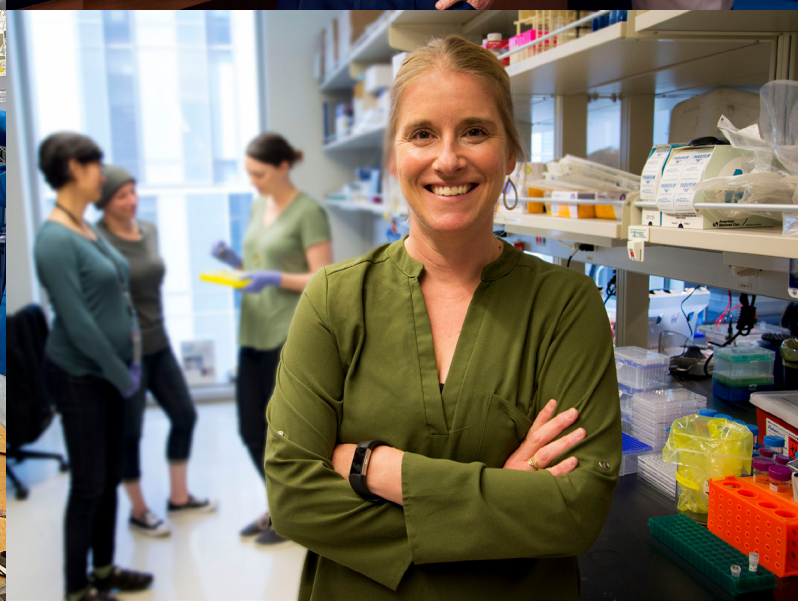


Research for a Better Tomorrow

2023 National Glaucoma Research Projects

BrightFocus® Foundation | National Glaucoma Research

Advancing Research Toward a Cure

An estimated 80 million people around the world have glaucoma, with 111 million projected to have it by 2040. In the United States, where the disease disproportionately affects and is a leading cause of blindness among African American and Latino communities, more than three million people live with glaucoma.

National Glaucoma Research, a BrightFocus Foundation program, is on a mission to cure this sight-stealing disease.

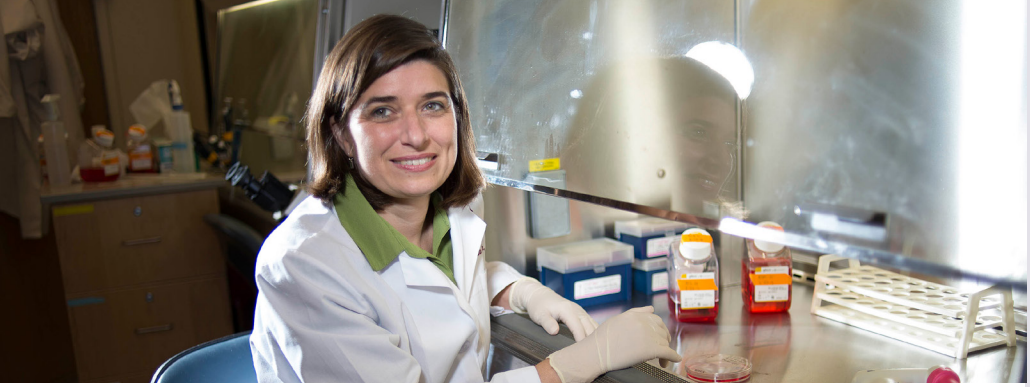
We believe that by providing initial funding for highly innovative experimental research and creative ideas, we can spark revolutionary approaches and vision-saving breakthroughs.

We're funding 61 active research projects worldwide.

Since inception:

Nearly **$50 million** in research grants awarded

1,607 scientists supported across 487 grants



National Glaucoma Research

Meet the Innovators

BrightFocus Foundation's National Glaucoma Research program is one of the world's leading nonprofit funders of glaucoma research.

