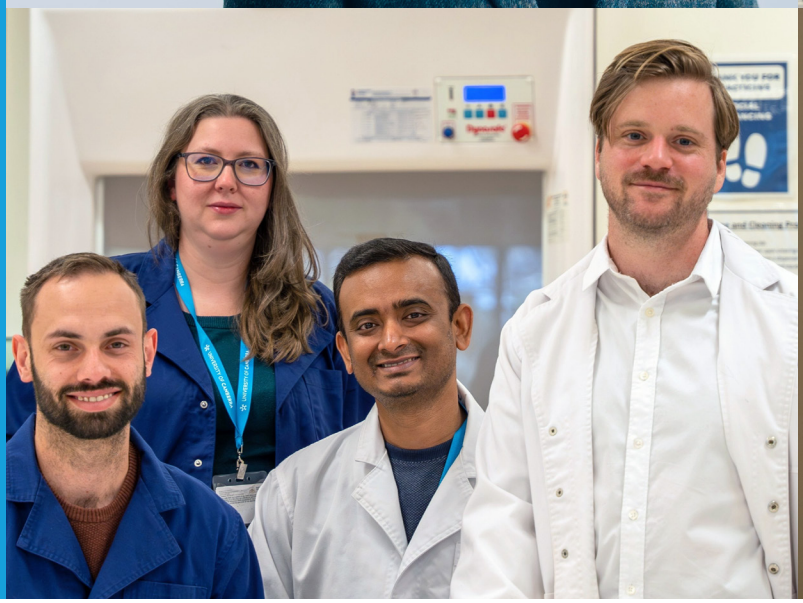
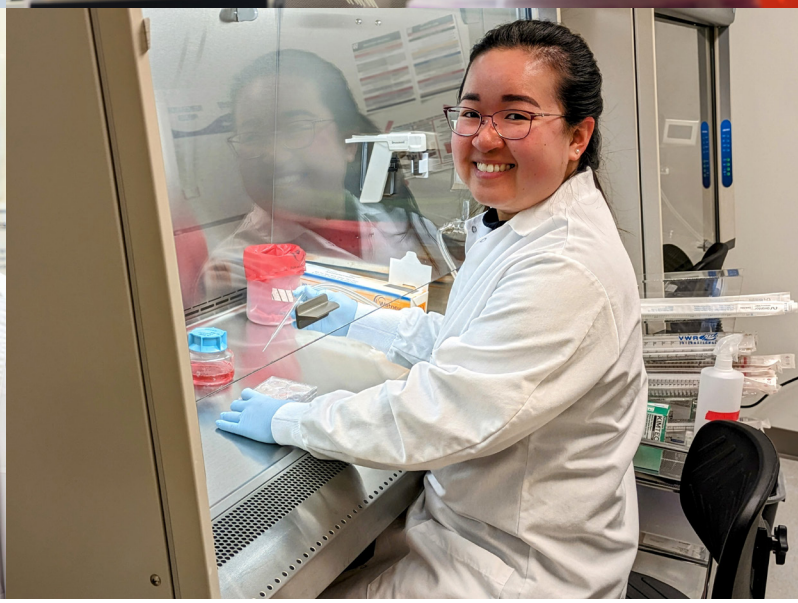
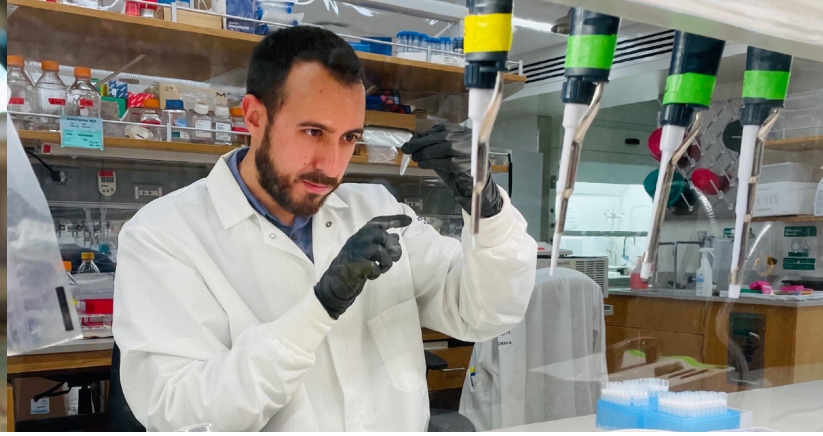


Research for a Better Tomorrow

2023 Macular Degeneration Research Projects

BrightFocus® Foundation | Macular Degeneration Research



Advancing Research Toward a Cure

Macular Degeneration Research, a BrightFocus Foundation program, is on a mission to cure and raise awareness about this sight-stealing disease impacting an estimated 20 million U.S. adults.

We believe that by providing initial funding for highly innovative experimental research and creative ideas, we can spark revolutionary approaches and vision-saving breakthroughs for this leading cause of blindness in people over age 50 worldwide.

We're funding 58 active research projects worldwide.

Since inception:

Nearly **$50 million** in research grants awarded

1,115 scientists supported across 338 grants

Macular Degeneration Research

Meet the Innovators

Research holds the key to finding a cure. Thanks to generous donor support, we have invested more than $50 million in groundbreaking studies aimed at furthering our understanding of the causes and potential prevention, treatment, and cure of macular degeneration.

Macular Degeneration Research invests in a wide range of innovative scientific approaches, from exploring ways to regenerate damaged cells to the influence of early-life events, diet, and nutrition on disease risk. By tackling the disease from many angles, we leave no stone unturned.

This research portfolio provides an overview of our current Macular Degeneration Research grant projects. Grants are vetted through a rigorous evaluation process by the world's top scientists and clinicians who serve on our scientific review committee.

We are deeply grateful to our donors, whose generosity makes it possible to fund the next generation of researchers pursuing novel, bold, and promising science for tomorrow's cure.

Explore all active grants:

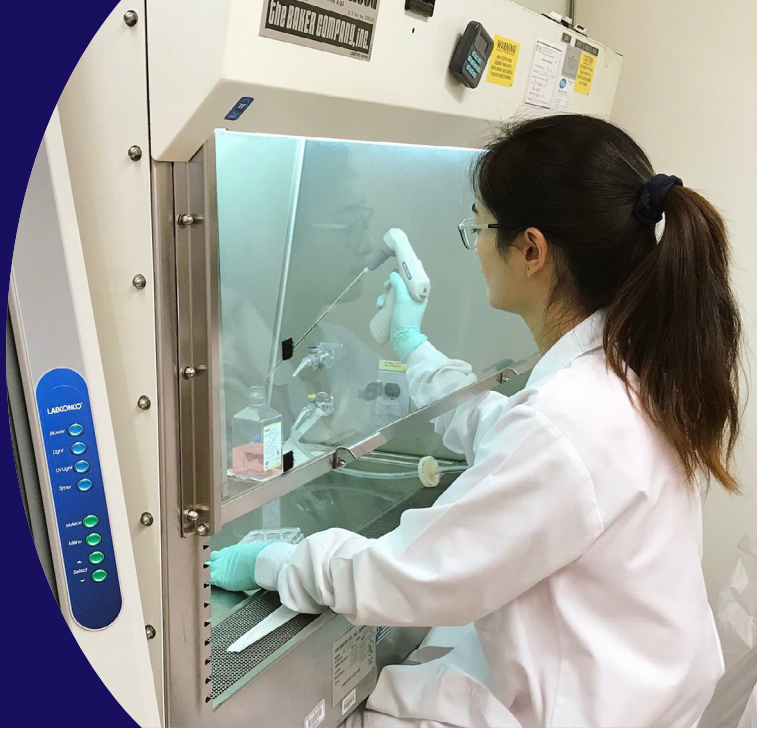
brightfocus.org/MDRgrants

Contents

Cover: *Macular Degeneration Research grantees.*

Note: *This portfolio reflects awarded grants as of July 25, 2023.*

Cell Metabolism



Above: *Dr. Shu in the lab, working with cell cultures to test compounds that might be protective against AMD. Photo courtesy of Daisy Shu, PhD, Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School.*

The retinal pigment epithelium (RPE) is a single layer of cells at the back of the eye next to the retina. Its health and ability to support the nerve cells of the retina depend on well-functioning cell metabolism as a source of energy.

