A possible new treatment for wet age-related macular degeneration (AMD) has been identified by researchers at Harvard Medical School. Supported by a Macular Degeneration Research grant, Ye Sun, MD, PhD, and her colleagues developed a strategy to prevent and manage neovascular AMD by modulating the immune-vascular pathway.

Myeloid cells are young cells that develop into germ-fighting white blood cells, such as macrophages, which absorb and digest bacteria and cellular debris. During the development of wet AMD, these macrophages get recruited from general circulation into the eyes. Once there, they release inflammation-producing cytokine molecules that stimulate abnormal blood vessel development, or neovascularization, in the retina.

Using mouse models, Harvard researchers explored the influence of a key mediator of inflammation, a gene known as SOCS3, on macrophages and inflammatory cytokine production. SOCS3 is an acronym for "suppressor of cytokine signaling 3."

Subsequent laboratory analysis of eyes treated in this manner showed that the overexpression of SOCS3 in myeloid-derived cells suppressed retinal neovascularization. The excess SOCS3 did so by suppressing the movement of macrophages and the secretion of inflammatory molecules into the retina. This was also confirmed using small molecules that mimic SOCS3.

This study opens the possibility to modulate immune-vascular crosstalk via SOCS3 as a potential treatment to prevent abnormal vessel growth in wet AMD.
PRESIDENT’S CORNER

I’m excited about the progress we’re making against AMD!

As our cover story shows, a researcher we fund has identified a new treatment that may prevent the abnormal blood vessel growth that affects people with macular degeneration.

I’m delighted by the advances we’ve made in learning how genes can affect the development of AMD. Understanding how genes influence AMD risk and inform treatment approaches are an important and growing focus of research. And thanks to you, Macular Degeneration Research can fund the top experts who will advance scientific knowledge in this area.

Your generosity makes all of our sight-saving work possible. With your ongoing support, we will continue to tackle macular degeneration on multiple fronts until we find a cure. Thank you!

Stacy Pagos Haller
President

NEW RESEARCH IS HELPING US UNDERSTAND HOW CELLS TRANSITION FROM HEALTH TO DISEASE, AND IT’S ALSO DRAWING PARALLELS BETWEEN RETINAL CELLS AND THOSE OF OTHER BODY TISSUES.

PARALLELS FOUND BETWEEN AMD CHANGES AND LIVER CELLS

Cells’ transition from one state to another is often accompanied by changes in gene expression and protein modification. Understanding these changes offers deep insight into how the cells function in normal and pathological states. New research funded by Macular Degeneration Research identifies molecular alterations that occur when cells in the retinal pigment epithelium (RPE) transition to a mesenchymal state—a change that enables them to migrate and can contribute to age-related macular degeneration (AMD).

Although transition is a part of the normal cellular process, it is also activated in cancer cells. Researchers also found similar modifications in liver cells. Their findings of linked metabolic pathways opens the door to discover new treatments for a variety of RPE diseases, including AMD.

This research was funded in part by a grant to Donald Zack, MD, PhD, of the Wilmer Eye Institute at Johns Hopkins. Dr. Zack is a past grantee in both the Macular Degeneration Research and National (Continued on next page)
Glaucoma Research programs.

For this work, the researchers studied large-scale changes in protein expression (proteomics) and protein phosphorylation of RPE cells undergoing epithelial-mesenchymal transition (EMT). They identified over 8,000 proteins and over 9,000 phosphorylated proteins.

Identifying the common pathways between different diseases can lead to shared treatment approaches with drugs that have already been approved or drugs that are still being developed.

HOW A HIGH-FAT DIET INFLUENCES AMD

In mouse models, a steady diet of high-fat foods altered retinal genes in ways that increased the risk of macular degeneration.

New research by Macular Degeneration Research–funded scientist Dimitra Skondra, MD, PhD, at the University of Chicago, has shown that a high-fat diet is capable of influencing genes related to the retina in ways that may contribute to age-related macular degeneration (AMD), by turning off some genes and turning on others.

