Casey Researcher Explores Link Between Macular Degeneration and the Gut

When it comes to investigating the origins of macular degeneration, Phoebe Lin, M.D., Ph.D., is casting her eye on a novel area of exploration — the diverse community of bacteria and other microscopic creatures that inhabit our intestines.

Recent research is finding a connection between this collection of microorganisms in the intestinal tract, called the “gut microbiome,” and the development of diseases like diabetes and heart disease, as well as inflammatory bowel disease. Dr. Lin, who specializes in retinal and inflammatory eye diseases at OHSU Casey Eye Institute, is drawing on these discoveries to learn how the bacteria in our gut affect the health of our eyes. For the past several years, her lab has been studying this intriguing relationship between gut bacteria and eye inflammation.

“The microbiome has a very complex, interactive relationship with its human hosts,” says Dr. Linn. “Bacteria can be good or bad, depending on the context, with each person having his or her unique composition,” she says, adding that the trillions of bacterial cells in our intestines outnumber our own cells by ten to one.

Your microbiome’s makeup is shaped by many factors, such as your age, diet, genetics, health habits, and environment. At birth, the majority of bacteria in your gut comes from your mother, but evolves and becomes more varied by adulthood. After age 65, however, its diversity lessens.
Thanks to recent advances in DNA sequencing technology, scientists are now able to identify and characterize the hundreds of bacterial species residing in our bodies. Much of this progress is due to the resources and support of the federal government’s Human Microbiome Project, which maintains a massive database of these microbes along with their genetic information.

With this information at hand, scientists are delving into the role these tiny guests play in our health, such as helping the body digest certain foods, produce vitamins and fend off disease, says Dr. Lin.

“What we know is that the gut microbiome can shape our immunity. For instance, certain bacteria, such as some types of Clostridia, make biochemicals that can regulate our immune system and decrease inflammation,” says Dr. Lin.

As research in the field progresses, scientists like Dr. Lin suspect that bacterial processes and components may be a factor in AMD, similar to the way gut bacteria impacts heart disease. Bacteria can send out signals that activate immune cells and trigger inflammation, spurring the formation of fatty deposits. “Both diseases are characterized by the presence of these deposits — drusen in AMD and atherosclerotic plaques in cardiovascular disease,” says Dr. Lin. Interestingly, the two diseases share other risk factors, such as smoking, obesity, and high cholesterol.

Dr. Lin and her research team hope to shed light on the causes of AMD by examining this complex connection between the microbiome and human eye diseases. The study will compare the microbiome of individuals with advanced AMD to those without the disease, looking for differences in the way lipids — or fats — are processed and the role of inflammation in setting off the disease. They will also examine whether some genes associated with AMD influence the types of bacteria you have in your intestines. “In animal models, we’ve found that certain gene variations linked to immune disorders changes the microbiome composition,” says Dr. Lin, who will be collaborating with researchers at the Pacific Northwest National Lab in Richland, Wash. and at the University of California San Diego. The study is being funded in part by the Macular Degeneration Center.

“While much remains to be discovered, these are important first steps. With this information, we hope to gain more insight into the causes of AMD, and use that knowledge to develop new therapies,” says Dr. Lin. In the future, those treatments may include changes in diet in order to repopulate the microbiome and reprogram the immune system.

To view Dr. Lin’s presentation on the microbiome at the Center’s public seminar last April, visit www.caseyamd.com
Research at the Macular Degeneration Center

New Study Aimed at Advanced Dry AMD

Diagnosed with geographic atrophy (GA), a form of advanced AMD, Lee Smith can tell that his eyesight has significantly deteriorated in the last nine months. He no longer drives at night and finds it difficult to read without a magnifier or additional lighting. “It’s frustrating in many ways,” says the 91-year-old retired stockbroker. So when Smith was offered the chance to enroll in a new clinical trial for GA at Casey Eye Institute, he was enthusiastic about trying something that may help him and others.

“In people with GA, patches of underlying cell tissue in the macula become damaged and stop working, causing severe central vision loss,” says retina specialist Christina Flaxel, M.D., principal investigator of the Phase 3 study at Casey. Unfortunately, no proven treatments are available for GA, which can hamper your ability to read, drive and perform other activities that require sharp, straight-ahead vision.

The multi-center clinical trial is investigating whether the medication Lampalizumab is safe and can slow progression of the disease. It will also look to see if the study drug works differently in carriers of specific gene mutations linked to increased risk of AMD.

The drug, given by injection, is designed to block protein factor D, an enzyme in our immune system’s alternate complement pathway, which regulates inflammation. “Although we still don’t know what sets off AMD, scientific studies suggest that certain proteins in this biological pathway may play a role,” says Dr. Flaxel. Earlier trials of Lampalizumab were encouraging, reducing progression of disease by 20 percent and by 44 percent in a sub group of study patients with a particular gene variation.