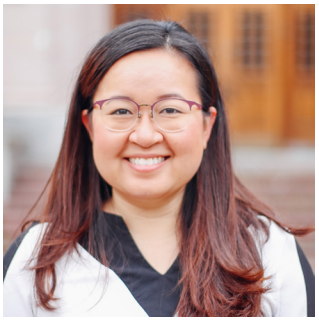
Grantees are examining the decline in cellular and mitochondrial ("cell powerhouse") energy production in the RPE and other retinal cells as possible triggers of age-related macular degeneration, or AMD.

Macular Degeneration Research-funded investigators are exploring how an imbalance between energy needs and production could contribute to the disease and are finding ways to restore health to the aging eye by improving cellular metabolism.

Getting to the Root of Fat Transport Dysfunction in AMD

Catharina Grubaugh, PhD | University of Pennsylvania
Mentor: Kathleen Boesze-Battaglia, PhD

This project focuses on a retinal pigment epithelium protein that drives lipid packaging. Researchers will knock out production of microsomal triglyceride transfer protein in the eye to study the effects of its absence. They then will study the added effects of aging and a high-fat diet, two risk factors for age-related macular degeneration. The results are expected to highlight potential treatments for defective lipid transport in the eye for preventing or slowing disease progress.



Interactions of Immune Proteins and Glucose Breakdown in Severe, Hereditary AMD

Rayne Lim, PhD | University of Washington
Mentor: Jennifer Chao, MD, PhD

This project relies on a model of a severe, inherited form of age-related macular degeneration to study the interactions of glucose breakdown and the complement pathway, an immune process. Researchers will evaluate how adding the normal form of the gene to cells affects disease-related changes to the retinal pigment epithelium. This is the first such study of the links between complement pathway activity and glucose metabolism in this context and is expected to highlight treatment targets.

Elucidating the Role of Metabolic Reprogramming in RPE Dysfunction and Inflammation in AMD

Daisy Yao Shu, PhD | Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School
Mentor: Leo A. Kim, MD, PhD

This proposal seeks to increase our understanding of the interplay between metabolism and inflammation in age-related macular degeneration. Resveratrol (found in red wine) is a drug known to enhance metabolic function and suppress inflammation. Its efficacy in blocking tumor necrosis factor-alpha, or TNF-α, will be tested as a potential drug target for age-related macular degeneration.

Transcriptional Regulation of Cellular Organelle Function in the Retinal Pigment Epithelium

Mallika Valapala, PhD | Indiana University

This proposal addresses strategies by which the degradative ability of lysosomes (cellular organelle) can be enhanced or restored to augment clearance of cellular waste that declines with advanced age. These strategies help keep the intracellular environment of the cell clean and promote overall cellular health.

Macular Degeneration, Metabolism, and a Novel Mitigation Strategy

Thomas Wubben, MD, PhD | University of Michigan

While the exact cause of age-related macular degeneration remains unknown, deregulation of cellular metabolism is believed to be critical to its pathogenesis. This project will reveal the significance of modulating metabolic targets important in macular degeneration, which may have immediately translatable applications to clinically treat patients.

Quick Facts

- Macular degeneration is a disease of the retina that affects the macula in the back of the eye.
- Because the early signs are often subtle, many people may not notice symptoms until vision begins to fade.
- The disease is most common in people over age 60, which is why it is often called age-related macular degeneration, or AMD.

Diet & Nutrition's Impact on Age-Related Macular Degeneration Risk

The current treatment for preventing progression of intermediate age-related macular degeneration, or AMD, is a supplement combination that showed effectiveness in two large National Institutes of Health studies.

The AREDS2 (Age-Related Eye Disease Study 2) eye formula combines vitamins C and E, the pigments lutein and zeaxanthin, and zinc and copper. Investigators are exploring how to increase uptake of carotenoids (pigments like lutein and zeaxanthin that give fresh produce their bright red, yellow, and orange colors), an important nutrient in macular health. A Mediterranean-style diet rich in fish, whole grains, fruits, and leafy vegetables also is of interest.

Our diet helps shape a healthy immune response, including through effects on the microorganisms that live on and inside our body, such as gut bacteria. Ideally, these dietary findings will translate into clinical use and "vision healthy" lifestyles.

Exploring the Role of Gut Bacteria in Early AMD

Christopher Hammond, MD, MRCP, FRCOphth | King's College London (UK)

The gut microbiome can influence and modify the body's immune responses and may be relevant in age-related macular degeneration. The aim of this project is to explore the role of the gut microbiome in this condition, which may enhance understanding of the disease and support development of new therapies for age-related macular degeneration.

The Gut Bacteria and AMD in Aging Women

Amy Millen, PhD | University at Buffalo

Studying gut bacteria as a modifiable risk factor for age-related macular degeneration is relevant to public health. Evidence of a protective association between certain gut bacteria profiles and age-related macular degeneration could lead in the long term to easily implemented, low-cost interventions to modify the gut bacteria with diet or highlight potential metabolic pathways for treatment to prevent age-related macular degeneration.

How AMD Risk Factors Interact in Disease Development

Freya Mowat, PhD | University of Wisconsin-Madison

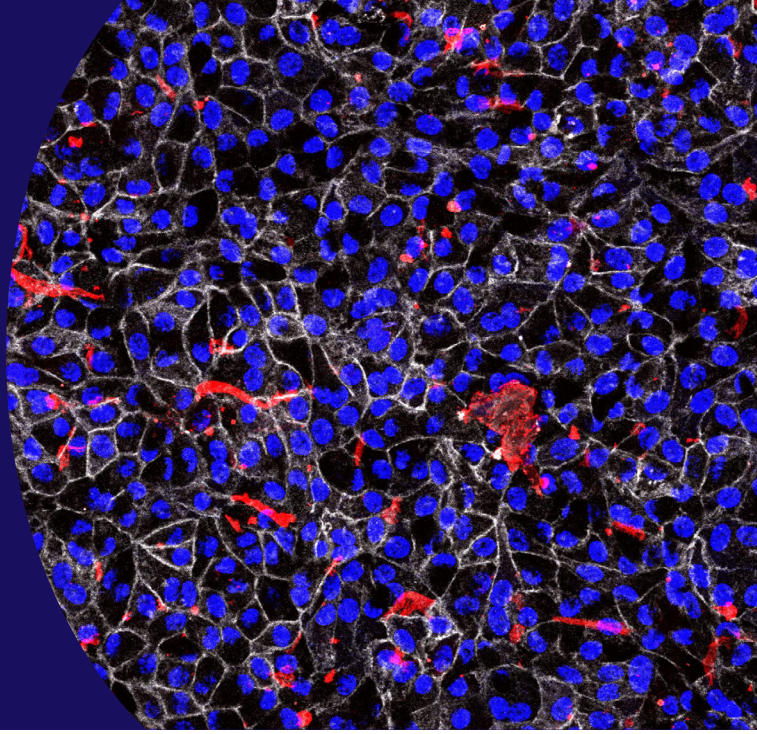
Researchers will characterize how genetics, age, and diet interact in age-related macular degeneration risk as the basis for a tool for therapeutics development and testing. A novel aspect is the focus on how these factors affect DNA methylation, which has not been clarified, especially in early stages of the disease. Such a model could be used to test whether candidate therapies prevent accumulation of methylation changes associated with these risk factors.

