

Across the Research Spectrum

Expanding Our Innovative 360° Approach

2022 Macular Degeneration Research Projects



**BrightFocus®
Foundation**

**Macular
Degeneration
Research**



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Research**

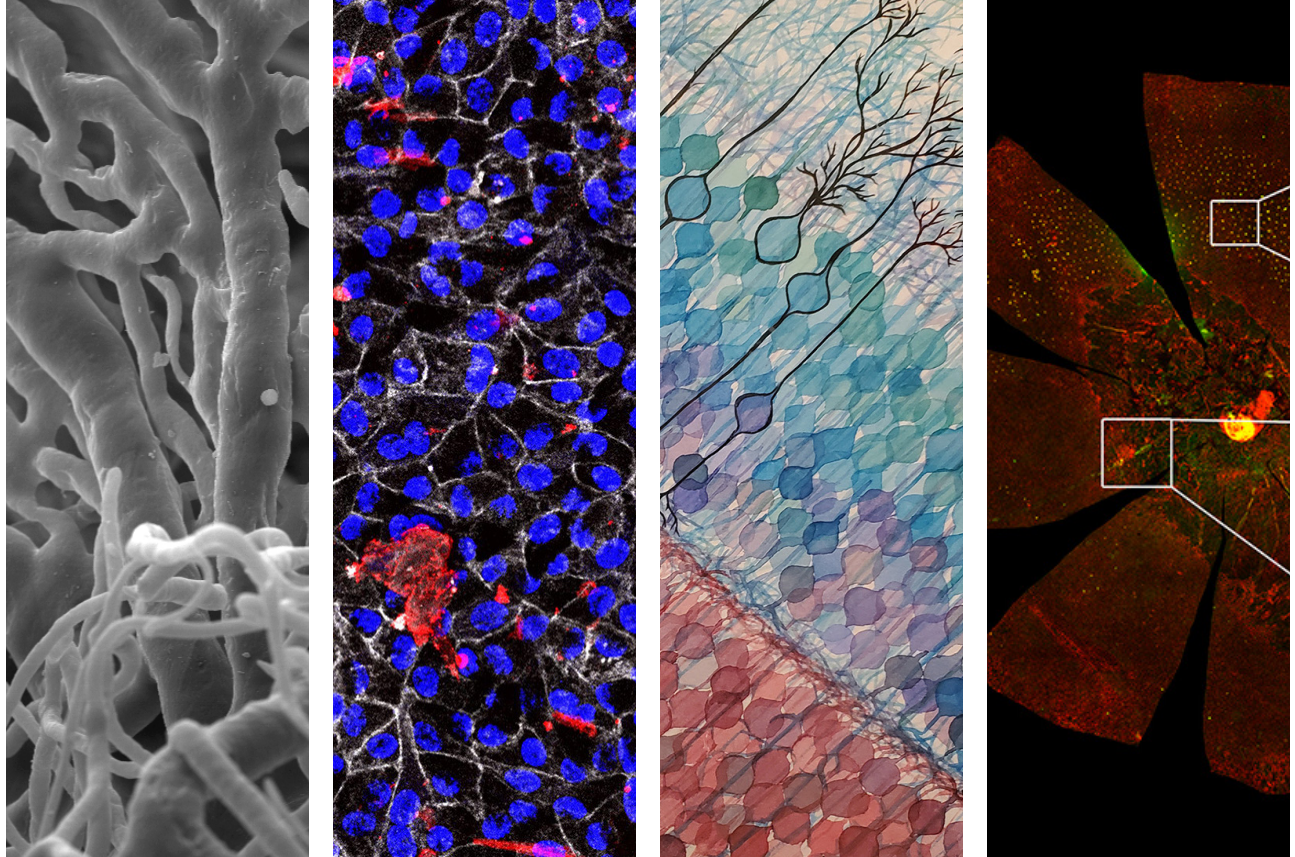
We're Funding 58 Projects Worldwide This Year.

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Age-related macular degeneration (AMD is the leading cause of blindness in people over age 50 worldwide.

AMD is expected to affect 288 million people by 2040.



Left to right: Page 6, Page 8, Page 26, Page 16.

An estimated 20 million adults in the United States have some form of macular degeneration, according to new studies. This alarming figure takes into consideration both the wet and dry forms, as well as geographic atrophy, the advanced form of dry AMD.

Much work is needed to develop treatments and cures for macular degeneration in all its forms.

Through the generosity of our donors, Macular Degeneration Research (MDR), a BrightFocus Foundation program, has awarded nearly \$46 million to fund

research projects on the causes and potential prevention, treatment, and cure of this disease.

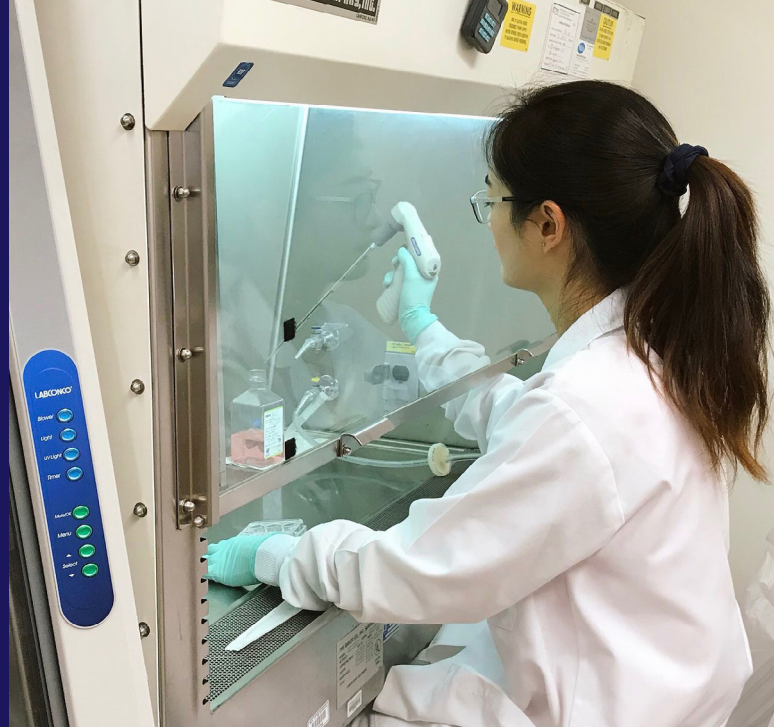
MDR is funding studies exploring the influence of early-life events on AMD. From a disease-in-a-dish approach to screening for FDA-approved drugs, MDR has invested in several promising avenues of research that cover a broad array of innovative scientific approaches.

As of July 15, 2022, MDR has awarded 58 cutting-edge macular degeneration projects worldwide.