We invest in a wide range of innovative scientific approaches, exploring the root causes of and prevention strategies and treatments to end glaucoma. National Glaucoma Research-funded investigators are advancing newer imaging techniques and strategies for early detection, exploring exercise to slow vision loss, and finding new ways to control eye pressure—taking a 360-degree approach to ending this disease.

This research portfolio provides an overview of our current grant projects. Grants are vetted through a rigorous evaluation process by the world's top scientists and clinicians who serve on our scientific review committee.

We are deeply grateful to our donors, whose generosity makes it possible to fund the next generation of researchers pursuing novel, bold, and promising science for tomorrow's cure.

Explore all active grants:

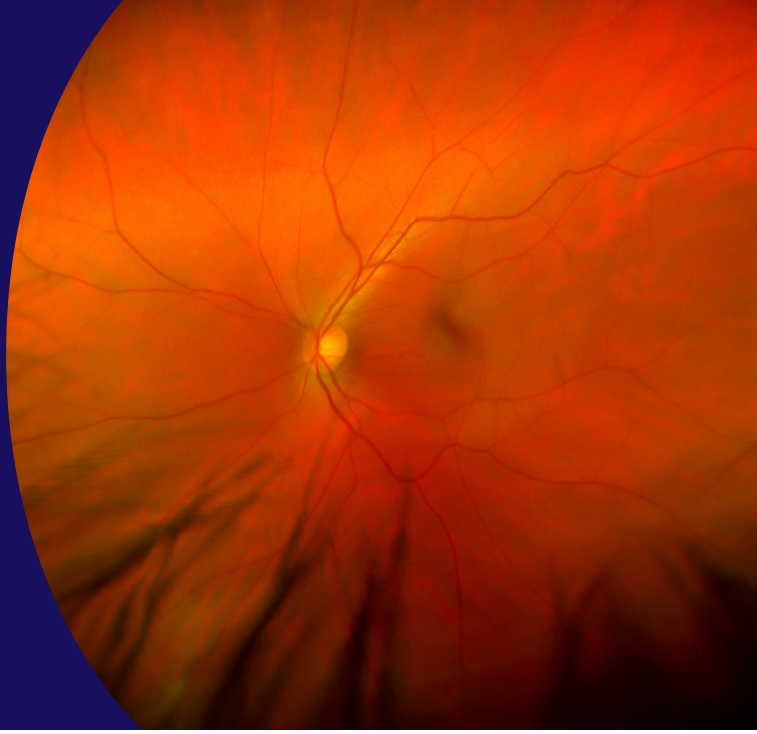
brightfocus.org/NGRgrants

Contents

Cover: National Glaucoma Research grantees.

Note: This portfolio reflects awarded grants as of July 25, 2023.

Controlling Eye Pressure in New Ways



Above: *View inside of the eye showing a healthy retina, optic nerve, and macula.*

Elevated eye pressure, or intraocular pressure (IOP), exists in most forms of glaucoma and can occur when aqueous humor, the fluid that constantly bathes the front of the eye, cannot drain properly.

Normally aqueous humor drains through a spongy tissue known as the trabecular meshwork and flows into Schlemm's canal (SC), a ring-like passageway that then delivers it to the blood stream.

Blockages and other forms of resistance to the outflow of aqueous humor can raise eye pressure.

The Role of Podosomes in Regulating Eye Pressure

Michael G. Anderson, PhD | University of Iowa

For this project, researchers will test the role of podosomes, small fingerlike protrusions of cells, and their effect on eye pressure. This work will lead to important information about the cell biology of glaucoma, including possibly identifying the precise molecular location of outflow resistance. The findings also may point to compounds altering podosomes as potential new glaucoma therapies.

Next-Generation Glaucoma Drugs to Selectively Release the Pressure-Building Block in Schlemm's Canal*

C. Ross Ethier, PhD | Georgia Tech Research Corporation

Endothelial cells of the inner wall of Schlemm's canal (SC) play a key role in homeostatic control mechanisms that maintain intraocular pressure (IOP) within a target range. The long-term goal of this project is to develop novel therapies that directly target SC cells to improve IOP control. These targeted therapies will be highly effective because of their specificity and thus greatly benefit glaucoma patients.

