Global Network Locates Additional AMD Genes

The Macular Degeneration Center at Casey Eye Institute participated in a large international study that significantly expanded the number of genetic factors known to play a role in age-related macular degeneration (AMD).

The Center was one of 26 research sites worldwide conducting the study of about 43,000 people as part of the International AMD Genomics Consortium. The study, published in the online journal *Nature Genetics* in December, was supported by the National Eye Institute, part of the National Institutes of Health (NIH).

“This is the largest study of its kind investigating AMD, and its findings represent a significant advance in our understanding of the genetic basis of the disease,” says Michael L. Klein, M.D., Casey’s lead investigator of the study and co-director of the Macular Degeneration Center. “By uncovering the biological mechanisms that drive AMD, we can develop more effective, targeted methods of prevention and treatment,” he says.

Tammy Martin, Ph.D., associate professor of ophthalmology at Casey, was also a study author.

AMD is a progressive disease that can damage central vision. A combination of genetic, environmental and lifestyle risk factors, such as smoking, influence the risk of advanced AMD, says Dr. Klein. Currently, there are no clinically approved treatments for advanced dry AMD, known as geographic atrophy (GA). Although treatments are available for the other advanced form, neovascular or “wet” AMD, therapies do not cure the condition, nor work for everyone.

The consortium collected and analyzed genetic information from 43,566 people to identify common

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Center Launching into New Space

OHSU Casey Eye Institute is planning a new facility that will enable the Macular Degeneration Center to better accommodate patients and strengthen its top-caliber research program as it enters a new era in ophthalmology.

Located adjacent to the current structure on Marquam Hill, the 60,000 square foot building will house the Macular Degeneration Center, as well as the Elks Children’s Eye Clinic, Casey’s Translational Clinical Trials Reading Center and additional space for research and patient care.

Bolstering this undertaking is a $5 million gift from Wyoming business leader and philanthropist John S. Wold to support the Macular Degeneration Center.

The building project, expected to begin in summer 2017, is part of the recently launched Onward OHSU campaign to support key initiatives at the university.

“Because we now have better treatments for age-related macular degeneration, the demand for clinical services is burgeoning,” says David J. Wilson M.D., Director of OHSU Casey Eye Institute and Chair of the Department of Ophthalmology in the OHSU School of Medicine. “That demand is expected to escalate even more as the population in the U.S. and other developed countries grows older,” he adds, noting that “the risk of blindness from age-related eye disorders like macular degeneration is enormous.”

The estimated number of people with AMD is projected to more than double from 2.1 million to 5.4 million between 2010 and 2050, according to the National Eye Institute.

Clinical care areas in the new space will be designed to reflect advances in the delivery of eye care, leading to greater efficiency and convenience for patients. For example, state-of-the-art imaging, such as Optical Coherence Tomography (OCT) will be seamlessly incorporated into the patient’s clinic appointment to improve patient flow and experience of care.

“Imaging technology like OCT has advanced to the point where it’s become an essential part of a patient’s visit, helping diagnose macular degeneration and determine whether a treatment is working,” notes Christina Flaxel, M.D., co-director of the Macular Degeneration Center.

With its expanded space and proximity to Casey’s Reading Center, the Macular Degeneration Center will also be able to ramp up its well-regarded bench-to-bedside research of promising therapies to prevent and treat AMD. The Reading Center is made up of physicians and staff who design and evaluate clinical trials for eye diseases, and interpret the studies’ diagnostic and imaging tests.

“Since its beginning more
A Word of Thanks

In this issue of Insight, you will read about Casey Eye Institute’s exciting plans to build a new facility that will include the Macular Degeneration Center. By moving into expanded space next to our current location on Marquam Hill, we can better accommodate the growing number of people diagnosed with age-related macular degeneration (AMD) and at the same time, build on our accomplishments in basic and clinical research. Some of these efforts – including a recently published study of AMD genes and clinical trials of promising therapies - are covered in this publication.

These achievements are the result of your generous philanthropic and community support, including ongoing gifts from many longtime donors and from those contributing for the first time. In fact, it was an endowment from George and Carolyn Goodall that led to the Center’s establishment two decades ago. Their legacy, facilitated by Portland attorney Roscoe Nelson, helped create one of the most unique, multi-disciplinary programs in the nation for AMD. In addition to our outstanding research and patient care services, we are one of the few centers in the U.S. that offers a vibrant public education program, such as the upcoming Macular Degeneration and Low Vision Expo.