Cover: Photoreceptors are studied in a CRISPR-modified frog model where they are damaged in ways similar to AMD. Photo courtesy of Brittany Carr, PhD, University of British Columbia, Canada.

Note: Co-principal investigator and fellowship mentor institutions are listed if different from the PI.

Cell Metabolism



The health of the retinal pigment epithelium (RPE), a single layer of cells at the back of the eye next to the retina, and its 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 the cellular and mitochondrial (“cell powerhouse”) energy production in the RPE and other retinal cells as possible triggers of AMD.

MDR-funded studies 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.

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.



Targeting Proline Metabolism in AMD

Jianhai Du, PhD | 9/1/20 – 8/31/22

West Virginia University Research Corporation

Co-Principal Investigator: Deborah Ferrington, PhD, Doheny Eye Institute

In this proposal, researchers will test mechanisms for utilization of an amino acid, proline, in AMD and will investigate approaches to rescuing defects in the RPE cells from AMD by targeting proline metabolism.

www.brightfocus.org/grant/M2020141



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

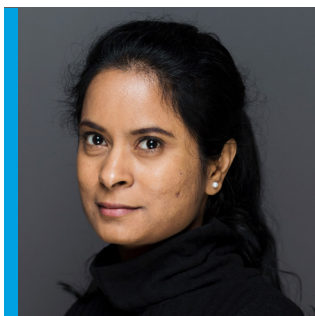
Daisy Yao Shu, PhD | 7/1/21 – 6/30/23

Schepens Eye Research Institute, Massachusetts Eye and Ear,

Harvard Medical School | Fellowship Mentor: Magali Saint Geniez, PhD

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

www.brightfocus.org/grant/M2021010F



Transcriptional Regulation of Cellular Organelle Function in the Retinal Pigment Epithelium

Mallika Valapala, PhD | 7/1/21 – 6/30/24

Indiana University Bloomington

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.

www.brightfocus.org/grant/M2021019N



Macular Degeneration, Metabolism, and a Novel Mitigation Strategy

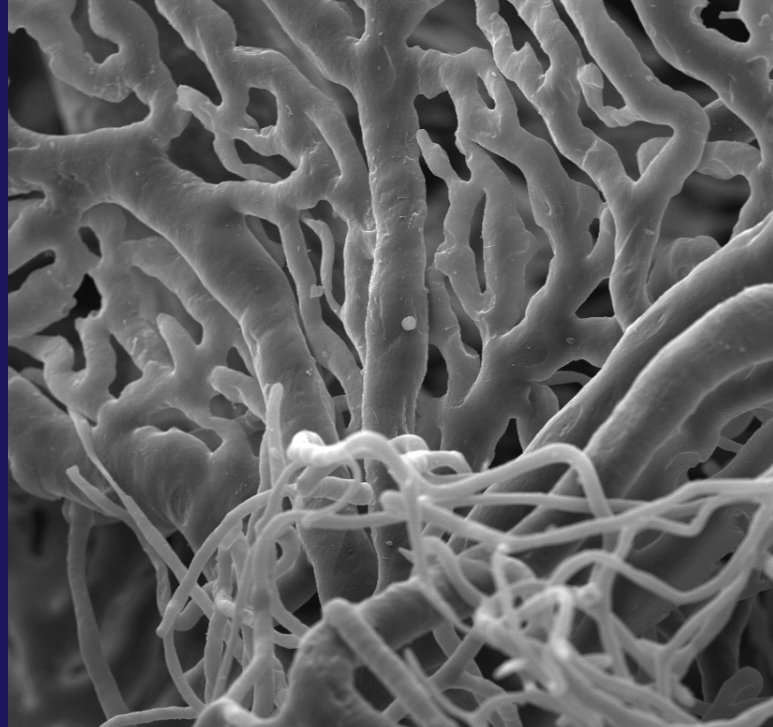
Thomas Wubben, MD, PhD | 7/1/22 – 6/30/25

University of Michigan

While the exact cause of AMD 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.

www.brightfocus.org/grant/M2022008N

Diet & Nutrition's Impact on AMD Risk



Currently, the best treatment protocol to prevent the intermediate stage of AMD from worsening to the advanced stage, dry or wet, is taking eye vitamins, as determined by two large NIH studies, including the Age-Related Eye Disease Study 2 (AREDS2).

The AREDS2 eye vitamin formula combines specific dosages of vitamins C and E, the carotenoids lutein and zeaxanthin, and the minerals zinc and copper.

Research is showing there may be additional ways to lower risk, given how sensitive the eye is to nutritional intake and possible deficiencies.

Ways to increase the body's uptake of carotenoids (molecules that make fresh produce bright red, yellow, and orange), an important nutrient vital to macular health, are being explored, as are the benefits of a Mediterranean-style diet rich in fish, whole grains, and a variety of healthy fruits and vegetables (especially leafy greens).

Our diet affects how our body responds to disease and helps shape a healthy immune response by influencing the microorganisms that live within our body (including gut bacteria).

Ideally, these dietary findings will translate into current clinical practice and "vision healthy" lifestyles.

Above: A cast of mouse choroidal (large) and retinal (small) blood vessels imaged by environmental scanning electron microscopy. Choroidal blood vessels are affected in AMD. Photo courtesy of Przemyslaw Sapieha, PhD, Hôpital Maisonneuve-Rosemont, Canada.

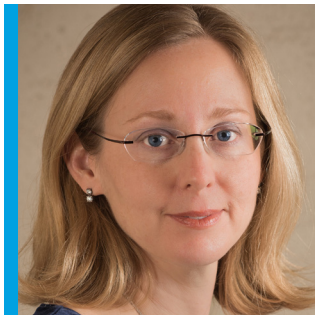


Exploring the Role of Gut Bacteria in Early AMD

Christopher Hammond, MD, MRCP, FRCOphth | 9/1/20 – 8/31/23
King's College London (UK)

The gut microbiome can influence and modify the body's immune responses and may be of relevance in AMD. Therefore, the aim of this project is to explore the role of the gut microbiome in AMD, which may help us better understand the disease to develop new therapies for AMD.

www.brightfocus.org/grant/M2020277



The Gut Bacteria and AMD in Aging Women

Amy Millen, PhD | 9/1/20 – 8/31/23
University at Buffalo

The proposed research to study the gut bacteria as a modifiable risk factor for AMD is relevant to public health. Evidence of a protective association between certain profiles of the gut bacteria content and AMD 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 AMD.

