

**BOLDLY EXPLORING**

**RESEARCH INSPIRING HOPE**

**2021 Macular Degeneration Research Projects**



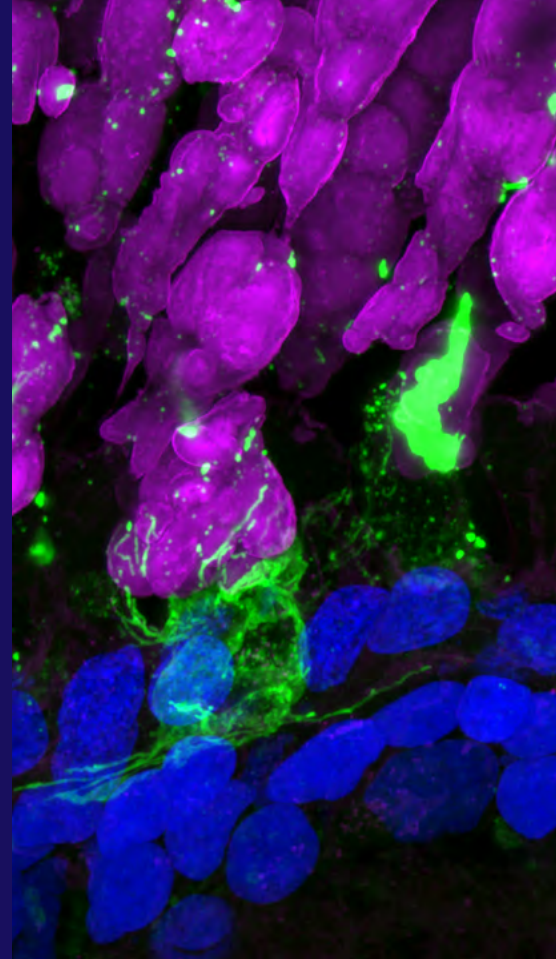
**BrightFocus<sup>®</sup>  
Foundation**

**Macular  
Degeneration  
Research**



MACULAR  
DEGENERATION  
RESEARCH

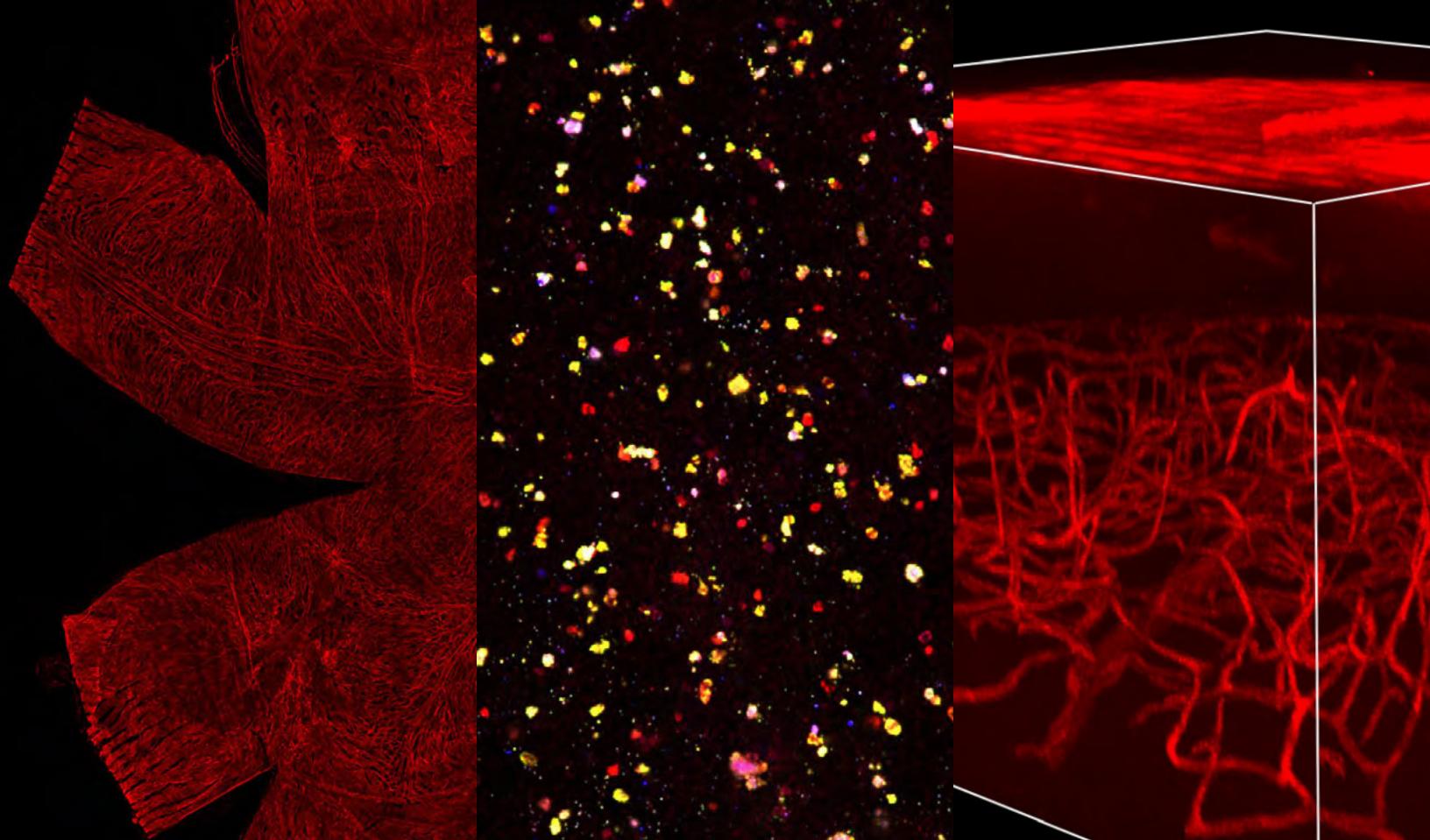
# WE'RE FUNDING 52 PROJECTS WORLDWIDE THIS YEAR IN RESEARCH.



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Advanced forms of age-related macular degeneration (AMD) are a leading cause of vision loss and irreversible blindness in Americans age 60 years and older, as well as throughout the world.



