Cell Models Reveal a Shared Early Pathway to Macular Disorders

Ruchira Singh, PhD, of the University of Rochester, is hopeful that different macular disorders could one day be stopped by treatments aimed at some of the earliest cellular changes that these diseases have in common. This is based on her recent research showing that there are similarities in the lead-up to different forms of age-related macular degeneration (AMD) that might lend themselves to shared treatments.

That’s good news, because shared therapies could be less costly to develop and more effective to use than separate therapies for each disease subtype.

With help from a Macular Degeneration Research grant, Dr. Singh is currently studying the role of different cells in the eye that are affected in AMD. Her lab’s work replicates early aspects of AMD using cell models created from living cells from adults. Known as human induced pluripotent stem cells (hiPSCs), they can differentiate into nearly all cell types. In this case, Dr. Singh is using eye cells.

Now Dr. Singh, her postdoctoral researcher Chad Galloway, PhD, and a group of international collaborators have reached a successful turning point in their investigations. Using hiPSC models, the researchers were able to replicate two early features...
of AMD: 1) the development of drusen, and 2) the accumulation of extracellular protein matrix (ECM) in Bruch’s membrane, a layer of cells between the retinal pigmented epithelium (RPE) and the choroid layer filled with blood vessels. Drusen formation and ECM accumulation are hallmarks of early AMD.

According to their study, published in Proceedings of the National Academy of Sciences, similar molecular changes occurred even in RPE cells derived from patients with rare genetic macular dystrophies. This suggests that the disease plays out through shared mechanisms that could potentially be stopped by the same early treatment.

It is this possibility that drives Dr. Singh. “I know that… my work with patient-derived stem cells will one day lead to treatments and possibly cures for retinal and neurodegenerative diseases,” she recently shared with Macular Degeneration Research. “I would sincerely like to thank the donors for funding my research project and moving my research program forward.”

Vision scientists funded by Macular Degeneration Research are tackling AMD on multiple fronts. And their tireless work gives us hope for the future.

I’m delighted that we’re able to support the work of Ruchira Singh, PhD. As our cover story shows, she and a group of international researchers are making important strides in identifying early changes that are common among AMD and other macular disorders. This raises the prospect of early treatments that could one day arrest these diseases before people lose their vision.

Another grantee, Sheldon Rowan, PhD, is studying the impact of diet and gut bacteria on the development of AMD, which could lead to new ways to prevent and treat this disease.

Innovative studies like these are only possible with help from friends like you. Thank you for your continued support as we work toward a future free of AMD.

President’s Corner

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Stacy Pagos Haller
President

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This hiPSC model shows early drusen formation in RPE.
Importance of Gut Bacteria in the Development of AMD

Diet can affect our risk of developing AMD. But how? The answer could be related to the bacteria living symbiotically in our guts, known as the microbiome.

Macular Degeneration Research-funded scientist Sheldon Rowan, PhD, of Tufts University, is testing whether high-glycemic diets can lead to an altered gut microbiome and contribute to AMD. Diets high in sugar and starch are linked to a greater risk for this disease compared to low-glycemic diets rich in fruits, vegetables, and fish.

In this study, mice will be fed either a high- or low-glycemic diet. Measuring metabolites affected by the composition of gut bacteria will help determine how much the gut microbiome either protects against, or contributes to, AMD.

In addition, some mice will receive antibiotics, which remove both harmful and beneficial bacteria. Dr. Rowan and his team will then swap out gut bacteria between the high- and low-glycemic mice to clarify how much of the dietary impact is modulated solely by the gut microbiome.

When complete, this study will help clarify the importance and role of gut bacteria. If results show it does help protect against AMD, this could lead to the development of new probiotic treatments or drug targets.

To register, call 800-437-2423 or go to brightfocus.org/eyechats.
Clinical Trials for AMD

*Interview with Benjamin Kim, MD*

A clinical trial at the University of Pennsylvania, supported by BrightFocus’ Macular Degeneration Research program, is testing whether alpha lipoic acid can slow down the growth of geographic atrophy, an advanced form of dry AMD.