The Study of Segmental Aqueous Outflow in Uveal Drainage Pathway

Haiyan Gong, MD, PhD | Boston University

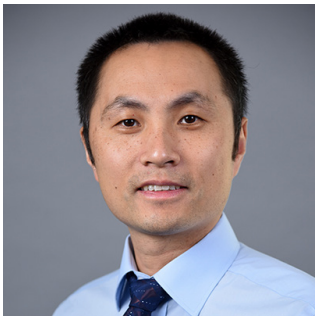
Uveal outflow, one of two routes for fluid drainage from the eye, plays a role in maintaining normal pressure inside the eye (IOP). Prostaglandin analogue drugs lower increased IOP in glaucoma by enhancing uveal outflow. This group recently found that uveal outflow is segmental, or nonuniform, around the eye, although the regulating factors involved are unclear. The researchers will further investigate segmental uveal outflow and the factors that may regulate it.

A Novel Gene-Therapy Approach for Glaucoma*

Simon John, PhD | Columbia University
Co-Principal Investigator: Krish Kizhatil, PhD, The Jackson Laboratory

The aim of this project is to develop and test resources for Schlemm's canal-specific targeting and expression of genes for gene therapy. Successful development of this targeted therapy will help control eye pressure more effectively and provide better treatment options for glaucoma patients.

**Part of a joint research award for a collaborative interinstitutional grant.*



An Effective Tool for Understanding Dysfunctional Eye Drainage in Glaucoma

Weiming Mao, PhD | Indiana University School of Medicine

For this project, researchers will develop a mouse model of eye drainage dysfunction in glaucoma that will allow for more straightforward investigations of how fluid buildup occurs. The tool is expected to support scientists in better understanding how glaucoma develops and offer a way to test candidate treatments.

Building a Better Model to Screen for Intraocular Pressure-Lowering Glaucoma Drugs

Darryl Overby, PhD | Imperial College London (UK)

Researchers will assess Schlemm's canal cells, which modulate fluid drainage from the eye, for their role in the fluid buildup of glaucoma. The team will recreate the natural environment of these cells to test how they form a barrier to fluid outflow and to test candidate treatments. The model is expected to support faster evaluation and transition of candidate drugs into clinical testing for glaucoma.

Developing New Drugs to Lower Eye Pressure in Glaucoma*

Darryl Overby, PhD | Imperial College London (UK)
Co-Principal Investigator: Joseph M. Sherwood, PhD

This group has identified a particular cell type (Schlemm's canal cells) that regulates eye pressure by controlling the drainage of aqueous humor from the eye. In this project, they will develop and apply novel screening technologies to identify new drugs to lower eye pressure by improving aqueous humor drainage across Schlemm's canal cells.

Small Molecular Compounds for Glaucoma Therapy

Chan Young Park, PhD | Harvard T.H. Chan School of Public Health

Fluid in the eyes of people with glaucoma has a higher concentration of an important chemical compared with fluid in healthy eyes. This chemical, a growth factor, acts on tissues to make them stiffer, which increases the chance of glaucoma. For this work, researchers will test remodilins, a new drug, for its ability to return stiffened tissues to a softer state.

Long-Lasting, Nonsurgical Treatment for Eye Pressure in Glaucoma

Mark Prausnitz, PhD | Georgia Institute of Technology

The aim of this project is to test the safety and efficacy of an expanding gel to relieve fluid buildup in the eye in glaucoma. The injectable gel could offer a nonsurgical, nondrug treatment of eye pressure in glaucoma that could last months. Success will set the stage to move into clinical trials.