Most recently, a transformative gift to the Macular Degeneration Center from Wyoming business leader John S. Wold will have a significant impact on our work, fueling the development of new discoveries to improve the diagnosis, prevention and treatment of this leading cause of adult blindness. Mr. Wold, who suffers from advanced macular degeneration, is hopeful that his philanthropic support will help bring an end to this devastating disease.

As we move into this new stage of exploration and patient care – and into new space to support these efforts – all of us at the Macular Degeneration Center thank you for entrusting us with this vital mission to end vision loss from macular degeneration. We look forward to updating you on our progress.

Sincerely,

Michael L. Klein, M.D.
Co-director, Macular Degeneration Center

Christina J. Flaxel, M.D.
Co-director, Macular Degeneration Center

To learn more about Casey’s building campaign and how you can be involved, visit www.onwardohsu.org
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and rare variations in genetic coding—called variants—associated with AMD. About half of the patients in the study had macular degeneration and about half did not.

“Because this study involved such a large population of AMD patients and controls, we were able to locate a number of new sites across the genome that may be connected to the disease,” says Dr. Klein.

As a result of the study’s findings, there are now 52 genetic variants associated with AMD. These variants are located among 34 regions of the genome; 16 of which had not been previously linked to AMD.

“The investigation is akin to looking at a Google map of the United States and attempting to pinpoint several leaders and satellite operations in a crime syndicate,” says a co-leader of the study, Anand Swaroop, Ph.D., chief of NEI’s Neurobiology- Neurodegeneration and Repair Laboratory. “It’s possible to find the key players by zooming in and seeing specific regions in rich detail, but first you have to know where to look. Pooling the genetic information from such a large population is what allowed us to look across the genome for possible culprits in AMD, even very small, very rare ones.”

For the first time the researchers also identified a variant linked to wet AMD, which may point to reasons why therapy for this form of AMD is effective for some people but not everyone.

“Even with the pooling of genetic information from such a large population, the variants identified by the international consortium still cannot account for all of the heritability of AMD,” says Grace L. Shen, Ph.D., a group leader and director of the retinal diseases program at NEI. “We are, however, on track for discovering important variant genes that may play a role in AMD heritability.”
New Retina Faculty at Casey

The Macular Degeneration Center welcomes **J. Peter Campbell, M.D., M.P.H.**, who specializes in adult and pediatric medical and surgical retina, including research and treatment of macular degeneration. Dr. Campbell, a vitreo-retinal fellow at Casey Eye Institute from 2012 to 2014, returned to Casey after serving as Assistant Chief of Service at Wilmer Eye Institute at Johns Hopkins Hospital in Baltimore, Maryland.

Dr. Campbell says it was Casey’s high caliber, caring staff that drew him back to Portland. “I had the good fortune of doing my fellowship here and got to know how Casey works behind the scenes. I feel really blessed to be at a place that is full of people who not only seem to enjoy their work, but who also are really good at it,” he says.

A native of Wooster, Ohio, Dr. Campbell earned his medical degree from Johns Hopkins University School of Medicine, and a master’s degree from the university’s Bloomberg School of Public Health. A residency in ophthalmology followed at Johns Hopkins Hospital’s Wilmer Eye Institute.

Dr. Campbell’s current research focuses on using imaging technology to improve the care of patients with retinal disease, domestically and overseas. He also is involved with other retina research projects, including an upcoming clinical trial that uses a refillable implant to deliver a wet AMD medication over the long term. “This type of treatment option is the future and it is exciting to be a part of its evaluation,” says Dr. Campbell. (See page 6 for more information about the LADDER study.)

As a retina specialist, Dr. Campbell says he enjoys caring for the many macular degeneration patients in his practice. “I really value those interactions with these patients and hearing their stories, especially since they have lived through so much,” he says.

**Other new faces:**

**Kavita Bhavsar, M.D.**, a retina specialist practicing full time at the VA Portland Health Care System, is seeing patients one half day a week at Casey. Before coming to Portland, Dr. Bhavsar completed subspecialty training in medical retina and uveitis through the Vitreous- Retina-Macula Consultants of New York, in conjunction with Columbia University and Manhattan Eye, Ear & Throat Hospital in New York City, N.Y. A fellowship in electrophysiology and inherited retinal disease followed at Moorfields Eye Hospital in London, England.

