

F.Y. eye

A QUARTERLY NEWSLETTER

Casey takes on unique challenges of eye cancer

Casey Eye Institute's ocular oncology program is one of the few of its kind in the Pacific Northwest and the only one in Oregon. Ocular oncologists Alison Skalet, M.D., Ph.D., and David Wilson, M.D., work with a team of radiation oncologists, eye pathologists, medical oncologists and specialists in retina, cornea and oculofacial plastic surgery to treat patients of all ages with both non-cancerous and cancerous tumors.

Here's a look at some of our most recent innovative efforts in the lab, community and clinic to combat cancers of the eye.

OCULAR MELANOMA: EXPLORING NEW AVENUES TO SAVE LIVES



Alison Skalet, M.D., Ph.D., is conducting leading-edge research to improve the diagnosis and treatment of eye cancers.

Last fall, Stephanie Arnet was days away from relocating to the Pacific Northwest when she began to lose vision in her right eye. Stationed in Virginia with the U.S. Army, the married mother of three was told she had ocular melanoma, a rare and aggressive type of eye cancer that mainly strikes adults.

"Luckily, I was being transferred to Portland, where Casey Eye Institute has one of the top programs in the country" for eye cancer, said Stephanie, who is a military recruiter.

In February, Dr. Skalet, treated the 30-year old with plaque brachytherapy, in which a tiny device that delivers a highly concentrated dose of radiation to the tumor is temporarily implanted in the eye.

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Dear Friends

ONWARD. That's the theme of OHSU's current campaign to transform human health. The initiatives profiled in this issue clearly demonstrate how Casey is embracing this theme on all fronts - from construction of a new facility that will enable all of our programs to grow and thrive, to innovative efforts in research and patient care.

Happily, the new building's plans were not only approved by the Portland Design Commission, they were applauded. In the words of the commission's chair, "... we hope that you (NBBJ, the project's architects) will design many more buildings in Portland. Our only regret is that the building is not downtown, so that more people will see it." I look forward to keeping you informed about the project's progress and the unique features that will make it a "site for the senses."

This issue also features Casey's Ocular Oncology service, which is a vital resource for children and adults with cancer of the eye. Proper care of these uncommon but potentially lethal conditions requires a highly skilled multidisciplinary care team. As the article describes, Dr. Alison Skalet has expanded this critical service by bringing new diagnostic and treatment advances to the care of these patients.

Similarly, Casey's Vision Rehabilitation Center is an essential resource for those with severe vision loss. This year we have added a provider who will be a great asset to this service, helping people of all ages make the most of their remaining vision.

Sincerely,

David J. Wilson, M.D.

Thiele-Petti Chair, Department of Ophthalmology

Director, Casey Eye Institute

A site to behold: Casey celebrates groundbreaking of new facility

With expansion, sight-saving programs can flourish

The Casey Eye Institute community - including longtime partners from the Oregon State Elks - celebrated the groundbreaking of the new Elks Children's Eye Clinic in early June. Located adjacent to the eye institute on Marquam Hill, the 60,000 square-foot building is named in honor of the fraternal organization, which pledged \$20 million toward construction of the new facility.

During the ceremony, Casey director David Wilson, M.D., noted that the aim of the expansion is to address the challenge of preventable blindness. The new facility not only will be the nation's first free-standing eye institute for pediatric patients, it will also house leading-edge programs for macular degeneration, genetic eye disease, imaging technology and more.

Joining Dr. Wilson on the podium were OHSU president Joseph E. Robertson, M.D., M.B.A., and Jim Damon, of the Oregon State Elks Association.



With shovels in hand, Jim Damon, L, Dr. David Wilson, center and Dr. Joe Robertson, R, officially kick off construction of the new Elks Children's Eye Clinic. The building is set to be completed in 2020.

Please join us in fulfilling this vision

For more information about the Casey expansion project, please contact Sarah Nevue, Senior Director of Development, OHSU Foundation at 503-552-0683.

