fact that I would likely go blind. It was unsettling to start hoping for something different. What if it didn't work?" she said.

After her initial tests with her retinal specialist in Colorado, Hambright arrived in Portland for more tests, to confirm that she had usable cells. "Those were the longest three days of my life," said Hambright.

Hambright received the go-ahead in December 2019 and they scheduled the surgery for May 2020. And then Covid-19 hit. Hambright assumed her procedure would be cancelled, but the team at Casey decided that the surgery was essential – it had the potential to transform her life.

During the procedure, the surgeon injected a normal copy of the RPE65 gene into each retina, next to the defective genes. The hope was that the normal genes would take over.

In the mountains on a clear night I feel like I am in a disco ball surrounded by stars and planets

A new relationship with light

Hambright noticed the difference almost immediately. "Within days of surgery I was noticing a whole new relationship with light. Things looked radioactive, glowing and intense. Eventually, my brain was able to process the new information."

Now she's able to do things she hasn't done since childhood, like read books; or ever, like seeing stars. "In the mountains on a clear night I feel like I am in a disco ball surrounded by stars and planets," said Hambright.

"What's unique about these patients is that they've been told their entire life that they'll eventually go blind. That burden can profoundly influence their life expectations," said Hambright's surgeon, Steven Bailey, M.D., associate professor of ophthalmology in the OHSU School of Medicine. "This novel treatment gives hope—people have come from as far away as Australia for the procedure."

JoDee Hambright poses outside while enjoying her improved vision after she received Luxturna gene therapy for her inherited retinal disease.

Hambright's success story would not have been possible without the leadership of David J. Wilson, M.D., the Paul H. Casey Chair and director of Casey, who anticipated how important gene therapy would become. Philanthropy also played a role: A transformational gift from Paul Casey in 2010 led to an additional $10 million in industry and philanthropic support for gene therapy research.

The team at Casey is excited about the future of gene therapy. Luxturna's success has the potential to lead to better treatments for a range of eye diseases, including problems like age-related macular degeneration, the leading cause of vision loss in the U.S.

"We've had good results with almost every patient," says Mark Pennesi, M.D., Ph.D., associate professor of ophthalmology and Kenneth C. Swan Professor of Ophthalmology in the OHSU School of Medicine; and chief of the Paul H. Casey ophthalmic genetics division at OHSU Casey Eye Institute. "I love hearing the stories at the one-month post-surgery visit. One patient asked his mom, 'What are all these lights inside the car?' He had never seen the dashboard properly. Another parent broke down in tears of joy, telling us that she was finally able to go back to work because her 12-year-old son could now see well enough to be independent after school."

Dr. Bailey notes that "This treatment was built on decades of research into understanding ophthalmic genetics, molecular techniques to transfer gene products into targeted host cells, improved retinal imaging techniques, and advances in vitreo-retinal surgery. Now we're seeing decades of research bear fruit. It's an exciting time for gene therapy."

Finding the other 50% of patients with glaucoma

How can we improve the evaluation and care of patients with glaucoma? Glaucoma is one of the leading causes of legal blindness and affects about six percent of adult Americans. It has an even higher prevalence in Black and Latinx populations. As glaucoma is asymptomatic until its advanced stages, it is common that severe disease happens more often in groups that have limited access to eye care. Half of the patients with glaucoma in the U.S remain undiagnosed.

The Covid-19 pandemic provides an interesting insight into how we might establish a population-based approach to address glaucoma and find that other half of patients who remain undiagnosed. During the past two years, restrictions on in-person visits changed how we use many types of technology to provide ongoing care for patients with glaucoma.

Researchers and doctors at Casey have focused their efforts to provide the framework for expanding this change in patient care to provide improved screening, diagnosis and care of patients with glaucoma.

At the forefront of early glaucoma diagnosis

First of all, researchers with Casey's Center for Ophthalmic Optics and Lasers (COOL lab) demonstrated that the non-invasive imaging technology OCT angiography is a reliable way to detect glaucoma early by viewing blood vessels in the eye. OCT angiography could be a technology we are able to use to screen many people for the unsuspected presence of glaucoma.