www.brightfocus.org/grant/M2020227



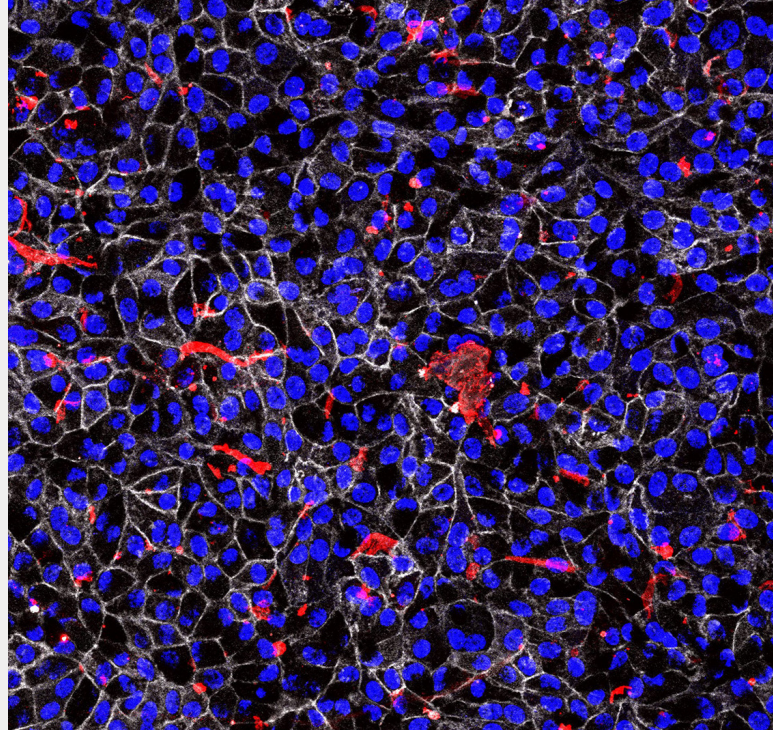
The Molecular Events in Early Life That Lead to AMD

Przemyslaw Sapieha, PhD | 7/1/22 – 6/30/25
Hôpital Maisonneuve-Rosemont (CANADA)

Immune cells, which play a key role in the aberrant blood vessel growth during AMD, are altered following encounters with pathogens, as well as during persistent events such as obesity, potentially impacting disease development. In this proposal, we will assess whether immune cells are modified in a way that increases the risk of AMD following weight gain and subsequent weight loss. Understanding how immune cells respond in the context of past obesity will allow us to gain insight on mechanisms that cause AMD and potentially lead the way to developing targeted interventions.

www.brightfocus.org/grant/M20220151

Drusen Formation & Immune Response



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 (RPE) cell layer and trigger an immune response.

In fact, when spotted on a comprehensive eye exam, drusen often are the first sign of AMD, and 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 therefore focusing on specific aspects of the immune response, including testing drugs that can clear the waste deposits that contribute to AMD.

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.



A New Animal Model of Severe Age-Related Macular Degeneration

Brittany Carr, PhD | 7/1/21 – 6/30/23

University of British Columbia (CANADA)

Fellowship Mentor: Orson Moritz, PhD

This study involves characterizing a new animal model of AMD that will provide significant insight into the relationship between reticular pseudodrusen (RPD) and AMD progression. Establishing RPD as an early indicator of AMD and understanding its role in AMD progression will result in more effective prevention of AMD-associated blindness.

www.brightfocus.org/grant/M2021001F



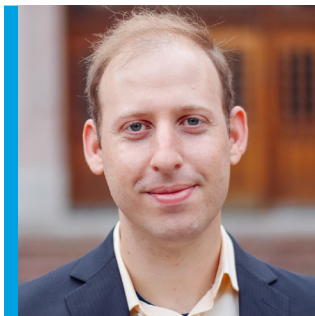
Understanding the Role of Inflammation in AMD

Sayan Ghosh, PhD | 7/1/21 – 6/30/23

University of Pittsburgh | Fellowship Mentor: Debasish Sinha, PhD

In this proposal, using their genetically engineered mouse models, researchers aim to understand if their gene of interest regulates retinal inflammation and degeneration as seen in AMD, through the interaction between infiltrating inflammatory cells (neutrophils) and the immune cells (retinal microglia). Understanding these molecular changes may provide novel background for future drug discoveries for atrophic AMD.

www.brightfocus.org/grant/M2021005F



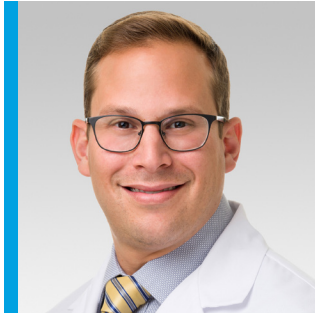
Can Fatty Acid Oxidation Influence Drusen Levels in the Eye?

Daniel Hass, PhD | 7/1/22 – 6/30/24

University of Washington | Fellowship Mentor: James Hurley, PhD

This study determines the effect of a small molecule on fatty acid metabolism, cell function, and deposit levels in multiple cell culture and mouse models of AMD. This small molecule has been tested in humans in clinical trials and is safe, so if it is also effective at decreasing deposit levels, the transition to clinical use may be more rapid than for untested treatments.

www.brightfocus.org/grant/M2022003F



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

Jeremy Lavine, MD, PhD | 7/1/21 – 6/30/24

Northwestern University Feinberg School of Medicine

Mentors: Harris R. Perlman, PhD & Amani Fawzi, MD

The premise of this study is that there are macrophage (immune cell) subtypes, and classical-derived macrophages promote wet AMD, while non-classical macrophages block wet AMD. This group has identified a macrophage subset that expresses blood vessel growth factors derived from classical macrophages and is present in patients with wet AMD. They further aim to identify non-classical-derived macrophage subsets and demonstrate that they inhibit experimental wet AMD.

www.brightfocus.org/grant/M2021016N



Evaluating a Novel Mechanism and Target for Wet AMD

Priyatham Mettu, MD | 9/1/20 – 12/31/22

Duke University Eye Center

This study proposes that the severe form of wet AMD is caused by inflammatory cells called macrophages and identifies a novel molecular target that controls the activity of these inflammatory cells. The purpose of this project is to better understand this molecular target and determine whether medicines that block this target could be effective novel treatments for patients with wet AMD.

www.brightfocus.org/grant/M2020168



Ciliary Lipids in RPE Repair: A Novel Target for AMD

Ke Ning, MD | 7/1/21 – 6/30/23

Stanford University

Fellowship Mentors: Yang Sun, MD, PhD & Vinit Mahajan, MD, PhD

Researchers in this study have discovered a novel role of RPE cilia (that looks like an antenna) that is related to the control of RPE repair in mice; loss of these organelles promotes cell proliferation and wound healing. They propose to study how this organelle mediates cell proliferation and wound healing. The result of this study will help us understand how antenna works in RPE proliferation and targeting this mechanism for drug development in AMD.