Honors and Awards



Phoebe Lin, M.D., Ph.D.

Phoebe Lin, M.D., Ph.D., was selected as the first recipient of the OHSU School of Medicine's Physician-Scientist Transitional Support Award. Dr. Lin, who is associate professor of ophthalmology, OHSU School of Medicine, will receive \$100,000 over a two-year period to pursue basic research in ocular immunology.

The award is meant to sustain the momentum for junior physician-scientists who have established a promising path to discovery and who need to bridge the funding gap while they seek long-term research support.

"Her experience and scholarly productivity as a physician-scientist are remarkable, and we are highly confident that she will succeed in transitioning to an R01 (independent funding) during her time in the program," the selection committee wrote.

Dr. Lin, who specializes in inflammation of the eye – or uveitis – said that being a clinician-scientist takes time and effort, but is immensely rewarding. She is particularly motivated by the need for more effective uveitis treatments.

"I'm asking the questions my patients inspire me to ask, designing experiments to answer those questions and testing them in my lab," she said in a School of Medicine blog post. "And while it may not help them today, I hope it will help patients 10 years down the line."

Dr. Lin also recently received a \$50,000 2018 Alcon Research Institute Young Investigator Grant to fund her research studying alterations in the gut microbiota associated with advanced age-related macular degeneration.

Mary J. Kelley, Ph.D., associate professor of ophthalmology, OHSU School of Medicine, was a recipient of a Shaffer Grant for Innovative Research. The \$40,000 award, given by the Glaucoma Research Foundation, will support Dr. Kelley's work exploring novel glaucoma treatment approaches.

Stephen Planck, Ph.D., professor of ophthalmology, OHSU School of Medicine, was honored with the prestigious School of Medicine's 2018 Dr. Edward J. Keenan Faculty Award for Distinguished Teaching of Medical Students. Dr. Planck, who has taught courses on the histology of the eye, was recognized for his many years of outstanding teaching and mentorship to OHSU medical students.

Benjamin Sivyver, Ph.D., assistant professor of ophthalmology, OHSU School of Medicine, received the Dr. Douglas H. Johnson Award for Glaucoma Research from the Bright Focus Foundation. The \$150,000 award will support Dr. Sivyver's work studying glaucoma-induced changes in retinal cells. It is a collaborative project between the Sivyver and Morrison laboratories at Casey and the von Gersdorff laboratory in the OHSU Vollum Institute.

Three OHSU researchers received funding awards from the Knights Templar Foundation to support vision related research:

Patrick C. Kerstein, Ph.D., a postdoctoral fellow with the OHSU Vollum Institute, received \$65,000 to examine how a unique retinal nerve cell expresses an important developmental gene and enables people to perceive light intensity, contrast, orientation and motion.

Allison Loh, M.D., assistant professor of ophthalmology, OHSU School of Medicine, received \$57,000 to develop a non-invasive imaging method to detect glaucoma in children before the condition causes irreversible blindness.

Dan Jiang, Ph.D., a postdoctoral researcher at Casey Eye Institute, received \$65,000 to evaluate a drug's ability to treat inherited retinal degeneration, the cause of blindness in about 4.5 million people worldwide.



Accompanied by members of the Knights Templar Foundation are L to R: Allison Loh, M.D., Patrick Kerstein, Ph.D. and Dan Jiang, Ph.D.

Unique eye cancer challenges

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Stephanie's recent follow-up visit at Casey showed she has responded well to the treatment, which is considered highly effective for her condition. "It was tough waiting and not knowing what would be found at the exam," she admitted.

Physician-scientists like Dr. Skalet are determined to lessen some of the uncertainties of ocular melanoma by searching for better ways to predict and detect the spread of the disease and monitor response to treatment.

Ocular melanoma arises from cells that produce the dark-colored pigment melanin. Diagnosed in about 2,000 adults in the U.S. each year, it can spread to other organs – especially the liver – but remain undetectable for many years even with conventional imaging and blood tests, according to the Ocular Melanoma Foundation. Although their names are similar, ocular melanoma is distinct from the more common melanoma of the skin.