**BrightFocus:** What does your clinical trial do?

**Dr. Kim:** The atrophy (death of retinal tissue) that develops in advanced AMD causes about 20 percent of the legal blindness in the U.S., and no treatment is available. The GALA (geographic atrophy lipoic acid) trial is testing if the atrophy can be slowed by alpha lipoic acid. This is a potent antioxidant that can prevent the damaging effects of oxidative stress and iron overload in AMD.

**BrightFocus:** Why are clinical trials important?

**Dr. Kim:** They’re tremendously important for evidence-based medicine. Physicians need high-quality data to be confident that a recommended treatment will help patients and not have concerning side effects. This can only be achieved through carefully designed clinical trials.

**BrightFocus:** What advice would you give to someone considering volunteering for a clinical trial?

**Dr. Kim:** I recommend being proactive and discussing this with your physician. Depending on the disease, there sometimes are various clinical trials at different stages of development. Ultimately, each participant has to weigh their own potential risks and benefits and discuss with their physician to make the best decision about trial participation.

**BrightFocus:** Is there a misperception that the public has about clinical trials that you would like to correct?

**Dr. Kim:** While many people appreciate the importance of clinical trials, some may have concerns about participating in one. However, trials are rigorously designed to maximize patient safety and monitor for any safety issues that could develop. Additionally, we must also remember that many therapies approved by the U.S. Food and Drug Administration are available only because people took part in such trials.

**BrightFocus:** Are you hopeful for the future of vision research?

**Dr. Kim:** I’m very hopeful. There have been astounding developments in ophthalmology. Scientists, study participants, and funding organizations like BrightFocus are really making a difference.

To read the full interview and to learn more about this trial and clinical trials available in your area, please visit brightfocus.org/AMDtrials. This series of articles promoting awareness of clinical trials is supported in part by an educational sponsorship from Biogen. BrightFocus is solely responsible for the content of this article.
For people with vision loss due to AMD, being able to function safely in the kitchen is a key part of remaining independent at home. Here are a few tips that may help:

**Lighting:** When cooking, people need to see package details and read recipes. Overhead lights can cast a shadow over the workplace, making it hard to function. Consider adding task lights, such as a pendant lamp that hangs over a food preparation area or a desk lamp on your counter.

**Microwaves:** Microwaves mounted over the stove can be dangerous. “People often can spill hot liquids onto themselves as they are getting food out from a higher surface,” says Dr. Orli Weisser-Pike, a doctor of occupational therapy and a certified low-vision therapist. It’s safer to place the microwave either on top of or underneath the counter. If you have trouble seeing the numbers on the microwave, mark the gridlines between them so they’re easier to distinguish.

**Ovens:** You may also want to mark your oven panel for select features, such as the start and stop buttons, or the numeral five. Be judicious—too many markings will make it cluttered and hard to use. Weisser-Pike recommends an oven where the dials or panels are in front, not back. Cooks with impaired vision often want to lean over the stove to see the dials closely, which increases their risk for getting hurt.

Many ovens now have a touchscreen panel, but it can be easier to turn an old-fashioned dial than try to figure out a digital touchscreen. It also may be safer to cook with a smaller appliance, such as a toaster oven or slow cooker.

**Liquids:** Pour liquids over a bowl or sink so any spills are easier to clean up. For increased visibility, use a contrasting color. This can be as simple as pouring milk into a blue bowl.

**Knives:** Finger guards are an economical way to help protect your fingers when cutting foods. Alternately, you can get inexpensive chopping appliances. It can also help to use a cutting board of a contrasting color. For example, to bring out the shape of a white onion, chop it on a red plastic cutting board.
Help Find a Cure for AMD and Receive Payments for Life

A charitable gift annuity is a perfect way to receive income for life and create a legacy of fighting AMD that benefits future generations.

To establish an annuity, you make a gift using cash, marketable securities, or other assets. In exchange, you receive fixed payments for life. Your payment rate is set at the time of your gift and never fluctuates, regardless of changes in the stock market, interest rates, or inflation. You benefit in several ways:

• Guaranteed lifetime income
• The option to receive payments annually, semi-annually, quarterly, or monthly
• Income tax benefits
• Competitive annuity payment rates

To learn more about charitable gift annuities, please contact Lauren Fields, Manager of Planned Giving, at 855-345-6637 or Lfields@brightfocus.org.