OHSU

CASEY EYE
Institute

Innovations

2022

JEFF FARRELL

Contents

From the directors

Long-term vision yields innovations

After celebrating 75 years as an institute, we reflect that innovation rarely happens in a flash of brilliance. Instead, innovations change health care after building on a sustained commitment to discovery. Throughout our history, OHSU Casey Eye Institute has invested in the long-term, foundational aspects of innovation, which has led to remarkable breakthroughs in vision health. In just one example, consider the advent of optical coherence tomography (OCT). This invention went from an interesting gadget to an essential tool that is rapidly advancing into new and novel applications. Many of our clinician scientists are stretching the concepts of what's possible with this technology, including investigating opportunities in ultrawide-field and visible-light OCT, handheld operation, artificial intelligence algorithms and more.

Another hallmark of our institute is the openness to multidisciplinary collaborations. Whether in cross-functional teams among our faculty or in multidisciplinary clinics across our health system, we see added value for our patients by working together. When someone suffers facial paralysis, for example, we are part of the team providing treatments to preserve corneal sensation and nerve transfer procedures.

Through all this work, we are also creating the clinicians and researchers of tomorrow. As examples, glaucoma researcher Ted Acott, Ph.D., has taught and mentored some of today's leading scientists in glaucoma research and John Ng, M.D., is one the most highly recognized instructors for oculoplastics in the country.

Still, we need more trained people to create access to eye care for preventing blindness, especially among the underserved and underinsured. That's why we are investing in community health programs to expand our reach throughout Oregon. We are currently training community health workers and clinical staff as vision health navigators in the Oregon Vision Health Network. Our first cohort of nine community health workers have finished training and are serving the rural community of Hood River, Oregon.

We are honored to share some of the highlights of this year's transformative work occurring at OHSU Casey Eye Institute. We are proud to be on the leading-edge of discovery while perpetuating inspiration in a new generation of innovators.

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ANDREAS K. LAUER, M.D.
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PETERSON PROFESSOR OF OPHTHALMOLOGY AND PROFESSOR OF BIOMEDICAL ENGINEERING; ASSOCIATE DIRECTOR, CASEY EYE INSTITUTE

Expediting care for adults and children with ocular impacts from facial paralysis

▶ John Ng, M.D., MS, FACS, is an orbital surgeon with expertise in ophthalmic plastic, orbital, lacrimal and reconstructive surgery for adult and pediatric patients. He is pictured here with other members of the Facial Nerve Center team during their multidisciplinary clinic at Casey Eye Institite.

The OHSU Facial Nerve Center housed inside the OHSU Casey Eye Institute offers multidisciplinary treatment for children and adults with facial nerve disorders. Our team includes some of the top experts in the nation in facial reconstructive and plastic surgery. John Ng, M.D., MS, FACS, chief of the Division of Oculofacial Plastics, Orbital and Reconstructive Surgery is the co-director of the center with reconstructive facial plastic surgeon and otolaryngologist Myriam Loyo Li, M.D.

"Facial paralysis is a fairly common issue, and one that has profound psychosocial effects. For maintaining eye health, the best care is early care. By centralizing all services in one physical location, we treat children and adults holistically, avoiding fragmented care and unnecessary delays for patients."

John Ng, M.D., MS, FACS

"Facial paralysis is a fairly common issue, and one that has profound psychosocial effects," Ng said. "For maintaining eye health, the best care is early care. By centralizing all services in one physical location, we treat children and adults holistically, avoiding fragmented care and unnecessary delays for patients. Our collaborative team evaluates each patient and determines a care plan. A combined surgical plan means we can often perform several procedures in one anesthetic operating room session."

The most common ophthalmic need in facial paralysis is eye protection. Bell's palsy, stroke and other facial nerve injuries can put the eyes at risk for corneal exposure from sagging lower eyelids and inability to completely close the eyelids. Ng provides medical and surgical procedures to improve these conditions for both temporary and long-lasting facial paralysis. Other nonsurgical therapies available include custom scleral lenses and rehabilitation services.