"As treatment options improve for this disease, it's vitally important we identify patients whose cancer is likely to metastasize," said Dr. Skalet, associate professor of ophthalmology, OHSU School of Medicine, adding that a promising new drug is currently being tested in clinical trials.

"If successful, this project will be the first step in creating a noninvasive and repeatable 'liquid biopsy' for patients with ocular melanoma."

– Alison Skalet, M.D., Ph.D.

A "liquid" biopsy for eye tumors

In other types of cancer, tissue biopsies of the tumor help doctors learn more about the patient's tumor and its chances of spreading. Since taking a biopsy of the eye tumor is technically challenging and poses risk to vision, Dr. Skalet and her basic science collaborator, Melissa Wong, Ph.D., are investigating less invasive and possibly more effective alternatives. Dr. Wong is an associate professor in the

Departments of Cell, Developmental, and Cancer Biology, OHSU School of Medicine.

Earlier this year, Dr. Skalet was awarded \$150,000 by the American Association for Cancer Research and the Ocular Melanoma Foundation to pursue novel research of a recently recognized type of tumor cell called "circulating hybrid tumor cells" or CHCs.

The research will involve evaluating the numbers of CHCs in the blood of ocular melanoma patients, said Dr. Skalet. "We will study whether CHC levels predict the risk for spread of the tumor, comparing this to existing tumor testing methods and clinical staging. We will also determine whether we can isolate CHCs from the blood to perform the same testing that currently requires tumor biopsies.

"If successful, this project will be the first step in creating a noninvasive and repeatable 'liquid biopsy' for patients with ocular melanoma. It will allow all patients to benefit from the newest predictive testing and open the door to repeated testing over time to detect metastatic disease and monitor responses to treatment," she said.

Measuring levels of CHCs in the blood also may help with early diagnosis of ocular melanoma in the future, said Dr. Skalet, who also recently received a separate \$40,000 grant from the Medical Research Foundation to pursue research in this area. "Studies of this unique cell population may transform how we diagnose and monitor patients with ocular melanoma. I am hopeful we will make discoveries that improve patient survival for this deadly disease."

CHILDHOOD EYE CANCER: CATCHING IT EARLY, EXPANDING TREATMENT OPTIONS

Dr. Skalet is also working to make sure that children with a form of eye cancer called retinoblastoma have the best opportunity of retaining vision and surviving the disease. From 2015 to 2017, she served on

an expert panel from the American Association of Ophthalmic Oncologists and Pathologists which published the first set of screening guidelines for children at risk for retinoblastoma. Dr. Skalet was the first author of the consensus report, which appeared in the March 2018 issue of *Ophthalmology*.

“Retinoblastoma, which can be inherited, is the most common eye cancer in children,” said Dr. Skalet. “However, survival and vision outcomes are excellent if retinoblastoma is diagnosed and treated in the beginning stages, when tumors are small.”

The report outlines a strategy for screening eye examinations based on a child’s risk for disease and recommends that children with a family history of retinoblastoma undergo genetic testing early on to clarify their risk. Youngsters who do not carry the gene mutation can avoid unnecessary eye exams while those who test positive need to be followed closely as they are very likely to develop the disease.

“Our goal is to improve outcomes for at-risk children by raising awareness of the need for dedicated eye exams and improving access to genetic counseling and testing,” said Dr. Skalet. The guidelines have been endorsed by a number of medical organizations, including the American Academy of Ophthalmology and the American Academy of Pediatrics.

A new addition to the treatment toolbox

Should a child be diagnosed with retinoblastoma, Casey’s ocular oncology program offers a comprehensive array of the latest diagnostic and treatment services. In July, OHSU began offering a new treatment called intra-arterial chemotherapy as an alternative to systemic chemotherapy or surgical removal of the eye. The procedure was developed in Japan and further refined in New York City before expanding to other centers.