Mechanisms Controlling Aqueous Humor Drainage in Mouse Models

Ester Reina-Torres, PhD | Imperial College London (UK)
Mentors: Darryl Overby, PhD; W. Daniel Stamer, PhD, Duke University

A lack of understanding of how the eye controls fluid outflow is the main reason for not having effective therapeutics to lower intraocular pressure and treat glaucoma. These researchers will use a mouse model of ocular hypertension to better understand how fluid outflow from the eye becomes impaired. This project will further our understanding of aqueous humor drainage, supporting development of more effective drugs to lower eye pressure and treat glaucoma.

Next-Generation Glaucoma Drug Development*

W. Daniel Stamer, PhD | Duke University

For this project, researchers will screen candidate molecular biology tools that could be used to target drugs to different eye structures affected by glaucoma. The eye structures are the trabecular network, which controls fluid drainage from the eye, and Schlemm's canal, where draining fluid passes to the circulatory system. Fine-tuning ways to target each of these separately could open new paths to drug development in glaucoma.

Understanding What Causes Glaucoma

Above: *An ophthalmologist checks the eyes.*

Ultimately, glaucoma threatens sight by damaging the optic nerve at the back of the eye, which carries light signals from the eye to the brain. Our knowledge of how and when glaucoma damages nerve cells remains imprecise. It's linked mostly to chronic pressure increases inside the eye, referred to as elevated intraocular pressure (IOP), which may arise from the eye's inability to drain fluid properly.

National Glaucoma Research is funding studies on genetics, including studies addressing racial and ethnic disparities in disease incidence and onset. Other projects include developing more sensitive methods for studying onset and projects to develop new research models to promote a better understanding of glaucoma that may lead to new therapies.

Mechanisms of Angle Development and Glaucoma

Revathi Balasubramanian, PhD | Columbia University

In several cases of glaucoma and especially early-onset glaucoma, drainage structures that regulate eye pressure are affected. To address this, researchers need to understand the genetics of drainage structure development. This group has developed a mouse model of early-onset glaucoma. Combining this model with the latest imaging methods, they will determine how drainage structures develop and how abnormalities in drainage tissue contribute to glaucoma.

Genetics of Glaucoma in Africa

Kathryn Burdon, PhD | University of Tasmania (Australia)
Co-Principal Investigator: Girum Gessesse, MD, St. Paul's Hospital Millennium Medical College (Ethiopia)

Genetics can play a role in predicting who requires early treatment for glaucoma, and there is a stark lack of data from non-European populations, particularly those from Africa, which has one of the highest burdens of glaucoma. For this work, researchers are investigating the genetics of glaucoma in Ethiopia. The findings will expand our understanding of glaucoma and possibly enhance the utility of genetic information in the diagnosis and management of glaucoma for patients worldwide.

Deciphering the Local Effect of Glaucoma Risk Factors on Axonal Mitochondria

Romain Cartoni, PhD | Duke University Medical Center

Mitochondria are cell organelles responsible for key processes such as energy production and programmed cell death regulation. In retinal ganglion cells (RGCs) affected by glaucoma, however, these structures and their functions are impaired. For this study, researchers will uncover regulators of mitochondrial functions involved in glaucomatous conditions, especially in the axons of RGCs. The findings may highlight novel therapeutic targets.

Genetically Engineering a New Animal Model to Find Cures for Glaucoma

F. Kent Hamra, PhD | University of Texas Southwestern Medical Center

For this project, researchers will generate novel visual systems for inventing new glaucoma medicines. They plan to use animal models that are genetically engineered to express clinically relevant, heritable human glaucoma-causing genes. The aim of the work is to create a model that researchers can use to identify candidate therapies targeting these genes that hold potential against glaucoma in humans.

The Genetics of Glaucoma in Individuals of Caucasian and African Ancestry

Michael Hauser, PhD | Duke University

Researchers will examine the expression levels of glaucoma-associated genes in individual retinal cells and the effects of different versions of these genes. The studies will yield basic information that will advance our understanding of the disease and could lead to development of new glaucoma treatments. Most crucial, the team will follow up on new findings in African Americans, a group disproportionately affected by glaucoma.