For patients with prolonged or congenital paralysis, Ng and the Facial Nerve team can provide nerve grafts, neurotized free muscle transfers and facial suspension. OHSU is the only center in Oregon with microsurgical procedures for nerve transfer and free muscle transfers for facial reanimation. Ng performs minimally invasive corneal neurotization, a technique of grafting a healthy donor nerve to the affected eye to restore sensation. Only a handful of centers around the country offer this corneal reinnervation expertise.

For patients with incomplete paralysis, hemifacial spasms and synkinesis, Ng uses selective chemodenervation (i.e., Botox treatments).

"Time is of the essence in facial paralysis," Ng said. "Our co-managed approach and combined multispecialty clinic all under one roof consolidates patient visits into as few trips as possible. This results in streamlined care that is better for all patients, but especially for those traveling long distances to the center, including most of the western states and Alaska."

OHSU FACIAL NERVE CENTER TEAM

- Pediatric plastic and reconstructive surgery
- Adult facial plastic and reconstructive surgery
- Otolaryngology surgery
- Oculofacial plastics, orbital and reconstructive surgery
- Head and Neck Oncology and Orbital Oncology
- Speech-language pathology
- Physical therapy, facial specialty
- Optometry, contact lens specialty
- Social work

CENTRAL HUB FOR PERIPHERAL NERVE DYSFUNCTION

The Facial Nerve Center is part of the OHSU Nerve Center, which is unique on the West Coast for our multidisciplinary approach to nerve disorders. We bring the collective expertise of neurology, neurosurgery, ophthalmology, orthopedics, otolaryngology/head and neck surgery, physical medicine and plastic surgery to bear on determining the right treatment options for each patient. Additionally, we have support systems for patients in the OHSU Rehabilitation Services, OHSU Comprehensive Pain Center and OHSU Neurology.

FACIAL NERVE TREATMENTS

- Nerve transfers and free muscle transfers (gracilis free muscle transfer)
- Regional muscle transfer and static suspension
- Selective surgical neurolysis and selective myectomy
- Surgery for brow and eyelid paralysis, including brow lift surgery, eyelid weight placement and ectropion correction
- Neuromodulation with botulinum toxin
- Scleral contact lenses
- Rehabilitation services, including mirror therapy, massage therapy, exercise, pain control and motor control therapy

TECHNOLOGY AND INNOVATION

Our specialists use the latest surgical techniques and the most advanced technology available anywhere.