Currently, an estimated 11 million Americans have some form of macular degeneration, and that number is expected to double by 2050. This alarming prediction takes into account both wet and dry forms as well as geographic atrophy—the advanced form of dry AMD, which has long been without an effective treatment.

Much work is needed to develop treatments and cures for macular degeneration in all its forms. Through the generosity of our donors, Macular

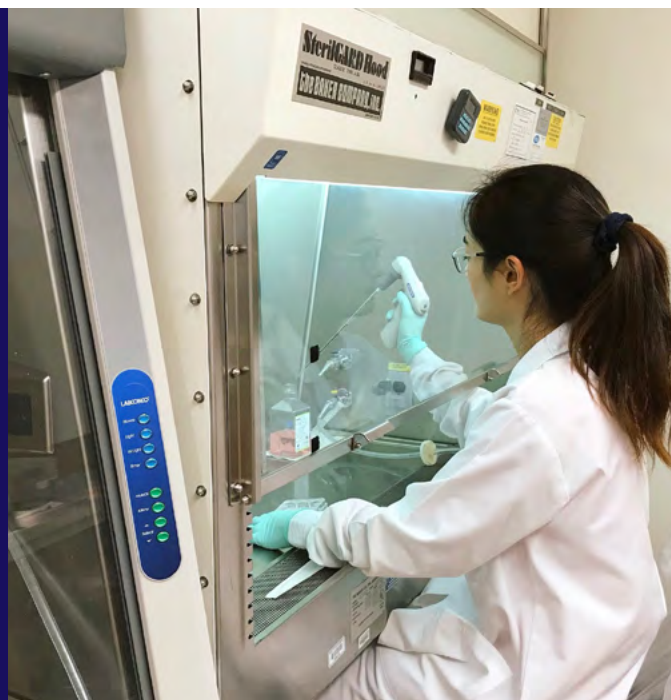
Degeneration Research (MDR), a BrightFocus Foundation program, has awarded nearly \$40 million to fund research projects on the causes and potential prevention, treatment, and cure of this disease. MDR funds have been invested in several promising avenues of research that cover a broad array of innovative scientific approaches. We hope that you enjoy this look at this research portfolio, which is made possible through the generosity of MDR donors in the United States and worldwide.

*Co-principal investigator and fellowship mentor institutions are listed if different than the PI.*

*Cover: Scientists are studying specialized cellular particles (shown here in green and red) that protect vision by “taking out the trash,” i.e., removing lipids and other debris near the retina. (Courtesy of Aparna Lakkaraju, PhD, University of California, San Francisco)*

*Above left to right: Close-up view of rod (purple) and cone (green) photoreceptors in a frog model of AMD. (Courtesy of Brittany Carr, PhD, University of British Columbia, Canada); A cross-section of the choriocapillaris, or “bed” of blood vessels that feeds the retinal area. (Courtesy of Benjamin Thomson, PhD, Northwestern University); Phagosomes—a part of the retinal “housekeeping” team—are being studied for their role in macular degeneration. (Courtesy of Antonio Escudero Paniagua, PhD, University of California, Los Angeles); Advanced imaging shows retinal blood flow in microvessels, providing insight into “wet” AMD. (Courtesy of Tyson Kim, PhD, University of California, San Francisco)*

# CELL METABOLISM



The retinal pigment epithelium (RPE) is a single layer of cells at the back of the eye next to the retina. The health of RPE cells, and their ability to support the nerve cells of the retina, depend on well-functioning RPE cell metabolism as a source of energy. Grantees are currently looking at the decline in the cellular and mitochondrial (“cell powerhouse”) energy production in the RPE and other retinal cells as possible triggers to AMD. Macular Degeneration

Research-funded studies are trying to understand how an imbalance between energy needs and production may 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. (Courtesy of Daisy Shu, PhD, The Schepens Eye Research Institute Massachusetts Eye and Ear & Harvard Medical School)*



## **Jianhai Du, PhD**

(9/1/20 - 8/31/22)

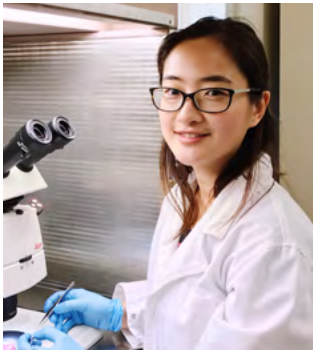
*West Virginia University Research Corporation, Morgantown*

Co-Principal Investigator: Deborah Ferrington, PhD

## **Targeting Proline Metabolism in AMD**

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](http://www.brightfocus.org/grant/M2020141)



**Daisy Shu, PhD**

(7/1/21 – 6/30/23)

*The Schepens Eye Research Institute Massachusetts Eye and Ear, Harvard Medical School*

Fellowship Mentor: Magali Saint Geniez, PhD

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

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 (TNFa) will be tested as a potential drug target for AMD.

[www.brightfocus.org/grant/M2021010F](http://www.brightfocus.org/grant/M2021010F)



**Mallika Valapala, PhD**

(7/1/21 – 6/30/24)

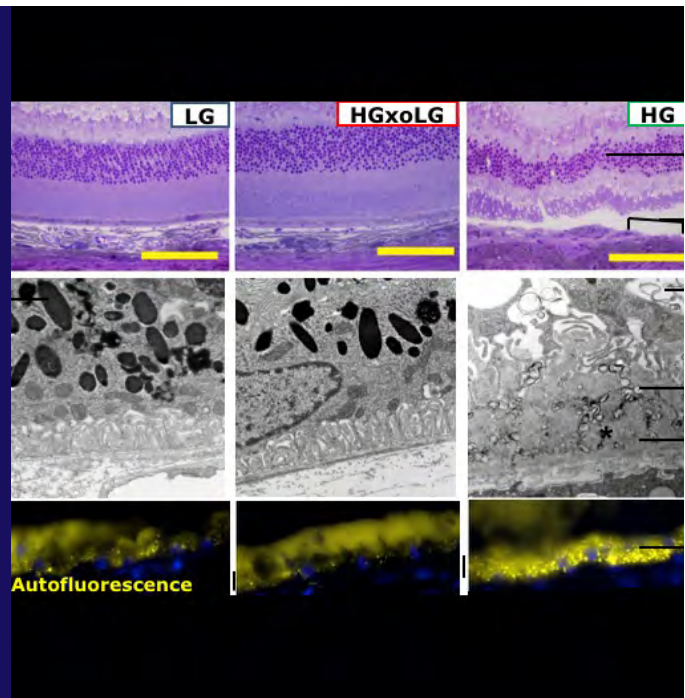
*Indiana University*

### **Transcriptional Regulation of Cellular Organelle Function in the Retinal Pigment Epithelium**

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](http://www.brightfocus.org/grant/M2021019N)

