

RETINA RESEARCH FOUNDATION NEWSLETTER

Foresight for Sight

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The Retina – A Window To Assessing Overall Health

Most likely you have heard the quote attributed to many, including William Shakespeare, Leonardo Da Vinci, the philosopher Cicero, and even the Bible: “the eyes are the windows to the soul,” but what you might not be as familiar with is that vision scientists are exploring how the eye, and specifically the retina, is a window to understanding your overall health. Imagine, in the future, a simple, non-invasive look into your eyes might provide a clear picture of your biological age, general health, or identify a number of systemic vascular and neurological health concerns you may have. Damage to retina blood vessels may reflect early signs of nerve damage due to diabetes, cardiovascular disease, kidney disease or dementia, even cancer -- diseases that are all associated with increased risks of mortality. The health of retina blood vessels also may reveal glaucoma and age-related macular degeneration.

The concept of examining the retina to better understand systemic health is not new, but with recent improvements in retinal imaging and automated data analysis, the concept is much closer to becoming a clinical tool available to physicians. A recent study published in the British Journal of Ophthalmology by Dr. Mingguang He, a professor of ophthalmic epidemiology, University of Melbourne Australia, used retinal imaging and machine deep learning to identify a “retina age gap” – the difference between a person’s biological age and their age from birth. For each year difference, there was a 2% increase in the risk of death from any cause, and larger gaps of three, five and 10 years were significantly associated with up to a 67% higher risk of death from specific diseases. Researchers believe the retinal age gap is an independent predictor of increased mortality risk, and these findings also suggest that retinal age

may be a clinically significant biomarker of aging¹. The use of retinal imaging biomarkers, as medical indicators, shows great potential for aiding in clinical diagnosis and as indicators of disease progression. In the U.S. and UK, similar work is being conducted as well as research related to standardization of image acquisition protocols, parameters for storage and analysis of imaging data so that data can be shared across research groups and used in development of large data sets. RRF supports related imaging research through work with scientists at the McPherson Eye Research Institute at the University of Wisconsin, Madison. Visit retinaresearchfnd.org to learn more about these efforts.



Examination of the retina provides the only view of the human vascular system possible without making an incision.

Retinal imaging technology is a particularly helpful tool in diagnosing and treating retinal disease caused by diabetes. Diabetes affects the blood vessels in the retina, termed diabetic retinopathy, an effect that can also be observed in people with pre-diabetes. Often an ophthalmologist might be the first health professional to suspect undiagnosed diabetes. According to the CDC, more than one in 10 of every adult over the age

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of 20 has diabetes. Within the U.S. population of 330 million, that is nearly 30 million diagnosed people. An additional 86 million have pre-diabetes, and it is estimated that eight million people are undiagnosed. Consequently, uncontrolled diabetes leading to diabetic retinopathy is the primary cause of vision loss in working age adults. An estimated 4.1 million Americans are affected by retinopathy, and 899,000 have more severe vision-threatening retinopathy. Because of the sheer impact of diabetes on vision health, RRF sponsors a number of research projects that focus on this area.

1 Zhu Z, Shi D, Guankai P, et al. Retinal age gap as a predictive biomarker for mortality risk. British Journal of Ophthalmology. Published Online First: 18 January 2022. doi: 10.1136/bjophthalmol-2021-319807

RRF Pilot Study Researchers Newly Funded in 2022

During 2022, the RRF basic research pilot program is funding the work of 20 vision researchers at top-tier universities and institutes across the country. In addition to the existing multi-year grant recipients, two additional researchers received grants this year:



Ann C. Morris, PhD, Department of Biology
University of Kentucky, Lexington, Kentucky

Retinal Damage and Regeneration in the African Spiny Mouse (Acomys cahirinus): A Novel Mammalian Model for Translational Research



Ming Zhang, MD, PhD, Department of Cellular Biology & Anatomy
Augusta University, Medical College of Georgia, Augusta, Georgia

The Roles of RIP kinase 3 in the Development of AMD-like Pathologies during Cytomegalovirus Ocular Latency

Please visit retinaresearchfnd.org to learn more about the novel research conducted by this year's pilot study researchers.

