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Friends and colleagues,

As we celebrate 75 years of our department, we recognize the efforts of our predecessors at OHSU Casey Eye Institute in creating a climate of innovation and collaboration that is still a driving force for us today. Today, we are making fantastic strides in performing gene-editing, harnessing artificial intelligence and using spectroscopic optical coherence tomography among other discoveries—all a distant dream in 1945.

For our next chapter, perhaps the most exciting endeavor will be our efforts to flip the traditional encounter model to a population-based approach. We are designing our programs to address the prevalence of blindness in Oregon, while seeking to overcome some of the inequities and barriers in the delivery of quality care.

It is an ambitious project, but we are taking the first steps next year with the opening of two new clinics using a community-based model.

One clinic will be located inside the Portland metro area and the other will be in Hood River, a more rural community about 65 miles outside of Portland. Community health workers will be trained to provide sophisticated evaluation of patients, including imaging with optical coherence tomography. Patient data will be transmitted to OHSU Casey Eye Institute for interpretation by an artificial intelligence algorithm to screen for patients who need specialist care. We anticipate expanding this model to 10 clinics over the next five years. As these clinics evolve, we want to improve the vision health among all Oregonians.

Our vision is to redefine the standards of eye care for the people whom we serve in Oregon and beyond. We are honored to share some of the highlights of this year’s transformative work occurring at OHSU Casey Eye Institute.
Pioneering the first-ever CRISPR gene editing in vivo

On Feb. 25, 2020, OHSU Casey Eye Institute led a unique moment in human history—the first gene editing procedure in a living person in all of medicine.

As part of the BRILLIANCE clinical trial, the procedure seeks to repair mutations in the CEP290 gene that causes Leber congenital amaurosis type 10 (also known as LCA10 and CEP290-related retinal dystrophy). Andreas K. Lauer, M.D., internationally recognized as one of the leading ocular gene therapy surgeons, performed the operation that edits the mutated gene using CRISPR technology.

“We have the ability to snip out the abnormal DNA in a cell,” he said. “We’re not altering the person’s genetics, only changing the DNA at a molecular level in a very local area of the retina, and not even whole retina, just in a specific functional area and in a deliberate and controlled way. To do this for the first time in a human being—that’s an amazing initial step.”

Mark Pennesi, M.D., Ph.D., who leads OHSU’s involvement in the trial and is the chief of the OHSU Casey Eye Institute’s Paul H. Casey Ophthalmic Genetics Division, said the significance of this first use of CRISPR in vivo has implications beyond ophthalmology.

“Being able to edit genes inside the human body is incredibly profound,” he said. “Beyond potentially offering treatment for a previously untreatable form of blindness, in vivo gene editing could also enable treatments for a much wider range of diseases.”

Patients with Leber congenital amaurosis type 10 can now have hope that treatment will be possible to prevent, halt or reverse blindness for them and their children.

“As we become more comfortable with treating these patients, there will be opportunities to treat younger patients before degeneration occurs and preserve vision at an earlier stage,” Lauer said.

The outlook is changing for previously untreatable retinal dystrophies, Pennesi noted.

“As ophthalmologists, we need to be aware of the evolving opportunities for these patients,” he said. “We are entering an era of new therapy for those who otherwise would become irreversibly blind. For the first time, we are offering hope for these patients and their families and improving quality of life.”

The clinical trial sponsored by Allergan/Editas Medicine continues with a second patient scheduled at another eye center. Casey Eye Institute treated the third patient on January 21, 2021 and will continue to participate and enroll patients.

“It is a tremendous privilege to be doing this work,” Lauer said. “We are trying to alter the way we practice medicine through innovation.”

An epicenter for ocular gene therapy trials

OHSU Casey Eye Institute has invested in creating ideal conditions for cutting-edge clinical trials by having facilities, staff and technology to push the boundaries of what’s possible. For example, we were one of the first institutions in the country to administer the first federally approved gene therapy for biallelic RPE65 mutation-associated retinal dystrophy. Resources that make this type of cutting-edge treatment possible include:

- Dedicated space in a new 60,000-square-foot building for the Paul H. Casey Ophthalmic Genetics Division, with imaging technology integrated into exam spaces and a mobility maze
- Intraoperative OCT
- Experienced surgical and OR team, which has performed more than 150 ocular gene therapy procedures
- Three ophthalmic geneticists
- Eight clinical trial coordinators
- 14 clinical trials investigating new genetic treatments for ophthalmic conditions
- 50 vision-related clinical trials overall
Using data analytics to solve real-world workflow challenges

OHSU Casey Eye Institute is a pioneer in the use of computers to support patient care. We were among the earliest adopters of electronic health record systems (EHRs) in the country. Utilizing data from these systems, OHSU Casey Eye Institute informaticists created novel computer models designed to maximize clinic productivity without reducing patient satisfaction. Using new scheduling templates based on these models, average wait times in pediatric eye clinics reduced by 15 percent while clinic volumes increased by 15 percent.