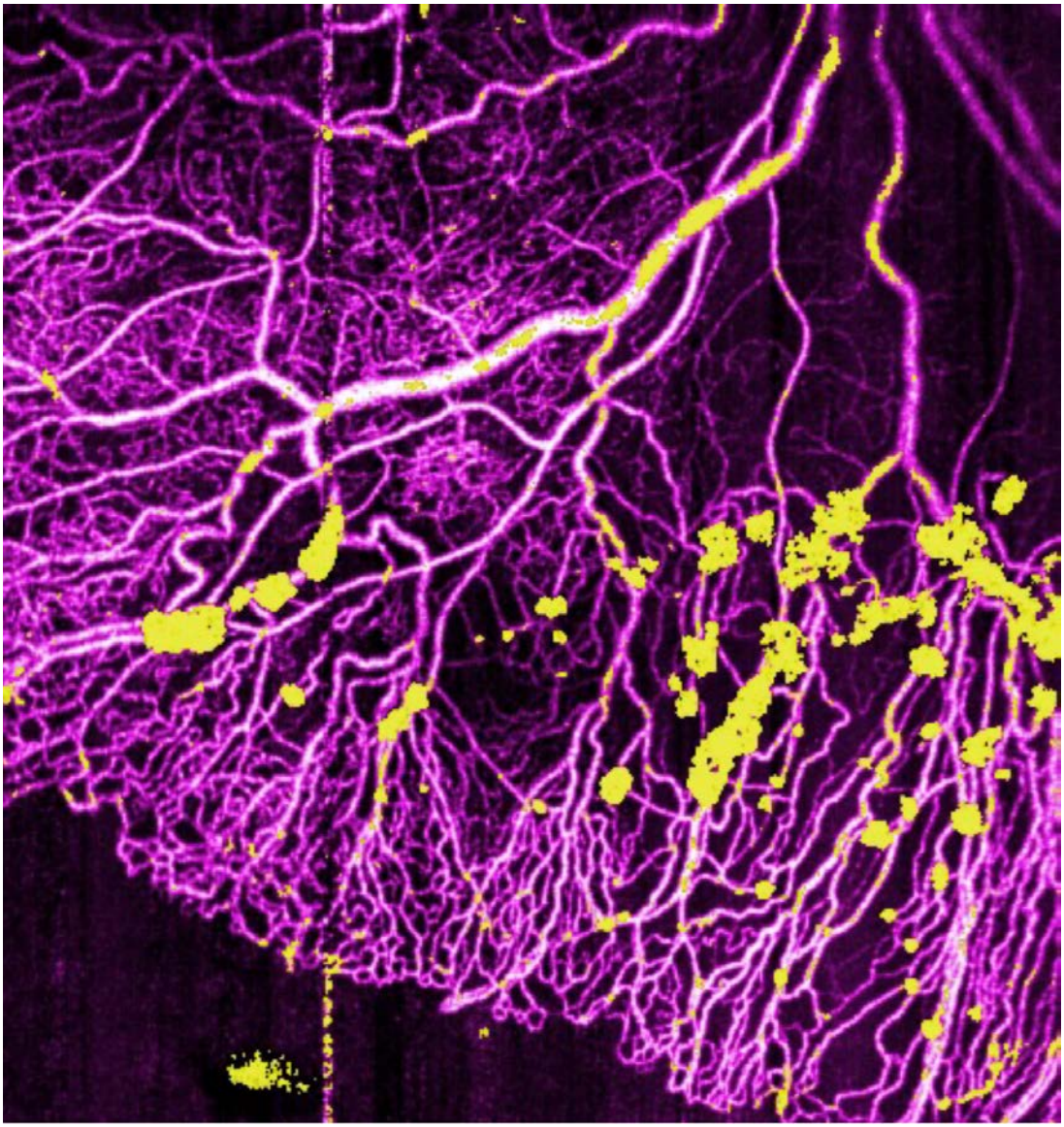
Microsurgical techniques to perform reinnervation for motor recovery in facial paralysis and sensory recovery of the cornea.

Intraoperative nerve stimulation to precisely identify nerves.

Cutting-edge technology for custom contact lenses.

Cutting-edge development of treatments for aberrant tearing management (crocodile tearing), including the Jones Tube, Frosted Jones Tube and Narrow Lumen Jones Tube – all invented at OHSU.

Groundbreaking work in ultrawide-field represents next evolution of optical coherence tomography



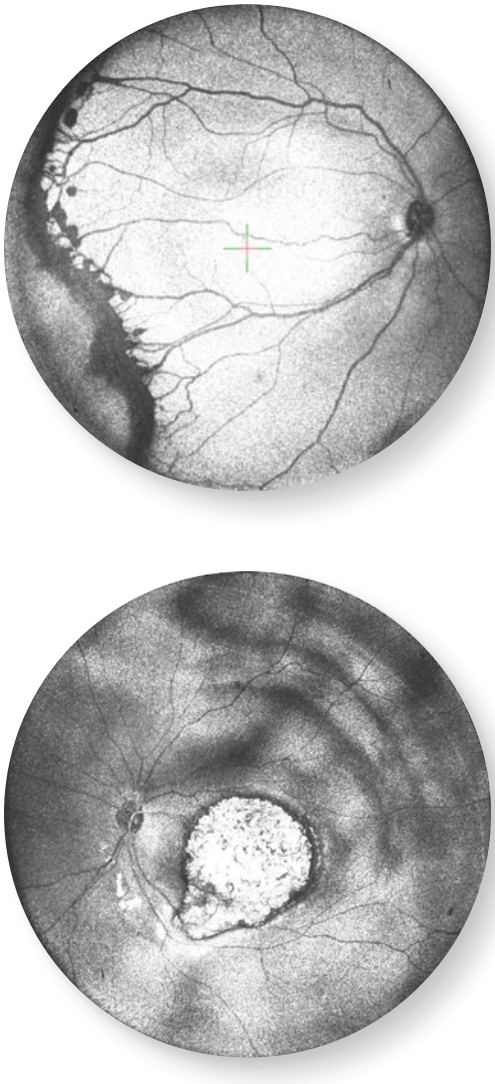
▶ 40-degree field-of-view en face retinal OCT angiography in an eye with incontinentia pigmenti show incompletely developed retinal vasculature and preretinal neovascularization (yellow).