“Testing this medication in a larger population will also provide us with some meaningful answers about the mechanisms of this disease and how genetic makeup influences response to AMD treatment. We are excited to be part of this promising effort,” says Dr. Flaxel.

The Lampalizumab study is open to people age 50 and over who meet other eligibility criteria. For more information, contact study coordinators Mitchell Schain, 503 494-3115 or Shelley Hanel, 503 494-1986

Advanced Imaging Update

For several years, Casey researchers have been testing groundbreaking 3D optical coherence tomography (OCT) technology for macular degeneration, diabetic eye disease and glaucoma. Recently, the team published new findings in the Proceedings of the National Academy of Sciences (PNAS) showing that this imaging system, called OCT angiography, has considerable advantages over more invasive approaches for the diagnosis and care of these blinding eye conditions.

The new OCT technology, invented by Casey investigators Yali Jia, Ph.D. and David Huang, M.D., Ph.D., is a non-invasive alternative to conventional angiography, which requires an intravenous injection of a contrast dye to illuminate the problem blood vessels. It not only allows physicians to view blood vessels more quickly and easily, but measures their blood flow and density. This information is very useful and may help physicians detect wet AMD sooner and decide whether treatments are working, says Steven Bailey, M.D., who is a co-principal investigator of Casey’s OCT trial for wet AMD. This past spring, Dr. Bailey discussed his team’s research at the International Retinal Imaging Symposium in Los Angeles and presented a poster on that topic at the annual meeting of the Association for Research (Continued on page 4)
Research at the Macular Degeneration Center (Continued from page 3)

in Vision and Ophthalmology (ARVO). Casey will host an international summit on OCT angiography featuring top researchers and clinical pioneers of this new technology this summer.

The OCT trials for macular degeneration are ongoing. In addition to studies for wet AMD, investigators are also comparing how retinal anatomy and blood flow differ among study patients in dry AMD.

For more information, contact Shahrzad Mohammadi, study coordinator, at 503 494-7398.

Genetics of Age-Related Macular Degeneration Study

Tammy Martin, Ph.D., presented a poster at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO) in April detailing recent findings from the Macular Degeneration Center’s Genetics of AMD Study. The research project studied 24 genes linked to AMD within a large group of 152 families affected by the disease. “At Casey, we have a unique collection of families with multiple members diagnosed with AMD. This enables us to study the degree of heritability within our group of families and to calculate how much these 24 genetic variants contributed to that genetic cause,” explains Dr. Martin, one of the study’s investigators. Although the researchers found that some of these genes played a role, their data suggests that there are additional, yet to be discovered, genetic risk factors that contributed to the disease.

The research team included principal investigator Michael Klein, M.D. and Matthew Johnson, Ph.D.

The Genetics of AMD Study, supported by a major grant from the National Eye Institute, is being carried out in partnership with genetic statisticians at the University of Texas Rio Grande Valley’s medical school, as well as other collaborators in the U.S. and elsewhere. The group is using advanced whole genome sequencing technology to identify AMD genes in these large families and other groups. Understanding the genetic mechanisms of AMD will lead to more accurate early detection and precise treatments.

For more information, contact Jennifer Maykoski, study coordinator, at 503 494-3064.

Other Clinical Trials

Wet AMD Combination Therapy

Purpose: To study the safety and effectiveness of a medication (Fovista) that blocks a protein that causes abnormal blood vessels to grow in wet AMD. The study drug is injected monthly along with one of the current wet AMD medications, which targets a different source of abnormal blood vessel growth. The hope is that this combination approach will be more effective than using one medication and will lead to better vision and extend time in between treatments. The Phase 3 study is recruiting people age 55 and older with active wet AMD. Other eligibility criteria may also apply.

Contact Shelley Hanel, study coordinator, at 503 494-1986.
Brimonidine for Dry AMD

Purpose: To learn if an implantable medication, Brimonidine, is safe and effective for treating geographic atrophy (GA) in dry AMD. Brimonidine, used in eye drop form to treat glaucoma, has been shown to protect cells in the retina. In this Phase 2 study, a tiny pellet is implanted in the eye that releases the medication to the retina over a sustained period of time. To be eligible, you must be 55 years or older and have GA in the study eye that results in moderate vision loss. Other eligibility criteria may also apply.

Contact Ann Lundquist, study coordinator, at 503 494-6364.

Gene Therapy for Wet AMD

Purpose: To evaluate the safety and dosing levels of a gene-based treatment, RetinoStat®, for wet AMD. In this study, two helpful genes are delivered directly to the retina, where they activate proteins that block abnormal blood vessel growth in a sustained fashion. Enrollment is closed and results are expected by the end of 2015.

Contact Ann Lundquist, study coordinator, at 503 494-6364.

SEATTLE Study for Dry AMD

Purpose: To learn if an oral study medication, emixustat hydrochloride, slows progression to advanced dry AMD (geographic atrophy) compared to placebo in people with dry AMD. The oral medication is designed to reduce the amount of byproducts in the retina, which can damage eye cells. Enrollment is closed and study patients are being followed.

