



**Macular
Degeneration
Research**

News

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HOW MACULAR DEGENERATION AND LUPUS SHARE AN INFLAMMATORY PATHWAY

An international team of scientists has identified a new biological link between age-related macular degeneration (AMD) and lupus. Their studies, funded in part by Macular Degeneration Research, support the development of various new treatments for AMD.

When pathogens, such as harmful bacteria or viruses, enter the human body, molecules called inflammasomes trigger an immune response to fight off the pathogens. However, inflammasomes can trigger a response without the presence of a pathogen, causing inflammation.



A shared inflammatory pathway between AMD and lupus leads to the use of existing drugs to treat both diseases.

Researchers have discovered a pathway by which inflammasomes are triggered, and that these disease-activating molecules are shared by AMD and lupus but with different results. In lupus, inflammation leads to joint pain, rashes, and fevers; in AMD, it leads to degeneration of the retinal pigment epithelium (RPE), a layer of cells that nourish and maintain the health of the eye.

The pathway begins with cellular stress caused by aging, which triggers the production of a special type of ribonucleic acid (RNA). These RNAs are sensed by an enzyme called DDX17, which activates the inflammasomes.

The discovery of a single pathway that contributes to multiple diseases is incredibly impactful. Scientists hope it means that drugs used to treat one disease will effectively treat the other disease as well. This study supports the use of a new class of drugs (Kamudevines) to treat diseases like AMD that share this inflammatory pathway.

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A variety of resources are available for people living with macular degeneration. To receive a copy of our Resource List, which has information about government programs, transportation assistance, and other special services, please call Macular Degeneration Research at 855-345-6637 or visit our website at brightfocus.org/MDRresources.

Macular Degeneration Research is a BrightFocus Foundation Program

22512 Gateway Center Drive, Clarksburg, MD 20871 • 855-345-6637 • brightfocus.org/MDRmatch



PRESIDENT'S CORNER

Cutting-edge science is expanding our understanding of macular degeneration. Thanks to generous supporters like you, research projects and clinical trials funded by Macular Degeneration Research are giving people living with macular degeneration new hope for better prevention and treatments.

As you'll read in this newsletter, we're exploring shared inflammatory pathways between lupus and AMD, whereby drugs used to treat one disease can potentially treat both. Plus, you'll find helpful information about promising treatments, such as a potential one-time gene therapy treatment for AMD that could last up to three years.

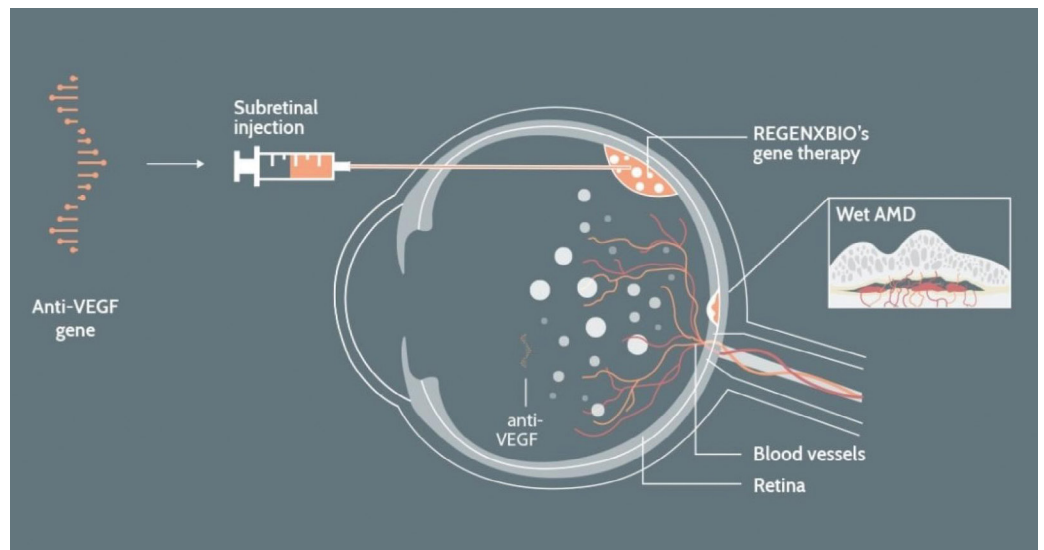
Working together, we're supporting groundbreaking science to help people protect their sight. Thank you for making this progress possible.

Stacy Pagos Haller
President

ONE-TIME GENE THERAPY FOR WET AMD

Arshad Khanani, MD, director of clinical research at a large Nevada eye clinic, spoke at a *BrightFocus Chat* discussion hosted by Macular Degeneration Research. He shared an overview of an exciting new treatment for age-related macular degeneration (AMD) that is currently in the clinical trial stage of development.

The discussion covered RGX-314, a proposed gene therapy being developed by a biotechnology firm in Rockwell, Maryland. This therapy was developed to treat wet AMD and is being heralded as a game changer. It is designed to be a potential one-time treatment that can last up to three years in some patients.



Arshad Khanani offers an overview of a new gene therapy treatment for wet AMD.

The therapy uses a viral vector to deliver a gene to the back of the eye. This gene encodes an antibody fragment that binds to and neutralizes vascular endothelial growth factor (VEGF) activity, halting the growth of new blood vessels.

This treatment is designed to be used by patients who respond to the traditional monthly anti-VEGF compounds and injections that are the current standard of care. In current trials, roughly two-thirds of patients required no further injections after the gene therapy treatment, thereby providing a higher quality of life for patients with wet AMD.