The Molecular Events in Early Life That Lead to AMD

Przemyslaw Sapieha, PhD | Hôpital Maisonneuve-Rosemont (Canada)

Immune cells play a key role in aberrant blood vessel growth during age-related macular degeneration. They change because of pathogen encounters and in chronic states such as obesity. Researchers will assess whether immune cells change in a way that increases risk for age-related macular degeneration after weight gain and subsequent weight loss. The work will yield insights into mechanisms underlying age-related macular degeneration, potentially opening a path to targeted interventions.

Drusen Formation & Immune Response



Above: *An image of patient-derived induced pluripotent stem cells, differentiated to RPE cells, showing the cell boundaries in white and vitronectins, proteins found in drusen, in red. Photo courtesy of Daniel Hass, PhD, University of Washington.*

As the eye ages, it becomes less efficient at removing waste. Deposits of extracellular waste products containing fats and proteins, known as drusen, may collect within and beneath the retinal pigment epithelium cell layer and trigger an immune response. In fact, when spotted on a comprehensive eye exam, drusen often are the first sign of age-related macular degeneration, or AMD; increases in the number and size of drusen may cause the immune system to kick into overdrive.

Ultimately, an out-of-control immune response may reach a tipping point and damage cells in the macula, or central part of the eye, which provides sharp central vision. Researchers are focusing on specific aspects of the immune response, including testing drugs that can clear the waste deposits that contribute to AMD.

A New Animal Model of Severe Age-Related Macular Degeneration

Brittany Carr, PhD | University of British Columbia (Canada)
Mentor: Orson Moritz, PhD

This study involves characterizing a new animal model of age-related macular degeneration that will facilitate insights into the relationship between disease progression and reticular pseudodrusen, or RPD. Establishing RPD as an early indicator of age-related macular degeneration and understanding its role in disease progression will result in more effective prevention of blindness associated with the condition.

Can Fatty Acid Oxidation Influence Drusen Levels in the Eye?

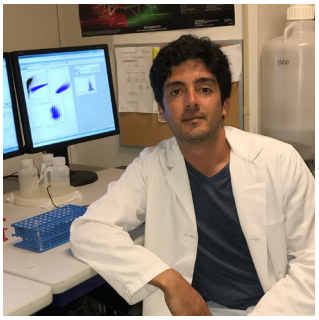
Daniel Hass, PhD | University of Washington
Mentor: James Hurley, PhD

Researchers will establish the effect of a small molecule on fatty acid metabolism, cell function, and deposit levels in multiple cell culture and mouse models of age-related macular degeneration. The small molecule in this study has been tested in humans in clinical trials, indicating its safety. If it is effective at decreasing deposit levels, the transition to clinical use may be more rapid than for untested treatments.

Origin, Heterogeneity, and Function of Immune Cells in a Wet AMD Model

Jeremy Lavine, MD, PhD | Northwestern University Feinberg School of Medicine
Mentors: Harris R. Perlman, PhD & Amani Fawzi, MD

Macrophages are immune cells present in different subtypes, with classical-derived macrophages promoting wet age-related macular degeneration and nonclassical macrophages blocking its development. This group has identified a macrophage subset that expresses blood vessel growth factors derived from classical macrophages and is present in patients with wet age-related macular degeneration. The researchers aim to identify nonclassically derived macrophage subsets and establish their inhibition of experimental wet age-related macular degeneration.



Tracking How Rare Eye Immune Cells Respond to Damage in AMD

Abdelilah Majdoubi, PhD | Yale University
Mentor: Brian Hafler, MD, PhD

Microglia in the retina are the focus of this project, which will expand our understanding of how these retinal immune support cells react to damage in age-related macular degeneration. Researchers will genetically analyze an unusually expansive bank of tissues for this work, which they expect to yield treatment targets, especially related to the C3 complement pathway, an immune response pathway closely implicated in age-related macular degeneration.

Ciliary Lipids in RPE Repair: A Novel Target for AMD

Ke Ning, MD | Stanford University
Mentors: Yang Sun, MD, PhD & Vinit Mahajan, MD, PhD

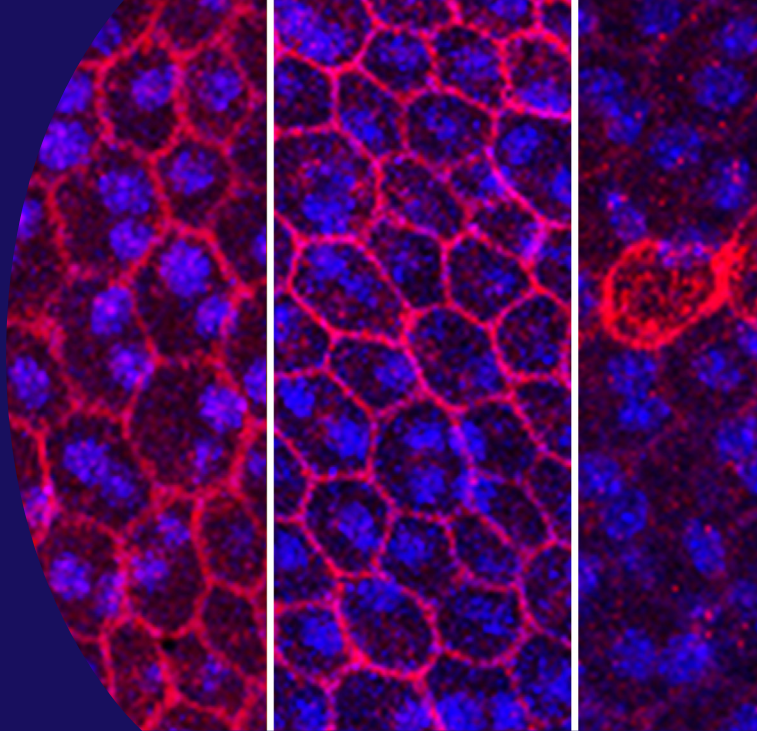
Researchers have discovered a novel role of an organelle, the antenna-like retinal pigment epithelium (RPE) cilia, involving control of RPE repair in mice. Having shown that loss of these organelles promotes cell proliferation and wound healing, this group will study how the RPE cilia mediate these two processes. The results will facilitate understanding of how this organelle works in RPE proliferation, highlighting targets for drug development.