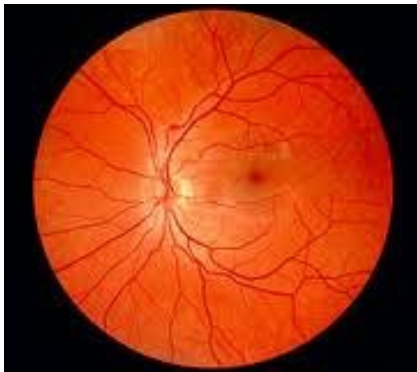


Retina Research Foundation is dedicated to the eradication of retina disease through programs in research and education.
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Diabetes Impact on the Retina

From the Ophthalmologist's Perspective

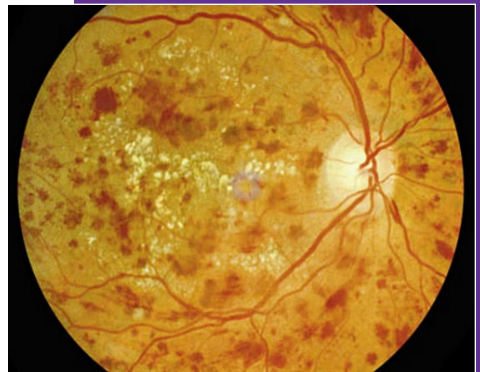
High blood sugar can damage the tiny blood vessels that bring oxygen and nutrients to the retina. This is known as diabetic retinopathy (DR), and it can lead to vision loss. Pools of blood, or hemorrhages, on the retina of an eye are visible in both of the images below, on the right. The tiny white areas, "cotton-wool spots" are caused by a lack of blood flow to the small retinal blood vessels and can be an indication of a serious medical condition, in this case, DR. Over time, these clinically evident signs of DR can cause



For comparison, a normal, healthy retina image.



Retina images with hemorrhages, cotton-wool spots and abnormal blood vessel growth.



the growth of new abnormal blood vessels and scarring that lead to vision loss. DR is the leading cause of new cases of blindness in U.S. working-age adults, people between the ages of 20 and 74.

Diabetic Retinopathy Impact on Vision

From the Patient's Perspective

The leading cause of blindness in American adults is diabetic retinopathy (DR), a common complication of diabetes. It is characterized by progressive damage to the blood vessels of the retina, the light-sensitive tissue at the back of the eye that is necessary for good vision. DR progresses through four stages, mild nonproliferative retinopathy (microaneurysms), moderate nonproliferative retinopathy (blockage in some retinal vessels), severe nonproliferative retinopathy (more vessels are blocked leading to deprived retina from blood supply leading to growing new blood vessels), and proliferative retinopathy (most advanced stage). Diabetic retinopathy usually affects both eyes.

Important for you to know is that the risks of DR are reduced through disease management, which includes good control of blood sugar, blood pressure, and lipid abnormalities. Early diagnosis of DR and timely treatment reduce the risk of vision loss; however, as many as 50% of patients are not getting their eyes examined or are diagnosed too late for treatment to be effective.



RRF Research Focused on Retinal Disease Caused by Diabetes

The damage that diabetes may inflict on human sight can be devastating and vision threatening. The retina is susceptible to the long-term consequences of unmanaged diabetes, both type I and type II, but this damage does not happen quickly, providing time and opportunity to reduce or even prevent vision loss. Following are brief synopses of the work of five RRF researchers interested in understanding this problem and ultimately finding therapeutic solutions to save the vision of those with diabetes.



Lih Kuo, PhD

Lih Kuo, PhD

Department of Medical Physiology, Texas A&M University Health Science Center, Bryan, TX

PROJECT: *Activation of Endothelin-dependent RhoA/ROCK Pathway Elicits Retinal Microvascular Dysfunction in Diabetic Retinopathy*

Dr. Kuo researches the development of the abnormal, small blood vessels in diabetic retinopathy to understand the mechanisms responsible and to develop strategies/tools for the prevention/treatment of this sight-threatening disease. Proper function of the retina depends on an adequate supply of blood (oxygen/nutrients) to the retina, and dysfunction of the retinal microcirculation could lead to disease development. Dr. Kuo has found that in the diabetic retina, the synthesis of vasoconstrictor/inflammation agent endothelin-1 (ET-1) from endothelin converting enzyme (ECE) is elevated, and the vascular signaling molecules, RhoA kinase (ROCK) and arginase enzyme, are upregulated. By investigating these vascular signaling pathways in the initiation and development of diabetic retinopathy, Dr. Kuo plans to develop pharmacological strategies for disease prevention and treatment for early onset type-1 diabetes related retinal disease.



Milam A. Brantley, Jr., MD, PhD

Milam A. Brantley, Jr., MD, PhD

Department of Ophthalmology & Visual Sciences, Vanderbilt University Medical Center, Nashville, TN

PROJECT: *The cellular mechanisms by which arginine and citrulline promote vision threatening diabetic retinopathy*

Dr. Brantley studies the actions, which take place at the cellular level that cause blood vessels in the retina to become permeable or leaky, resulting in diabetic retinopathy. He specifically researches precisely how citrulline and arginine, two essential amino acids, alter the cells in the retina that are involved in diabetic retinopathy. When the body converts citrulline into arginine, it creates nitric acid, a gas that helps dilate blood vessels to improve blood flow. Dr. Brantley's work will determine exactly how arginine and citrulline function in retinal endothelial cells to cause retinopathy as well as how they may be able to modify current treatments for DR. He believes these studies will help in developing new ways of treating, or even preventing, diabetic retinopathy.