OHSU Casey Eye Institute is a leader in noninvasive imaging technology to detect vascular changes in the eye, an underlying pathology of several eye diseases that can lead to blindness. A world-recognized leader in optical coherence tomography (OCT) structural and angiographic imaging, David Huang, M.D., Ph.D., runs the Center for Ophthalmic Optics and Lasers, or COOL Lab, at OHSU Casey Eye Institute. With his team, Huang is currently pioneering new applications of this extraordinary technology.

"In our original prototype, we were getting 40 axial scans, or image lines, per second," said Huang, who co-invented the technology in 1991. "Current OCT systems get hundreds of thousands of axial scans per second, making it feasible to image wide areas of the retina with ultrawide-field OCT systems. Several of our faculty are working on different applications. It's exciting because a lot of pathologies happen in the periphery of the eyes. This area of research represents an open canvas for designing innovative technology to improve clinical practices and standards."

Developing AI in diabetic retinopathy

Yali Jia, Ph.D., transformed OCT angiography (OCTA) by developing split-spectrum amplitude decorrelation angiography (SSADA), a highly efficient algorithm that made clinical OCTA feasible. Jia remains at the forefront of OCTA imaging research in retinal diseases. She's



▲ (Top) En face OCT image with a clear demarcation line from an infant (ROP, Stage 3) with preretinal neovascularization acquired by the handheld 105-degree OCT. (Bottom) En face OCT showing an elevated tumor from a 5-month-old patient with bilateral retinoblastoma.

▶ The imaging process of an infant in the neonatal intensive care unit with J. Peter Campbell, M.D., M.P.H., and Yifan Jian, Ph.D.

now developing an algorithm to provide fast, automatic and reliable biomarkers for diabetic retinopathy progression using ultrawide-field OCTA, a noninvasive method to detect capillary dropout and neovascularization.

"Dr. Jia's work is the most important recent advance for the evaluation of diabetic retinopathy, one of the top three blinding diseases," Huang said.

Inventing a handheld device for retinopathy of prematurity and retinoblastoma

Yifan Jian, Ph.D., has developed a portable ultrawide-field OCT/OCTA prototype that J. Peter Campbell, M.D., M.P.H., is using in the neonatal intensive care unit to examine infants for retinopathy of prematurity (ROP). The handheld device can obtain a 105° OCT or a 55° OCTA in just 1.5 seconds. This is ideal for detecting retinal neovascularization in the periphery. This noninvasive method provides rapid real-time data for disease screening in a population at risk for blindness.

Alison Skalet, M.D., an ocular oncologist at Casey Eye Institute, is using this ultrawide-field OCT system to evaluate the extent of ocular tumors and their response to treatment. The portable system is particularly useful in retinoblastoma, an eye cancer of childhood that can be fatal if not treated in time. Though developing this

"Current OCT systems get hundreds of thousands of axial scans per second, making it feasible to image wide areas of the retina with ultrawide-field OCT systems. Several of our faculty are working on different applications. It's exciting because a lot of pathologies happen in the periphery of the eyes. This area of research represents an open canvas for designing innovative technology to improve clinical practices and standards."

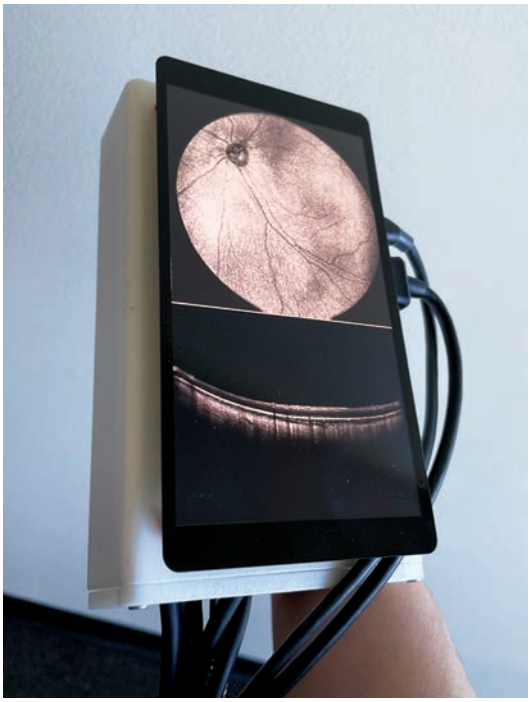
David Huang, M.D., Ph.D.

technology for pediatric patients, it may also translate to adults.