A Newly Discovered Eye Immune Environment in AMD

James Walsh, MD, PhD | Washington University in St. Louis
Mentor: Jonathan Kipnis, PhD

The goal of this project is to explore a newly identified local immune environment in the choroid, a supportive layer for the retina at the back of the eye. The work is novel as a first look at this local immunity in the eye and its potential role in age-related macular degeneration. Uncovering immune targets specific to the eye in this disease could lead to rapid development of treatments affecting these targets.

Genes & Age-Related Macular Degeneration



Above: *Understanding the role of MYRF transcription factor, which controls expression of other genes in the RPE. Images from models with normal level (left), low level (middle), and absence (right) of MYRF are studied by following the expression of an RPE membrane marker, shown in red. Photo courtesy of Lev Prasov, MD, PhD, University of Michigan.*

Most forms of macular degeneration are not linked to any single genetic mutation. Instead, susceptibility to age-related macular degeneration, or AMD, is scattered over a number of small irregularities of genes called single nucleotide polymorphisms (SNPs).

SNPs can arise spontaneously or be inherited, and their impact is tempered by factors such as age, overall health and nutrition, and exposure to cigarette smoke, sunlight, and other toxins.

Targeted gene research could lower the risk of AMD by blocking or replacing signals from genes that trigger disease and defend retinal pigment epithelium (RPE) cells against oxidative stress from aging and other causes.

The Role of Mitochondrial Dysfunction in AMD

Navdeep Gogna, PhD | The Jackson Laboratory
Mentor: Patsy M. Nishina, PhD

The project aim is to characterize the effects of a risk-related gene, ARMS2, on mitochondrial dysfunction and fat processing in age-related macular degeneration. This work is the first to investigate how a specific ARMS2 variant influences mitochondrial function and fat processing and leads to increased risk for age-related macular degeneration. Researchers expect the findings to highlight new treatment targets for the disease.

Investigating Genetic or Immune Factors in AMD

Michelle Grunin, PhD | Hebrew University of Jerusalem (Israel)
Mentors: Shai Carmi, PhD & Jonathan L. Haines, PhD

Researchers will use novel technological tools and newly available diverse ancestry reference panels to identify new genetic risk factors for age-related macular degeneration and new genetic or immune system-related treatment targets. This group will use the genetics available through the International Age-Related Macular Degeneration Genomics Consortium, with over 50,000 samples, to investigate these issues on a large scale. Inclusion of multiethnic participants will support discovery of rare genetic variants.

Generating a Precision Model for AMD Research

Jürgen Naggert, PhD | The Jackson Laboratory

This proposal aims to develop animal models that mimic human disease and allow for determining the function of human genes that increase the risk of developing age-related macular degeneration. This work has the potential to greatly facilitate the development of new treatment strategies.

Mouse Models for Subretinal Fibrosis

Patsy M. Nishina, PhD | The Jackson Laboratory
Co-Principal Investigator: Jürgen Naggert, PhD

Tissue damage in the back of the eye may lead to formation of scar tissue, or fibrosis, which causes vision impairment. In this study, researchers will characterize two new genetic models of subretinal fibrosis, a common complication of wet age-related macular degeneration, and provide insights into pathways that may underlie the disease.

Gene Regulation of RPE Maintenance

Lev Prasov, MD, PhD | University of Michigan

This group has identified a new gene that controls expression of other genes in the retinal pigment epithelium (RPE) and leads to dysfunction. Researchers will evaluate the role of this gene in maintaining adult RPE function and its ability to protect against stresses that lead to age-related macular degeneration. The findings may open new avenues for treatment of the disease by targeting this gene or its downstream targets.

Functional Characterization of Genetic Regulatory Effects of AMD Risk Variants

Rinki Ratnapriya, PhD | Baylor College of Medicine
Mentor: John Timothy Stout, MD, PhD

For this work, researchers will integrate findings from genome-wide association studies with findings related to the transcriptome (representing protein-coding regions of genes) and epigenome (representing molecular tags on DNA that affect its use). The aim is to identify underlying causal genetic variants, regulatory elements, and target genes to address major gaps in mechanistic understanding of age-related macular degeneration.

Profiling of Immune Cell Subtypes in AMD Patients and Controls

Philip Ruzycki, PhD | Washington University in St. Louis
Co-Principal Investigator: Rajendra Apte, MD, PhD

For this project, researchers will seek to understand the genetic basis of age-related macular degeneration. By leveraging the most innovative genomic techniques available, they will gain insights into biomarkers for disease progression and identify novel targets for preventive therapeutics.

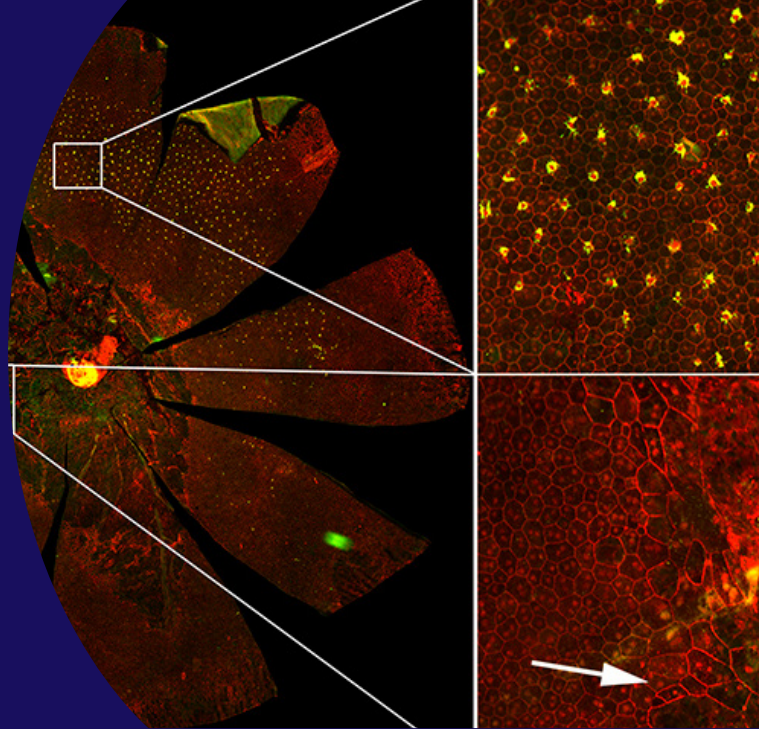
This award is supported by the Ivan Bowen Family Foundation.

Machine Learning to Predict AMD-Associated Genetic Variant Impact

Leah VandenBosch, PhD | Seattle Children's Hospital
Mentor: Timothy Cherry, PhD

For this project, researchers will apply machine learning to human retinal and retinal pigmented epithelium genomic data. They aim to predict how variations in the noncoding regions, which are stretches of DNA that do not code for proteins, contribute directly to age-related macular degeneration.

Geographic Atrophy



Above: *In an animal model of geographic atrophy, RPE cell boundaries (red) are lost in the central region, and microglia (green) are recruited to the area to protect the tissue. Photo courtesy of Claudio Punzo, PhD, University of Massachusetts Chan Medical School.*

Some people with age-related macular degeneration, or AMD, will develop geographic atrophy, an advanced and severe form of dry AMD that can lead to permanent vision loss. In geographic atrophy, regions of cells in the retina waste away and die (atrophy), resulting in dead zones and an expanding blind spot near the center of the visual field.