BrightFocus Chats are free, monthly discussions with leaders in vision research and care. You can sign up to be notified of upcoming chats or listen to recordings of previous chats at this link: brightfocus.org/chats.

DNA MODIFICATION AND GENE EXPRESSION IN AMD

Thanks to Macular Degeneration Research funding, Willard Freeman, PhD, and Ana J. Chucair-Elliott, PhD, with Oklahoma Medical Research Foundation, are studying how the retinal epigenome—a record of the chemical changes to the DNA—modifies with aging and contributes to age-related macular degeneration (AMD).

Using specially engineered laboratory models containing glial cells (the cells that control inflammation in the retina), researchers will study age-related changes in DNA modification. These studies will develop both unique mouse models and new techniques to measure the epigenome and how it causes AMD, providing effective tools for scientists to use in the future.

This study will also generate cell-type specific data across the lifespan of a subject, which has not been generated for the



Willard Freeman, PhD

retina before. Researchers hope this data will provide new insights into how aging contributes to AMD risk so they can identify candidates for cell- and gender-specific epigenome editing to prevent or reverse maladaptive retina aging, thereby providing new targets for treating AMD.



New research allows for a comprehensive study of aging DNA.

NEW TREATMENTS FOR AMD

The advancement of scientific understanding around macular degeneration has led to a significant number of new drugs that will likely improve the quality of life and efficacy of treatments for people with this disease.

For wet age-related macular degeneration (AMD), the standard treatments are intraocular injections of drugs that block vascular endothelial growth factor (VEGF). These drugs usually need to be injected at least every three months, depending on the patient and the drug.

The recently approved drug Vabysmo targets both VEGF and another related protein called angiopoietin-2 (Ang-2). Based on clinical trials, this drug can be given as infrequently as once every four months in about 50 percent of patients. Higher-dose Eylea is also being tested and may last as long as four months in about half of treated patients.

One recently approved implant (Susvimo), which is placed in the wall of the eye, stores a drug called Lucentis and then slowly releases it over a six-month period, resulting in fewer eye injections. The device can then be refilled during an office visit.

Another drug that blocks VEGF by inhibiting its receptor is called Sunitinib. One form (GB-102) is injected into the eye as a depot for prolonged release. It lasted at least six months in a phase I/IIa clinical trial. It's now moving to phase III trials.

OPT-302 is a new drug that targets VEGF-C and VEGF-D, and it is now in phase II trials. OPT-302 is injected in combination with a traditional VEGF inhibitor. Results of this trial show that patients receiving monthly injections of OPT-302 in combination with Lucentis had better visual acuity outcomes than those who received Lucentis alone.

These are just a few of the upcoming treatments we are excited about. Thank you for making these breakthroughs possible through your support of Macular Degeneration Research.



Please share this newsletter with others who may be interested!

Register for

BrightFocus®
Chats

Recently diagnosed with AMD? Know someone who has it? Receive helpful information from our FREE monthly phone call with doctors, researchers, and experts in the field on timely topics. You can submit questions before or during the event. Transcripts and audio recordings are available afterward on our website.

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

 **Macular Degeneration Research**



Macular Degeneration Research is a program of BrightFocus Foundation, a charitable organization that complies with all 20 rigorous BBB Wise Giving Alliance Standards.

CORRECTING MACULAR DEGENERATION DEFECTS

A critical part of our visual process is the recycling of a special molecule, called a chromatophore, after exposure to light. This is done by a molecular pump that allows the cell to regenerate the active form of the chromatophore. Some diseases of the eye result in misfolding of proteins and the malfunction of the pump, called ABCA4, which can eventually lead to blindness.

Stephen Aller, PhD, and Alecia K. Gross, PhD, at the University of Alabama at Birmingham, received a grant from Macular Degeneration Research that may lead to the discovery of new FDA-approved treatments for visual diseases such as macular degeneration.

Dr. Aller and his team are determining the three-dimensional structure of the active form of ABCA4 and adapting a drug-screening assessment previously used for cystic fibrosis to identify novel compounds that could be developed into drugs for treating visual problems related to defective ABCA1 folding.

The two aims of their research are innovative since, to date, no complete autonomous pump that utilizes the energy from ATP of any protein family in the human genome has been determined in a dimeric configuration. Similarly, no yeast-based assay using protein folding readout has been applied to ABCA1 in the visual process. This work could lead to the identification of new drugs to treat macular degeneration through the processes of drug screening and cutting-edge rational drug design.





Charitable remainder trusts let you take care of your loved ones first and help fight AMD in the future.

PROVIDE SECURITY FOR YOUR LOVED ONES ... AND HELP FIGHT AMD!

One way you can benefit your loved ones and also help Macular Degeneration Research is to create a charitable remainder trust. This provides income to loved ones for the rest of their lives or for a term of years. After that, the remainder goes to Macular Degeneration Research to help fight this disease.

How It Works

1. You decide which assets to donate. Popular options include cash, stocks, or real estate.
2. You choose whom you would like to benefit from the trust.
3. Those beneficiaries will receive income for the rest of their lives or for a specified number of years.
4. After the specified term, the remaining assets are given to Macular Degeneration Research to support our mission.

How You Benefit

- ✓ When you itemize, you receive a potential income tax charitable deduction for a portion of the full fair-market value (not the cost basis) of the assets placed in the trust.
- ✓ Upfront capital gains taxes are eliminated when you fund the trust with long-term appreciated property.
- ✓ You feel fulfilled, knowing you are helping fight AMD.

If you have questions, please contact Charlie Thomas, Planned Giving Manager, at 301-556-9362 or plannedgiving@brightfocus.org.



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