A winner of the Portland Design Commission's 3rd Annual Design Excellence Award, the new Elks Children's Eye Clinic is designed to accommodate the unique needs of eye care patients and evoke a sense of wonder. Features include:

- *Contrasting colors used throughout to help patients safely navigate their surroundings and dark, quiet areas for dilating patients.*
- *A striking glass sky bridge to Casey's existing building which dramatically changes color in response to outside lighting conditions.*
- *Welcoming outdoor areas, including a sensory garden with seating and pathways.*

Completion of New Eye Clinic Building within View

Less than two years after breaking ground, OHSU Casey Eye Institute's new Elks Children's Eye Clinic is on time and on budget for completion next summer. The five-story structure's glass and metal façade is taking shape and workers have begun installing special glass panels in the sky bridge that will connect to the existing Casey facility on Marquam Hill.

The 60,000-square-foot building will be the nation's first freestanding eye institute for pediatric patients and will also house the Wold Family Macular Degeneration Center, retina services, the Paul H. Casey Ophthalmic Genetics Division, vision rehabilitation and a clinical trials center.

"The expansion project demonstrates Casey's strong commitment to ending preventable blindness in Oregon and beyond," said Casey director David Wilson, M.D., adding that it will give Casey the necessary tools, technology and collaborative space to build on its strengths in patient care, research and community outreach.

The new facility will help grow patient capacity by a third in 10 years and enable gene therapy clinical trials and treatments to quadruple in five years.

The $50 million building is made possible by a $20 million pledge from the Oregon State Elks, a $7.5 million donation from the Wold family, a $5 million bequest from Paul Casey and numerous gifts from other generous supporters.

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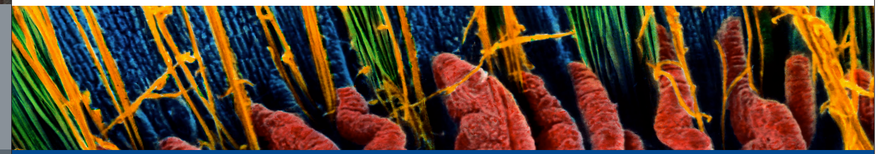


Publications

Between May and October 2019, Casey Eye Institute faculty published 78 research papers in leading national and international medical journals. Here is a sampling of some of this important work.

Detection of nonexudative choroidal neovascularization and progression to exudative choroidal neovascularization using OCT angiography. Bailey ST, Thaware O, Wang J, Hagag AM, Zhang X, Flaxel CJ, Lauer AK, Hwang TS, Lin P, Huang D, Jia Y. Ophthalmol Retina 2019; 3:629-36.

Casey clinicians and scientists studied the use of optical coherence tomography angiography (OCT-A), an imaging technology largely developed at Casey, to the diagnosis of "wet" and "dry" macular degeneration. This paper demonstrates potential applications of OCT-A to improve the monitoring and treatment of patients with macular degeneration.

Lipid nanoparticles for delivery of messenger RNA to the back of the eye. Patel S, Ryals RC, Weller KK, Pennesi ME, Sahay G. J Control Release 2019; 303:91-100.

Remarkable advances have occurred in gene therapy for inherited retinal degenerations, which were previously considered untreatable. Casey performs more gene therapy trials than any other institution in the country. In this paper, Casey researchers and collaborators study the use of lipid nanoparticles to deliver messenger RNA to the retina. This paper may provide new approaches for gene therapy.

Corneal higher-order aberrations in Descemet Membrane Endothelial Keratoplasty versus Ultrathin DSAEK in the Descemet Endothelial Thickness Comparison Trial: a randomized clinical trial. Duggan MJ, Rose-Nussbaumer J, Lin CC, Austin A, Labadzinzki PC, Chamberlain WD. Ophthalmology 2019; 126:946-57.

Casey clinicians, researchers, and collaborators report findings from a clinical trial comparing two methods of performing corneal transplantation surgery. Casey surgeons are at the forefront of developing and testing new procedures, and this paper helps identify the best surgical procedures for patient care.

Automated fundus image quality assessment in retinopathy of prematurity using deep convolutional neural networks. Coyner AS, Swan R, Campbell JP, Ostmo S, Brown JM, Kalpathy-Cramer J, Kim SJ, Jonas KE, Chan RVP, Chiang MF. Ophthalmol Retina 2019; 3:444-50.