During the IAC procedure, doctors thread a catheter through the groin, the carotid artery and into the ophthalmic artery that supplies blood to the eye while



Stephanie Arnet, with husband Tyler, is undergoing treatment for ocular melanoma. Medical researchers like Dr. Skalet are exploring better ways to predict and detect the spread of the disease and monitor response to treatment.

the patient is under anesthesia. The chemotherapy drug is then injected directly into the tumor. The number of treatments necessary varies.

“This is a fairly complex therapy involving a multi-disciplinary team that includes pediatric and ocular oncologists, a neuro-interventional radiologist, a pediatric anesthesiologist and other medical professionals,” said Dr. Skalet, adding that the OHSU program has been under development for more than a year. In July, the team treated its first patient, a 1-year old girl who had not responded sufficiently to systemic chemotherapy and laser therapy.

“The addition of intra-arterial chemotherapy allows us to treat even the most challenging of retinoblastoma cases and offers an excellent chance for saving the eye,” said Dr. Skalet. “I expect many children will benefit from our new program.”

New specialist joins Vision Rehabilitation Center

Adopts team approach to patient care



Alan Labrum, O.D.

Alan Labrum, O.D., says he was drawn to the field of vision rehabilitation because he enjoys helping people and building relationships with them. "I like to sit down with patients so I can get to know them and understand their needs – and that's especially important when caring for people who are dealing with visual disabilities."

Dr. Labrum joins clinical director John Boyer, O.D., at OHSU Casey Eye Institute's Evelyn L. Jones Vision Rehabilitation Center, which provides full vision exams and personalized plans for children and adults with vision loss. Those plans may include demonstrating and prescribing visual aids and adaptive technologies, recommendations for better lighting and contrast, and teaching patients how to do familiar tasks in new ways.

After earning his optometry degree from the Illinois College of Optometry in 2013, the Vancouver, B.C. native moved to northern British Columbia to practice primary optometry care. Finding that services for people with visual disabilities are limited – especially in rural areas - he returned to Chicago to complete a residency in vision rehabilitation and ocular disease from the Illinois College of Optometry and Chicago Lighthouse.

Dr. Labrum said he plans to adopt a team approach when caring for patients with visual disabilities. "It's important that optometrists work with other professionals in the field to meet their extensive needs," he said, adding that he often refers patients to Casey's social worker for counseling. The Vision Rehabilitation Center also plans to add occupational therapy services in the future.

Dr. Labrum sees patients at Casey's Vision Rehabilitation Center at the OHSU Center for Health and Healing, 3303 SW Bond Ave., in Portland. For more information or to make an appointment or referral, please call 503-494-3098.

Casey hosts global summit on cutting-edge imaging technology

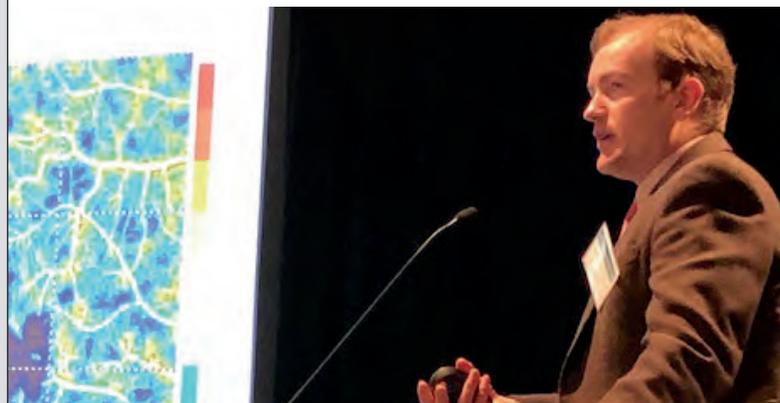
More than 130 vision scientists and clinicians from around the world met in Portland in August for OHSU Casey Eye Institute's fourth Optical Coherence Tomography Angiography (OCTA) Summit. Experts from as far away as France and Japan discussed advances in this revolutionary imaging technology that noninvasively visualizes blood vessels, blood flow and eye structures in a matter of minutes.

