

Current Macular Degeneration Research Projects

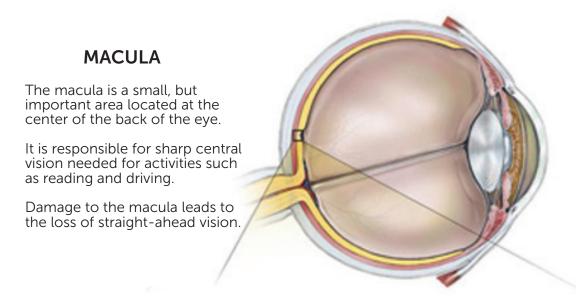
Advanced forms of age-related macular degeneration (AMD) are a leading cause of vision loss and irreversible blindness in Americans age 60 years and older, as well as throughout the world. Currently, as many as 11 million Americans have some form of macular degeneration, including both early and advanced 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 more than \$26 million to fund research projects on the causes and potential prevention, treatment, and cure of this disease.

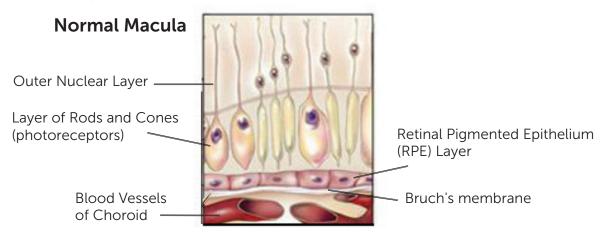
Macular Degeneration Research invests in several promising avenues of research to defeat age-related macular degeneration. We fund a broad array of scientific approaches, encompassing innovative projects falling into the following categories:

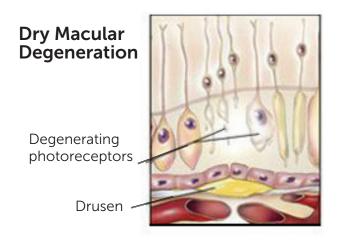
- Understanding Early AMD
- Insights into Geographic Atrophy
- Role of Metabolism in AMD
- Drusen Formation and Immune Response
- Genes and AMD
- How Diet and Nutrition Affect AMD Risk
- Innovative Approaches to AMD Treatment
- Regenerating Cells Damaged by AMD

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, 2018. 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 2/7/2019.

Schematic Diagram of the Macula







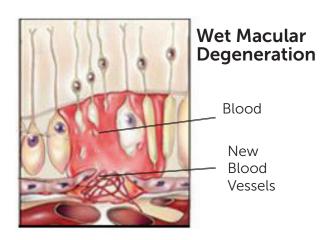


Illustration by Bob Morreale provided courtesy of BrightFocus Foundation

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.



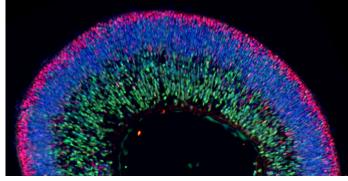
Maria Valeria Canto-Soler, PhD (7/1/16 - 6/30/19) University of Colorado, Denver

A New Model of a Human Retina in a Dish to Study AMD

The goal of this study is to develop the first "human retina in a dish" model...to provide a unique biological system to investigate the initial triggers leading to AMD and to develop treatments to stop its progress.

www.brightfocus.org/grant/M2016119 Recipient of The Helen Juanita Reed 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



Noriko Esumi, MD, PhD (7/1/15 - 6/30/19) Johns Hopkins University, Baltimore, MD

Resistance to Oxidative Stress: A New Strategy for AMD

The goal of this project is to develop new strategies for prevention and treatment of AMD, more specifically to test a molecule that promotes stress resistance and longevity on the survival and integrity of the RPE, a critical cell for AMD.

www.brightfocus.org/grant/M2015220 Recipient of The Helen Juanita Reed Award



Kaustabh Ghosh, PhD (7/1/16 - 6/30/19) University of California, Riverside

Understanding the Role of Increased Vessel Stiffness in Cell Death Associated with AMD

This project investigates the hypothesis that aging leads to stiffening of blood vessels in the eye that, in turn, exacerbates the pathogenesis of AMD by causing inflammation-mediated vascular degeneration.

www.brightfocus.org/grant/M2016161



Chi Luu, PhD (7/1/18 - 6/30/20) Centre for Eye Research Australia, Melbourne 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 (7/1/17 - 6/30/19) University of Calgary, 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.



Debasish Sinha, PhD (7/1/16 - 6/30/19) University of Pittsburgh, PA

Novel Therapeutic Targets for the Treatment of Early AMD

The proposed studies in this project are aimed at developing novel small molecules that could be tested as a therapy for early AMD. www.brightfocus.org/grant/M2016056

Insights into Geographic Atrophy

Geographic atrophy (GA) is an advanced form of dry age-related macular degeneration (AMD). GA 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. Currently there is no treatment for GA. 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.