Determining the Genetic Element on Human Chromosome 9 That Increases the Risk for Glaucoma

Gareth Howell, PhD | The Jackson Laboratory

Human genetic studies show glaucoma is caused by a combination of genetic risk factors, but few specific changes have been pinpointed. This gap is severely hampering the ability to identify people at risk for developing glaucoma and is interfering with the development of new treatments. For this study, researchers will target the specific genetic element in a genomic region that shows one of the strongest associations with glaucoma.

Defining the Role of a New Protein Target in Fluid Buildup in Glaucoma

Rupalatha Maddala, PhD | Duke University School of Medicine
Co-Principal Investigators: Pratap Challa, MD & Vasantha Rao, PhD

In this project, researchers will assess the role of septins, proteins that are implicated in glaucoma, in fluid drainage from the eye. They will focus on the trabecular meshwork, which is where fluid drains from the eye, and how septins affect the function of this area. The findings will highlight specific features of septins and their role in fluid pressure in the eye that could be targets in glaucoma treatment.

A Possible Link Between Glaucoma and Alzheimer's Disease

Nick Marsh-Armstrong, PhD | University of California, Davis

Researchers will use live imaging of the optic nerve in models to determine whether an agent believed to be central to Alzheimer's disease might be released from axons together with mitochondria (the energy powerhouse of cells). If its release is linked to that of mitochondria, it would have profound implications for both Alzheimer's disease and glaucoma.

Human Stem Cell Modeling of the *APBB2* Risk Variant for Glaucoma

Jason Meyer, PhD | Indiana University School of Medicine

Recently, a variant in a gene, *APBB2*, was identified as significantly associated with glaucoma in African Americans, offering a novel opportunity to explore the degeneration of retinal ganglion cells (RGCs) associated with the increased risk. Researchers will focus on using adult stem cells and CRISPR/Cas9 gene editing as an in vitro model to study the effects of this gene variant on RGCs and how it may lead to glaucomatous neurodegeneration.

Mapping Scleral Fibroblasts and Their Significance in Glaucoma

Ian Pitha, MD, PhD | Johns Hopkins University School of Medicine

Damage to the nerve cells occurs because the pressure within the eye pinches the nerve at the optic nerve head. Intraocular pressure reduction alleviates this pinching and allows the cell to function properly. The aim of this work is to generate a better understanding of how the wall of the eye remodels in glaucoma and to test an approach to prevent the nerve cells' pinching by altering this process.

Investigating Risk Factors for Primary Open-Angle Glaucoma in Individuals of African Ancestry

Alberta Thiadens, MD, PhD | Erasmus Medical Center (The Netherlands)

Co-Principal Investigator: Caroline C.W. Klaver, MD, PhD

Researchers will focus on nutritional and environmental influences and ancestry-related anatomical variation of the eye that might explain the higher vulnerability of the optic nerve in people of African ancestry. The findings will enhance understanding of why glaucoma is so frequent and severe in people of African ancestry, yield knowledge about the causes of glaucoma, and further the aim of curing and preventing this disease.

Understanding Alterations in an Early Experimental Glaucoma Model

Hongli Yang, PhD | Good Samaritan Foundation, Legacy Health System

Co-Principal Investigator: Priya Chaudhary, PhD

The goal of this proposal is to identify the cellular and molecular alterations underlying structural change in an experimental model. Overall, this project will inform and enhance the interpretation of human optical coherence tomography imaging, advance our understanding of pathophysiologic mechanisms in glaucoma, and provide guidance to improve therapeutic options before glaucomatous damage becomes permanent and untreatable.

Imaging & Exploring the Eye-Brain Connection

***Above**: The optic nerve and its visual link from the eye to the brain.*

Eye changes associated with glaucoma contribute to tiny blind spots, known as visual field defects, which can advance to vision loss and blindness. The speed and likelihood of this progression vary from person to person. Early diagnosis is key, and considerable progress has been made in eye imaging to detect the tiniest changes preceding glaucoma.