Casey investigators and collaborators developed an artificial intelligence system for measuring the quality of retinal images. Technologies such as imaging, telemedicine, and artificial intelligence have revolutionized eye care, yet images must be of adequate quality for diagnosis. This paper provides a method for automatically measuring image quality.

Using registry data to characterize the incidence and causes of blindness in Oregon. Brinks MV, Redd T, Lambert WE, Zaback T, Randall J, Field T, Wilson D. PLos One. 2019; 14:e0220983.

Casey clinicians and researchers identify the leading causes of blindness in Oregon by analyzing registry data over several decades. This paper is significant because previously, there was little reliable data about the prevalence of blinding eye disease in Oregon. Understanding these causes will allow for better approaches toward improving eye health on a population level.

CASEY EYE *Institute*
OHSU

WINTER 2020

Researchers Join Forces in Tackling Glaucoma

Glaucoma is a sneaky disease. Its damage is subtle and gradual, and may even begin before you notice problems with your eyesight. However, its effects are irreversible and can lead to significant visual disability.

Nearly 3 million American are living with glaucoma, considered a leading cause of permanent blindness worldwide. Although the disease can be detected during a dilated eye exam and managed with medical, laser and surgical treatments, in many cases, those measures may be too little, too late.

While some glaucomas are related to a specific medical condition, how and why the disease develops remains unclear for the majority of cases.

Kate Keller, Ph.D., (foreground) and Ted Acott, Ph.D., (background) are among a team of Casey scientists conducting innovative glaucoma research on the aqueous humor and trabecular meshwork. (OHSU)

At OHSU Casey Eye Institute, scientists are working together to better understand glaucoma's underpinnings, gaining insights that will lead to new and more effective ways to diagnose and treat glaucoma before damage occurs.

Their accomplishments are an outgrowth of Casey's decades of leadership in the field of glaucoma research, which continues to earn international recognition and attract significant funding from the National Institutes of Health, Research to Prevent Blindness and other leading organizations. In October, Casey scientists Ted Acott, Ph.D., John Morrison, M.D., and other glaucoma researchers played prominent roles in a symposium sponsored by the International Society for Eye Research and the Bright Focus Foundation.

"Many patients are affected by the limitations, costs and side effects of our current therapies. This is what drives the collaborations between practitioners and researchers, creating a sense of urgency to address all aspects of the disease," said Beth Edmunds, M.D., Ph.D., director of Casey's glaucoma division and associate professor of ophthalmology.

DIFFERENT ANGLES OF INVESTIGATION

Glaucoma affects the area in front of the lens (anterior) as well as the back of the eye (posterior), and researchers typically focus their work on one of these regions.

At the Lamfrom Biomedical Research Building on the OHSU campus, NIH-supported investigators such as Janice Vranka, Ph.D., are studying the molecular properties that

(continued on page 4)

Dear Friends

The year is 2020, but Oregon's vision is 20/80. That's the corrected vision of most of the state's population who have macular degeneration, glaucoma or diabetes - the three major causes of blindness in Oregon (go to url for our methodology). People with 20/80 vision that can't be corrected with lenses or treatments may have difficulty doing everyday tasks, and are at risk of social isolation, depression and shorter life span.

While it may seem strange to measure the vision of a state, it gauges our progress toward ending preventable blindness in Oregon. The good news is that we are making headway in our mission through the combined efforts of research scientists, government-sponsored funding, pharmaceutical company investment and donor-supported programs.

Much of our progress is due to such remarkable developments as optical coherence tomography. As you will read in this issue, this noninvasive technology detects early complications of glaucoma, macular degeneration and diabetic eye disease so treatment can begin before severe vision loss occurs. New biologic therapies offer effective treatments for macular degeneration and diabetic eye disease, conditions that before lead to blindness. And gene therapy now holds the promise of correcting a group of inherited eye conditions largely responsible for childhood blindness.

Yet much work remains to improve Oregon's vision to 20/40, which has little vision impairment. Meeting that target will require greater public awareness of the importance of sight. For 2020, we have developed a host of activities to enable an exchange of ideas on this topic. The Eye Love Project (www.theeyeloveproject.com) is a mobile multi-media exhibit that celebrates the wonder of vision and drives awareness of the importance of eye health. The year 2020 is a great opportunity to consider the prevalence and impact of eye disease. I hope you will join us and participate in The Eye Love Project.

Sincerely,
David J. Wilson, M.D.
Thiele-Petti Chair, Department of Ophthalmology

Honors and Awards

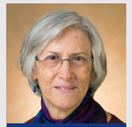
Derek Louie, O.D.

