

Current Macular Degeneration Research Projects

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, as many as 11 million Americans have some form of macular degeneration, including both early and advanced stages of the wet and dry forms. This number is expected to double by 2050. Much more work is needed to develop effective treatments and cures. Through the generosity of our donors, Macular Degeneration Research, a BrightFocus Foundation program, has awarded nearly \$30 million to fund research projects on the causes and potential prevention, treatment, and cure of this disease.

Macular Degeneration Research invests in several promising avenues of research to defeat age-related macular degeneration. We fund a broad array of scientific approaches, encompassing innovative projects falling into the following categories:

- **Understanding Early AMD**
- **Insights into Geographic Atrophy**
- **Role of Cell Metabolism in AMD**
- **Drusen Formation and Immune Response**
- **Genes and AMD**
- **How Diet and Nutrition Affect AMD Risk**
- **Innovative Approaches to AMD Treatment**
- **Regenerating Cells Damaged by AMD**

Note: The funding statistics and inclusion of research grants in this yearbook are based upon award offers and grants that were active as of July 1, 2019. Excerpts are from research profiles available at BrightFocus.org and may have been edited for clarity and space constraints. This information is accurate as of Sept 5, 2019.

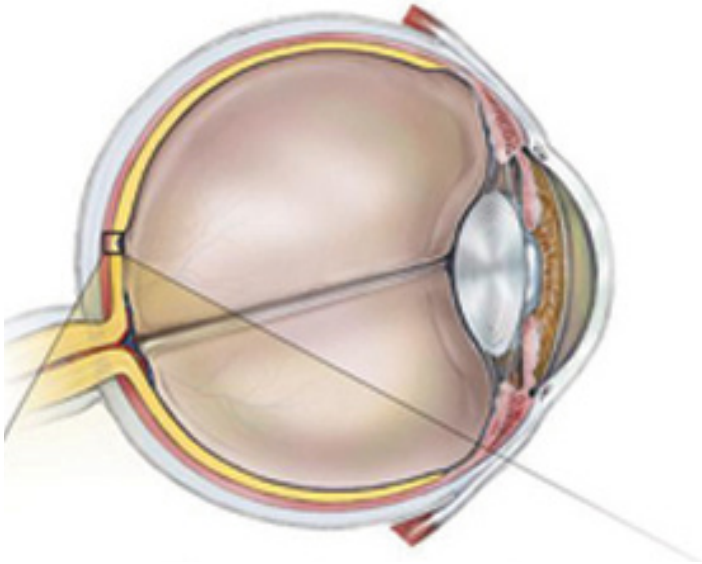
Schematic Diagram of the Macula

MACULA

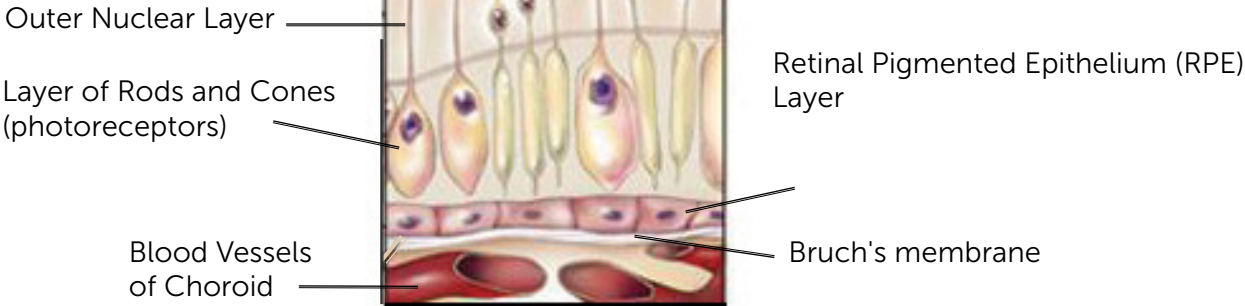
The macula is a small, but important area located at the center of the back of the eye.

It is responsible for sharp central vision needed for activities such as reading and driving.