“OHSU Casey Eye Institute is unique in having a dedicated informatics group that works closely with clinicians,” said Michelle R. Hribar, Ph.D., a clinical informaticist working in Ophthalmology. “In doing this project, members of the informatics group spent hours in clinic observing and timing the workflow, getting to know the clinicians and talking with the scheduling staff. Our result is a model we believe other clinics can take and apply their data to with similar outcomes. Our next goal is to expand this model to other subspecialties in ophthalmology, such as glaucoma.”

OHSU Casey Eye Institute was one of the first institutions to use EHR audit log data for modeling clinic workflow. EHR systems are required to record audit logs that track users’ actions in the EHR, including timestamps. Hribar mined millions of timestamps from audit logs for the simulation models of clinic days at OHSU Casey Eye Institute. After thousands of simulations, Hribar learned how to plan

Simulations support reopening during pandemic

The simulation models were a huge asset when OHSU Casey Eye Institute began to ramp up patient volume following the initial COVID-19 shutdown. “We used the models not only to simulate wait times but to determine how to schedule patients using new safety guidelines. We looked at if we would have enough exam rooms if patients waited there for dilation instead of in the waiting room, for example, and how many patients would be in line waiting to check in at the front desk,” Hribar said. “As a result, we were able to confidently make decisions about how to reopen clinics safely and efficiently.”

Our studies showed that scheduling patients according to their visit lengths improved patient wait times. In the original schedule, patients with longer visits (darker icon) were often scheduled in the first appointments of the clinic so they wouldn’t extend the length of the clinic. This resulted in more wait times than when patients with shorter visits (lighter icon) were scheduled first in our new schedules.
“Wait times can be a barrier to good eye care. Research in this area is an important part of how we respectfully treat patients within the context of their lives, not just for more efficient clinics. That’s one way informatics fits into our philosophy of delivering better health.”

Michelle R. Hribar, Ph.D.

for patients more efficiently throughout the day.

“If you can schedule patients whose exams are going to take a short time and have less variability at the beginning of clinic, you can avoid the snowball effect of delays that lead to long wait times,” Hribar said. “Scheduling the patients with longer appointment times near the end of the clinic allows better wait times for everyone.”

Hribar recently received a grant to integrate the model into EHRs for use in real time by clinic schedulers. This will expand the models into more clinics at Casey and throughout OHSU. Hribar is also part of the National Research Network for Audit Log Data, a national group of more than 100 researchers using this type of data. She is leading a national workgroup developing measures based on audit log data; initial measures relate to clinician EHR burden.

“We hope our work will shape functionality and design of EHRs in the future,” Hribar said.

Informatics and big data have enormous potential for improving the patient experience, she believes.

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Elks Center for Ophthalmic Informatics

OHSU Casey Eye Institute is an international leader in ophthalmology informatics, which is the application of computer and information technologies to improve the quality and delivery of eye care. Casey’s Elks Center for Ophthalmic Informatics is an epicenter for innovation in using telemedicine and “big data” to improve the quality and delivery of ophthalmic care.
Investigating spectroscopic OCT to measure capillary oximetry

Ophthalmic imaging expert Yali Jia, Ph.D. and her team constructed a spectroscopic optical coherence tomography (OCT) instrument using visible-light band. They paired this instrument with a novel algorithm to extract the blood oxygen saturation in retinal capillaries in a preclinical model. Jia’s lab is the first to bring this technology to the capillary level.

“If we can detect vascular oxygenation alteration before patients have vascular morphological changes, it will be a breakthrough as an early marker of disease,” Jia said. “Detection of capillary oxygenation impairment is even more appealing than that of major vessels. This technology has applications for retinal diseases and glaucoma but could also impact imaging for all vascular diseases, including stroke.”

Jia’s lab is now concentrating on realizing this potential tool for clinical use. Compared to conventional methods, OCT oximetry can provide three-dimensional information on specific vessels. It is also efficient, since the data can be processed from the same scans that generate structural OCT and OCT angiography.

Using the same device, Jia’s lab has also worked to generate cellular-level retina images in a preclinical model by improving the hardware sensitivity and software registration accuracy. The images produced by visible-light OCT (vis-OCT) provide finer axial resolution than near-infrared OCT for a given wavelength bandwidth.