Derek Louie, O.D., was elected president of the Oregon Board of Optometry for 2020. He has served on the governor-appointed board for the past four years.

John Ng, M.D., has been appointed to the editorial board of the Ophthalmic Plastic Orbital and Reconstructive Surgery Journal

Alison Skalet, M.D., Ph.D., was selected as an F1000Prime Faculty Member. These peer-nominated, internationally-renowned researchers select and recommend articles they consider to be highly important to others working both in their field and beyond.

Hiroyuki Nakai, M.D., Ph.D., received the Stein Innovation Award from Research to Prevent Blindness. The $300,000 award supports his work developing viral vectors for ophthalmic gene therapy.



Martha Neuringer, Ph.D.

Martha Neuringer, Ph.D., received the Helen Keller Award at the 10th annual Gained in Translation Symposium at OHSU. The award recognizes a scientist whose body of work is well-respected and has translational components that contribute to reducing suffering from blindness.

Shandiz Tehrani, M.D., Ph.D., was invited to participate as an expert on the U.S. Preventive Task Force's "Screening for Impaired Visual Acuity and Glaucoma in Older Adults."

Kate Keller, Ph.D., and **Michael F. Chiang, M.D.,** received a five-year, $765,000 NIH grant to train vision research scientists. The competitive grant program provides salary funding for graduate students in the laboratories of **Catherine Morgans, Ph.D., (Colin Wakeham**) and **Ted Acott, Ph.D., (Samuel Berk),** and a postdoctoral fellow in the laboratory of **Yan Li, Ph.D.,** and **David Huang, M.D., Ph.D., (Elias Pavlatos).** Berk also is a recent recipient of OHSU's Tartar Trust Fellowship, which supports research career development in the School of Medicine.

Tackling Glaucoma

continued from page 1

control the way fluid is transported across the trabecular meshwork (TM), a spongy triangle of tissue at the front of the eye. Open-angle glaucoma is the most common form in Western populations and often develops when the fluid inside the eye – called the aqueous humor – is hindered as it flows out through the TM. This obstruction causes a build-up of pressure that over time can harm the optic nerve and cause vision loss.

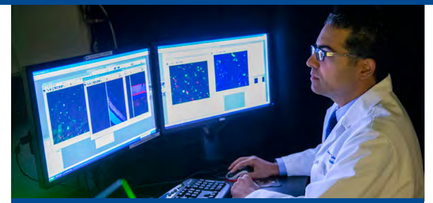
Shedding light on the inner workings of the TM is key to the development of improved glaucoma therapies, said Vranka, assistant professor of ophthalmology.

For Kate Keller, Ph.D., understanding how proteins in the TM regulate eye pressure may lead to new glaucoma treatments. In healthy eyes, TM cells manufacture proteins that aid the flow of the aqueous humor, said Keller, associate professor of ophthalmology.

"But in glaucoma, these proteins are slightly different and may cause the outflow channel in the trabecular meshwork to become clogged. Our aim is to look at the differences in these proteins and better understand how they are organized differently than proteins in healthy eyes," said Keller, whose research was recently published in the journal of Investigative Ophthalmology and Visual Science.

Keller is also collaborating with Mary Wirtz, Ph.D., professor of ophthalmology and molecular & medical genetics, whose lab is zeroing in on genes linked to glaucoma. Several years ago, Wirtz identified a gene variant in large families with glaucoma that may contribute to the TM's proper functioning, said Wirtz, who is teaming up with Keller to learn more about the gene's interactions and role in regulating eye pressure. "The exciting thing about these discoveries is that they will contribute to better cures that correct this gene mutation."

Their colleague, Mary Kelley, Ph.D., is also focusing on the TM, adopting a different yet equally intriguing approach. An associate professor of ophthalmology, she is the principal investigator of an NIH study examining the role of stem cell therapy in treating glaucoma. In 2017, Kelley won the prestigious Lewis Rudin Glaucoma Prize from the New York Academy of Medicine for showing for the first time that specialized TM cells can be created from stem cells, reintroduced into eyes with glaucoma and correct the underlying cause of the disease.



Shandiz Tehrani, M.D., Ph.D., views images of ocular tissue from a confocal microscope. Dr. Tehrani is exploring novel treatment approaches for glaucoma. (OHSU)

Much of this impressive work is built on the research of Acott, who for nearly 40 years has made crucial contributions to our understanding of how the aqueous humor is regulated and how this affects glaucoma. Acott, professor of ophthalmology and biochemistry & molecular biology, was a keynote speaker at the October international symposium, serves on the editorial boards of several leading medical journals and has been recognized for mentoring numerous glaucoma researchers.