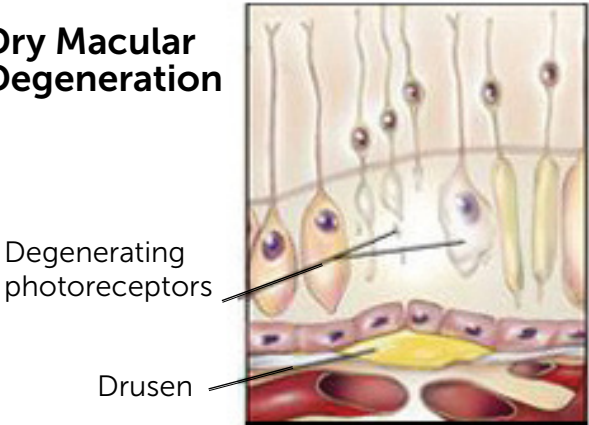
Damage to the macula leads to the loss of straight-ahead vision.



Normal Macula



Dry Macular Degeneration



Wet Macular Degeneration

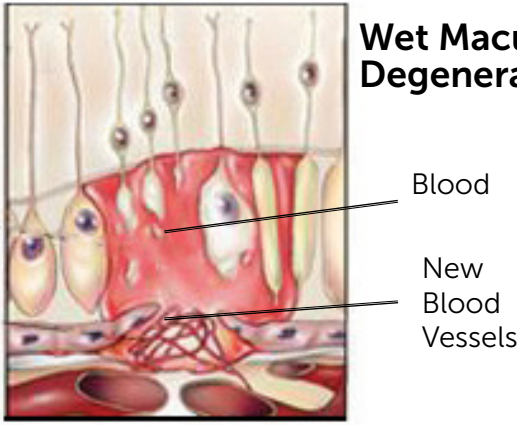


Illustration by Bob Morreale, provided courtesy of BrightFocus Foundation

Understanding Early 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, oxidative stress, inflammation, and other factors causing the immune system to kick in and overact. The scientific exploration that Macular Degeneration Research is funding will expand our understanding and open new and earlier treatment avenues.



Tim Corson, PhD (7/1/19 – 6/30/21)
Indiana University, Indianapolis

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

Recipient of The Carolyn K. McGillvray Award.



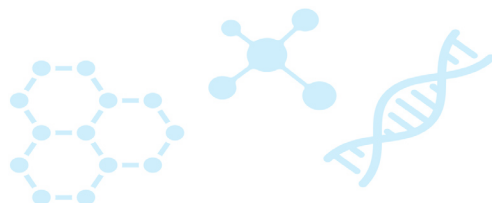
Xi-Qin Ding, PhD (7/1/18 - 6/30/20)
University of Oklahoma Health Sciences Center, Oklahoma City

Thyroid Hormone Regulation in AMD

Thyroid hormone (TH) regulates cell growth, differentiation, and metabolism, and has recently been associated with increased risk of AMD. This study will investigate TH regulation and determine whether suppressing TH signaling protects the retinal pigment epithelium against damage.

www.brightfocus.org/grant/M2018107

Recipient of The Elizabeth Anderson Award for Macular Degeneration Research.





Haijiang Lin, MD, PhD (7/1/19 - 6/30/21)
University of Massachusetts Medical School, Worcester
Co-Principal Investigator: **Bo Tian, PhD**

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



Chi Luu, PhD (7/1/18 - 6/30/20)
Centre for Eye Research Australia, East Melbourne, Australia
Co-Principal Investigators: **Robyn Guymer, PhD** and **Gregory Dusting, PhD**

The Role of "Good Cholesterol" in AMD

The overall aim of this research project is to explore the role and therapeutic benefit of "good cholesterol" in AMD.
www.brightfocus.org/grant/M2018144



Sarah McFarlane, PhD (7/1/2017 – 3/30/20)
University of Calgary, Alberta, Canada

Aberrant Blood Vessel Growth in AMD: A New Animal Model

This study aims to develop a genetic animal model which can be used to rapidly identify novel, safe and effective drugs for the treatment of wet AMD.
www.brightfocus.org/grant/M2017002