The first treatments for geographic atrophy were approved by the Food and Drug Administration in 2023, and several other promising treatments are undergoing testing in clinical trials. Macular Degeneration Research is funding innovative research into new drugs and ways to manage and treat this complex form of AMD responsible for around 20% of cases of legal blindness in North America.

A New Method for Prediction of the Two Advanced Types of AMD

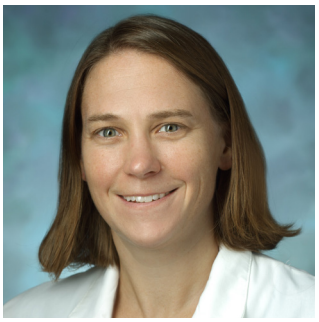
Paul Baird, PhD | The University of Melbourne (Australia)
Co-Principal Investigators: Adam Kowalczyk, PhD & Alice Pebay, PhD

This proposal brings together different areas of medicine and biology and applies advances in high throughput computing and big data analysis to aid our understanding and advancement of treatments for age-related macular degeneration, particularly the dry form. This study will identify genes that interact with each other as well as with other factors known to be involved in increased risk of age-related macular degeneration such as age, gender, and smoking.

Investigating Multiarmed Cell Death (PANoptosis) in Dry AMD Progression

Lucia Celkova, PhD | Trinity College Dublin (Ireland)
Mentor: Matthew Campbell, PhD

The aim of this research is to explore a master "decision maker" that could integrate and process these triggers and guide the fate of retinal pigment epithelium (RPE) cells toward either survival or death. Through this work, researchers expect to gain a better understanding of the complex process underlying RPE cell death and to identify potential new targets and strategies for therapeutic intervention in dry age-related macular degeneration.

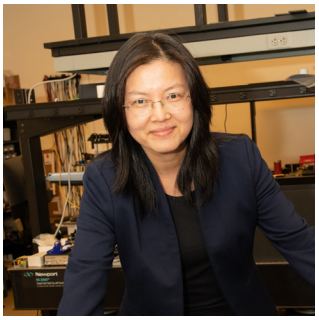


Understanding the Role of Support Cells, Known as Glia, in Geographic Atrophy

Malia Edwards, PhD | Wilmer Eye Institute, Johns Hopkins University

For this work, researchers will take a novel approach to studying geographic atrophy by investigating the role of glial cells. These cells, traditionally considered only support cells, are altered in geographic atrophy. In the proposed studies, the team will investigate how changes to these cells may influence disease progression and the effectiveness of treatments.

This award is supported by the Victor and Anna Mae Charitable Foundation.



Imaging Tiny Blood Vessels in the Eye for Markers of AMD

Yali Jia, PhD | Oregon Health & Science University

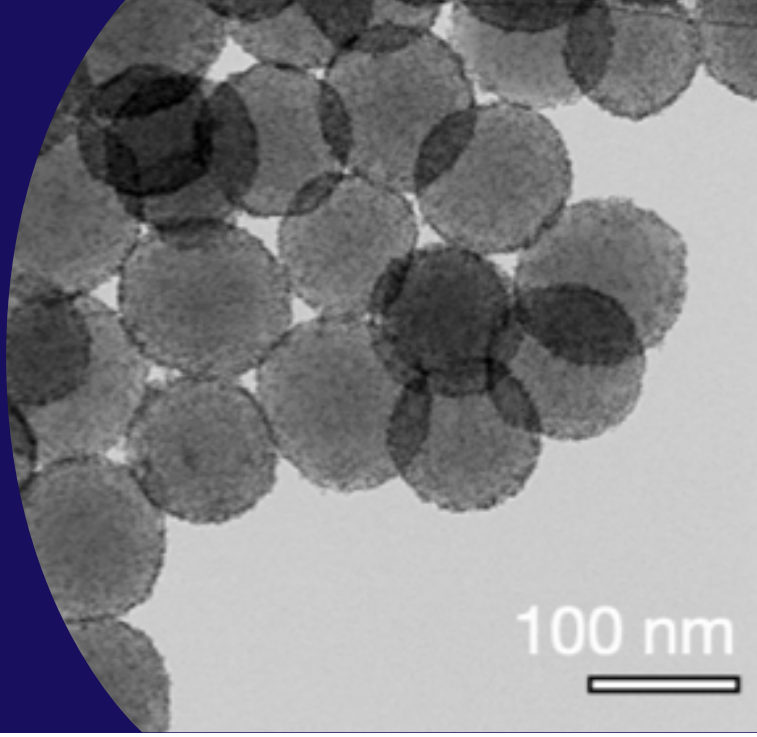
For this project, researchers will develop an imaging device that tracks blood flow in the eye as a disease marker in age-related macular degeneration. With this cost-effective tool, researchers will identify features that specifically undergo changes during progression of the disease to characterize biomarkers of the process. The tool is expected to allow prediction of development and progression of specific features of age-related macular degeneration, including geographic atrophy.

Cellular Scale Characterization of the RPE-Photoreceptor Complex in a Model for Geographic Atrophy Progression

Kristen Bowles Johnson, PhD, OD | Indiana University
Mentors: Donald T. Miller, PhD & Jennifer J. Hunter, PhD, University of Rochester

In this study, researchers will use a camera called an adaptive optics ophthalmoscope to take pictures of fluorescent clumps in retinal pigment epithelium cells and measure how sick photoreceptors become as the disease progresses. The results could characterize biomarkers for identifying patients most likely to benefit from a specific treatment and for determining treatment efficacy.

Innovative Approaches to Treatments



Above: *Cerium (Ce) ion imaging is used to understand the antioxidative activity of ceria-coated melanin nanoparticles (CMNPs), which may provide a potential treatment for AMD. Photo courtesy of Yong-Su Kwon, PhD, University of North Carolina at Chapel Hill.*

One day, we may be able to detect signs that age-related macular degeneration, or AMD, is developing and take early steps to defend against it.

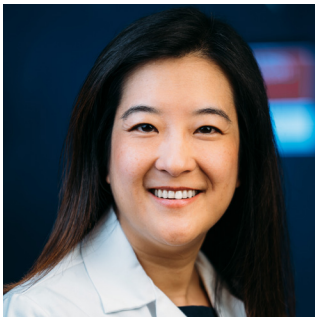
Macular Degeneration Research is funding research into unique ways to protect the retinal pigment epithelium (RPE) and retina before sight damage has occurred, including drugs that enhance immune functioning and improve the eye's ability to clear lipids/fats and other waste that could lead to inflammation in AMD.

New imaging techniques will support better tracking of disease progression over time, and gene therapy is being evaluated as a possibility for treating AMD.

Functional Imaging of the Human Retina Using Noninvasive Technology

Andrew Browne, MD, PhD | University of California, Irvine
Mentor: Krzysztof Palczewski, PhD

In this study, researchers will develop a camera for use in humans and directly examine the causes of age-related macular degeneration. Researchers will combine microscopy technology that is already used to study models with a device that can noninvasively acquire images at high enough resolution to reveal events inside the cell.