# DIET & NUTRITION'S IMPACT ON AMD RISK



Currently, eye vitamins resulting from two large studies conducted by the National Institutes of Health, the AREDS2 [Age-Related Eye Disease Study 2] formula, are the standard treatment recommended to prevent intermediate-stage age-related macular degeneration (AMD) from worsening to advanced AMD (dry or wet). The formula for these AREDS2 eye vitamins 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. Carotenoids (molecules that give the bright red, yellow, and orange colors to fresh produce) are vital to macular health, and there may be ways to increase the body's uptake of this important nutrient. A "Mediterranean-style" diet rich in fish, whole grains, and a variety of healthy fruits and vegetables (especially

leafy greens) may also be beneficial. Research is showing that our diets may influence how our body responds to disease and help shape a healthy immune response by influencing the composition and function of the microorganisms that live within our body (including gut bacteria). The hope is that all these findings may rapidly translate to current clinical practice and be incorporated into "vision-healthy" lifestyles.

*Above: Retinal tissue is compared in animals fed a low glycemic diet (left), a high glycemic diet (right), and transitioning from one to the other (middle). The image at right shows evidence of macular degeneration, including photoreceptor degeneration and atrophy of surrounding tissue (top row); empty vacuoles and loss of protective pigmentation (middle); and autofluorescence (yellow staining) from the accumulation of lipofuscin and other waste products. (Courtesy of Sheldon Rowan, PhD, Tufts University, Boston, MA. Adapted from Rowan et al, Proc Natl Acad Sci U S A. 2017 May 30;114(22):E4472-E4481. doi: 10.1073/pnas.1702302114)*



**Christopher Hammond, MD, MRCP, FRCOphth**

(9/1/20 - 8/31/22)

*King's College London, United Kingdom*

**Exploring the Role of Gut Bacteria in Early AMD**

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](http://www.brightfocus.org/grant/M2020277)



**Amy Millen, PhD**

(9/1/20 - 8/31/22)

*University of New York at Buffalo*

**The Gut Bacteria and AMD in Aging Women**

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](http://www.brightfocus.org/grant/M2020227)



**Dimitra Skondra, MD, PhD**

(7/1/18 - 6/30/22)

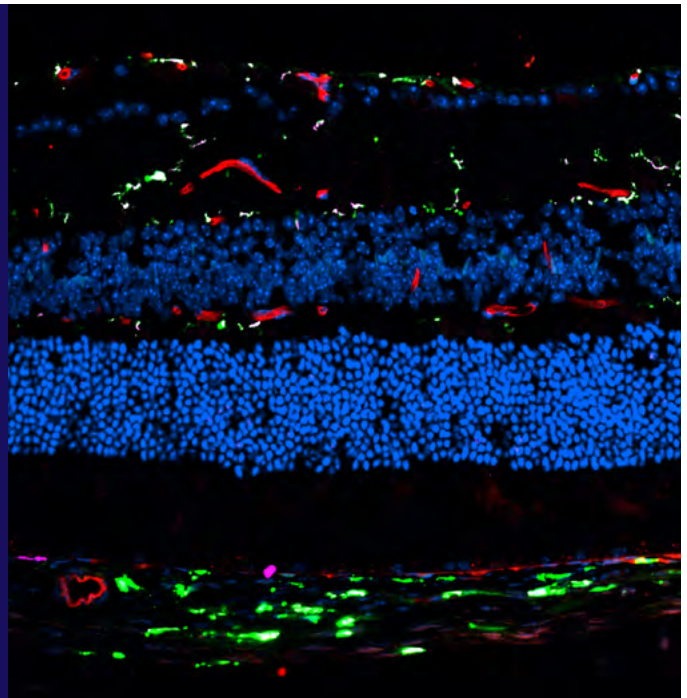
*University of Chicago, Chicago, IL*

**Role of Diet and Gut Microbes in Macular Degeneration**

The goal of this proposal is to study whether gut microbiome could be the missing link that connects lifestyle factors, like diet, and genetic risk, to the development of AMD.

[www.brightfocus.org/grant/M2018042](http://www.brightfocus.org/grant/M2018042)

# 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 age-related macular degeneration (AMD), and increases in the number and size of drusen may cause the immune system to kick into overtime. 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. Thus, researchers are focusing on specific aspects of the immune response, including numerous inflammatory factors, and the eye's own built-in defense molecules, called microglia, to learn exactly how they interact and participate in AMD.

*Above: Scientists are focusing on the role of different immune cells in and near the retina, shown here. (Courtesy of Jeremy Lavine, MD, PhD, Northwestern University Feinberg School of Medicine, Chicago)*



**Brittany Carr, PhD**

(7/1/21 – 6/30/23)

*University of British Columbia (Canada)*

Fellowship Mentor: Orson Moritz, PhD

## **New Model to Tracking the Development of Reticular Pseudodrusen and AMD**

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](http://www.brightfocus.org/grant/M2021001F)





**Sayan Ghosh, PhD**

(7/1/21 – 6/30/23)

*University of Pittsburgh*

Fellowship Mentor: Debasish Sinha, PhD

### **Understanding the Role of Inflammation in AMD**

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](http://www.brightfocus.org/grant/M2021005F)



**Jeremy Lavine, MD, PhD**

(7/1/21 – 6/30/24)

*Northwestern University Feinberg School of Medicine*

Co-mentors: Harris R. Perlman, PhD & Amani Fawzi, MD

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

The premise of this study is that there are macrophage (immune cell) subtypes, and classically-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](http://www.brightfocus.org/grant/M2021016N)



**Alexander Marneros, MD, PhD**

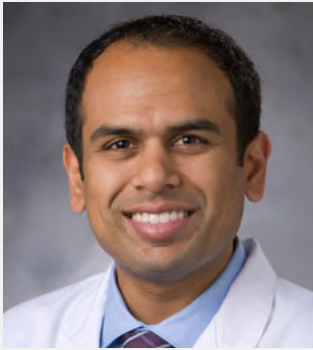
(7/1/19 – 6/30/22)

*Massachusetts General Hospital, Harvard Medical School, Boston*

### **Inhibiting Inflammation to Prevent Wet AMD**

This study aims to identify which cell types in the eye are important for mediating the effects of the inflammasome, a protein complex identified as a likely contributor to the inflammation that promotes “wet” AMD. This will enable the researchers to selectively target these specific cell types and to develop novel pharmacologic treatments while reducing therapeutic side effects in other cell types.