Ming Zhang, MD, PhD (7/1/19 – 6/30/21)
Augusta University Research Institute, GA

Association Between Cytomegalovirus Infection in the Eye and the Development of AMD

The purpose of this study is to investigate if cytomegalovirus (CMV), a common virus, that stays dormant in the human eyes and how reactivation of this virus contributes to the development of AMD. This study will further explore strategies to inhibit virus reactivation and alleviate development of AMD induced by CMV reactivation in the eye.
www.brightfocus.org/grant/M2019035

This grant is made possible by support from the Nancy Ferguson Seeley Trust in memory of Mildred F. Ferguson.

Insights into Geographic Atrophy

Geographic atrophy (GA) is an advanced form of dry age-related macular degeneration (AMD). Geographic atrophy is “dry” 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 (“geographic”). Currently there is no treatment for geographic atrophy. Macular Degeneration Research is funding investigations into new drugs and ways to manage and treat this devastating disease. It’s urgently needed research which could one day result in the first successful therapies.



Paul Baird, PhD (7/1/19 – 6/30/21)

The University of Melbourne, Australia

Co-Principal Investigator: **Adam Kowalczyk, PhD and Alice Pebay, PhD**

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

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, sex of an individual and smoking.

www.brightfocus.org/grant/M2019093



Yingbin Fu, PhD (7/1/18 - 6/30/20)

Baylor College of Medicine, Houston, TX

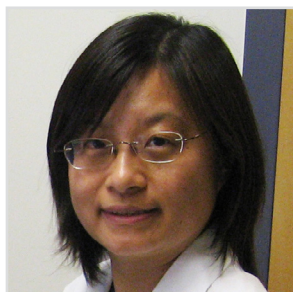
A Novel Method to Treat Both the Wet and Dry Forms of AMD

The objective of this project is to develop a highly innovative and effective treatment strategy to target the underlying causes of both the wet and dry forms of AMD.

www.brightfocus.org/grant/M2018142

Role of Cell Metabolism in AMD

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



Jing Chen, PhD (7/1/17 - 6/30/20)

Boston Children’s Hospital, MA; Harvard Medical School, MA

Protecting RPE and Photoreceptors in AMD

This work aims to investigate the molecular processes through which dysregulation of factors controlling oxidative stress impairs RPE and photoreceptor cell metabolism and their survival in AMD.

www.brightfocus.org/grant/M2017161



Yan Chen, PhD (7/1/2017 - 6/30/20)

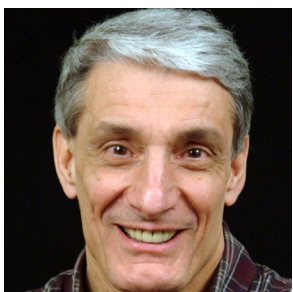
The University of Texas Medical Branch at Galveston

Co-Principal Investigator: **Dean Jones, PhD**

Metabolic Pathways of the Retina in Health and AMD

This project studies the mechanisms of energy production and regulation, in both healthy and diseased eyes, particularly those with AMD.

www.brightfocus.org/grant/M2017186



Michael Paulaitis, PhD (7/1/17 - 3/01/20)

Johns Hopkins University, Baltimore, MD

Co-Principal Investigator: **James T. Handa, MD**

MicroRNAs and Mitochondrial Dysfunction in AMD

The overall goal of this project is to test the novel concept that a recently discovered class of small non-coding ribonucleic acids (RNAs), which are called microRNAs and are packaged and secreted by RPE cells, have gone ‘haywire’ in AMD. These microRNAs can predict the status of mitochondrial function in these cells and influence mitochondrial function in neighboring RPE cells through vesicle-mediated intercellular transfer of the microRNAs.

www.brightfocus.org/grant/M2017060



Raju Rajala, PhD (7/1/19 – 6/30/21)
University of Oklahoma Health Sciences Center, Oklahoma City