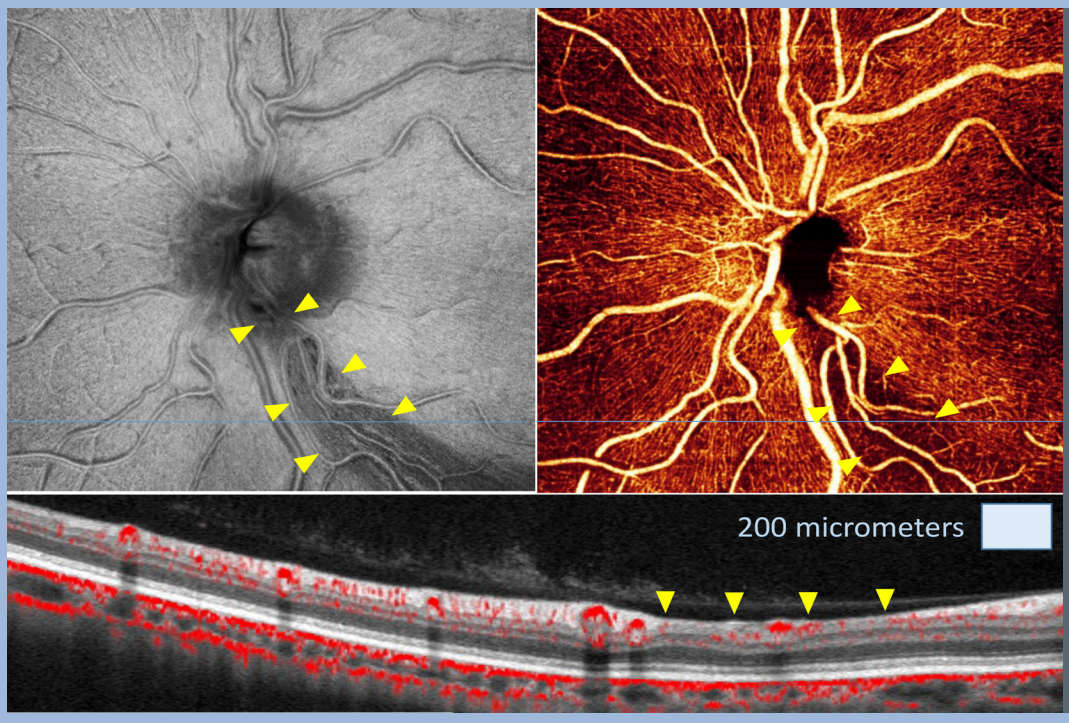
Secondly, Casey researchers are also developing artificial intelligence algorithms for looking at eye images to recognize those patients with glaucoma. This is another way doctors can detect glaucoma early in large populations.

Finally, The Roundhouse Foundation has provided funding to implement this approach in pilot sites throughout Oregon. By making a diagnosis early in patients without symptoms, many who lack easy access to quality eye care, we will have the best chance of reducing the prevalence of vision loss from glaucoma in Oregon and beyond.

Getting it right

The evolution of the way we diagnose and care for glaucoma requires careful study, and Casey's team of leading experts are working together to conduct just such an analysis. David Huang, M.D., Ph.D., and Yali Jia, Ph.D., in the COOL lab will provide unparalleled expertise in imaging. Michelle Hribar, Ph.D., and Hiroshi Ishikawa, M.D., Ph.D., will develop artificial intelligence processing applications. Finally, the Casey Community Outreach Program, led by Mitchell Brinks, M.D., M.P.H., and Verian Wedeking, is building a network of community health workers in Oregon to support the implementation of this approach in high-risk populations.

Casey's glaucoma division has embraced this project, and Aiyin Chen, M.D., one of Casey's glaucoma specialists, will be evaluating whether these tools and technologies can be successful in early glaucoma screening and detection.



Images from the left eye of a glaucoma patient. The photograph (left) shows subtle thinning of the rim of the optic disc and loss of nerve fibers (arrowheads) in the inferotemporal sector. OCT angiography (right) shows loss of capillary blood vessels that supply the nerve fibers. The cross-sectional OCT angiography (bottom) shows thinning of the nerve fiber layer (yellow arrows). Loss of the blood vessels is a very sensitive measure of glaucoma, and is evident as lack of capillaries (red dots) in that layer.

Expansion of residency program strengthens learning and service opportunities

Adding a new class of residents improves ophthalmology training experience

The inaugural integrated internship residents started in July, 2021. The group of 5 pose in front of the OHSU Center for Health and Healing during orientation with program director Dr. Thomas Hwang (far left) and education manager Susan Minnieweather (far right).