[www.brightfocus.org/grant/M2019184](http://www.brightfocus.org/grant/M2019184)



**Priyatham Mettu, MD** (9/1/20 - 8/31/22)  
*Duke University Eye Center, Durham, NC*

### **Evaluating a Novel Mechanism and Target for Wet AMD**

This study proposes that the severe form of wet AMD is caused by inflammatory cells called macrophages and have identified 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](http://www.brightfocus.org/grant/M2020168)



**Ke Ning, MD** (7/1/21 – 6/30/23)  
*Stanford University*

Fellowship Co-mentors: Yang Sun, MD, PhD & Vinit Mahajan, MD, PhD

### **Ciliary Lipids in RPE Repair: A Novel Target for AMD**

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](http://www.brightfocus.org/grant/M2021008F)



**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*

### **Role of Lipids (Deposits) in Causing Dry AMD**

Researchers in this study propose to characterize the role of a new protein which is involved in processing lipids, a process which has long 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](http://www.brightfocus.org/grant/M2020271)

*Recipient of The Elizabeth Anderson Award for Macular Degeneration Research.*



**Ye Sun, MD, PhD**  
*Boston Children's Hospital, MA*

(7/1/19 – 6/30/22)

### **A Novel Negative Immune Regulator to Control Wet AMD**

This study aims to investigate a novel negative-immune regulator that may suppress inflammation-induced abnormal vessel growth in AMD by altering the immune-vascular crosstalk. Furthermore, novel activators of this immune regulator will be evaluated in a pre-clinical animal model of AMD to determine if this treatment is effective in preventing or slowing development of AMD-like pathologies.

**[www.brightfocus.org/grant/M2019114](http://www.brightfocus.org/grant/M2019114)**

*This grant is made possible by support from Dr. H. James and Carole Free*

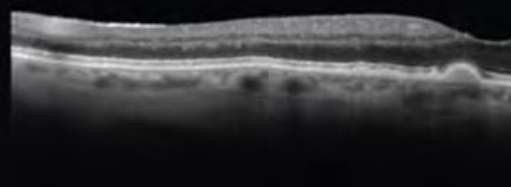
# GENES & AMD

AMD  
ARMS2 GT  
CFH CC

Right Eye



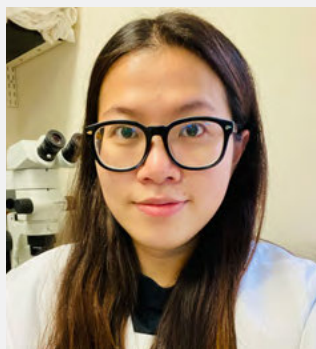
AMD  
ARMS2 GT  
CFH CC



Most forms of macular degeneration are not linked to any single genetic mutation. Instead, susceptibility to age-related macular degeneration (AMD) is scattered over a number of small irregularities of genes called single nucleotide polymorphisms (SNPs). SNPs may arise spontaneously or be inherited, and their impact is tempered by other factors, such as age, overall health and nutrition, and exposure to cigarette smoke, sunlight, and other toxins. Despite their relatively indirect influence, genes may be one way to lower the risk of AMD, if

researchers can block or replace signals from genes that trigger disease, and promote the survival and integrity of the retinal pigment epithelium (RPE) cells when they encounter oxidative stress from aging and other causes.

*Above: Imaging techniques are used to study AMD lesions associated with an AMD risk gene called ARMS2. In addition, in a cell model of AMD, researchers are attempting to modify AMD risk genes using CRISPR/Cas9 gene editing technology. (Courtesy of Ya-Ju Chang, PhD, Columbia University Medical Center)*



**Ya-Ju Chang, PhD**

(7/1/21 – 6/30/23)

Columbia University Medical Center

Fellowship Mentor: Stephen Tsang, MD, PhD

## CRISPR Genome Engineering in AMD Risk Alleles

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](http://www.brightfocus.org/grant/M2021002F)



**Willard Freeman, PhD** (9/1/20 - 8/31/22)  
*Oklahoma Medical Research Foundation, Oklahoma City*  
Co-Principal Investigator: Ana J Chucair-Elliott, PhD

### **Immune Cell Specific DNA Modifications and Gene Expression in AMD**

Aging is the major risk factor for AMD but how aging, along with gender, lead 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](http://www.brightfocus.org/grant/M2020207)



**Michelle Grunin, PhD** (7/1/21 - 6/30/23)  
*Hebrew University of Jerusalem, Israel*  
Fellowship Co-mentors: Shai Carmi, PhD & Jonathan L. Haines, PhD

### **Integrated Immunogenomics to Develop Translational Treatment for AMD**

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. Utilizing multiethnic participants will allow for discovery of rare genetic variants not previously investigated.

[www.brightfocus.org/grant/M2021006F](http://www.brightfocus.org/grant/M2021006F)



**Jurgen Naggert, PhD** (9/1/20 - 8/31/22)  
*The Jackson Laboratory, Bar Harbor, ME*

### **Generating Precision Model for AMD Research**

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](http://www.brightfocus.org/grant/M2020284)



**Rinki Ratnapriya, PhD**

(7/1/21 – 6/30/24)

*Baylor College of Medicine*

Mentor: John Timothy Stout, MD, PhD

### **Functional Characterization of Genetic Regulatory Effects of AMD Risk Variants**

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 mechanistic understanding of AMD.