Pioneering new methods for scleral lens fitting

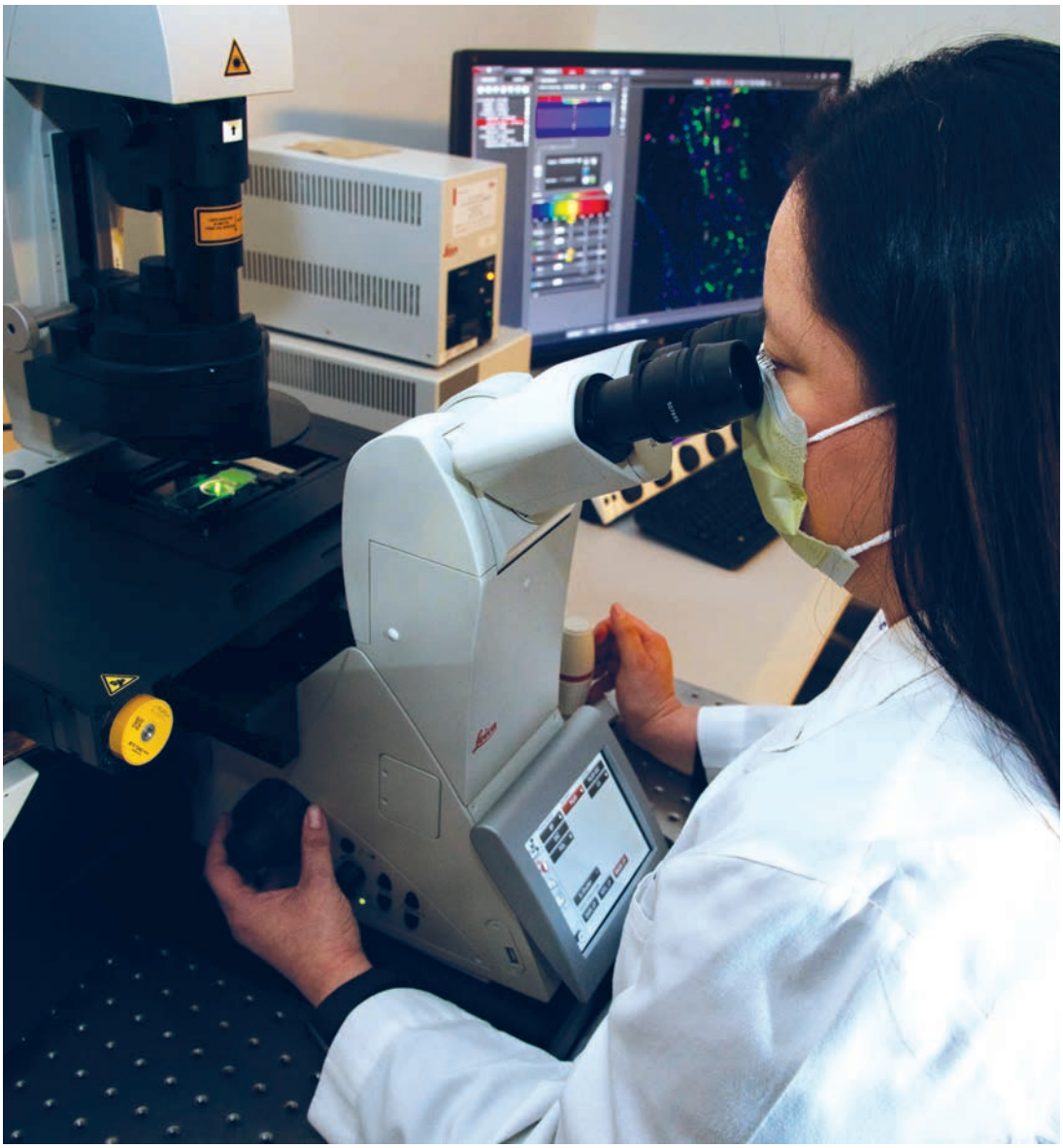
With more than 20 years of research together using OCT for the anterior of the eye, Huang and research assistant professor Yan Li, Ph.D., are now using an ultrahigh-speed/ultrawide-field OCT for corneoscleral topography. The prototype can scan 22 mm wide and 10 mm deep, covering the whole anterior eye. Their purpose is to improve scleral lens fittings for people with irregular ocular surfaces.