A Novel Method for Modeling AMD in a Dish

Jennifer Chao, MD, PhD | University of Washington

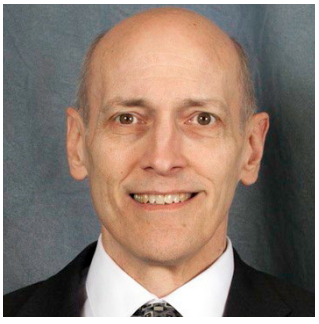
The goal of this proposal is to develop and study a three-dimensional model that mimics the microvascular networks and structure formed by the retinal pigmented epithelium (RPE) cells and choriocapillaris of the eye. This model will allow study of the essential elements of RPE-related diseases, such as drusen deposition, blood flow effects, and blood vessel permeability.

Identifying FDA-Approved Drugs to Reverse Dry AMD

Steffi Daniel, PhD | University of Texas Southwestern Medical Center
Mentor: John Hulleman, PhD

This study will employ a novel "disease in a dish" system to screen for more than 1,500 Food and Drug Administration-approved drugs for their ability to reverse disease. Lead drugs from this screen also will be extensively and rigorously tested in a preclinical model system. If successful, the results from this study will contribute toward transforming age-related macular degeneration therapeutics.

This award is supported by the Ivan Bowen Family Foundation.



Ocustatin for Treatment of Intermediate AMD

John Edwards, MS, MBA | Drusolv Therapeutics
Co-Principal Investigators: Joan Miller, MD & Demetrios Vavvas, MD, PhD, Harvard University

The goal of this project is to develop a novel, high-dose reformulation of oral atorvastatin for early intervention in age-related macular degeneration.

New Automated Method to Predict AMD Progression

Joelle Hallak, PhD | University of Illinois Chicago
Co-Principal Investigators: Daniel Rubin, MD, Theodore Leng, MD, FACS & Luis de Sisternes, PhD, Stanford University; Carl Zeiss, Meditech

The aim of this proposal is to develop a tool to predict the chances of age-related macular degeneration progression on a personalized, patient-by-patient basis, using images of the retina and the patient's genetic, historical, demographic, and behavioral data.

What Squirrels Can Teach Us About Treating AMD

Sangeetha Kandoi, PhD | University of California, San Francisco
Mentor: Deepak A. Lamba, MBBS, PhD

The main goal of this project is to trace how the squirrel eye rescues the retina from hibernation stress damage that is similar to age-related macular degeneration. Researchers will explore the molecular steps that the eyes of the 13-lined ground squirrel undergo for these repairs. The ultimate goal of this work is to develop therapies that could, as with these squirrels at each annual wakening, restore damaged vision.

Advanced Imaging Studies in a Model of Type 3 Neovascular AMD

Tyson Kim, MD, PhD | University of California, San Francisco
Mentors: Douglas Gould, PhD, Aparna Lakkaraju, PhD & Dan Schwartz, MD

This project focuses on formation of chorioretinal anastomoses, fusions that arise between the retinal and choroidal vascular networks. Using models of neovascular age-related macular degeneration, researchers will develop an advanced imaging method for looking deep into the living eye at cellular resolution to gain molecular information. They also will measure blood flow in individual microvessels. The findings will support development of more effective treatments for neovascular age-related macular degeneration.

Dark Matter: Developing a Nanoantioxidant-Based Therapeutic System for AMD

Yongsu Kwon, PhD | University of North Carolina at Chapel Hill
Mentor: Han Zongchao, MD, PhD

The aim of this study is to develop a new combination antioxidant system to scavenge free radicals, which are the toxic waste products that gradually build up in cells over time. The findings may demonstrate long-term effects and reduced damage in age-related macular degeneration.

How Does Mechanical Stress Injure the Retinal Pigment Epithelium in AMD?

Aparna Lakkaraju, PhD | University of California, San Francisco

In this study, researchers will use advanced live imaging of the retina along with genetic and molecular approaches. They will study how insoluble aggregates mechanically stress the retinal pigmented epithelium (RPE), leading to atrophy and detachment of RPE cells and permanent vision loss. At each step, the researchers will evaluate drugs that can preserve the health of the RPE and prevent RPE loss in disease models.

Recipient of the Lorraine Maresca Award.

Stem Cell Therapy for Early AMD

Narendra Pandala, PhD | University of Iowa
Mentor: Budd Tucker, PhD

The aim of this project is to use adult-derived stem cells to restore tiny blood vessels in the eye that are lost at the onset of age-related macular degeneration. To encourage the stem cells to repopulate the lost capillaries, researchers will test a biomaterial that supports targeted injection of the cells. They expect their work to yield an injectable stem cell delivery system with possible clinical applications.

Immune Cell Traps in Inflammation and Wet AMD

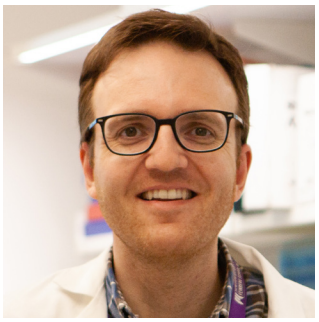
Matthew Rutar, PhD | University of Canberra (Australia)

The aim of this project is to explore the role of neutrophil extracellular traps, or NETs, in neovascular age-related macular degeneration. Researchers will use mouse models and donor tissues to test candidate inhibitors of NET activity. Current therapies are focused on limiting rogue growth of blood vessels, so identifying new targets related to inflammation offers new opportunities for treatment.

Stem Cell-Based Approaches to Identify New Drugs for Treating Dry AMD

Srinivasa Rao Sripathi, PhD | Retina Foundation of the Southwest

The aim of this project is to develop novel treatments for age-related macular degeneration by utilizing stem cell-derived retinal pigment epithelium (RPE) cells to screen for molecules (potential drugs) that inhibit RPE damage and reduce epithelial-mesenchymal transition to help RPE cells maintain their integrity.



Understanding the Link Between Blood Vessels in the Eye and Vision Loss

Benjamin Thomson, PhD | Northwestern University-Chicago Campus

Typical wet age-related macular degeneration is most commonly seen in patients of European ancestry, but similar disease in patients of Asian and African ancestry is more commonly associated with polypoidal choroidal vasculopathy (PCV). This work will characterize the role of a recently identified, important blood vessel regulatory system (known as the angiopoietin signaling pathway) in PCV and test new drug candidates targeting this pathway.

A New Approach to Modeling Subretinal Tissue

Elizabeth Vargis, PhD | Utah State University

This team of biological engineers proposes to design a multilayered model with human retinal cells and blood vessels that realistically mimics the back of the eye. This model will be subjected to varying disease conditions to test and develop treatments that can effectively stop vision loss.

A Novel Method for Treating Wet AMD Reversibly With Single Intraocular Injection

Shusheng Wang, PhD | Tulane University
Co-Principal Investigator: Bo Yu, PhD

The study aim is to establish a novel gene regulation system that can turn off vascular endothelial growth factor, or VEGF, a gene responsible for the growth of new blood vessels. The aim is to reduce levels of VEGF protein in wet age-related macular degeneration. This gene system combines potency, tight control of VEGF, and safety and can be used to treat the disease with just one intraocular injection.