www.brightfocus.org/grant/M2021008F



Role of Lipids (Deposits) in Causing Dry AMD

Dorota Skowronska-Krawczyk, PhD | 9/1/20 - 8/31/22

University of California, Irvine | Co-Principal Investigator: Daniel Chao, MD, PhD, University of California, San Diego

Researchers in this study propose to characterize the role of a new protein that is involved in processing lipids, a process that has long been thought to play an important role in macular degeneration. This study will explore the relationship of inflammation with this protein in creating these lipid deposits in the eye and will explore the function of this protein in human cell lines to see whether this can serve as a target for AMD.

www.brightfocus.org/grant/M2020271

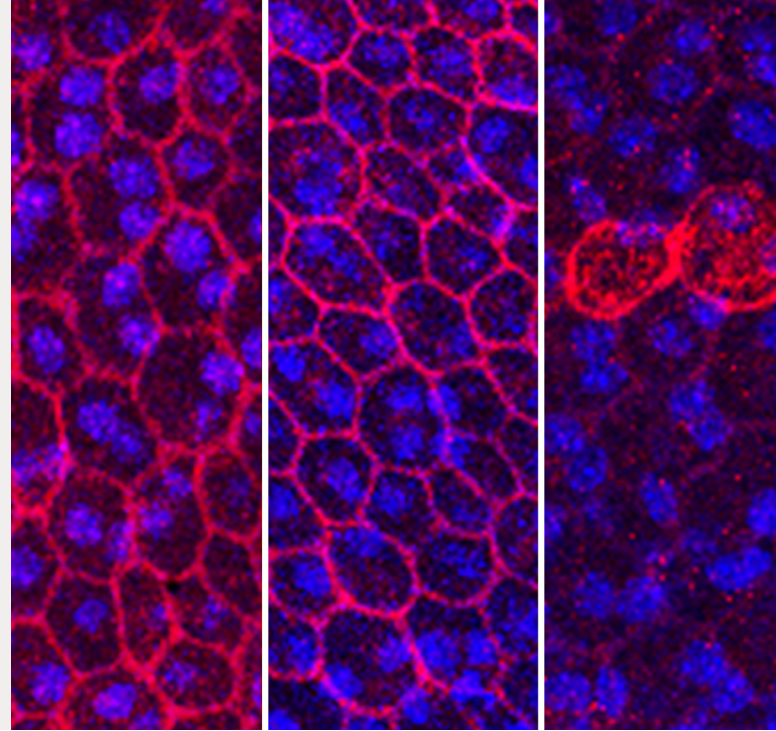
A recipient of the Elizabeth Anderson Award for Macular Degeneration Research.

Nearly  20 million

adults in the U.S. have some form of macular degeneration

almost double the previous estimate of 11 million people

Genes & AMD

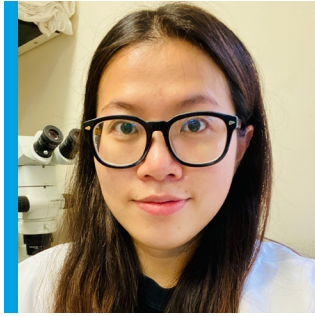


Most forms of macular degeneration are not linked to any single genetic mutation. Instead, susceptibility to AMD is scattered over a number of small irregularities of genes called single nucleotide polymorphisms (SNPs).

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.

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 a RPE membrane marker, shown in red. Photo courtesy of Lev Prasov, MD, PhD, University of Michigan.



CRISPR Genome Engineering in AMD Risk Alleles

Ya-Ju Chang, PhD | 7/1/21 – 6/30/23

Columbia University Irving Medical Center

Fellowship Mentor: Stephen T. Tsang, MD, PhD

In the study, the researcher plans to address the knowledge gap in our understanding of the cause of AMD by developing a stem cell model capable of mimicking AMD in human patients. The cutting-edge gene-editing tool, CRISPR/Cas9, will be used to convert AMD risk genes from the high-risk to low-risk variants in AMD patient-derived stem cells and evaluate the effect on the cells' defense against oxidative stress.

www.brightfocus.org/grant/M2021002F



Immune Cell-Specific DNA Modifications and Gene Expression in AMD

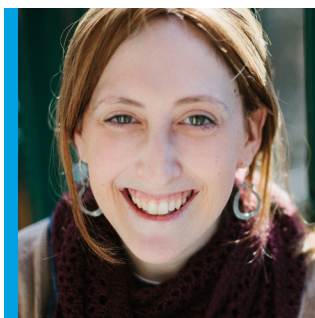
Willard Freeman, PhD | 9/1/20 - 8/31/22

Oklahoma Medical Research Foundation

Co-Principal Investigator: Ana J. Chucair-Elliott, PhD

Aging is the major risk factor for AMD, but how aging, along with gender, leads to the development of the disease is not understood. This study will look at how DNA alterations, known as epigenetic modifications, are able to influence gene expression and retina function/acuity in specific immune cells like the microglia and Müller cells, respectively, considering age and sex as parameters.

www.brightfocus.org/grant/M2020207



Investigating Genetic or Immune Factors in Age-Related Macular Degeneration

Michelle Grunin, PhD | 7/1/21 – 6/30/23

Hebrew University of Jerusalem (ISRAEL)

Fellowship Mentors: Shai Carmi, PhD & Jonathan L. Haines, PhD

This study will use novel technological tools and diverse ancestry reference panels that were previously unavailable to identify new genetic risk factors for AMD and possible new genetic or immune system targets for treatment of the disease. Researchers will utilize the existing genetics of the International Age-Related Macular Degeneration Genomics Consortium, with over 50,000 samples, to investigate these issues on a large scale.

www.brightfocus.org/grant/M2021006F



Generating a Precision Model for AMD Research

Jürgen Naggert, PhD | 9/1/20 – 2/28/23

The Jackson Laboratory

This proposal aims at developing animal models that mimic human disease and allow us to determine the function of human genes that increase the risk of developing AMD. This has the potential to greatly facilitate development of new treatment strategies.

www.brightfocus.org/grant/M2020284



Mouse Models for Subretinal Fibrosis

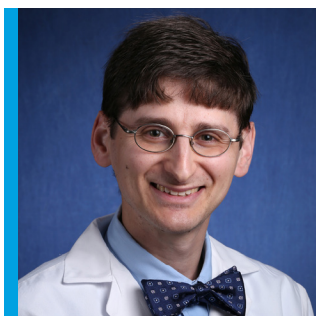
Patsy M. Nishina, PhD | 7/1/22 – 6/30/25

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 that causes vision impairment. This study will characterize two new genetic models that develop subretinal fibrosis, a common complication of wet AMD, and provide insights into pathways that may underlie the disease.

www.brightfocus.org/grant/M20220161



Gene Regulation of RPE Maintenance

Lev Prasov, MD, PhD | 7/1/22 – 6/30/25

University of Michigan

This group has identified a new gene that controls expression of other genes in the RPE and leads to dysfunction. This proposal evaluates the role of this gene in maintaining adult RPE function and its ability to protect against stresses that lead to AMD. Understanding this may open new avenues for treatment of AMD by targeting this gene or its downstream targets.

www.brightfocus.org/grant/M2022011N

Recipient of the Dr. Joe G. Hollyfield Award for Macular Degeneration Research.