[www.brightfocus.org/grant/M2021017N](http://www.brightfocus.org/grant/M2021017N)



**Philip Ruzycki, PhD**

(9/1/20 - 8/31/22)

*Washington University in Saint Louis, MO*

Co-Principal Investigator: Rajendra Apte, MD, PhD

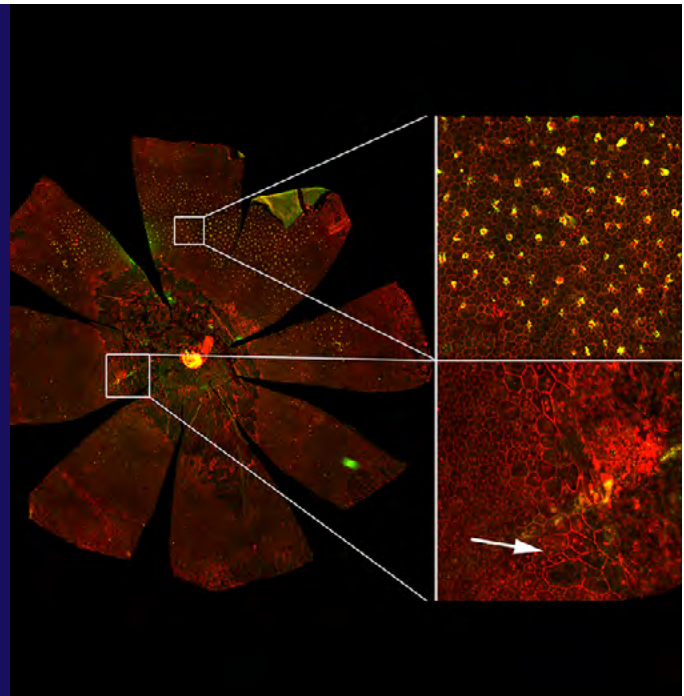
### **Profiling of Immune Cell Subtypes in AMD Patients and Controls**

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 preventative therapeutics.

[www.brightfocus.org/grant/M2020115](http://www.brightfocus.org/grant/M2020115)

*This award is made possible by support from The Ivan Bowen Family Foundation.*

# GEOGRAPHIC ATROPHY



Geographic atrophy (GA) is an advanced form of age-related macular degeneration (AMD). It is sometimes referred to as “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 in discovery and/or development. Macular Degeneration Research 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, retinal-pigmented epithelium cell boundaries (in red) are lost in the central region, and microglia (in green) are recruited to the area to protect the tissue. (Courtesy of Claudio Punzo, PhD, University of Massachusetts Medical School, Worcester)*



**Malia Edwards, PhD**

(9/1/20 - 8/31/22)

*Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD*

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

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](http://www.brightfocus.org/grant/M2020174)