"We want to be able to map an individual's eye shape and provide a custom design for each eye, like a tailored suit that fits precisely for comfort and quality of vision." Huang said.



◀ (Left) A prototype of the portable handheld OCT device with OCT module and computer. (Right) A close-up of the probe with a 5.5-inch display capable of real-time en face visualization.

Extraordinary teamwork model generates breakthroughs in glaucoma research



▶ Diana Lozano, Ph.D., is a member of the glaucoma research team. Her research focuses on which gene and protein responses might protect from pressureinduced axonal injury.

Glaucoma researchers at OHSU Casey Eye Institute work cooperatively to improve glaucoma care. Many institutions study either anterior mechanisms that affect aqueous humor outflow dynamics or posterior mechanisms of glaucomatous optic nerve damage. In contrast, our glaucoma research encompasses both, forming a team that currently holds 14 grants, representing over $24 million in total funding from the National Institutes of Health.

"The longitudinal dedication and the sheer breadth of the work on the glaucoma problem by our group is remarkable," said clinician-scientist John Morrison, M.D., whose glaucoma research career began in the early 1980s.

Anterior research

Much of this impressive work builds on the research of Ted Acott, Ph.D., who has made crucial contributions over the last 40 years to understanding how aqueous humor outflow is regulated by the trabecular meshwork (TM) and how this affects glaucoma. Acott has mentored several members of the team who have stayed at OHSU to continue their basic science research. Areas of interest include:

- **TM:** Kate Keller, Ph.D., studies proteins and gene expression in TM cells and how cells communicate. She also studies the effect of netarsudil (Rhopressa) on the actin cytoskeleton and how it stimulates phagocytosis to clear outflow channels in TM tissue.
- **Stem cells:** Mary Kelley, Ph.D., winner of the 2017 Lewis Rudin Glaucoma Prize from the New York Academy of Medicine, is studying how autologous stem cells transplanted to the TM might restore intraocular pressure (IOP) homeostasis.
- **Gene variants:** Geneticist Mary Wirtz, Ph.D., has identified genes linked to glaucoma, including one variant that may affect TM tissue and eye pressure regulation. Studies are underway to elucidate the effects of this gene variant on TM cell function.
- **TM outflow:** The late Janice Vranka, Ph.D., investigated outflow regulation through the TM, showing how regional molecular and biomechanical differences in the extracellular matrix produce a pattern of high and low aqueous humor outflow regions.

Knowledge gained from these studies will lead to better understanding of the causes of glaucoma as well as improved treatments for increasing aqueous humor outflow and IOP, a major risk factor for glaucoma.

Posterior research

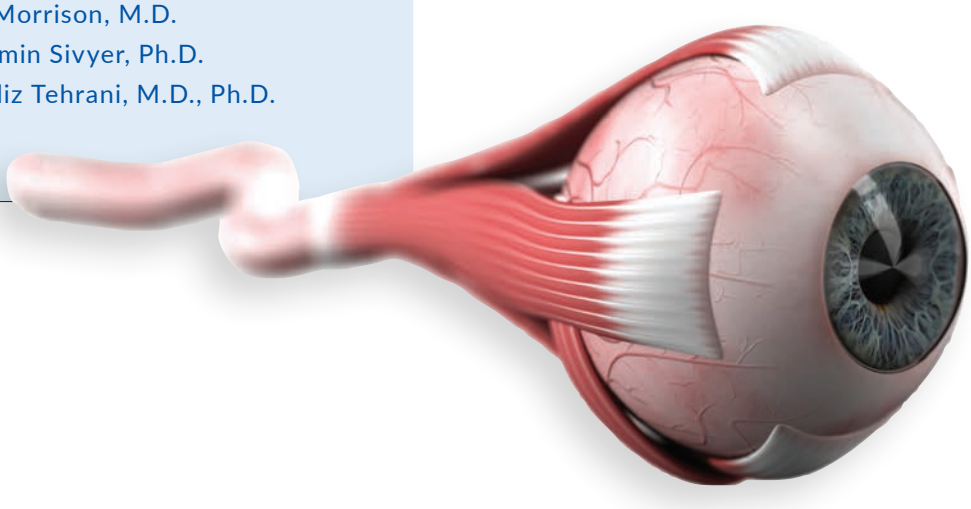
In the early 1990s, Morrison and his associate, Elaine Johnson, Sc.D., pioneered the development of preclinical models of glaucoma. They initially described gene and cellular responses to chronically elevated IOP within the optic nerve