FOCUSING ON THE OPTIC NERVE

"We have a strong research group studying the front of the eye, but that is only part of the story," said Morrison, explaining that scientists also want to understand the changes that occur in the back of the eye when eye pressure is elevated, especially before glaucoma is detected.

Morrison, whose glaucoma research spans three decades, is joining forces with other Casey investigators studying retinal ganglion cells and their axons, which form the optic nerve and send images to the brain. The optic nerve, composed of approximately a million retinal ganglion cell axons, exits the eye at the optic nerve head, which is the initial site of injury from glaucoma. Morrison, who is professor of ophthalmology, is particularly interested in learning how these cells' genes, and those of the optic nerve head, respond to the accumulating effects of elevated eye pressure and damage the optic nerve.

One of those researchers, Benjamin Sivyer, Ph.D., recently was awarded a major grant from the BrightFocus Foundation to develop more sensitive methods for studying the onset of glaucoma. Sivyer, assistant professor of ophthalmology, said his goal is to pinpoint beginning changes to retinal ganglion cells following injury to the optic nerve. "We hope our research will lead to earlier diagnosis of glaucoma," he said, and more importantly, uncover mechanisms in the retina that will slow or stop the death of these cells.

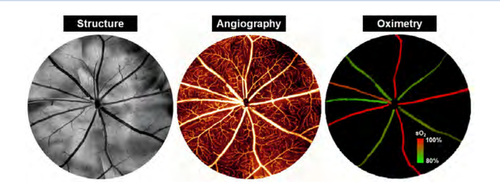
Physician-scientist Shandiz Tehrani, M.D., Ph.D., associate professor of ophthalmology, is among the first to repurpose a small molecule drug to prevent optic nerve axons from degenerating. Called fasudil, the drug is approved for use outside the U.S. for stroke and other neuro-degenerative conditions.

"Our early findings showed that fasudil protected optic nerve axons by 50 percent in a small animal model of glaucoma. This was our first clue that a small molecule administered as a drop, injection or pill may directly protect axons against glaucoma," said Tehrani, whose work is supported by the NIH and Research to Prevent Blindness. Tehrani and his team hope these investigations will eventually pave the way for new neuroprotective glaucoma therapies.

Innovative Imaging Tools Probe Glaucoma's Effects

OHSU Casey Eye Institute scientists are harnessing the power of advanced imaging technologies to learn what changes may occur in the back of the eye in patients with glaucoma.

At the heart of this work is the development of Optical Coherence Tomography (OCT), a commonly used, noninvasive technique that uses light waves to capture highly detailed cross-sectional images of the inner eye. Led by David Huang, M.D., Ph.D., professor of ophthalmology and biomedical engineering, and co-inventor of OCT technology, a team of scientists at the Casey Center for Ophthalmic Optics and Lasers (COOL) lab has been using this technology to devise new ways of monitoring tissue loss in glaucoma. This includes the addition of software that allows them to map out the eye's smallest capillaries and measure blood flow in seconds.



These visible-light OCT images show the inner eye's structures, blood flow and oxygen content of capillaries. Researchers are studying this technology to improve early detection and management of glaucoma (OHSU/Yali Jia, Ph.D.)

In collaboration with Casey Eye Institute's glaucoma investigators, COOL lab researchers are now determining how retinal blood flow is altered in glaucoma, and how this might be improved by conventional pressure-lowering glaucoma treatments.

Recently, COOL lab ophthalmic imaging expert Yali Jia, Ph.D., and glaucoma physician-scientist John Morrison, M.D., have begun collaborating on research using an enhanced type of optical coherence tomography called visible light OCT.

This newer OCT system, developed by Jia and her team at Casey, builds on these current imaging technologies by employing a laser with visible light to determine oxygen content within retinal blood vessels.

Currently, the researchers are refining visible light OCT technology so it is capable of measuring oxygen levels in the capillaries most likely affected by glaucoma, said Jia, associate professor of ophthalmology and biomedical engineering. Altered oxygen levels may be early signs of glaucoma's progression and affect a patients' susceptibility to elevated eye pressure.

"Visible light OCT provides a meaningful interpretation of the effects of glaucoma in 'real time,'" said Morrison, professor of ophthalmology. "We hope these investigations will provide new insights into the disease and improve our ability to detect and manage glaucoma in its earliest stages, before vision is affected."