Defective Energy Utilization in AMD

RPE cells of the retina provide nourishment to the photoreceptor cells for normal visual functions. Recent studies show that in AMD patients' retinas and tissues from aged mouse, expression of two metabolic enzymes is increased in the RPE and is decreased in the photoreceptors which are opposite to that seen in normal retinas. This proposal aims to study these two enzyme alterations and also reprogram their expression to reduce the AMD phenotype.

www.brightfocus.org/grant/M2019168

Recipient of The Elizabeth Anderson Award for Macular Degeneration Research.



Magali Saint-Geniez, PhD (7/1/18 - 6/30/20)
Massachusetts Eye and Ear, Boston; Harvard Medical School, Boston

Investigation of a New Target in AMD

This project aims to study a novel pathogenic mechanism responsible for impaired RPE metabolism and progression to the advanced "wet" form of AMD. Results from this study may open up new avenues for efficient and specific therapeutic strategies.

www.brightfocus.org/grant/M2018064



Drusen Formation and Immune Response

As the eye ages, it becomes less efficient at removing waste. Deposits of extra cellular 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 increase in these number and size of these 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.



John Hulleman, PhD (7/1/18 - 6/30/20)
University of Texas Southwestern, Dallas

Conditional Control of Inflammation in Retinal Degenerative Diseases

The goal of this project is to slow or prevent damage to the RPE by using small molecules to stop local inflammatory signals and complement activation that has been associated with macular degeneration.

www.brightfocus.org/grant/M2018099



Alexander Marneros, MD, PhD (7/1/19 – 6/30/21)
Massachusetts General Hospital, Boston; 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



Ye Sun, MD, PhD (7/1/19 – 6/30/21)

Boston Children's Hospital, MA

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

Genes and AMD

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.



Michael Farkas, PhD (7/1/19 – 6/30/21)

SUNY Buffalo, NY

The Role of Long Non-coding RNAs in HTRA1 Regulation

This study aims to elucidate the role of two novel long non-coding RNAs in the regulation of HTRA1, a gene associated with high risk of developing AMD.

www.brightfocus.org/grant/M2019108



Rosario Fernandez-Godino, PhD (7/1/18 - 6/30/20)

Massachusetts Eye and Ear and Harvard Medical School, Boston

The Relationship Between Genetic Predisposition and Age in AMD

This study aims to create a cell-based model to discover the primary mechanisms activated by the combination of aging and genetic variants in complement genes in patients with early AMD. Based on the results, drugs could be designed to stop these mechanisms before they lead to major damage and complete loss of vision.

www.brightfocus.org/grant/M2018115

This grant is made possible in part by support from the Ivan Bowen Family Foundation.



Mark Kleinman, MD (7/1/18 - 6/30/20)
East Tennessee State University, Johnson City

A New Method to Regulate Gene Expression Pathways in AMD

The goal of this project is to utilize CRISPR/Cas9 gene editing to study epigenetic signatures/influences on inflammatory genes in experimental models of AMD.

www.brightfocus.org/grant/M2018193



William Scott, PhD (7/1/18 - 6/30/20)
University of Miami, FL

Co-Principal Investigator: Margaret A. Pericak-Vance, PhD

Using Genetics and Retinal Imaging to Predict Progression to Advanced AMD

The goal of this project is to identify genetic factors that influence progression of AMD from early stages, where vision loss is less severe, to late stages, where there is significant visual impairment. Identifying genetic factors that predict faster or slower progression could also provide targets for the development of potential therapies.

www.brightfocus.org/grant/M2018112

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

How Diet and Nutrition Affect AMD Risk

Currently, eye vitamins that follow the AREDS2 [Age-Related Eye Disease Study 2] formula are the standard treatment aimed at preventing 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 color to fresh produce) are vital to macular health, and there may be ways to increase the body's uptake of this important nutrient. Our diets may also influence how our body responds to disease and help shape a healthy immune response by influencing the composition and function of the micro-organisms that live within our body (aka, our gut bacteria). The hope is that all these findings may rapidly translate to current clinical practice and be incorporated into "vision-healthy" lifestyles.