National Glaucoma Research grantees are developing and leveraging new technologies to look at the individual retinal ganglion cells (RGCs) of the eye and their nerve fibers, which carry light signals to the brain—a challenging task because RGCs are almost transparent and difficult to image. Scientists also are investigating disruptions in how cells communicate in glaucoma. The findings could result in earlier detection of and new ways to treat glaucoma.

Alterations of the Sleep-Regulating Systems in Glaucoma

Ji Won Bang, PhD | New York University School of Medicine
Mentors: Kevin C. Chan, PhD & Joel Schuman, MD; Yuka Sasaki, PhD, Brown University

Researchers will use multimodal brain neuroimaging, clinical ophthalmic assessments, and sleep quality assessments in early-stage and advanced-stage glaucoma patients and healthy participants. The outcomes should provide a mechanistic account of the high incidence of sleep disorders in glaucoma and could lead to therapeutic advancements benefiting millions of people.

Improved Imaging of the Outflow Pathway in the Living Human Eye

Alessandra Carmichael-Martins, PhD | Indiana University Bloomington
Mentor: Stephen Burns, PhD

This work is expected to enable researchers and clinicians to achieve three-dimensional images of the drainage structures in the living human eye at cellular-level resolution. This tool will facilitate a deeper understanding of changes within the trabecular meshwork associated with age, glaucoma, and treatment.

A Novel Tool for Seeing Neuron Cells in Eyes with Glaucoma

Yali Jia, PhD | Oregon Health & Science University
Co-Principal Investigator: Shaohua Pi, PhD

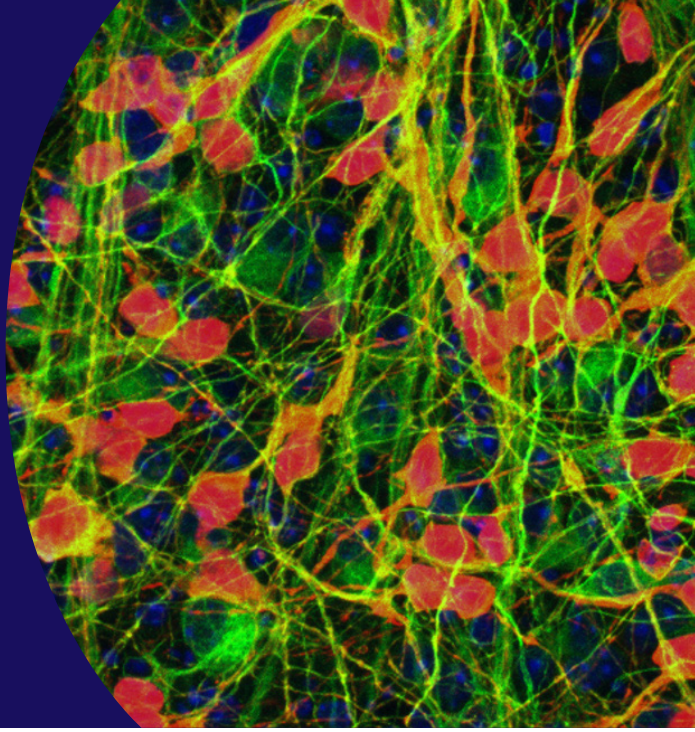
Researchers aim to improve the current state-of-the-art ocular imaging systems using optical tools originally developed for astronomy. These improvements will enhance image quality so that even individual cells in the eye can be clearly seen. The goal of this study is to image glaucoma models using this instrument in order to discover new and improved indicators of glaucoma progression and to advance our understanding of the nature of the disease.