Functional Characterization of Genetic Regulatory Effects of AMD Risk Variants

Rinki Ratnapriya, PhD | 7/1/21 – 6/30/24

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

In this proposal, researchers will integrate the genome-wide associated studies (GWAS) findings with transcriptome (protein coding region) and epigenome (DNA modification markers) data to identify underlying causal variants, regulatory elements, and target genes to address major gaps in the mechanistic understanding of AMD.

www.brightfocus.org/grant/M2021017N



Profiling of Immune Cell Subtypes in AMD Patients and Controls

Philip Ruzycski, PhD | 9/1/20 – 8/31/23

Washington University in Saint Louis

Co-Principal Investigator: Rajendra Apte, MD, PhD

This project seeks to understand the genetic basis of AMD. By leveraging the most innovative genomic techniques available, researchers in this study will gain insights into biomarkers for disease progression and identify novel targets for preventive therapeutics.

www.brightfocus.org/grant/M2020115

This award is made possible with the support of the Ivan Bowen Family Foundation.



Machine Learning to Predict AMD-Associated Genetic Variant Impact

Leah VandenBosch, PhD | 7/1/22 – 6/30/24

Seattle Children's Hospital

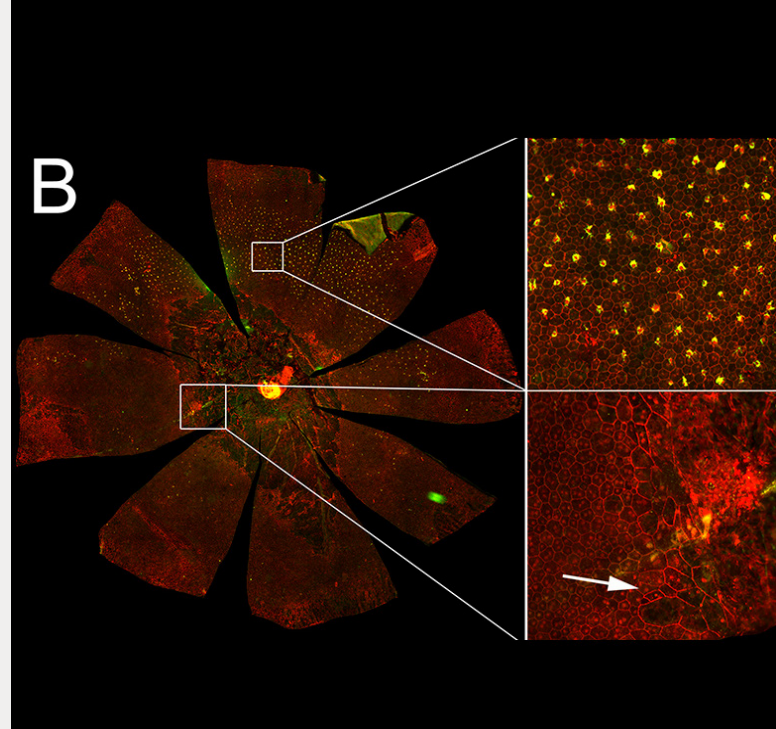
Co-Principal Investigator: Timothy Cherry, PhD

This study will apply machine learning to human retinal and RPE genomic data to predict the effect of variations in the noncoding regions, the regions of DNA with no known function to contribute directly to AMD.

www.brightfocus.org/grant/M2022006F

Recipient of the Helen Juanita Award for Macular Degeneration Research.

Geographic Atrophy



Geographic atrophy (GA), an advanced form of AMD, is sometimes called “dry” AMD because it lacks the fragile, leaky blood vessels seen in late-stage “wet” AMD. Instead, photoreceptors weaken and die (atrophy), resulting in dead zones and an expanding blind spot near the center of the visual field.

Currently, there is no approved treatment for GA, although several are underway. MDR is funding investigations into new drugs and ways to manage and treat this devastating disease. This urgently needed research could one day result in the first successful therapies.

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, UMass Chan Medical School.



Investigating Multiarmed Cell Death (PANoptosis) in Dry AMD Progression

Lucia Celkova, PhD | 7/1/22 – 6/30/24

Trinity College Dublin (IRELAND)

Fellowship Mentor: Matthew Campbell, PhD

The research proposed here aims to explore a master “decision maker” that could integrate and process these triggers and guide the fate of RPE cells either toward survival or death. Through this, we will not only gain a better understanding of the complex process underlying RPE cell death but also identify potential new targets and strategies for therapeutic intervention in dry AMD.

www.brightfocus.org/grant/M2022004F

A recipient of the Elizabeth Anderson Award for Macular Degeneration Research.



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

Paul Baird, PhD | 7/1/19 – 12/31/22

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 AMD, 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 AMD such as age, the sex of an individual, and smoking.

www.brightfocus.org/grant/M2019093



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

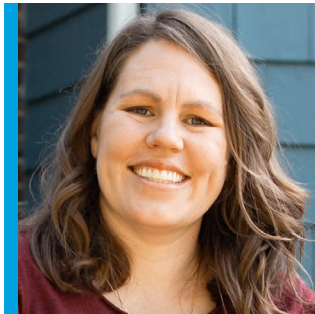
Malia Edwards, PhD | 9/1/20 – 8/31/23

Wilmer Eye Institute, Johns Hopkins University

This proposal will take a novel approach to studying GA by investigating the role of glial cells. These cells, traditionally considered only support cells, are altered in GA. The proposed studies will investigate how changes to these cells may influence disease progression and the effectiveness of treatments.

www.brightfocus.org/grant/M2020174

This grant was made possible in part by the support of the Victor and Anna Mae Charitable Foundation.