head (ONH), the site of axonal injury in glaucoma. Later, they developed a short-term, acute pressure elevation model. This has led to work by several other investigators, including:

- **Diana Lozano, Ph.D.,** has demonstrated which cells are responsible for ONH gene and protein response in chronic glaucoma, and that similar responses can appear sequentially following a discrete, short period of elevated IOP. She is now using this knowledge to determine which gene and protein responses might protect from pressure-induced axonal injury.
- Vision neuroscientist **Benjamin Sivyer, Ph.D.,** is using this short-term model to study the impact of pressure-induced optic nerve damage on retinal ganglion cells and their projections to the brain, providing information that may lead to new approaches to help these injured cells survive. In collaboration with a national team of glaucoma researchers, Sivyer recently received a National Eye Institute Audacious Goals Initiative U24 grant to understand barriers to using stem cell therapy to replace retinal ganglion cells.
- Clinician-scientist **Shandiz Tehrani, M.D., Ph.D.,** has used both chronic and acute animal models to determine how ONH astrocytes respond to elevated IOP, and is now using the short-term model to determine how these cells influence glaucomatous nerve injury. He has also developed a unique method of small molecule delivery to uncover mechanisms of astrocyte response and explore new treatments for preventing axonal degeneration.

Casey Glaucoma Research Team

Ted Acott, Ph.D.
Aiyin Chen, M.D.
Beth Edmunds, M.D., Ph.D.
David Huang, M.D., Ph.D.
Eliesa Ing, M.D.
Hiroshi Ishikawa, M.D.
Yali Jia, Ph.D.
Kate Keller, Ph.D.
Mary Kelley, Ph.D.
Diana Lozano, Ph.D.
John Morrison, M.D.
Benjamin Sivyer, Ph.D.
Shandiz Tehrani, M.D., Ph.D.



Collaboration leads to innovative new research targets

These investigators have formed active collaborations among their team and with other OHSU Casey Eye Institute investigators. These synergies create opportunities, according to Keller.

"The collegial environment in all of our labs allows for a lot of mentoring and excitement in discovery," she said. "Our shared purpose is to take our collective research and design new and novel therapeutics for glaucoma."

Collaborative research examples include:

- Keller, Lozano and Morrison have combined their expertise in anterior and posterior glaucoma research to generate a newly funded grant to understand the gene profile of IOP homeostasis. "Because we are working in two different aspects of the eye, our team can ask and answer questions that lead us in new directions with translational potential," Morrison said. "For example, our preclinical model allows Dr. Keller to use the living trabecular meshwork to confirm observations she previously could only make using cell and organ culture techniques."
- Morrison and Yali Jia, Ph.D., associate director of OHSU Casey Eye Institute's Center for Ophthalmic Optics and Lasers (COOL Lab), have an NIH grant to develop visible-light OCT angiography (OCTA) to image blood flow and determine oxygenation of retinal capillaries. This technology may provide new insights into the pathogenesis of glaucoma and lead to new, early indicators of glaucoma progression.
- David Huang M.D., Ph.D., director of the COOL Lab and co-inventor of optical coherence tomography (OCT), is collaborating with glaucoma specialists Beth Edmunds, M.D., Ph.D., Aiyin Chen, M.D., and Eliesa Ing, M.D., Tehrani and Morrison, to develop novel objective functional and structural OCT and OCTA technologies for glaucoma. These translational studies, funded by the NIH, offer exciting new opportunities to detect early glaucoma, and improve the sensitivity and accuracy of detecting significant disease progression.
- Hiroshi Ishikawa, M.D., who is also funded by the NIH and makes use of glaucoma clinical and image data, is collaborating with the IBM Watson Research Team for developing various deep-learning applications in clinical glaucoma. These include glaucoma diagnosis and estimation and prediction of visual function based on 3D retinal imaging data.