Increased Pressure in the Eye Affects the Neuronal Communications in the Brain

Prabhavathi Maddineni, PhD | University of North Texas Health Science Center at Fort Worth
Mentor: Gulab Zode, PhD

The optic nerve is part of the central nervous system and is connected to the brain, and pressure-induced optic nerve damage may also damage surrounding cells and neurons in the brain. The aim of this study is to ascertain how neurons in the brain communicate with each other in response to this pressure-induced damage.

Predicting Outcomes & Other Treatment Innovations



***Above**: The Johnson Laboratory induces human pluripotent stem cells to become retinal ganglion cells (RGCs), shown in red. They have developed methods that enable donor human RGCs to integrate into the retina of a recipient eye following transplantation, where they intermingle with the recipient's own RGCs, shown in green. Photo courtesy of Thomas V. Johnson III, MD, PhD, Wilmer Eye Institute, Johns Hopkins University School of Medicine.*

Approved treatments for glaucoma primarily focus on lowering eye pressure. Many therapies involving eye drops or surgery lower eye pressure effectively, but most require skill and consistency to achieve results or, as with surgery, present recognizable risks.

More reliable treatments and new therapies to address the underlying causes of glaucoma beyond changes in intraocular pressure are needed. National Glaucoma Research grantees are working to develop drugs that will lower eye pressure and protect against nerve cell injury and death, as well as genome-editing approaches to restore the function of the trabecular meshwork (a spongy tissue that drains fluids from the eye). Additional therapies include advancing stem cell transplantation, promoting lifestyle interventions, and identifying strategies to promote genetic testing with at-risk individuals.

Preventing Vision Loss by Predicting and Treating Exfoliation Syndrome Earlier in Patients

Karen Curtin, PhD | University of Utah
Co-Principal Investigator: Barbara M. Wirostko, MD

Researchers will explore thousands of medical records of exfoliation syndrome patients to find the clinical conditions and personal characteristics that correlate with changes in their eyes over time. They expect this work to provide direction to doctors who care for these patients and help prevent or delay vision loss from glaucoma through earlier medical treatment.

Biomechanical Phenotype of Normal-Tension Glaucoma

Michael Girard, PhD | Singapore Eye Research Institute, Singapore National Eye Centre (Singapore)
Co-Principal Investigators: Aung Tin, MBBS, PhD & Monisha E. Nongpiur, MBBS, PhD

To determine why some patients with normal eye pressure develop glaucoma, researchers will develop engineering and artificial intelligence tools to fully assess and understand the robustness of the optic nerve head (ONH) in individual patients. Their goal is to establish whether ONH robustness can support predictions of who is at risk of developing glaucoma damage. If successful, the findings will support earlier treatment in eyes that are identified as mechanically unstable.

Diagnosing Glaucoma in the Peripheral Retina

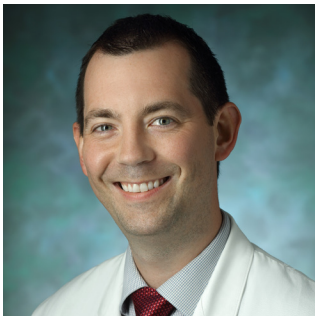
John Hetling, PhD | University of Illinois at Chicago
Co-Principal Investigators: Thasarat Vajaranant, MD & Jason McAnany, PhD

Early diagnosis of glaucoma is important because it leads to more effective treatment. Early glaucoma can affect central vision or peripheral vision, so both areas of vision should be tested. However, the best objective test for glaucoma evaluates only central vision. This project will give both central vision and peripheral vision tests to a group of glaucoma patients, to demonstrate that the new peripheral vision test helps to diagnose the disease.

Integrated Machine Learning Analysis of Biomarkers for Glaucoma Therapy

Pirro Hysi, MD, PhD | King's College London (UK)

Researchers will identify modifiable changes in metabolism or chemical modifications of DNA that lead to glaucoma. For this work, they will use powerful machine learning to stack millions of data points acquired through high-throughput platforms ("omics") in a very large number of individuals. With this exploration, they will identify robust signals of epigenetic and metabolic changes that together modulate glaucoma risk.