“Compared to other imaging modalities with cellular-level resolution, vis-OCT can maintain a depth of focus at a range encompassing nearly the entire retina. Using vis-OCT, these single neurons with different functions at different retina layers can be investigated simultaneously in a 3D volume scan.”

Jia believes vis-OCT could potentially replace traditional histology of tissue staining and collection.

“Vis-OCT is one of the most exciting new frontiers for clinical ophthalmology.”

Yali Jia, Ph.D.
Abundance of clinical trials

At OHSU Casey Eye Institute, we are rooted in a culture that questions the status quo and pushes the boundaries of what is possible. We are bringing new science and technology to the diagnosis and treatment of eye diseases. We accomplish this by creating a culture in which translational science can thrive. With dozens of clinical trials upcoming or underway, our clinician investigators collaborate with multidisciplinary research teams to make scientific progress toward eliminating preventable blindness for conditions such as retinitis pigmentosa, choroideremia, advanced dry macular degeneration. Some examples include:

- **Phase I/Ia Open Label Prospective Study of the Safety and Tolerability of the Human Retinal Progenitor Cell (hRPC) Therapy Candidate in the Treatment of Patients with Retinitis Pigmentosa.** (First patient treated January 12, 2021.)
- **STAR trial: A Randomized, Open Label, Outcomes-Assessor Masked, Prospective, Parallel Controlled Group, Phase 3 Clinical Trial of Retinal Gene Therapy for Choroideremia Using an Adeno-Associated Viral Vector (AAV2) Encoding Rab Escort Protein 1 (REP1).**
- **GEMINI trial: An Open-Label Safety Study of Retinal Gene Therapy for Choroideremia with Bilateral, Sequential Administration of Adeno-associated Viral Cector (AAV2) Encoding rab Escort Protein 1 (REP1). Phase I/I Study to Look at the Safety of Bilateral Administration of Gene Therapy for Choroideremia.**
- **BRILLIANCE trial: Open-Label, Single Ascending Dose Study to Evaluate the Safety, Tolerability, and Efficacy of EDIT-101 in Adult and Pediatric Participants with Leber Congenital Amaurosis Type 10 (LCA10), with Centrosomal Protein 290 (CEP290)-Related Retinal Degeneration Caused by a Compound Heterozygous or Homozygous Mutation Involving c.2991+1655A>G in Intron 26 (IVS26) of the CEP290 Gene (“LCA10-IVS26”).**
- **GALLEGO trial: A Phase II Multicenter, Randomized, Single-Blinded, Sham-Controlled Study to Assess Safety, Tolerability, and Efficacy of Intravitreal Injections of FHTR2163 in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration.**
- **GYROSCOPE: A Study of Disease Progression in Genetically Defined Subjects With Geographic Atrophy Secondary to Age-Related Macular Degeneration.**

Mobile eye clinic celebrates 10 years

OHSU Casey Eye Institute’s mobile eye clinic travels throughout Oregon to provide free eye exams with the purpose of identifying sight-threatening conditions in low-income adults before they can cause blindness. The mobile clinic is the only adult vision screening program in Oregon that offers complete eye exams under the supervision of an ophthalmologist who can diagnose serious eye conditions. OHSU Casey Eye Institute will be adding and equipping a second mobile clinic to expand coverage in 2021.

**OHSU Casey Community Outreach Program, 2010-present:**

- 300 clinic days held
- 10,015 people provided free eye exams
- 5,934 glasses prescriptions given
- 2,358 people received referrals for follow-up eye care
- 80 referrals for urgent needs that immediately threatened a person’s sight
- 28,482 volunteer hours
- 71 partner agencies and organizations have hosted the program’s mobile clinics

**New facility expands pediatric care and clinical trial capacity**

As 2020 came to a close, the new Oregon Elks Children’s Eye Clinic opened a new era in OHSU Casey Eye Institute. The new facility is a critical resource for growing programs to provide services for eliminating blindness. The Oregon Elks Children’s Eye Clinic is the nation’s first free-standing eye institute for pediatric patients. It is a world-class hub for innovative research, subspecialty patient care and leading-edge programs in gene therapy, preschool vision screening and telemedicine for retinopathy of prematurity. Also housed in the new building, the Wold Family Macular Degeneration Center will further Casey’s decades long work studying macular degeneration’s underlying causes and evaluating bench-to-bedside treatments, including gene and stem cell therapies. Additionally, the Ophthalmic Genetics Program will reside in the building to better accommodate the growing number of clinical trials, anticipating that patient volumes will triple in the next five years.

Above: Located next to OHSU Casey Eye Institute’s existing facility, the 60,000-square-foot Oregon Elks Children’s Eye Clinic houses research and patient care services for pediatric eye care, macular degeneration, ophthalmic genetics, imaging technology and more.

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