In this first-of-its-kind study, Dr. Skondra and her colleagues untangled the effects of a high-fat diet and the gut microbiome on the retina, by identifying how a high-fat diet in and of itself activates or represses retinal genes and influences diseases like AMD. The research also discovered new genes related to the retina, as well as shed light on the molecular and biochemical processes by which a high-fat diet is involved in AMD.

This study provides early evidence of a direct relationship between a high-fat diet and gene changes related to AMD, separate from the gut microbiome. The results raise the possibility that other interventions involving diet, or treatments directed to gene targets influenced by diet, could be beneficial to treat AMD. More research is needed to explore the potential treatment and prevention avenues raised by these findings.
Aspirin may be the closest thing to a wonder drug because, in addition to decreasing pain and fevers, it is sometimes prescribed by doctors to decrease the risk of heart attacks, strokes, or colorectal cancer.

Taking aspirin is not without its dangers, however, as there is some increased risk of bleeding from the gastrointestinal tract and hemorrhagic strokes.

Many people with macular degeneration ask if they should stop taking aspirin. Some have had heart attacks or strokes, after which their physicians put them on an aspirin regimen. Many eye doctors advise that whether or not you have AMD, it should not be a factor in the decision to take aspirin, given the current inconclusive state of clinical trial evidence.

It is best to follow the advice of your primary care physician concerning aspirin use, because they should be familiar with your current medications and medical history. For example, some people with certain risk factors or who take specific medications should not take aspirin. It is also important to note that all medicines have their own risks and benefits, and they should not be stopped or started without consulting your entire medical team first.

Please share this newsletter with others who may be interested!
For people with macular degeneration, visual rehabilitation (also known as low vision therapy) can help you adjust and function better with your remaining vision.

Start by letting your eye doctor or a low-vision specialist know what kinds of limitations your vision loss has caused. The doctor can then prescribe you optical tools, such as standing and handheld magnifiers, magnifying glasses, and telescopic devices.

They may also refer you to a vision rehab center, an eye clinic, or other organization where a low-vision therapist can help you adapt, and also make personalized recommendations for your situation.

Most people with low vision are surprised to find out how much information they can glean about their surroundings by using their other senses. A person can learn how to tune in using their sense of hearing to help with daily activities. For example, the hum of the refrigerator can signal that you are entering the kitchen.

Those with low vision can also learn to rely more on their sense of touch. Selecting clothes from the closet, for example, will be easier to do if a person focuses on the textures of fabrics and associates them with mental images of certain garments.

People spend a lifetime depending primarily on their central vision, and this habit is hard to break. However, for those with macular degeneration, their best vision probably lies somewhere in their peripheral (side) area of sight. If you have macular degeneration, make a conscious effort to locate this area and use it as fully as possible.
AUGUST IS NATIONAL MAKE-A-WILL MONTH

HOW A WILL CAN KEEP GIVING LONG INTO THE FUTURE

A will or living trust helps you protect your loved ones long after your lifetime, and it can also support the causes you care about. Here are a few basics about making a lasting difference for Macular Degeneration Research’s sight-saving work:

How to Make Your Gift

Including Macular Degeneration Research in your will or living trust is easy. Start by contacting us to request the official wording for your gift. Then, ask your estate planning attorney to use this language when you create your will or living trust. If you already have one of these legal documents, simply ask your attorney to update it.

Your Benefits

- It’s worry-free. You won’t give anything away until after your passing, so you can keep using your possessions and finances like normal.
- You have choices. You can give Macular Degeneration Research a specific item, an amount of money, a gift contingent upon certain events, or a percentage of your estate.

We’re Here to Help

We’ve partnered with FreeWill to make planned giving easier for you. Visit www.freewill.com/brightfocus to create your estate plan for free. If you have questions, please contact Charlie Thomas, our Planned Giving Manager, at 301-556-9362 or plannedgiving@brightfocus.org.