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Wenbo Zhang, PhD

Department of Ophthalmology & Visual Sciences, University of Texas Medical Branch, Galveston, TX

PROJECT: *Novel therapy for retinal neovascularization*

Dr. Wenbo Zhang seeks to understand mechanisms of retinal neuronal and blood vessel injury in forms of ischemic retinopathy, such as diabetic retinopathy, retinopathy of prematurity and glaucoma, which cause irreversible vision loss. His goal is to identify new and better therapeutic approaches to treat these vision-threatening diseases. Dr. Zhang has identified 85 genes in endothelial cells, the main type of cell found in the inside lining of blood vessels, that may have critical roles in the growth of new blood vessels. Some of these genes are responsible for producing cell surface proteins and others control key biological functions related to new blood vessel growth, but many aspects of these genes such as how their resulting proteins are expressed or localized have not been studied. With knowledge from research of a subset of the identified genes, Dr. Zhang hopes to develop biomarkers and characterize novel drug targets for safe, effective and specific management of retinal neovascularization.

Andrius Kazlauskas, PhD

Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, IL

PROJECT: *Hyperglycemia-induced mitochondrial adaptation*

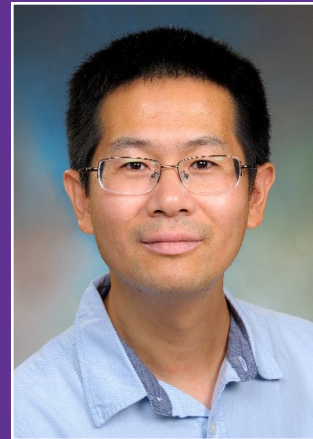
The long delay between the onset of diabetes mellitus and the development of retinopathy suggests the existence of processes that prevent the development of retinal disease. Dr. Kazlauskas discovered that prolonged hyperglycemia (HG) induces adaptation at the level of the mitochondria within primary human retinal endothelial cells (HRECs). Mitochondria produce energy necessary for healthy cell function, and the retina requires high levels of energy to function properly. Furthermore, such adaptation appears to be beneficial: it protects from the deleterious effects of hyperglycemia such as increased cell death. The purpose of Dr. Kazlauskas' project is to better understand hyperglycemia-induced mitochondrial adaptation (HIMA), which may provide the opportunity for therapeutic intervention.

Erika Eggers, PhD

Departments of Physiology and Biomedical Engineering, University of Arizona, Tucson, AZ

PROJECT: *Investigation and modulation of inner retinal dysfunction in diabetes*

Dr. Eggers researches some of the earliest identifiable retinal problems in diabetic patients -- visual deficits in the function of dim light-activated rod pathways that are not due to cell death but some unknown mechanism. Electrical recordings from diabetic retinas show dysfunction in the neurons that respond to light stimulus from rod and cone photoreceptors and relay that information to the brain. Dr. Eggers has found that diabetic retinas have low dopamine levels, and it is dopamine that allows the retina to adapt to increasing background light levels. Supplementation of dopamine can reduce inner retinal deficits in diabetes. Dr. Eggers is an expert in rod pathway signaling, and she will determine if this dopamine pathway signaling is specifically vulnerable to diabetic damage, and identify the mechanisms of dysfunction in order to develop prevention therapies for neuronal progression causing vision loss.



Wenbo Zhang, PhD



Andrius Kazlauskas, PhD



Erika Eggers, PhD

Rice University Researchers Looking For Vision Loss Study Participants

Researchers at Rice University are seeking to improve the mobility of people with vision loss and are currently conducting a study funded by the National Institutes of Health (NIH) National Eye Institute (NEI). If you or someone close to you have been diagnosed with age-related macular degeneration and live in or near Houston, please consider participation in this research.