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

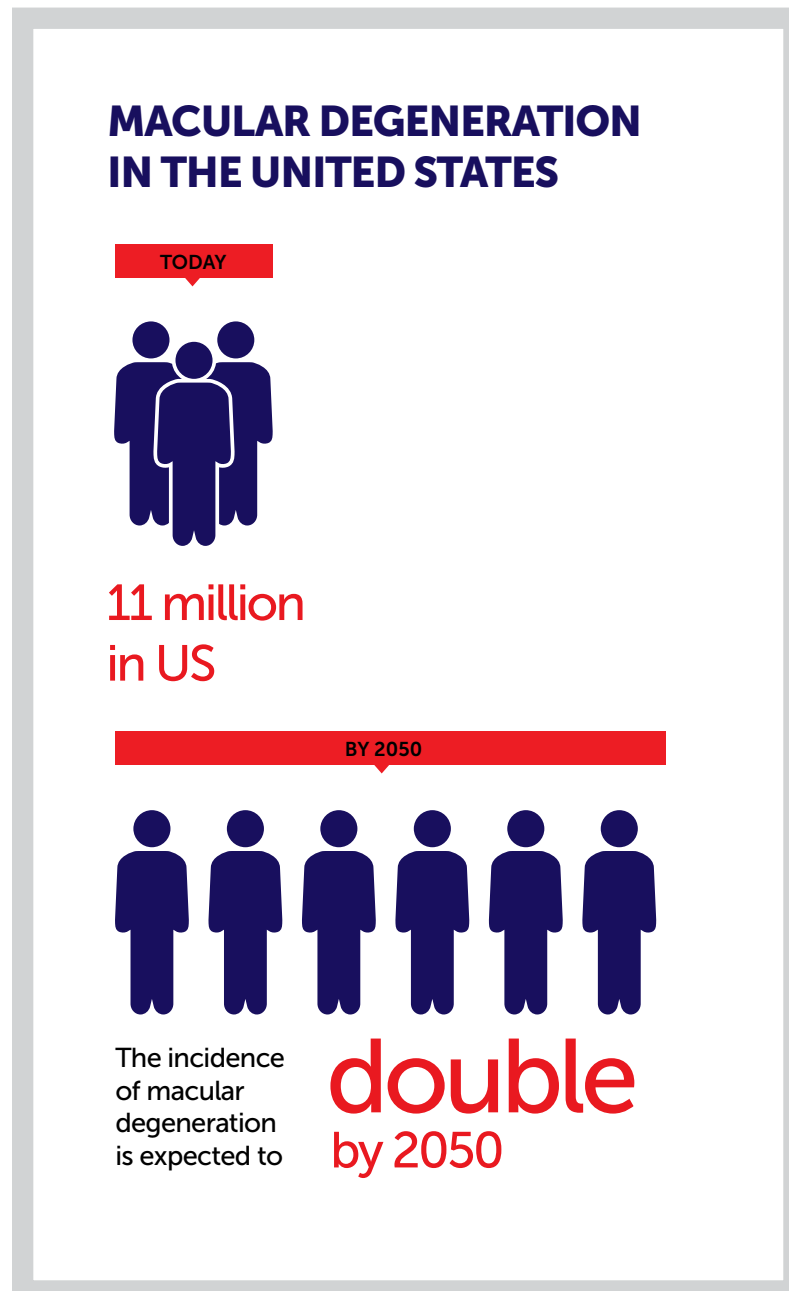


**Claudio Punzo, PhD** (9/1/20 - 8/31/22)  
*University of Massachusetts Medical School, Worcester, MA*

### **Elucidating How Smoking Causes Advanced AMD**

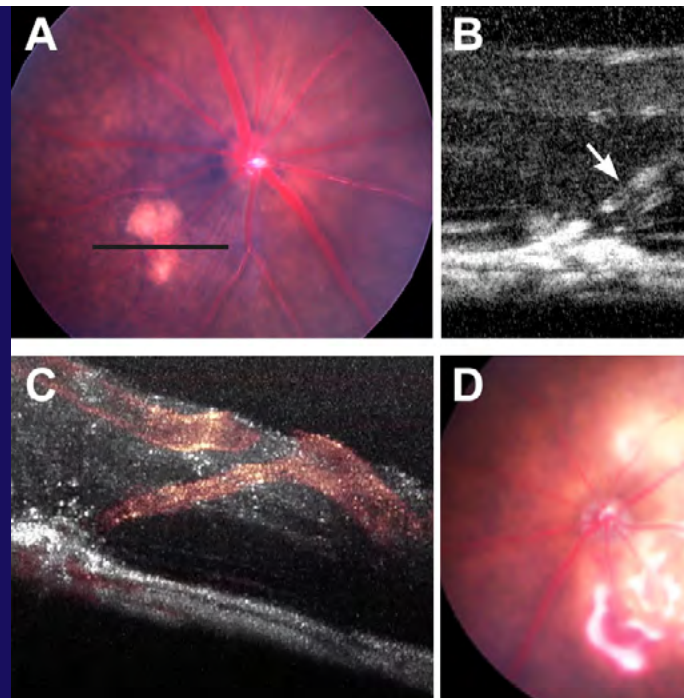
Among the non-genetic risk factors smoking, confers the highest risk for progression to the advanced stages of GA and wet AMD; however, how smoking contributes to AMD remains elusive. In this study, researchers propose that smoking causes advanced AMD pathologies by depletion of the second most abundant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

[www.brightfocus.org/grant/M2020016](http://www.brightfocus.org/grant/M2020016)





# INNOVATIVE APPROACHES TO AMD TREATMENTS



One day, we may be able to detect signs that age-related macular degeneration (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 at earlier stages, before damage to sight has occurred. These include drugs that enhance immune functioning and improve the eye's ability to clear lipids/fats and other waste that might otherwise lead to inflammation in AMD.

New imaging techniques are being developed that will help us to do a better job of tracking disease progression over time. Knowledge of genetics is advancing to the point that gene therapy is being evaluated as a possibility to treat AMD.

*Above: New imaging techniques, shown here in mice, are being pioneered to detect and repair leakages of blood and fluid into the macula, the central part of the retina responsible for straight ahead vision. (Courtesy of Tyson Kim, MD, PhD, University of California, San Francisco)*



**Stephen Aller, PhD**

(7/1/19 – 6/30/22)

*University of Alabama at Birmingham*

Co-Principal Investigator: Alecia K. Gross, PhD

## **The Three-Dimensional Structure of a Protein that Causes AMD**

A critical part of our visual process is the recycling of a special molecule, called a chromophore, after exposure to light by a molecular pump, called ABCA4 that allows the cell to regenerate the active form of the chromophore. A misfolding and malfunction of the pump in the eye can eventually lead to blindness in patients with early-onset macular degeneration. The researchers in this study propose to determine the three-dimensional structure of the active form of ABCA4, as well as to develop a drug selection process to discover new drugs that can correct folding defects of the ABCA4 pump to restore vision.

[www.brightfocus.org/grant/M2019212](http://www.brightfocus.org/grant/M2019212)



**Andrew Browne, MD, PhD**

(7/1/21 – 6/30/24)

*University of California, Irvine*

Mentor: Krzysztof Palczewski, PhD

### **Functional Imaging of the Human Retina Using Non-Invasive Technology**

This proposal seeks to develop a camera for use in humans and 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 non-invasively acquire images at such high resolution that they can reveal what is happening inside cells.

[www.brightfocus.org/grant/M2021013N](http://www.brightfocus.org/grant/M2021013N)



**Sabrina Carrella, PhD**

(11/1/20 – 10/31/22)

*Telethon Institute of Genetics and Medicine, FONDAZIONE TELETHON, Italy*

Co-Principal Investigator: Alessia Indrieri, PhD

### **A New Therapeutic Strategy to Treat AMD**

Researchers in this study have identified two small non-coding 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](http://www.brightfocus.org/grant/M2020184)



**Jennifer Chao, MD, PhD**

(9/1/20 - 8/31/22)

*University of Washington, Seattle, WA*

### **A Novel Method for Modeling AMD in a Dish**

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 epithelial (RPE) cells and choriocapillaris of the eye. This model will allow 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](http://www.brightfocus.org/grant/M2020217)

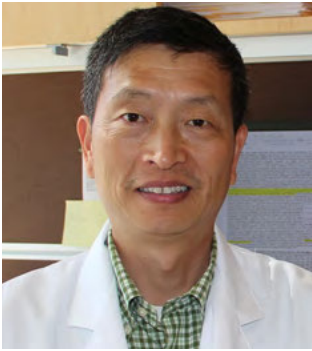


**Rony Chidiac, PhD** (7/1/21 – 6/30/23)  
*University of Toronto, Faculty of Pharmacy (Canada)*  
Fellowship Mentor: Stephane Angers, PhD

### **Novel Antibody-Based Agonist for Neovascular AMD**

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](http://www.brightfocus.org/grant/M2021003F)



**Zongchao Han, MD, PhD** (7/1/19 – 6/30/22)  
*The University of North Carolina at Chapel Hill*

### **A Selective Anti-Oxidant Nanoparticle to Treat AMD**

The goal of this project is to test the ability of a novel solution, generated by this team of researchers, to serve as a selective waste collector to pick up any specific free radicals (toxic waste products that gradually build up in the cells over time).