The summit represents Casey's global leadership in the development and research of OCTA technology, said David Huang, M.D., Ph.D., Peterson Professor of Ophthalmology and Biomedical Engineering at Casey, and one of the event's organizers. Other organizers were Brandon Lujan, M.D., associate professor of ophthalmology and Yali Jia, Ph.D., associate professor of ophthalmology.

"OHSU scientists developed the OCTA algorithms that made clinical applications in ophthalmology possible," said Dr. Huang, who was a co-inventor of the first OCT technology. He noted that current FDA-approved OCTA systems in the U.S. are based on OCTA technology licensed from OHSU.

Casey researchers, many of whom presented their work at the summit, continue to pioneer the use of OCTA and conduct NIH-supported research to apply OCTA in macular degeneration, diabetic retinopathy, glaucoma, and eye tumors.

Early research shows that OCTA may be useful in evaluating the very early and late stages of glaucoma. It may also help clinicians detect the beginnings of wet macular degeneration before visual symptoms occur.



Dr. Peter Campbell discusses use of OCT angiography in pediatric retinal disease at this summer's OCTA summit.



The late John S. Wold (above) and his family (right).
Photos courtesy of the Wold family

Wold family joins Casey in fight against macular degeneration

Two gifts totaling \$7.5 million from the late philanthropist John S. Wold and his family will help establish a new macular degeneration center at OHSU Casey Eye Institute.

“The Wold family’s generous investment will accelerate and build on Casey’s decades of research in macular degeneration. We are incredibly grateful for their support,” said David Wilson, M.D., director of the Casey Eye Institute and Thiele-Petti chair of ophthalmology in the OHSU School of Medicine.

In June, the Wold Foundation of Wyoming made a gift of \$2.5 million to combat macular degeneration, the leading cause of legal blindness in older Americans.

Combined with \$5 million that John S. Wold donated in 2015, the Wold Foundation’s gift will build and support the Wold Family Macular Degeneration Center. The center will be part of the new building next to Casey’s existing facility.

The Wold Family Macular Degeneration Center will allow Casey to expand its pioneering work to better understand the disease and develop more effective treatments. The center will create a collaborative



space with today’s most advanced medical technologies, bringing together experts in the areas of genomics, and gene and stem cell therapies. The center also will enhance patient care, offering state-of-the-art clinical and support services under one roof.

John S. Wold, who died in 2017 at age 100, was a businessman, geologist, inventor and former U.S. congressman. He suffered from age-related macular degeneration for the last 20 years of his life

“Our father never stopped thinking about how he could contribute to making the world a better place,” said his daughter, Priscilla Wold Longfield. “Macular degeneration significantly impacted his life but didn’t dampen his spirit. If anything, his condition made him even more committed to fighting this insidious disease. We can think of no better way to honor his legacy than to support Casey’s groundbreaking work in finding a cure for macular degeneration.”