Jianhai Du, PhD (7/1/16 - 6/30/19) West Virginia University, Morgantown Co-Principal Investigator: Jennifer Chao, MD, PhD

A New Method to Decrease Cell Death by Supplementation with NAD Metabolites

The goal of this project is to understand how energy metabolism is altered in AMD and test a nutritional approach to boost metabolism to prevent or rescue dry AMD.

www.brightfocus.org/grant/M2016047 This grant was made possible in part by the support from the Ivan Bowen Family Foundation.

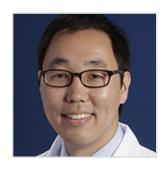


Yingbin Fu, PhD (7/1/18 - 6/30/20) Baylor College of Medicine, Houston, TX

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 Recipient of The Helen Juanita Reed Award



Benjamin Kim, MD (1/1/16 - 6/30/19) University of Pennsylvania, Philadelphia Co-Principal Investigators: Joshua Dunaief, MD, PhD and Maureen Maguire, PhD

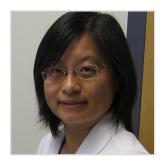
Evaluating Alpha Lipoic Acid as a Therapy for Geographic Atrophy

Through a Phase II pilot clinical trial, this study is testing alpha lipoic acid as a treatment for GA.

www.brightfocus.org/grant/CM2016971

Role of Metabolism in AMD

The retinal pigment epithelium (RPE) are a single layer of cells at the back of the eye next to the retina. Dysfunction in these cells is the starting point for age-related macular degeneration (AMD). RPE health and protective functions depend on their cellular metabolism as a source of energy. Grantees are currently looking at the decline in the cellular and mitochondrial ('cell powerhouse') energy production of the RPE and other retina cells as possible triggers to AMD. Macular Degeneration Research funded studies are trying to understand how an imbalance in this energy homeostasis 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 - 6/30/19) Boston Children's Hospital and 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 (7/1/17 - 6/30/19) 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.



Michael Paulaitis, PhD (7/1/17 - 6/30/19) Wilmer Eye Institute, 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 RNAs, so-called microRNAs, which 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.

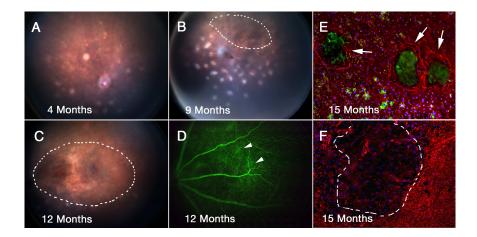
www.brightfocus.org/grant/M2017060



Claudio Punzo, PhD (7/1/17 - 6/30/19) University of Massachusetts School of Medicine, Worcester Role of the Light-sensing Photoreceptor Cells in AMD

The hypothesis of this study is that AMD is caused by age-related metabolic adaptations in photoreceptors. To test this hypothesis, a new mouse model with altered cell metabolism in photoreceptors is generated. This mouse model recapitulates many features of human AMD.

www.brightfocus.org/grant/M2017071



Courtesy of Dr. Punzo's Lab

New AMD model generated in Dr. Punzo's lab. (A-C) AMD progression to geographic atrophy (GA) in the same eye at ages indicated. Dotted area indicates the region with atrophy. (D) Angiography of the eye in (C) showing leakage of blood (arrowhead). (E, F) View of retinal-pigmented epithelium cells stained in red showing areas of atrophy (E: arrows; F: dotted line).



Magali Saint-Geniez, PhD (7/1/18 - 6/30/20)

The Schepens Eye Research Institute/Massachusetts Eye and Ear, and 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. Fatty deposits known as drusen may collect under the retina 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 many believe these 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 closely-focused 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.



Astra Dinculescu, PhD (7/1/17 - 6/30/19) University of Florida, Gainesville

Extracellular Deposits and Vision Loss in AMD

The goal of this study is to understand the factors contributing to the formation of drusen deposits, in order to develop a strategy to eliminate them and preserve vision in AMD patients.

www.brightfocus.org/grant/M2017035



Sarah Doyle, PhD (7/1/16 - 6/30/19) Trinity College Dublin, Ireland

Investigating How Loss of an "Off Switch" for Inflammation Contributes to AMD

AMD has elements that indicate that the inflammatory response is uncontrolled and persistent when low-level inflammation is observed. This research studies whether this active process of switching off the inflammatory response is lost in people with AMD.