[www.brightfocus.org/grant/M2019063](http://www.brightfocus.org/grant/M2019063)



**Tyson Kim, MD, PhD** (7/1/21 – 6/30/24)  
*University of California, San Francisco*  
Co-mentors: Douglas Gould, PhD, Aparna Lakkaraju, PhD & Dan Schwartz, MD

### **Advanced Imaging Studies in a Model of Type 3 Neovascular AMD**

In order to study the formation of chorioretinal anastomoses (CRA), which is 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](http://www.brightfocus.org/grant/M2021015N)



**Aparna Lakkaraju, PhD** (7/1/21 – 6/30/24)  
*University of California, San Francisco*

### **Does Aberrant Mechanotransduction Trigger RPE Atrophy in AMD?**

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 RPE 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](http://www.brightfocus.org/grant/M2021020I)



**Young Joo Sun, PhD** (7/1/21 – 6/30/23)  
*Stanford University*  
Fellowship Mentor: Vinit Mahajan, MD, PhD

### **Structure-based Development of HTRA1 Specific Inhibitors for AMD**

Researchers in this study propose to characterize the efficacy of their '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](http://www.brightfocus.org/grant/M2021011F)



**Benjamin Thomson, PhD** (7/1/21 – 6/30/24)  
*Northwestern University - Chicago Campus*

### **New Signaling Pathway in Blood Vessels as Target for Wet AMD**

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 (known as the angiotensin signaling pathway) in PCV, and test new drug candidates targeting this pathway.

[www.brightfocus.org/grant/M2021018N](http://www.brightfocus.org/grant/M2021018N)

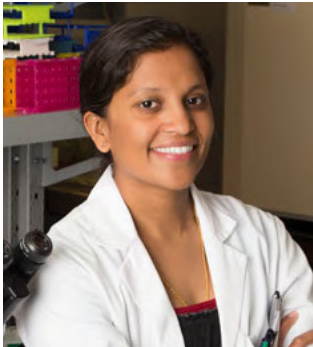


**MD Imam Uddin, PhD** (7/1/19 – 6/30/22)  
*Vanderbilt Eye Institute, Nashville, TN*

### **A Novel Gold Nanoparticle for the Treatment of AMD**

The goal of researchers in this study is to demonstrate, for the first time, how engineered gold nanoparticles can be used to treat AMD- specific genes, thereby overcoming the limitations of existing therapy. They will test this new technology for its safety, high sensitivity, and specificity in cells and in animal models of “wet” AMD

[www.brightfocus.org/grant/M2019023](http://www.brightfocus.org/grant/M2019023)



**Elizabeth Vargis, PhD** (7/1/19 – 6/30/22)  
*Utah State University, Logan*

### **A New Approach to Modeling Subretinal Tissue**

This team of biological engineers proposes to design a multi-layered 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](http://www.brightfocus.org/grant/M2019109)



**Shusheng Wang, PhD** (9/1/20 - 8/31/22)  
*Tulane University, New Orleans, LA*  
Co-Principal Investigator: Bo Yu, PhD

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

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](http://www.brightfocus.org/grant/M2020166)



**Yvette Wooff, PhD**

(7/1/21 – 6/30/23)

*The Australian National University*

Fellowship Mentor: Riccardo Natoli, PhD

### **Replenishment of MicroRNA Using Extracellular Vesicles for Treatment of AMD**

In the retina, extracellular vesicles (EV) are responsible for mediating essential communication and work by delivering molecular cargo, including small gene regulators called microRNA (miRNA), to target cells, and 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](http://www.brightfocus.org/grant/M2021012F)



**Glenn Yiu, MD, PhD**

(9/1/20 - 8/31/22)

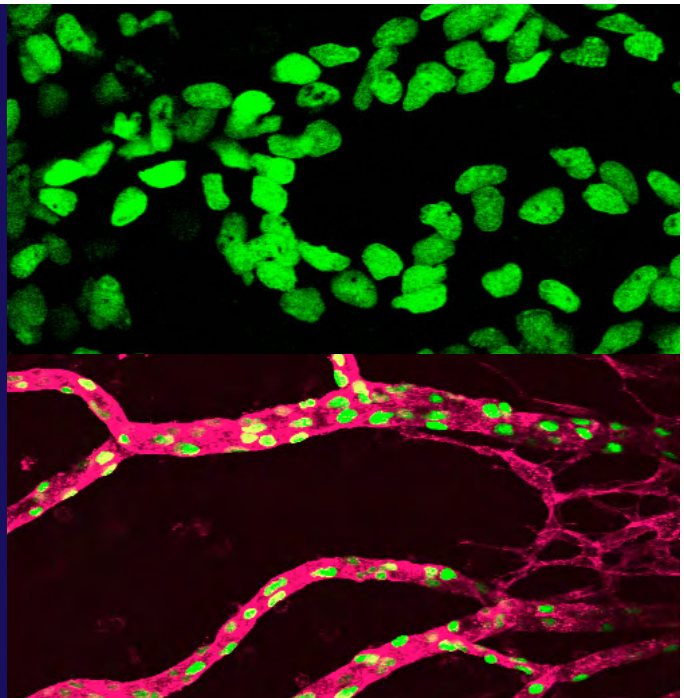
*University of California, Davis*

### **Development of Gene Editing as a Permanent Cure for Wet AMD**

This research proposal will address this healthcare crisis by developing a potential cure for wet AMD 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](http://www.brightfocus.org/grant/M2020247)

# REGENERATING DAMAGED CELLS



Unlike skin and other parts of the human body, the nerve cells of the eyes do not, for the most part, regrow or regenerate after damage has occurred. However, there is new hope for overcoming that biological limitation. Work is moving forward to regenerate and reconnect the eye's retinal cells that have been damaged by age-related macular degeneration (AMD), and to restore the underlying retinal pigment epithelium (RPE) cells that provide its nourishment and support. Grantees are recreating parts of the eye using induced

pluripotent stem cell (iPSC) technology, which are stem cells created from living adult tissue. Also, cell regeneration in other animal models is being studied with the hope of glean information that may be translated to therapy.