**Ambar Faridi, M.D.**, is a medical retina specialist at the VA Portland Health Care System and Casey. She is on the faculty of Casey’s Translational Clinical Trial Reading Center, where as a certified reader she participates in inherited retinal degeneration research. She also conducts studies on AMD and diabetic retinopathy. Dr Faridi, who completed her ophthalmology residency at Casey, is devoted to teaching and directs the resident Retina Imaging Conference and Retina Core Curriculum. She also staffs resident and fellow retina clinics.
Wet AMD

Ocular Implant (LADDER Study)

Purpose: To compare the effects of an ocular implant that releases one of three different doses of ranibizumab (Lucentis) to injections of ranibizumab. The study implant releases the study drug continuously for a prolonged period of time and can be refilled by your doctor when it is needed. This approach may decrease the need for frequent injections into the eye. This Phase 2 study will be recruiting newly diagnosed wet AMD patients age 50 or older who meet other eligibility criteria.

Contact: Ann Lundquist, 503 494-6364

Injectable Medication for Wet AMD (SEQUOIA Study)

Purpose: To compare the safety and effectiveness of the study drug abicipar pegol to ranibizumab (Lucentis) in patients with newly diagnosed wet AMD. Abicar pegol is an anti-VEGF agent that may be more long-lasting than some current therapies for wet AMD. This Phase 3 study will be recruiting patients age 50 or older who have at least one eye with wet AMD that has not been treated. Other eligibility requirements also apply.

Contact: Shelley Hanel, 503 494-1986

Dry AMD

Implantable Medication for Dry AMD (BEACON Study)

Purpose: To learn if an implantable medication, Brimonidine, is safe and effective for treating advanced AMD, called geographic atrophy (GA). In this Phase 2 study, a tiny pellet implanted in the eye releases the medication to the retina over a sustained period. Participants must be 55 years or older and have GA in the study eye that results in moderate vision loss, in addition to other eligibility criteria. Patients are not eligible if they have a history or active case of wet AMD.

Contact: Ann Lundquist, 503 494-6364

Lampalizumab for Advanced Dry AMD

Purpose: To evaluate the effectiveness and safety of lampalizumab in patients with advanced dry AMD. The medication targets an enzyme that may encourage dry AMD to develop. Researchers will examine the change in the area of GA over the course of
Other Studies

Advanced Imaging Trials
Purpose: To test the capabilities of optical coherence tomography (OCT) angiography in patients with AMD. Investigators are evaluating whether this new technology can visualize and measure blood vessel growth as well as fluorescein angiography, a more invasive imaging test.

Contact: Shahrzad Mohammadi, 503 494-7398

Genetics of AMD Studies
Purpose: To find genetic mechanisms associated with AMD, which will lead to more accurate early detection and precise treatments. Researchers are using advanced whole genome sequencing technology to uncover gene variations in large families and other populations affected by AMD. The study is supported in part by a major grant from the National Eye Institute.

Contact: Jennifer Maykoski, 503 494-3064

Association Between Advanced AMD and Changes in the Gut Microbiome
Purpose: To learn whether associations exist between gastrointestinal tract bacteria and AMD. Researchers will also explore the connection between an individual's genes and the activity of the gut bacteria. The study is limited to a select group of participants enrolled in the Genetics of AMD Study.

Contact: Jennifer Maykoski, 503 494-3064

SAVE THE DATE!
Join us for a day of information and inspiration!

Macular Degeneration and Low Vision Expo

Morning presentations by Casey faculty physicians:
- Macular degeneration basics and research update
- Choosing tinted lenses
- What's new in assistive technology

Afternoon sessions led by low vision experts:
- Basic introduction to iPhone and iPad devices
- Adjusting to vision loss

Exhibits of visual aids, new technologies and community services

Guest speaker Robert Purvis, Ph.D., shares his story as an AMD patient and low vision advocate.

Saturday, April 9, 2016
9 a.m. to 4 p.m.

Doubletree Hotel
Lloyd Center
1000 NE Multnomah Blvd.
Portland, Oregon

Free - Registration opens February 29, 2016
Register at www.caseyamd.com or call 503 494-8511
Connect with the Macular Degeneration Center!

Education and outreach is a top priority of Casey Eye Institute's Macular Degeneration Center, a national leader in research and patient care for age-related macular degeneration (AMD). If you’d like to be on our mailing list to receive the *Insight* newsletter and other information — or have a speaker for your group, please contact the center at 503 494-3537 or at kahnj@ohsu.edu.

Learn more about AMD and the work of the Macular Degeneration Center at www.caseyamd.com