Malia Edwards, PhD (7/1/16 - 6/30/19) Wilmer Eye Institute, Johns Hopkins University, Baltimore, MD A Study of Why Retinal Support Cells, Called Glia, Exit the Retina in AMD

The goal of this study is to identify glial cell changes in AMD and determine how these may affect AMD progression and treatment. www.brightfocus.org/grant/M2016198



Francesco Giorgianni, PhD (7/1/16 - 6/30/19) University of Tennessee Health Science Center, Memphis

Basic and Clinical Studies to Understand the Role of the CD5L/AIM Protein in AMD

The main objective of this research project is to reveal the mechanisms involved in AMD by studying two key pathological events that characterize AMD: the accumulation of drusen deposits and the death of retinal pigment epithelium cells (RPE).

www.brightfocus.org/grant/M2016068



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



Cristhian Ildefonso, PhD (7/1/17 - 6/30/19) University of Florida, Gainesville

Exploring the Role of Local and Systemic Inflammation in AMD

The goal of this research is to have a better mouse model of AMD by introducing pro-inflammatory cues, which may initiate the disease. In addition, a method of decreasing local inflammation in the eye will test the idea that this could help to protect vision.

www.brightfocus.org/grant/M2017126 Recipient of The Helen Juanita Reed Award



Daniel Saban, PhD (7/1/17 - 6/30/19) Duke University Eye Center, Durham, NC Targeting Immune Cells in AMD

This project seeks to identify the specific immune cell type that contributes to vision loss, and to devise a strategy that neutralizes such cells to ultimately help preserve vision in patients suffering from AMD.

www.brightfocus.org/grant/M2017183

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 RPE when it encounters oxidative stress from aging and other causes.



Rosario Fernandez-Godino, PhD (7/1/18 - 6/30/20) Massachusetts Eye and Ear, Harvard Medical School, Boston Too Much Debris as a Cause of AMD

My aim is 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; so that drugs can be designed to stop these mechanisms before they lead to major damage and legal blindness.

www.brightfocus.org/grant/M2018115 This grant is made possible by 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.



Philippe Mourrain, PhD (7/1/17 - 6/30/19)

Stanford University, California

Co-Principal Investigator: Romain Madelaine, PhD

Zebrafish Provides Insights into New AMD-Associated Genetic Mutation

This study will not only identify the actual impact of a non-coding human genetic mutation that causes AMD, but also will characterize how the evolutionarily conserved DNA region bearing the human mutation regulates its surrounding genes, potentially revealing the actual gene affected in AMD.

www.brightfocus.org/grant/M2017209 This grant is made possible by support from the Nancy F. Seeley Trust in memory of Mildred F. Ferguson.



Patsy Nishina, PhD (7/1/17 - 6/30/19) The Jackson Laboratory, Bar Harbor, ME Co-Principal Investigator: Martin Pera, PhD

DNA Changes That May Lead to AMD and Other Vision Diseases

This project will establish a research pipeline to examine the effects of the extracellular matrix-related genetic risk alleles in cultured RPE cells, and select those alleles that cause the greatest effects. They will then generate new mouse models that will be made available for the research community.

www.brightfocus.org/grant/M2017042



William Scott, PhD (7/1/18 - 6/30/20) Miller School of Medicine, 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

The current standard treatment for attempting to prevent progression from intermediate age-related macular degeneration (AMD) to advanced AMD (dry or wet) consists of eye vitamins that follow the AREDS2 [Age-Related Eye Disease Study 2] formula (with a specific combination of Vitamins C and E, the carotenoids lutein and zeaxanthin, zinc, and copper). However, 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. Vitamins C and E, also components of the AREDS2 formula, are being investigated to delay and/or prevent AMD progression. Our diets also may influence how our body responds to disease, and help shape a healthy immune response, and influence 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 be rapidly translated to the current clinical practice and incorporated into a healthy lifestyle.



Binxing Li, PhD (7/1/17 - 6/30/19)

Moran Eye Center, Salt Lake City, UT

Co-Principal Investigator: Paul S. Bernstein, MD, PhD

Delivering Sight-saving Nutrients to the Retina in AMD

The goal of this study is to understand the mechanism of scavenger receptor BI (SR-BI)-mediated macular carotenoid transport.

www.brightfocus.org/grant/M2017066



Trevor McGill, PhD (7/1/17 - 6/30/19) *Oregon Health & Science University, Portland*Nutritional Factors in the Development of AMD

The goal of this project is to determine whether being deprived of nutrients important for retinal health has consequences for the development of AMD, and to determine the mechanisms by which this occurs.

www.brightfocus.org/grant/M2017073
Recipient of The Carolyn K. McGillvray Award



Sheldon Rowan, PhD (7/1/17 - 6/30/19) 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



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 that found in the risk for AMD development.

www.brightfocus.org/grant/M2018042



Gaofeng Wang, PhD (7/1/17 - 6/30/19) Miller School of Medicine, University of Miami, Coral Gables, 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.