Contact Shelley Hanel, study coordinator, at 503 494-1986.

Remembering Harold Beal, Longtime Friend of Macular Degeneration Center

The Macular Degeneration Center lost a steadfast champion of its work with the passing in January of Harold Beal, who was 84.

Harold, along with his wife Verda, enthusiastically supported the Center’s research and outreach activities for more than a decade. In addition to serving on the Center’s Community Advisory Board, the two often volunteered at its community education programs and have been major contributors to the Macular Degeneration Center Fund.

For Harold, who had a passion for automobiles — both racing them and buying and salvaging their parts — losing eyesight from macular degeneration did not slow him down. With his wife’s help, he continued to go to work every day, using a video magnification system to help him read. “Giving up driving has been the toughest part of the disease,” he once recalled.

“As someone who contended with macular degeneration for many years, Harold wanted to do what he could to help today’s patients and provide hope to future generations. From participating in our Genetics of AMD Study to providing generous philanthropic support, Harold greatly contributed to our efforts in research and patient education,” says Michael Klein, M.D., co-director of the Macular Degeneration Center. “He led a remarkable life, and we will miss his gentle humor, kindness and determination to meet the challenges of his disease.”

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High Schooler’s High-tech Invention Helps Grandmother See

Like most grandparents, Marian Reekie is proud of her grandchildren. But the 81-year old Portland resident has an especially good reason to brag about her 14-year old grandson, Christopher Reekie. Visually impaired from advanced age-related macular degeneration — or AMD — Marian is able to see faces and read print for the first time in years thanks to a pair of video magnification glasses Christopher created on his own.

A ninth grader at Oregon Episcopal School, Christopher hatched the idea for the high-tech vision aid after noticing his grandmother’s eyesight was worsening as her disease progressed. “I could no longer drive, see things on my smart phone, read large print books or write,” says Marian, a patient at OHSU’s Casey Eye Institute. Eager to find something to help her, she flew to Colorado to try out a similar type of electronic glasses, but was disappointed in their quality, comfort and high price tag of $15,000.

“I had the idea that I could make something like this better and more affordable,” says Christopher, who financed the project called ‘Magniglass’ through a successful Kickstarter campaign. Last December, he presented his grandmother with a prototype version of the eyewear for Christmas.

Last January, Marian, Christopher and his father Ian Reekie demonstrated the glasses for John Boyer, O.D., clinical director of OHSU Casey Eye Institute’s Vision Rehabilitation Center. Christina Flaxel, M.D., a Casey retina specialist treating Marian for her AMD, suggested she and her grandson follow up with Dr. Boyer for his expert evaluation.

Christopher explained that Magniglass was pieced together “from the ground up” with components he found on the Internet. The device consists of high definition video glasses connected to a video feed from a small camera mounted to the top center of the glasses. The video signal is transmitted to a micro-computer mounted in a small box with a lightweight battery pack. One of the challenges was “writing the software code so that the video camera communicates seamlessly with the glasses and the software can manipulate the zoom and contrast,” he wrote on his Kickstarter page.

“The glasses are very adaptable and allow the wearer to control brightness, contrast, zoom and color saturation,” says Chris, adding that he plans to fine tune the device so the battery is smaller and the control buttons are easier to manipulate.

One of the glasses’ major pluses is that it allows her to distinguish faces, says Marian. “I saw my son’s face for the first time in years,” she says. When she donned the glasses during her visit with Dr. Boyer, she was delighted to find she could read the letters on the eye chart. Without them, it was nearly impossible, she says.
Mark your calendar!
2016 Macular Degeneration and Low Vision Expo

Saturday, April 9, 2016
Doubletree Hotel — Lloyd Center
Portland, OR
Free and open to the public

- Presentations by Casey faculty physicians
- Small group sessions to help with daily living
- Exhibits of visual aids and community resources

Details about registration, exhibits and event schedule will be mailed to newsletter subscribers in early 2016 and posted on our website, www.caseyamd.com

For more information or to be added to the Insight newsletter mailing list, call the Macular Degeneration Center at 503 494-3537 or email kahnj@ohsu.edu

Support for the Macular Degeneration Center Helps Hasten Progress

At Casey Eye Institute’s Macular Degeneration Center, we are confronting the challenges of age-related macular degeneration with outstanding programs in research, patient care and community education. Your contribution, no matter the size, helps sustain this vital work and fuels new, sight-saving discoveries. It is also a meaningful way to honor loved ones.

To make a donation to the Macular Degeneration Center, please use the enclosed contribution envelope or give online at http://amd.ohsufoundation.org Gifts also may be mailed to:

Macular Degeneration Center Fund
c/o OHSU Foundation
MS/45
PO Box 4000
Portland, OR 97208-9852

For more information about giving opportunities, including planned giving, please call the Macular Degeneration Center at 503 494-3537.
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