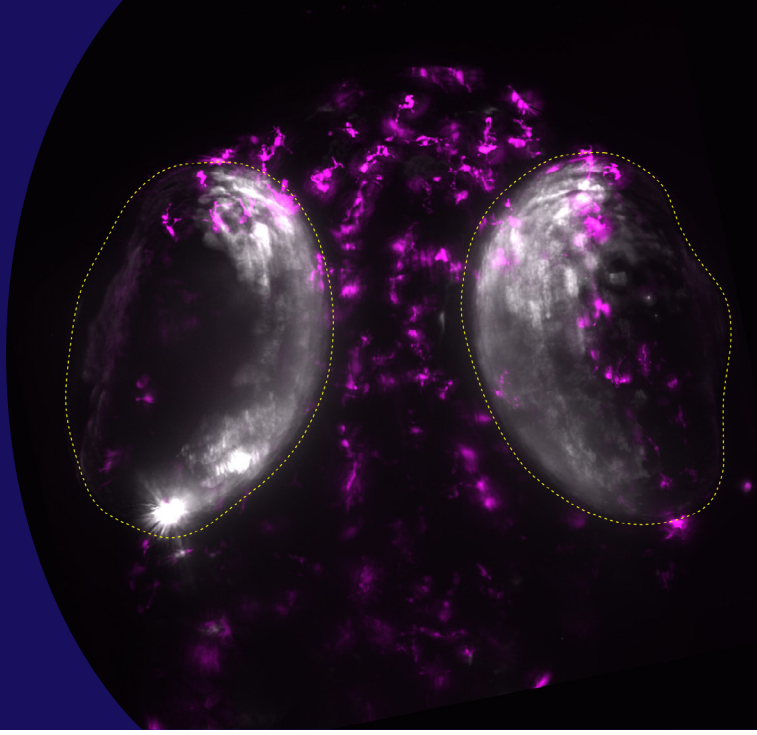
This award is supported by the Free Family Foundation.

Development of Gene Editing as a Permanent Cure for Wet AMD

Glenn Yiu, MD, PhD | University of California, Davis

For this work, researchers are tackling wet age-related macular degeneration by developing a potential cure using a powerful gene-editing technology called CRISPR. This innovative gene-editing system can permanently change the genes that cause this disease. The hope is that CRISPR can someday be used to preserve vision in the aging population.

Regenerating Damaged Cells



Above: *The retinal pigment epithelium, located at the back of the eye, is labeled in white and macrophages are shown in purple. Photo courtesy of Lyndsay Leach, PhD, University of Texas at Austin.*

Unlike human skin, the nerve cells of the eyes do not typically regrow or regenerate after damage has occurred. But there is new hope for overcoming this biological limitation.

Work is moving forward to regenerate and reconnect the eye's retinal cells that have been damaged by age-related macular degeneration, or AMD, and to restore the underlying retinal pigment epithelium (RPE) cells.

Grantees are recreating parts of the eye using human induced pluripotent stem cell (iPSC) technology—stem cells created from living adult tissue. Cell regeneration in animal models also is being studied for its applicability to human therapy.

Regenerative Response in Spiny Mice

Manas R. Biswal, PhD | University of South Florida

Degeneration of the neural retina and in the retinal pigment epithelium (RPE) is associated with the advanced atrophic form of dry age-related macular degeneration. Since photoreceptors in the neural retina and RPE cannot be replaced once they die, treatments boosting the endogenous factors to stimulate retinal tissue regeneration could be a novel therapeutic strategy. The goal is to study ocular regeneration following tissue injury in an animal model that could facilitate studies to develop potential treatments for dry age-related macular degeneration in humans.

This award is supported by the Free Family Foundation.

Discovery of New Methods to Regenerate Cone Photoreceptors

Mark Emerson, PhD | The City College of New York

Cone photoreceptors are the critical light-sensing sensory cells that are lost in age-related macular degeneration. Researchers will use high-resolution molecular techniques to identify genes that are normally active in forming cone photoreceptors. The team will identify gene candidates that can turn other retinal cells into cones as a way to develop new cone replacement therapies for age-related macular degeneration.

Uncovering Immune-Related Factors Driving Retinal Pigment Epithelium Repair

Lyndsay Leach, PhD | University of Texas at Austin

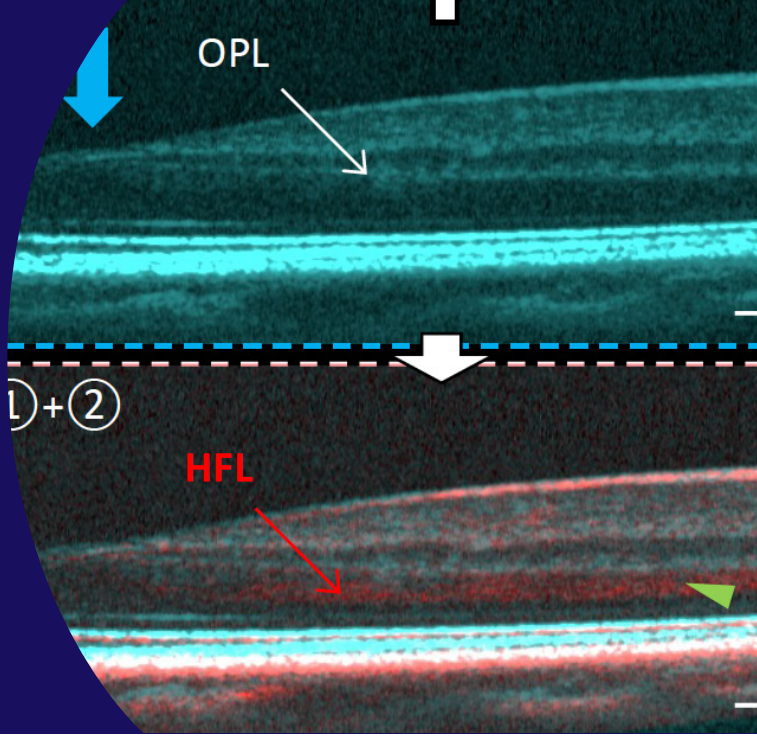
In this project using zebrafish as a lab model of tissue damage repair, researchers will examine how the immune response affects retinal pigment epithelium (RPE) repair. They expect to uncover novel factors in regenerating RPE that, in turn, represent candidates for treating or even reversing tissue loss in age-related macular degeneration.

Killifish: A Novel Model of AMD

Nicole C.L. Noel, PhD | University College London (UK)
Mentor: Ryan MacDonald, PhD

This work provides the unique opportunity to develop killifish as a retinal aging model, determine the cellular mechanisms that lead to age-related macular degeneration, and assess how healthy retinal aging can be promoted in a model of age-related retinal degeneration.

Understanding Early-Stage Age-Related Macular Degeneration



Above: *An advanced imaging technique to visualize a normally invisible retinal layer, Henle's fiber layer (HFL), and study its role in AMD. Photo courtesy of Yifan Jian, PhD, Oregon Health & Science University.*

While the exact cause of age-related macular degeneration, or AMD, is unknown, the strongest risk factor for developing the disease is changes in the eye that happen with age. Researchers believe that AMD begins in the retinal pigment epithelium (RPE), a layer of cells next to the retina that transports molecules in to nourish the retina and out to dispose of waste.

The RPE's ability to do this job can be compromised by age, genes, oxidative stress, inflammation, and other factors. Macular Degeneration Research is funding scientific exploration into the causes of AMD to open new and earlier treatment avenues.