Innovative Approaches to AMD Treatment

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.



Daniel Chao, MD, PhD (7/1/17 - 6/30/19) Shiley Eye Institute, University of California San Diego, La Jolla, CA

Drug Discovery in a Zebrafish Model of Wet AMD

The purpose of this grant is to develop zebrafish, a common organism with similarities to humans in genetics and biology, as a model for drug discovery for macular degeneration.

www.brightfocus.org/grant/M2017034



Kip Connor, PhD (7/1/16 - 6/30/19) Massachusetts Eye and Ear Infirmary and Harvard Medical School, Boston

Lipid Regulators of AMD

The goal of this proposal is to define the mechanism of action for potent bioactive lipid (fat) metabolites, and for their ability to suppress wet AMD. The data obtained from this study has clear potential to lead to new therapeutic molecules, targets, and strategies for specifically inhibiting wet AMD progression.

www.brightfocus.org/grant/M2016183



Rajendra Kumar-Singh, PhD (7/1/17 - 6/30/19) Tufts University, Boston, MA

Developing a Gene Therapy Against Complement Factors in AMD

The goal of this project is to determine the molecular factors responsible for pathology in AMD and to utilize that knowledge to develop therapies.



Marcelo Nociari, PhD (7/1/16 - 6/30/19)

Joan and Sanford I. Weill Medical College of Cornell University, NY Co-Principal Investigator: Enrique Rodriguez-Boulan, MD

Identification of Novel Treatments for Macular Degeneration by Alleviating Endoplasmic Reticulum Stress

This project proposes to fully characterize this new damaging pathway by which compartments within cells called endoplasmic reticulum (involved in protein synthesis) are stressed by modified fats called lipid-bisretinoids (LBs). LB's above a certain level or upon exposure to light become toxic and kill RPE cells, and this study will test whether targeting this pathway can prevent blindness in animal models of LB-driven retinal disease.

www.brightfocus.org/grant/M2016124



Florian Sennlaub, MD, PhD (7/1/18 - 6/30/20) Fondation Voir ed Entendre, Institut de la Vision, 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







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 directly impact the diagnosis and treatment of AMD patients, to stall the disease progression and prevent blindness.

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) 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 Poche, 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



Biju Thomas, PhD (7/1/16 - 6/30/19)

University of Southern California Roski Eye Institute, Los Angeles

Co-Principal Investigator: Danhong Zhu, PhD

Transplantation of iPS-RPE as a Polarized Monolayer

The study proposes to treat diseases such as AMD by transplanting into the retina a polarized monolayer (single layer) of RPE sheets derived from human iPSCs, which are stem cells that have been derived from healthy adult human tissue.



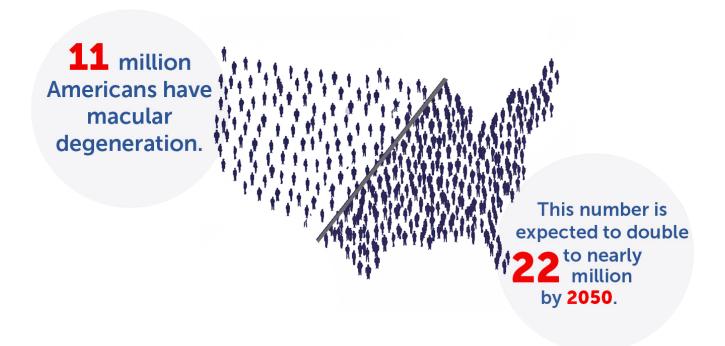


Karl Wahlin, PhD (7/1/18 - 6/30/20) University of California, San Diego

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 Recipient of The Carolyn K. McGillvray Award

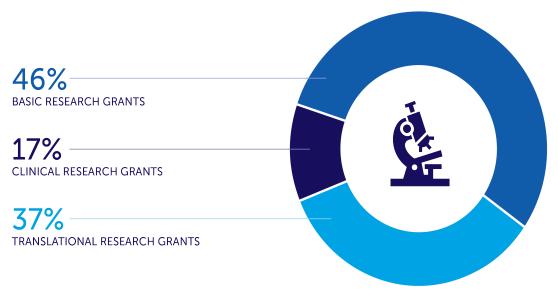


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> BrightFocus Grants at a Glance



Basic - Research that aims to better understand how a disease happens, and to obtain new ideas of how to stop the disease.

Clinical - Research involving volunteer participants to test the safety and effectiveness of drugs, devices, or other treatment candidates.

Translational - Research to move findings from the lab bench to the "bedside" by testing potential treatments.



Macular Degeneration Research, a BrightFocus Foundation program