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

Kristen Bowles Johnson, PhD, OD | 7/1/22 – 6/30/24

Indiana University Bloomington | Fellowship 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 (AOO) to take pictures of fluorescent clumps in RPE cells and measure how sick photoreceptors are as the disease progresses. Completion of this study could identify biomarkers to help identify patients most likely to benefit from a treatment and determination of treatment efficacy.

www.brightfocus.org/grant/M2022007F



Elucidating How Smoking Causes Advanced AMD

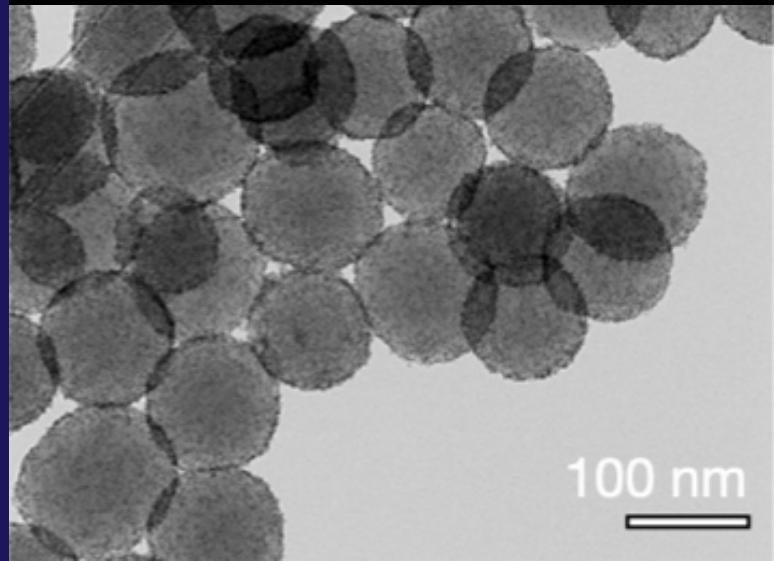
Claudio Punzo, PhD | 9/1/20 - 11/30/22

UMass Chan Medical School

Among the risk factors for AMD, smoking confers the highest risk for progression to the advanced stages of GA and wet AMD; however, how smoking contributes to AMD remains elusive. In this study, researchers propose that smoking causes advanced AMD pathologies by depletion of the second most abundant protein present in the serum.

www.brightfocus.org/grant/M2020016

Innovative Approaches to AMD Treatments



One day, we may be able to detect signs that AMD is developing and take early steps to defend against it.

MDR 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 help us better track disease progression over time, and gene therapy is being evaluated as a possibility to treat AMD.

Above: Image of cerium (Ce) ions 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.



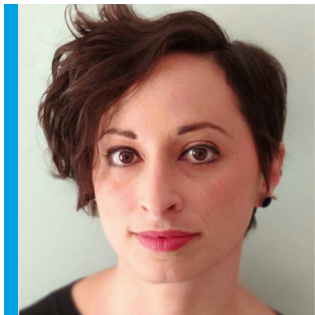
Functional Imaging of the Human Retina Using Noninvasive Technology

Andrew Browne, MD, PhD | 7/1/21 – 6/30/24

University of California, Irvine | Mentor: Krzysztof Palczewski, PhD

This proposal seeks to develop a camera for use in humans to directly examine the causes of AMD in human subjects. Researchers will translate the 2-photon (2P) microscopy technology already established to study models to a device that can noninvasively acquire images at such high resolution that they can reveal what is happening inside cells.

www.brightfocus.org/grant/M2021013N



A New Therapeutic Strategy to Treat AMD

Sabrina Carrella, PhD | 11/1/20 – 10/31/22

Telethon Institute of Genetics and Medicine (ITALY)

Co-Principal Investigator: Alessia Indrieri, PhD

Researchers in this study have identified two small noncoding ribonucleic acids (RNAs), called microRNAs, that are able to control many fundamental cellular processes and whose inhibition can protect the cells in the eye from damage and rescue vision. This proposal will test the beneficial effects of the inhibition of these two microRNAs in macular degeneration models and pave the way for novel therapeutic strategy for AMD.

www.brightfocus.org/grant/M2020184



A Novel Method for Modeling AMD in a Dish

Jennifer Chao, MD, PhD | 9/1/20 – 8/31/23

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 RPE cells and choriocapillaris of the eye. This model will allow the researcher to study the essential elements of RPE-related diseases, such as drusen deposition, blood flow effects, and blood vessel permeability.

www.brightfocus.org/grant/M2020217



Novel Antibody-Based Agonist for Neovascular AMD

Rony Chidiac, PhD | 7/1/21 – 6/30/23

University of Toronto (CANADA)

Fellowship Mentor: Stephane Angers, PhD

For the first time, researchers of this study could precisely activate one receptor of the many mimicking Wnt proteins and study its role in blood vessel formation and integrity. They aim to test this molecule's therapeutic potential in models mimicking the neovascular AMD. These synthetic agonists are attractive therapeutic modalities to control the formation of new blood vessels during neovascular AMD.

www.brightfocus.org/grant/M2021003F



Identifying FDA-Approved Drugs to Reverse Dry AMD

Steffi Daniel, PhD | 7/1/22 – 6/30/24

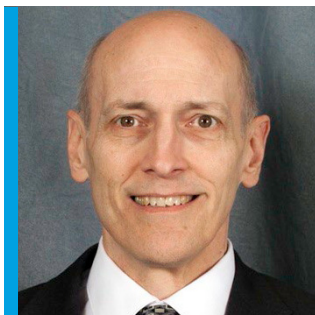
University of Texas Southwestern Medical Center

Fellowship Mentor: John Hulleman, PhD

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

www.brightfocus.org/grant/M2022005F

This award is made possible with support from the Ivan Bowen Family Foundation.



Ocustatin™ for Treatment of Intermediate AMD

John Edwards, MS, MBA | 3/31/22 – 2/28/24

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 AMD.

www.brightfocus.org/grant/CM2022001



New Automated Method to Predict AMD Progression

Joelle Hallak, PhD | 7/1/19 – 6/30/23

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

This proposal aims to develop a tool to predict the chances of AMD progression on a personalized, patient-by-patient basis by using images of the retina as well as the patient's genetic, historical, demographic, and behavioral data.

www.brightfocus.org/grant/M2019155



Advanced Imaging Studies in a Model of Type 3 Neovascular AMD

Tyson Kim, MD, PhD | 7/1/21 – 6/30/24

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

In order to study the formation of chorioretinal anastomoses, a lesion formed by the vascular fusions between the retinal and choroidal vascular networks, researchers in this study will develop an advanced imaging method to look deeper into the living eye with cellular resolution, molecular information, and the ability to measure blood flow down to individual microvessel in neovascular AMD models. This will provide insights to help develop more effective treatments for neovascular AMD.

www.brightfocus.org/grant/M2021015N



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

Yongsu Kwon, PhD | 7/1/22 – 6/30/24

University of North Carolina at Chapel Hill
Fellowship Mentor: Han Zongchao, MD, PhD

This study aims to develop a combination of a new antioxidant system to scavenge free radicals (toxic waste products that gradually build up in the cells over time), which can potentially achieve long-term effects and reduce the damage in AMD.

www.brightfocus.org/grant/M2022001F



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

Aparna Lakkaraju, PhD | 7/1/21 – 6/30/24

University of California, San Francisco

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

www.brightfocus.org/grant/M2021020I

Recipient of the Lorraine Maresca Award.