Examining the Role of Choroidal Blood Flow in AMD

Bradley Gelfand, PhD | University of Virginia

Researchers will use donor eyes and cutting-edge computer modeling to understand whether choroidal blood flow predisposes and contributes to age-related macular degeneration (AMD). Insights obtained from these studies could inspire new diagnostic and therapeutic tools targeting the choroidal blood vessels to improve AMD management.

Regulation of Capillary Blood Flow in the Choroid Vasculature

Albert Gonzales, PhD | University of Nevada, Reno

Researchers will examine how blood vessels can respond to light and change blood flow in the eye. This process is important not only for the delivery of vital oxygen and nutrients for cell survival but also for the removal of waste deposits that can lead to diseases like age-related macular degeneration. The completed work is expected to yield insights into the active physiological role of capillaries in the choroid vasculature.

Discovering an Invisible Layer in the Retina and Its Ties to AMD

Yifan Jian, PhD | Oregon Health & Science University
Mentor: Brandon Lujan, MD

In this study, researchers are developing a novel retina imaging device capable of volumetric directional optical coherence tomography. The aim is to measure a new candidate biomarker, the true thickness of the outer nuclear layer (ONL). The ability to measure ONL could lead to an improved understanding of the retinal degeneration in age-related macular degeneration and the effects of therapeutic interventions.

Identifying New Factors That Play a Role in Early-Onset Drusen Maculopathy

Yara T.E. Lechanteur, MD, PhD | Radboud University Nijmegen Medical Centre (The Netherlands)
Mentor: Frans Cremers, PhD

Researchers will evaluate young-onset cases of drusen maculopathy by studying family members of those who are affected and by looking at genetic factors and specific markers in blood samples. The aim is to identify new factors involved in this disease. Better knowledge about the disease can aid in the development of future therapies and may bring us a step closer toward treatment.

A Charity-Led, Big Data Resource for Discovery of Novel Biomarkers for Multiple Conditions Using Eye Scans

Wen Hwa Lee, PhD | Action Against AMD (UK)

The goal of this project is to build a prospective dataset of high-content images and three-dimensional subtissue retinal scans of 500,000 participants with consent for secondary use and linkage to other health datasets.

Identifying Signals That Draw Immune Cells to Damaged Tissues in Age-Related Macular Degeneration

Kelly Mulfaul, PhD | University of Iowa

For this project, researchers aim to identify the molecules that attract immune cells to damaged tissue in age-related macular degeneration. These cells are predicted to sometimes do more harm than good and to be involved in the death of choroid cells of the eye. An understanding of what draws these immune cells to the choroid at various stages of age-related macular degeneration will support the search for treatments based on the target stress signals.

Exploring the Role of Lipid Metabolism in AMD Pathogenesis

Rohini M. Nair, PhD | University of Pennsylvania
Mentor: Venkata Ramana Murthy Chavali, PhD

The aim of this study is to unravel the role of hepatic lipase in age-related macular degeneration. This molecule breaks down high-density lipoproteins into smaller, denser particles to be cleared away by systemic circulation. Clarifying its role in regulating cholesterol efflux using cellular models of retinal pigment epithelium derived from adult stem cells and animal models may support design of targeted therapies for slowing disease progression.

Macular- and Midperipheral-Specific iPSC-RPE Models to Discover Regional RPE Susceptibility in AMD

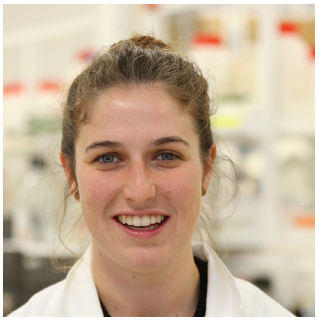
Davide Ortolan, PhD | National Eye Institute, NIH
Mentors: Kapil Bharti, PhD & Ruchi Sharma, PhD

This study will identify molecular and physiological differences between two populations of retinal pigment epithelium (RPE) cells, derived respectively from the central and peripheral retina, to determine what makes central RPE more vulnerable than peripheral RPE. This new knowledge, combined with the availability of an easily reproducible model of RPE in a dish, will eventually translate to the development of drugs that prevent vision loss caused by age-related macular degeneration.

Addressing the Link Between Impairment in Phagosome Degradation and AMD

Antonio Escudero Paniagua, PhD | University of California, Los Angeles
Mentor: David Williams, PhD

Researchers will investigate a cell structure called the phagosome, which forms around particles engulfed by a cell. They will compare phagosome stages between retinal pigment epithelium cells from patients with macular dystrophy and cells from unaffected patients and mouse models. The findings are expected to highlight new approaches to identifying and understanding how macular dystrophies arise and could be key to new strategies to stop or prevent them.



The Potential Role of the Cell's Sugar Coat in Age-Related Macular Degeneration

Jaclyn Swan, PhD | University of California, San Diego Health Sciences
Mentor: Pascal Gagneux, PhD

For this project, researchers will take a first look at the potential roles of the cell's glycocalyx, its carbohydrate coating, in age-related macular degeneration. The glycocalyx is important for cell communication and immunity but has received little attention in this condition. This project will fill that gap and test the hypothesis that glycocalyx changes could lead to immune dysregulation linked to age-related macular degeneration.

Catalyzing Life-Changing Breakthroughs

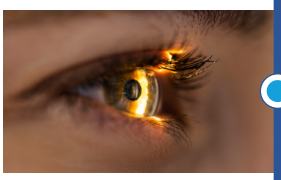
For the past 50 years, BrightFocus Foundation has funded the boldest research and what-if ideas to get us closer to cures for Alzheimer's disease, macular degeneration, and glaucoma, resulting in the novel treatments and diagnostic tools in use today. We also raise awareness and empower people with these diseases and their loved ones by sharing expert resources and information.

Macular Degeneration Research Milestones

Macular Degeneration Research

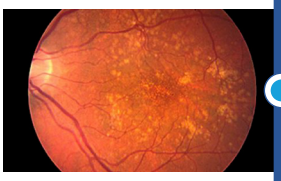
1999

Macular Degeneration Research, a BrightFocus Foundation program, is established.



2005

We supported fundamental research leading to the discovery of the **first anti-VEGF treatment for wet age-related macular degeneration**—still the gold standard for helping to slow or stop vision loss in people with wet AMD.



2006

Early research we funded laid the foundation for the **discovery of the complement pathway**, part of the immune system, as being involved in the onset of AMD. This discovery was central to the development of the first FDA-approved treatment for geographic atrophy in 2023.

2021

A Macular Degeneration Research-funded team develop the **irst-ever 3D cell matrix model of the human eye** that replicates wet AMD, a breakthrough discovery that can lead to a more personalized approach to treatment.

2021

Pioneering work by grantee Ilyas Washington, PhD, leads to an FDA Breakthrough Therapy designation for a **potential Stargardt disease treatment**, with possibilities for treating dry age-related macular degeneration—two vision diseases that can lead to blindness.

2022

An NIH clinical trial team successfully implants lab-grown retinal pigment epithelium cells into a patient with geographic atrophy—representing the **first-ever use of patient-derived stem cells for eye disease.** Earlier projects we funded helped pave the way for this groundbreaking surgery that could one day be used to prevent blindness.

Explore more breakthroughs: **brightfocusbold.org/breakthroughs**

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