Impacting the field

Forum addresses public health in global ophthalmology

Every other year, OHSU Casey Eye Institute hosts an international educational forum for leaders in the field to present evidence and discuss key aspects of ophthalmology in the public health setting. In 2021, our International Ophthalmology Program hosted a virtual summit in September. This year's topics included creating successful health initiatives in global ophthalmology, equity in eye health and implementing technological solutions to reducing global eye health disparities.

First free-standing eye institute for pediatric patients

The Oregon Elks Children's Eye Clinic celebrated its first year as 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. The new facility also houses the Wold Family Macular Degeneration Center and the Paul H. Casey Ophthalmic Genetics Program. The 60,000-square-foot building has allowed for the expansion of services and clinical trials, with 12 new faculty members joining the Casey team in 2021.

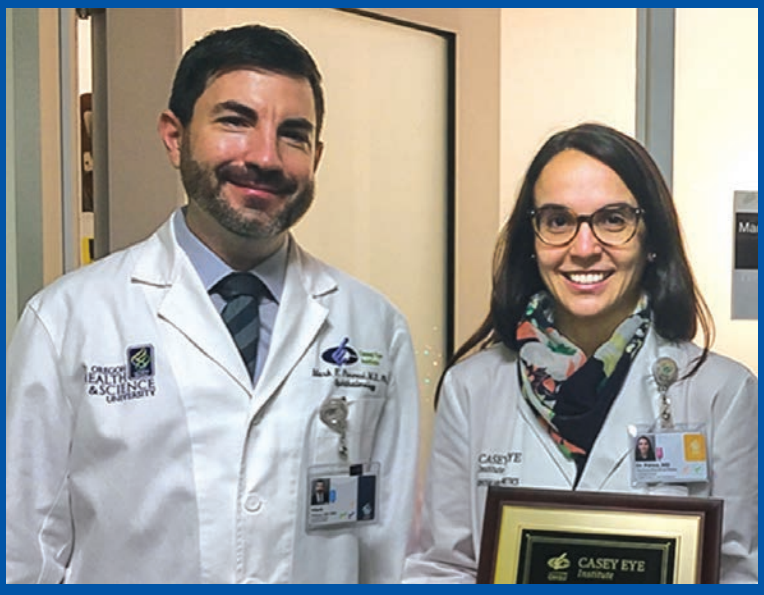
A unique feature of the Elks Children's Eye Clinic facility is a striking glass skybridge, which changes color in response to lighting conditions.

Philanthropy forwards public health efforts

With a recent $3.25 million dollar donation from The Roundhouse Foundation and Heather Killough, the Casey Community Outreach Program is expanding its ability to address critical vision health needs in Oregon using a three-pronged approach. The first is improving vision care access directly in local communities by training community healthcare workers. The second is increasing early detection of eye disease by expanding diagnostic testing through telehealth and informatics infrastructure. Lastly, deploying its second mobile eye care unit in the fall of 2022 will provide expanded vision care directly in communities throughout the state.

Support for vision loss at rehabilitation center

The Vision Rehabilitation Center at OHSU Casey Eye Institute offers assessment and treatment planning for the effects of vision loss. The only dedicated center in the region, the vision rehabilitation team includes optometrists, a social worker and a certified occupational and low vision therapist, Kathryn Marxen-Simonson, MSOT, OTR/L, CLVT. The team provides compassionate care with advanced diagnostic assessment and training in assistive technology to support vision loss. OHSU Casey Eye Institute also provides a vision loss patient support group in the Portland area.



International fellowship

Recipient of the 2021 Gillingham Pan-American Fellowship Experience, vitreoretinal surgeon Mariana Matioli da Palma, M.D. of São Paulo, Brazil served the fellowship at OHSU Casey Eye Institute. Her doctorate program is in the field of ocular genetics, an area that OHSU Casey Eye Institute is pioneering. In 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.

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