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

Srinivasa Rao Sripathi, PhD | 1/1/23 – 12/31/25

Retina Foundation of the Southwest

The aim of this project is to develop novel treatments for AMD by utilizing stem cell-derived RPE cells to screen for molecules (potential drugs) that inhibit RPE damage and reduce epithelial-mesenchymal transition (EMT) to help RPE maintain its integrity.

www.brightfocus.org/grant/M2022014N



Development of a Drug for Dry AMD

Young Joo Sun, PhD | 7/1/21 – 6/30/23

Stanford University | Fellowship Mentor: Vinit Mahajan, MD, PhD

Researchers in this study propose to characterize the efficacy of the lead-like compound that inhibits HTRA1 in cells. The success of this study will bring forth an HTRA1 inhibitor as a therapeutic candidate for AMD.

www.brightfocus.org/grant/M2021011F



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

Benjamin Thomson, PhD | 7/1/21 – 6/30/24
Northwestern University–Chicago Campus

Typical wet AMD is most commonly seen in patients of European ancestry; however, wet AMD–like disease in patients of Asian and African ancestry is more commonly associated with polypoidal choroidal vasculopathy (PCV). This proposal will characterize the role of a recently identified important blood vessel regulatory system in PCV and test new drug candidates targeting this pathway.

www.brightfocus.org/grant/M2021018N



A New Approach to Modeling Subretinal Tissue

Elizabeth Vargis, PhD | 7/1/19 – 12/30/23
Utah State University

This team of biological engineers proposes to design a multilayered model with human retina 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.

www.brightfocus.org/grant/M2019109



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

Shusheng Wang, PhD | 9/1/20 – 8/31/23
Tulane University | Co-Principal Investigator: Bo Yu, PhD

This study aims to establish a novel gene regulation system that can turn off the VEGF gene to reduce VEGF levels in wet AMD. This gene system combines potency, tight control of VEGF, and safety and can be used to treat AMD with just one ocular injection.

www.brightfocus.org/grant/M2020166

This award is made possible with the support of the Free Family Foundation.



Prescribing the Molecular Message of Retinal Health

Yvette Woof, PhD | 7/1/21 – 6/30/23

The Australian National University (AUSTRALIA)

Fellowship Mentor: Riccardo Natoli, PhD

In the retina, extracellular vesicles (EV) are responsible for mediating essential communication and work by delivering molecular cargo, including small gene regulators called microRNA, to target cells, which are reduced with degenerating retina. In this study, researchers will supplement the degenerating retina with essential retinal EV cargo derived from donor stem cells and investigate the effect on retinal health.

www.brightfocus.org/grant/M2021012F



Development of Gene Editing as a Permanent Cure for Wet AMD

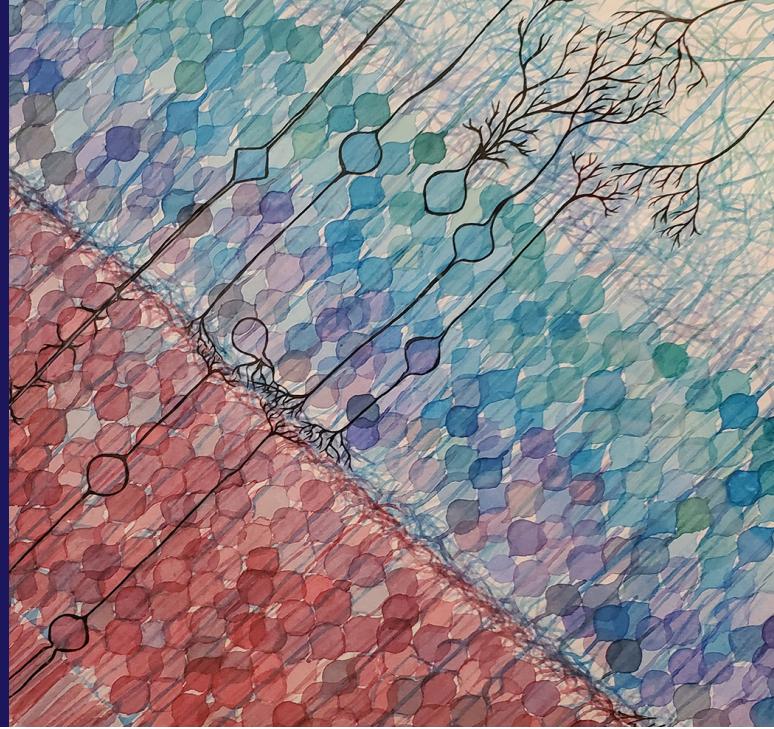
Glenn Yiu, MD, PhD | 9/1/20 – 8/31/23

University of California, Davis

This research proposal will address the health care crisis of wet AMD by developing a potential cure for it by using a powerful gene-editing technology called CRISPR. This innovative gene-editing system can permanently change the genes that cause wet AMD and can hopefully be used someday to save the vision of the aging population.

www.brightfocus.org/grant/M2020247

Regenerating Damaged Cells



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 AMD and to restore the underlying retinal pigment epithelium (RPE) cells.

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

Above: Illustration of different cell types of the retina, including rods, cones, and ganglion cells. Photo courtesy of Leah VandenBosch, PhD, Seattle Children's Hospital.



Regenerative Response in Spiny Mice

Manas R. Biswal, PhD | 7/1/22 – 6/30/25

University of South Florida

Degeneration of the neural retina and in the RPE is associated with the advanced atrophic form of dry AMD. 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 AMD in humans.

This award is made possible with the support of the Free Family Foundation.