Sheldon Rowan, PhD (7/1/17 - 6/30/20)
Tufts University, Boston, MA

Importance of Gut Bacteria in a Model of AMD

The goal of this proposal is to test whether the risk for developing AMD is based in part on our diet and nutrition, and relates to the composition and function of the micro-organisms that live within our guts, collectively known as the gut microbiome.

www.brightfocus.org/grant/M2017147

Recipient of The Elizabeth Anderson Award for Macular Degeneration Research

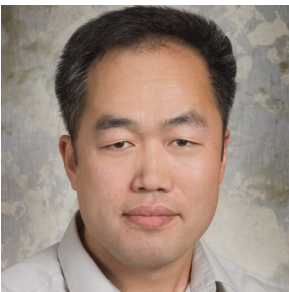


Dimitra Skondra, MD, PhD (7/1/18 - 6/30/20)
University of Chicago, IL

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



Gaofeng Wang, PhD (7/1/17 - 6/30/20)
University of Miami, FL

Co-Principal Investigator: **Rong Wen, MD, PhD**

Using Vitamin C to Treat AMD

This research aims to use vitamin C to inhibit the production of vascular endothelial growth factor (VEGF), a major factor promoting the growth of new blood vessels in the eye. Successful completion of this project will help to develop a treatment to delay and/or prevent AMD progression that is inexpensive and readily available for AMD patients.

www.brightfocus.org/grant/M2017081

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.



Stephen Aller, PhD (7/1/19 – 6/30/21)

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 chromatophore, after exposure to light by a molecular pump, called ABCA4 that allows the cell to regenerate the active form of the chromatophore. 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



Joelle Hallak, PhD (7/1/19 – 6/30/21)

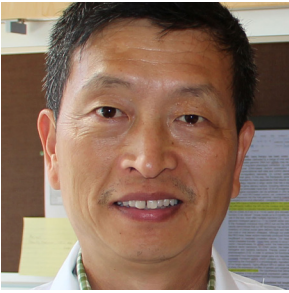
The University of Illinois, Chicago

Co-Principal Investigator: **Daniel Rubin, MS, MD, Theodore Leng, MD, FACS and Luis de Sisternes, PhD**

New Automated Method to Predict AMD Progression

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, and the patient's genetic, historical, demographic and behavioral data.

www.brightfocus.org/grant/M2019155



Zongchao Han, MD, PhD (7/1/19 – 6/30/21)
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



Florian Sennlaub, MD, PhD (7/1/18 - 6/30/20)
Fondation Voir et Entendre, Paris, France

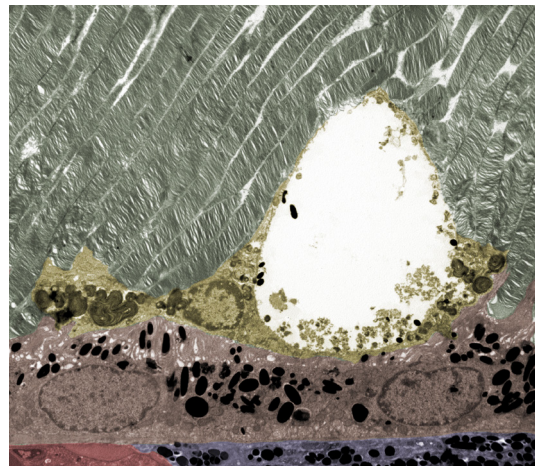
Understanding the Role of Sleep Apnea Syndrome in AMD

This project studies how experimental sleep apnea induces systemic immune cell activation and detrimental inflammation in the eye, which might explain the association of sleep apnea with AMD.

www.brightfocus.org/grant/M2018096

Courtesy of Dr. Sennlaub's Lab

Lipid (fat) bloated immune cell in between the retina (false color yellow) by electron microscopy.