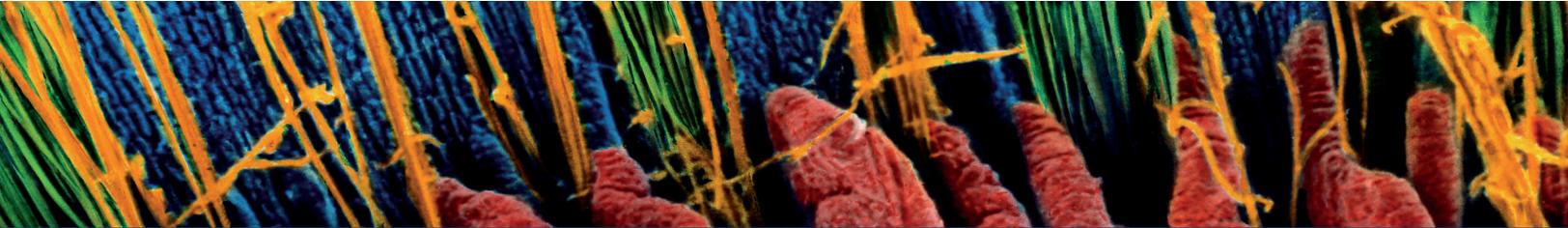


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Publications

Between January and June 2018, Casey Eye Institute faculty published 70 research papers in leading national and international medical journals. Here is a sampling of some of this important work.

Safety and efficacy of adalimumab in patients with noninfectious uveitis in an ongoing open label study: VISUAL III

Suhler EB, Adán A, Brézin AP, Fortin E, Goto H, Jaffe GJ, Kaburaki T, Kramer M, Lim LL, Muccioli C, Nguyen QD, Van Calster J, Cimino L, Kron M, Song AP, Liu J, Pathai S, Camez A, Schlaen A, van Velthoven MEJ, Vitale AT, Zierhut M, Tari S, Dick AD. *Ophthalmology* 2018; 125:1075-87. PMID: 29429764

Researchers collaborated in a major multi-center clinical trial of the anti-inflammatory drug adalimumab (Humira) for the treatment of uveitis.

Why it's important: Shows that adalimumab is able to improve vision while avoiding harmful side effects of other drugs. Casey is at the forefront of clinical trials of promising treatments to improve vision and health.

Estimating public and patient savings from basic research - A study of optical coherence tomography in managing antiangiogenic therapy

Windsor MA, Sun SJJ, Frick KD, Swanson EA, Rosenfeld PJ, Huang D. *Am J Ophthalmol.* 2018 Jan;185:115-122. PMID: 29224686

Casey plays a critical role in the development and application of revolutionary imaging technologies, such as OCT, to diagnose and manage eye disease. Leading health care economists evaluated the economic impact of OCT, largely invented through the work of Casey faculty member David Huang, M.D., Ph.D.

Why it's important: Shows that OCT saved the U.S. government \$9 billion and saved macular degeneration patients \$2.2 billion over seven years.

Results at 5 years after gene therapy for RPE65-deficient retinal dystrophy.

Pennesi ME, Weleber RG, Yang P, Whitebirch C, Thean B, Flotte TR, Humphries M, Chegarnov E, Beasley KN, Stout JT, Chulay JD. *Hum Gene Ther.* 2018 Jun 5. [Epub ahead of print] PMID: 29869534

Casey is an international leader in gene therapy for retinal dystrophies. Researchers report results of gene therapy in patients with Leber congenital amaurosis.

Why it's important: Illustrates how Casey's remarkable scientific and clinical innovations improve vision in patients once considered to have irreversible blindness.

The 2016 American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight) database: Characteristics and methods.

Chiang MF, Sommer A, Rich WL, Lum F, Parke DW 2nd. *Ophthalmology.* 2018; 125:1143-8. PMID: 29342435

Casey is a leader in applying information technology to eye care. Researchers worked with colleagues around the country to develop the American Academy of Ophthalmology IRIS Registry (the largest ambulatory disease registry in any field of medicine) and use it to improve eye care through data analytics.

Why it's important: Is an example of how informatics and "big data" have potential to revolutionize the field of ophthalmology.

In vivo small molecule delivery to the optic nerve in a rodent model

Tehrani S, Delf RK, Cepurna WO, Davis L, Johnson EC, Morrison JC. *Sci Rep.* 2018;8(1):4453. PMID: 29535357

For decades, Casey scientists have performed outstanding collaborative "translational research" - in which basic "bench" science is translated into knowledge that eventually benefits patients at the "bedside." In this study, researchers develop a new method for delivering drugs to the optic nerve in animal models.

Why it's important: Improves our understanding of optic nerve diseases and how better to treat them.