*Above: In an animal model, blood vessels of the eye are shown in red, and nearby, in green, are cells expressing a signaling molecule (Wnt) that determines cell fate. Researchers, including Dr. Poché, are looking for a way to induce eye cells to regenerate. (Courtesy of Ross Poché, PhD, Baylor College of Medicine)*



**Mark Emerson, PhD**

(9/1/20 - 8/31/22)

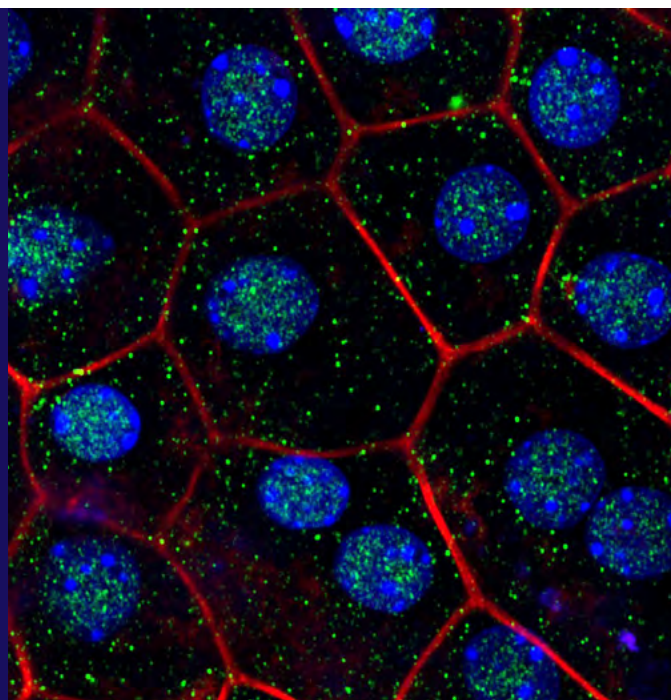
*The City College of New York, The City University of New York*

## Discovery of New Methods to Regenerate Cone Photoreceptors

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](http://www.brightfocus.org/grant/M2020157)

# UNDERSTANDING EARLY-STAGE AMD



Macular degeneration is a disease linked to not just one, but many, causes. Foremost are changes in the eye that happen with age—the strongest risk factor. It is generally thought that age-related macular degeneration (AMD) begins in the retinal pigment epithelium (RPE), a layer of cells next to the retina, whose job is to transport molecules in and out to nourish the retina and dispose of waste. The RPE's ability to do its job can be compromised by age,

genes, oxidative stress, inflammation, and other factors. BrightFocus' Macular Degeneration Research program is funding scientific exploration into AMD's contributing causes in order to expand our understanding and open new and earlier treatment avenues.

*Above: Microscopic image of the retinal pigmented epithelium, a layer of cells supporting the retina, reveals a characteristic "honeycomb" pattern. (Courtesy of Antonio Escudero Paniagua, PhD, University of California, Los Angeles)*



**Kapil Bharti, PhD**

(9/1/20 - 8/31/22)

*The National Eye Institute, Bethesda, MD*

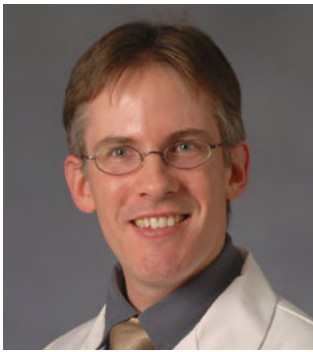
Co-Principal Investigator: Eric Nguyen, PhD

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

This research 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](http://www.brightfocus.org/grant/M2020258)





**Tim Corson, PhD**  
*Indiana University, Indianapolis*

(7/1/19 – 6/30/22)

### **A New Way to Target Abnormal Blood Vessel Growth in Wet AMD**

Researchers in this study will design and produce chemicals that will inhibit a newly discovered protein that, when blocked, will prevent blood vessel growth.

[www.brightfocus.org/grant/M2019069](http://www.brightfocus.org/grant/M2019069)



**Bradley Gelfand, PhD**  
*University of Virginia, Charlottesville*

(9/1/20 - 8/31/22)

### **Examining the Role of Choroidal Blood Flow in AMD**

In this proposal, 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](http://www.brightfocus.org/grant/M2020114)



**Rosario Fernandez-Godino, PhD**  
*The Schepens Eye Research Institute Massachusetts Eye and Ear, Harvard Medical School*

(3/1/22 – 2/28/25)

### **Understanding Bruch’s Membrane and their Relevance to the RPE Pathology in AMD**

In this proposal, researchers will evaluate the rigidity of eyes with and without AMD and how the elasticity of the retina impacts the function of the retinal cells. The results will contribute to bridge the gaps between aging and AMD as well as to improve existing therapeutic approaches for AMD patients, such as the RPE transplantation.

[www.brightfocus.org/grant/M2021014N](http://www.brightfocus.org/grant/M2021014N)



**Haijiang Lin, MD, PhD**  
*University of Massachusetts Medical School, Worcester*  
Co-Principal Investigator: Bo Tian, PhD

(7/1/19 - 10/31/22)

### **Investigation of Novel Pathogenesis and Therapeutic Strategy for AMD**

This study will identify new factor(s) contributing to the progression of AMD and explore methods to halt or reverse AMD retinal lesions. 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](http://www.brightfocus.org/grant/M2019074)



**Rohini M. Nair, PhD**

(7/1/21 – 6/30/23)

*University of Pennsylvania*

Fellowship Mentor: Venkata Ramana Murthy Chavali, PhD

### **Exploring the Role of Lipid Metabolism in AMD Pathogenesis**

This study aims to unravel the role of hepatic lipase (HL) that breaks down high-density lipoproteins (HDL) 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](http://www.brightfocus.org/grant/M2021007F)



**Davide Ortolan, PhD**

(7/1/21 – 6/30/23)

*National Eye Institute, NIH*

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

### **Macular and Mid-Peripheral Specific iPSC-RPE Models to Discover Regional RPE Susceptibility in AMD**

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. With this new knowledge, plus having an easily reproducible model in a dish, will eventually translate in the development of drugs to prevent vision loss caused by AMD.

[www.brightfocus.org/grant/M2021009F](http://www.brightfocus.org/grant/M2021009F)



**Antonio Escudero Paniagua, PhD**

(7/1/21 – 6/30/23)

*University of California, Los Angeles*

Fellowship Mentor: David Williams, PhD

### **Addressing the Link Between Impairment in Phagosome Degradation and AMD**

Researchers propose to investigate the maturation rate and the accumulation of specific phagosome (a vesicle formed around a particle engulfed by a phagocyte cell) 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](http://www.brightfocus.org/grant/M2021004F)

*Recipient of The Elizabeth Anderson Award for Macular Degeneration Research.*



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