Raunak Sinha, PhD (7/1/19 – 6/30/21)

University of Wisconsin, Madison

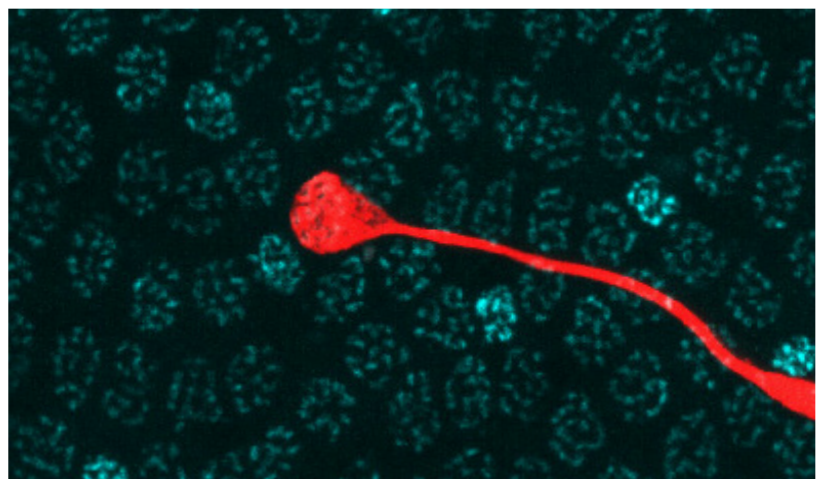
Understanding the First Step in Human Vision

Our everyday visual experience - including our ability to read this text - is dominated by signaling in a specialized region of the eye called the fovea, which is at the very center of the macula and constitutes an exquisite "high definition" array of photoreceptors, called cones. This study aims to provide the first detailed insight into how the sensors in the fovea work, to be able to devise vision restoration treatments for eye diseases such as AMD that affect the fovea.

www.brightfocus.org/grant/M2019131

Courtesy of Dr. Sinha's Lab

A cone photoreceptor, filled with red dye, overlaid on an array of other cone terminals (cyan) in the primate fovea.



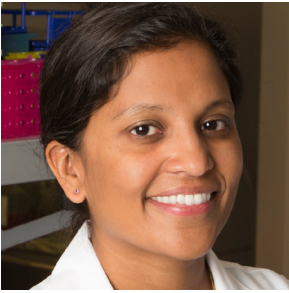
Imam Uddin, MD, PhD (7/1/19 – 6/30/21)

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



Elizabeth Vargis, PhD (7/1/19 – 6/30/21)
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

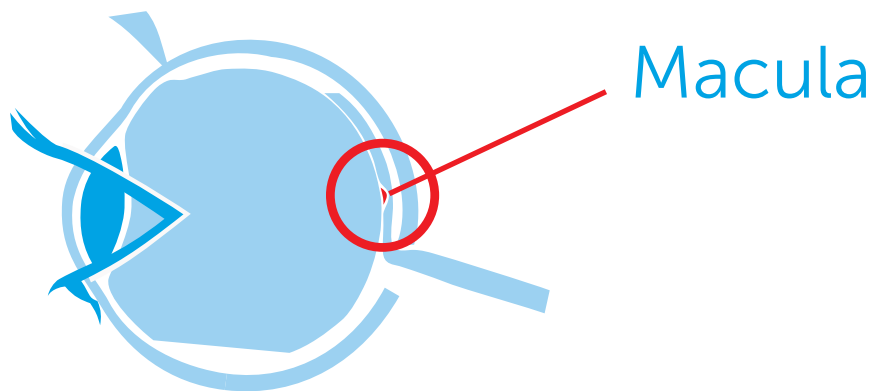


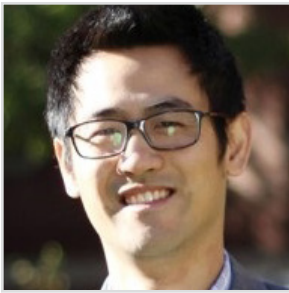
Zhichao Wu, PhD (7/1/19 – 6/30/21)
Centre for Eye Research Australia, East Melbourne