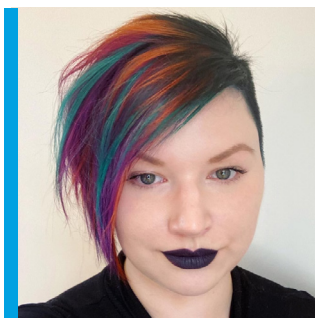
Discovery of New Methods to Regenerate Cone Photoreceptors

Mark Emerson, PhD | 9/1/20 – 8/31/23

The City College of New York

Cone photoreceptors are the critical light-sensing sensory cells that are lost in AMD. This project will use high-resolution molecular techniques to identify the genes normally found in forming cone photoreceptors that are sufficient to turn other retinal cells into cones to develop new cone-replacement therapies for AMD.

www.brightfocus.org/grant/M2020157



Killifish: A Novel Model of AMD

Nicole C. L. Noel, PhD | 7/1/22 – 6/30/24

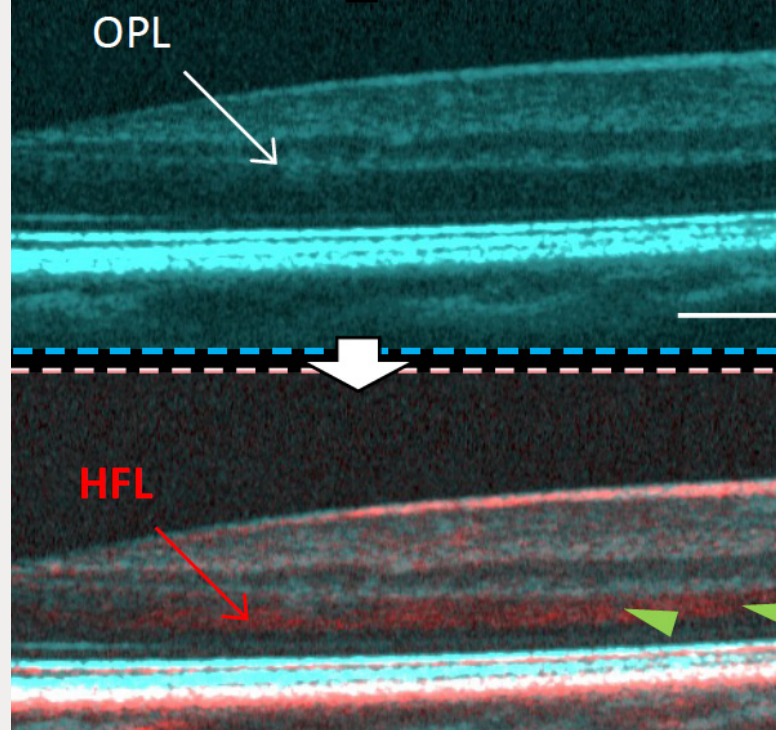
University College London (UK)

Fellowship 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 AMD, and assess how healthy retinal aging can be promoted in a model of age-related retinal degeneration.

www.brightfocus.org/grant/M2022002F

Understanding Early-Stage AMD



Macular degeneration is linked to many causes. Foremost are changes in the eye that happen with age—the strongest risk factor. It is believed 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. BrightFocus' MDR program is funding scientific exploration into the causes of AMD to open new and earlier treatment avenues.

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.



Engineered Eye Tissue Models to Analyze Mechanisms of Age-Related Vision Loss

Kapil Bharti, PhD | 9/1/20 – 8/31/22

National Eye Institute | Co-Principal Investigator: Eric Nguyen, PhD

This project uses 3D bio-printed human tissue models to clarify the role of retinal blood vessels in initiating and progressing macular degeneration. The completion of this project is expected to determine whether the retinal blood vessels can be effective therapeutic targets for countering macular degeneration and suggest novel therapeutics against the disease.

www.brightfocus.org/grant/M2020258



Examining the Role of Choroidal Blood Flow in AMD

Bradley Gelfand, PhD | 9/1/20 – 11/29/22

University of Virginia

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

www.brightfocus.org/grant/M2020114



Investigation of Novel Pathogenesis and Therapeutic Strategy for AMD

Haijiang Lin, MD, PhD | 7/1/19 – 10/31/22

UMass Chan Medical School

Co-Principal Investigator: Bo Tian, PhD

This study will identify new factor(s) contributing to the progression of AMD and explore methods to halt or reverse AMD retinal lesions. The overall goal is to gain a better understanding of the molecular mechanism of this disease and to develop novel effective therapies.

www.brightfocus.org/grant/M2019074



Regulation of Capillary Blood Flow in the Choroid Vasculature

Albert Gonzales, PhD | 7/1/22 – 6/30/25
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 deposit that can lead to diseases like AMD.

www.brightfocus.org/grant/M2022010N



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

Yifan Jian, PhD | 7/1/22 – 6/30/25
Oregon Health & Science University | Mentor: Brandon Lujan, MD

In this study, researchers are developing a novel retina imaging device, the volumetric directional optical coherence tomography, which can measure a new 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 AMD and the effects of therapeutic interventions.

www.brightfocus.org/grant/M2022009N



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

Yara T.E. Lechanteur, MD, PhD | 7/1/22 – 6/30/25
Radboud University Nijmegen Medical Centre (THE NETHERLANDS)
Mentor: Frans Cremers, PhD

Researchers propose to study young onset cases of AMD by studying their family members and looking at genetic factors and specific markers in blood samples. The aim is to identify new factors that are 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.

www.brightfocus.org/grant/M2022013N



Foresight: Charity-Led Big Data for Ophthalmology

Wen Hwa Lee, PhD | 3/31/22 – 3/30/24
Action Against AMD (UK)

Foresight will collect, aggregate, and share a first-in-class database of donated eye scans to enable early detection and next-generation treatment of retinal conditions and beyond.

www.brightfocus.org/grant/CM2022002



Exploring the Role of Lipid Metabolism in AMD Pathogenesis

Rohini M. Nair, PhD | 7/1/21 – 6/30/23

University of Pennsylvania

Fellowship Mentor: Venkata Ramana Murthy Chavali, PhD

This study aims to unravel the role of hepatic lipase that breaks down high-density lipoproteins to smaller, denser particles to be cleared away by systemic circulation. Understanding its role in regulating cholesterol efflux using cellular (iPSC-derived RPE cultures) and animal models would help design targeted therapies for slowing down the disease progression.

www.brightfocus.org/grant/M2021007F



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

Davide Ortolan, PhD | 7/1/21 – 6/30/23

National Eye Institute, NIH

Fellowship Mentors: Kapil Bharti, PhD & Ruchi Sharma, PhD

This study will identify molecular and physiological differences between the two populations of RPE cells (derived from the central and the peripheral retina) in a dish and will find which properties make the central RPE more vulnerable than peripheral RPE. This new knowledge, plus having an easily reproducible model in a dish, will eventually translate to the development of drugs that prevent vision loss caused by AMD.

www.brightfocus.org/grant/M2021009F



Addressing the Link Between Impairment in Phagosome Degradation and AMD

Antonio Escudero Paniagua, PhD | 7/1/21 – 6/30/23

University of California, Los Angeles

Fellowship Mentor: David Williams, PhD

Researchers propose to investigate the maturation rate and the accumulation of specific phagosome stages in RPE cells from macular dystrophy patients in comparison to cells from healthy patients and mice models. These studies will provide a paradigm shift in our identification and understanding of the etiology of macular dystrophies and could be key for the development of new strategies to stop or prevent them.

www.brightfocus.org/grant/M2021004F

A recipient of the Elizabeth Anderson Award for Macular Degeneration Research.



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