This past year has been very exciting for the residency program team, which prepared to welcome its inaugural class of integrated internship in July 2021. For the past few years, OHSU Casey Eye Institute's ophthalmology residency program has had 15 residents total, five per year over three years. The residents began the ophthalmology portion of their residency in the second year of training after completing an internship year between medical school and residency outside of OHSU. With this new integrated class, there are now five residents per year over four years, totaling 20 residents.

In 2021, the national governing body for accreditation of graduate medical education required that an internship year be included in ophthalmology residency programs nationwide. Casey was more than ready to make this change. "We have been preparing to expand our program for the last few years and are very excited to launch our new curriculum with the OHSU School of Medicine," said Susan Minnieweather, education manager.

The new integrated internship year provides a balanced introduction to general medicine and ophthalmology. An extra year of exposure to ophthalmology enriches resident learning, brings them closer to their fellow residents, and better prepares them to take primary call in their second year.

Culture of service

Many of our residents come to Casey with an amazing record of service, and they continue to make a difference while they are here. Service is a critical component of our residency program, as it helps residents become engaged in the community, address healthcare inequities and use their skills and knowledge to help underserved communities. Residents say that their service experiences at Casey are critical to their professional development, helping shape a career with dedication to volunteerism, empathy for their patients, and awareness of eye care access barriers and how to help reduce them.

Dr. Claire Mueller provides eye exams as a volunteer on the mobile clinic.

With the inaugural integrated internship class added in 2021, Thomas Hwang, M.D., residency program director wasted no time in encouraging new residents to volunteer with the program. "Service is an incredibly important part of residency training at Casey," said Dr. Hwang. "We want to train people who leave the program with the same idealism and commitment to make the world the better place that they come in with. How do we maintain that commitment and idealism? In addition to giving them all the support they need to nurture the sense of gratitude, we fuel it through opportunities for service."

The residents play a central role with the Casey Community Outreach Program Mobile Clinic, which is entirely donor-funded and provides free vision screenings to underserved communities throughout Oregon. As volunteers, the residents learn about helping patients with a wide variety of eye conditions, including many who have never received eye care before. They provide eye exams and referrals to community physicians, which helps them understand the healthcare system and how to be an advocate for their patients. Residents help make Casey's mission to reduce preventable blindness possible, having already volunteered about 120 hours with the outreach program from January through September 2021.

Casey Eye Institute has built a national reputation for providing a world-class ophthalmology education and was listed #8 in the Best Residency Program category in *Ophthalmology Times* 2020 Best Program Survey. Casey's residency program continues to be one of the most competitive in the country. Residents say its diverse, world-class clinical opportunities covering all ophthalmic subspecialties with top-notch teaching, a warm and supportive environment, and robust opportunities for research and impactful service as reasons they choose this program. Philanthropic support is critical to achieving the success of our program and allows us to provide the residents with state-of-the-art equipment, scholarly support, and facilities that are second-to-none.

Explosive growth of faculty carries momentum forward on heels of new building

After new building opened in 2020, growth continues in all areas of eye care and vision research

2020 was a very exciting year completing and opening the new Elks Children's Eye Clinic building. 2021 has been just as exciting with 12 new faculty members joining our research and eye care team.

As expected, the growth of our facilities has created room for growth in all aspects of eye care and vision research as we pursue our mission to eliminate preventable blindness and improve quality of life through leadership in the art, science and technology of 21st-century eye care.

By adding new faculty members in glaucoma, oculofacial plastics and reconstructive surgery, pediatric ophthalmology, ophthalmic genetics, neuro-ophthalmology and comprehensive ophthalmology, we are strengthening the eye care service we provide all around the region. Many of these new providers offer much-needed specialty care outside of major metropolitan areas at our clinics around Oregon and Southwest Washington. Some new faculty members, such as Dr. Hiroshi Ishikawa, will be strengthening our vision research program by focusing on providing new ways to diagnose and treat people with sight-threatening conditions such as glaucoma.

As we continue working to change how vision care is provided across our region, the nation and the world, the future is bright. By combining the best technology with the brightest minds in a collaborative environment, we are on track to transform the future of vision care.

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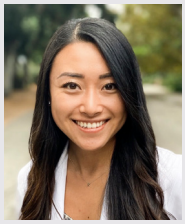

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