New Visual Function Tests to Enable Treatment Trials of AMD

This project examines whether a new and better method exists to measure the eye's ability to perceive different light levels within the area where tissue loss is occurring, thus enabling better evaluation of promising new treatments.

www.brightfocus.org/grant/M2019073





Ji Yi, PhD (7/1/18 - 6/30/20)

Boston Medical Center, MA

A New Imaging Method to Predict Neovascular AMD

This project proposes a non-invasive imaging technique to detect disease progression. If successful, the technique can be readily applied in clinics, and may directly impact the diagnosis and treatment of AMD patients as a way to stall disease progression and prevent blindness.

www.brightfocus.org/grant/M2018132

Regenerating Cells Damaged by AMD

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 hope, as 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 provides 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 gleaning information that may be translated to therapy.



Ross Poché, PhD (7/1/18 - 6/30/20)

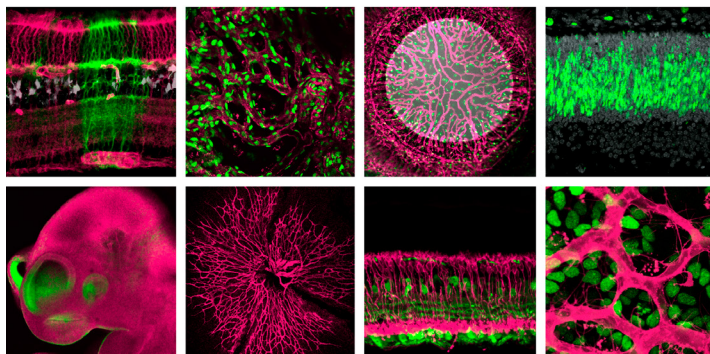
Baylor College of Medicine, Houston, TX

Reawakening the Ability of the Damaged Retina to Regenerate and Restore Vision

The project's main goal is to determine the biological reason why the human retina normally cannot undergo self-repair, also known as tissue regeneration.

www.brightfocus.org/grant/M2018022

Courtesy of Dr. Poché's Lab
Montage ocular imaging.





Karl Wahlin, PhD (7/1/18 - 6/30/20)

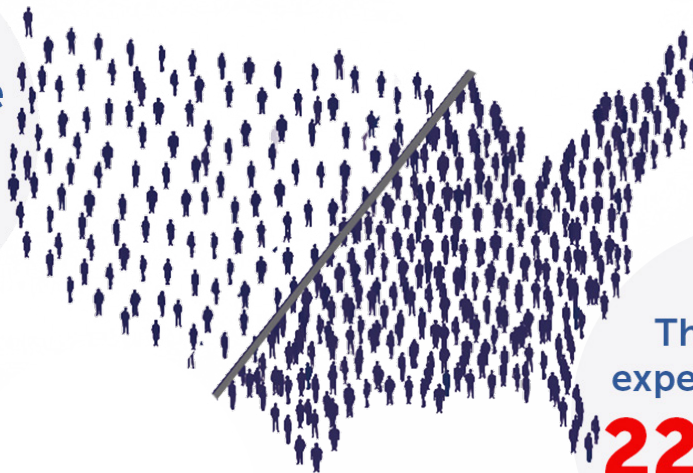
University of California, San Diego

Identifying Drugs that Block AMD Using Cell Lines with AMD-Associated Mutations

Using genetically engineered pluripotent stem cells harboring mutation in the complement gene, this study will develop a laboratory assay to monitor the progression of sub-RPE deposits. These cells will then be used to perform a small-molecule drug screen aimed at reducing sub-RPE deposits, which may in turn lead to new therapeutic targets for AMD.

www.brightfocus.org/grant/M2018175

11 million
Americans have
macular
degeneration.



This number is
expected to double
22 to nearly
million
by **2050**.



Macular Degeneration Research, a BrightFocus Foundation program