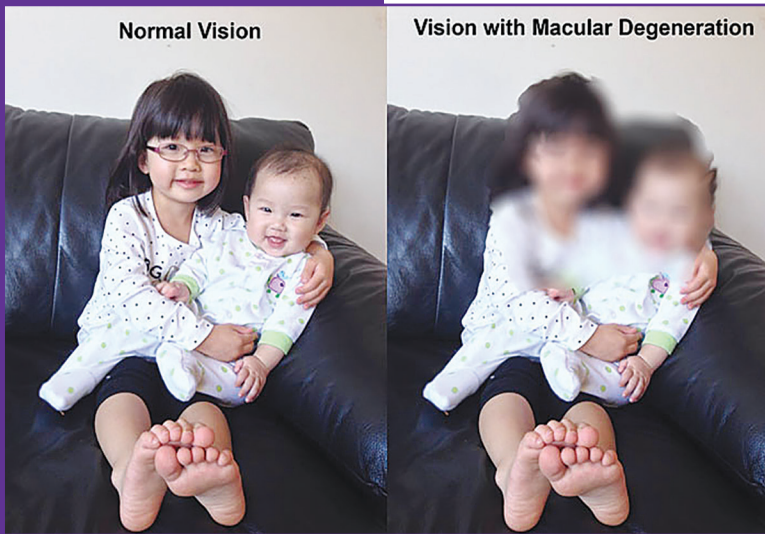


Photo courtesy of
DrOttoLee.com

Seeking Adults With Central Vision Loss For Research Study at Rice University, Houston, Texas

We seek adults with central vision loss (preferably due to age-related macular degeneration) to participate in a research study. The goal of this study is to learn how people use vision and hearing when they experience the world, particularly when they make judgments about collisions with obstacles in the environment. Study participants will be asked to perform tasks using computer displays of moving environments, including virtual reality, and to complete surveys.

Participants must meet eligibility requirements for the study, which will be determined by screening tests. Participation will consist of several sessions, each between about one to two hours in addition to a hearing exam and an eye exam. Each participant will receive up to \$300 plus up to \$60 for parking/transportation.

The research project will be conducted in Sewall Hall at Rice University, Houston, Texas. The hearing exam will take place at UTHealth in Houston. The eye exam will take place at Retina Consultants of Texas in Bellaire.

This research study has been reviewed and approved by Rice University Institutional Review Board. If you have concerns regarding this study or questions regarding your rights as a study participant, please contact Compliance Administrator-IRB, at Rice University.

Email: irb@rice.edu or telephone: 713-348-3586

If you are interested in participating or would like further information, please contact study personnel at VRLab@rice.edu or 713-348-2432, and provide your email address or phone number and mention this announcement.

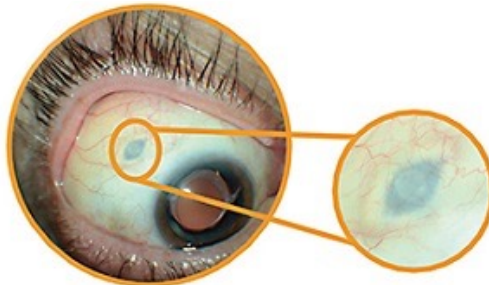
Treatment Advance for AMD

Abnormal blood vessels are found in the wet form of age-related macular degeneration (AMD), a leading cause of blindness for people age 60 and over in the U.S. This disease affects the macula, the part of the eye's retina that provides sharp, central vision needed for activities like reading. Wet AMD, or the neovascular form with abnormal, leaky blood vessels, can cause rapid and severe vision loss. Approximately 11 million people in the U.S. have AMD, of which 1.1 million have wet AMD. An effective treatment tool for this disease requires monthly injections of anti-VEGF therapy, a significant treatment burden for patients. If the injections are stopped, the risk of abnormal blood vessel regrowth is increased, and central vision may be permanently lost.

The FDA recently approved a port delivery system for continuous delivery of medication for wet AMD treatment to provide an alternative to standard of care eye injections. The implant can provide up to six months of anti-VEGF medication and is refillable. Ask your ophthalmologist if this new treatment option might be of benefit to you!



Port delivery system implant



View of implant in the eye

First-of-Its-Kind Therapeutic Approach for Wet Age-Related Macular Degeneration (AMD), Genetech. For more information, visit gene.com.

A GIFT TO RRF CAN SAVE SIGHT

Retina Research Foundation, a public foundation, supports research directed toward treating, preventing or curing all retinal diseases that damage and destroy vision. Your support is vital to the success of our efforts and every gift makes a difference. RRF accepts secure donations at retinaresearchfnd.org. You can also support RRF by making your online purchases through [amazonsmile](https://www.amazon.com/amazonsmile). Use the link on RRF's website or go to [smile.amazon.com](https://www.amazon.com/amazonsmile) to register and select RRF as your charity of choice. It's easy to give: once selected, all future purchases will result in an automatic donation to RRF of 0.5% of your purchases, at no additional cost to you. Thank you!

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- Margaret Barrow**
Lucy and David Barrow
- Robert Butner, MD, retina specialist**
Peter Forgash, MD, retina specialist
- Patrice Smith Clayton**
Dayln Schriewer
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IN HONOR OF

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Jamie Moeller
- Emmett A. and Lorine Humble**
Deral Humble
- Mary Farish Johnston**
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