New Tools for Leveraging Regenerative Medicine to Restore Sight in Glaucoma

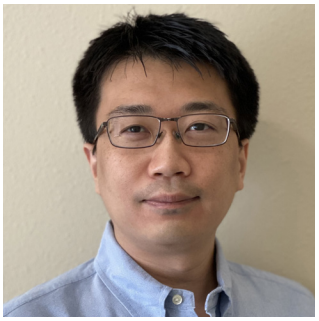
Thomas V. Johnson III, MD, PhD | Wilmer Eye Institute, Johns Hopkins University School of Medicine

To help usher in stem cell transplantation as a new approach toward treating glaucoma, these researchers plan to develop a novel, sensitive, rapid experimental tool that labels successful integration of transplanted neurons in the retinas of recipient eyes. They also will rigorously validate the experimental framework using multiple complementary techniques that include high-resolution, three-dimensional microscopy and measurements of electrical responses to light.

Can Progression of Glaucoma Be Slowed by Regular Exercise?

Andras Komáromy, DVM, PhD | Michigan State University

Using models of naturally occurring glaucoma, researchers will determine if regular, moderate-intensity exercise can slow glaucoma disease progression. They also plan to evaluate metabolic biomarkers of exercise-induced neuroprotection in this model. If results are positive, exercise would represent an easy, low-cost, beneficial therapy avenue for glaucoma patients.



Cellular-Scale Imaging in the Living Eye to Study Glaucoma Pathophysiology

Kazuhiro Kurokawa, PhD | Good Samaritan Foundation, Legacy Health System

There is an urgent need to detect glaucoma-related damage earlier, when treatment could preserve vision and even restore the health of the eye and optic nerve before irreversible damage occurs. Researchers will construct and test a new, advanced multifunctional imaging system capable of revealing astounding details in the living eye as small as single cells to transform the future of clinical testing for glaucoma.

An Optimal Form of Nerve Growth Factor as a New Neuroprotective Drug for Glaucoma

Silvia Marinelli, PhD | European Brain Research Institute (Italy)
Co-Principal Investigator: Francesca Malerba, PhD

For this project, researchers will dial down the negative effects of a naturally occurring molecule and boost its potential benefits as a glaucoma treatment. The optimized version of a "painless nerve growth factor" is expected to rescue retinal ganglion cells from progressive damage. The drug is already in clinical trials for other eye diseases.

Insights Into a Naturally Occurring Glaucoma Model

Amanda Melin, PhD | University of Calgary (Canada)
Co-Principal Investigator: James Higham, PhD, New York University

By leveraging access to a large, existing sample of eye tissues, researchers will examine genes expressed, their sequences, and the metabolites that are present in individuals with and without naturally occurring glaucoma-like phenotypes in a closely related animal model. These data hold great promise to guide genetic-screening panels used in the diagnosis and prognosis of glaucoma and to identify molecules in the blood that can be used for early detection and treatment.

Investigating the Mechanical Behavior of the Optic Nerve Head in Glaucoma

Thao Nguyen, PhD | Johns Hopkins University
Co-Principal Investigator: Harry A. Quigley, MD

Researchers will investigate the mechanical behavior of the optic nerve head (ONH) in glaucoma patients and determine how it may be altered by glaucoma damage. The results are expected to increase our understanding of how the mechanical properties and strain response of the ONH vary with age, sex, level of glaucoma damage, and structural features with the aim of enabling patient-specific glaucoma therapies.

Using Laser Pulses to Smooth the Way for Transplanted Retinal Ganglion Cells in Glaucoma

Karen Peynshaert, PhD | Ghent University (Belgium)
Mentor: Katrien Remaut, PhD

For this work, investigators will pilot the use of laser pulse technology to facilitate successful transplant of donor retinal ganglion cells in glaucoma. They will combine laser pulses with a heat-absorbing dye to make the smallest opening possible in the eye membrane to allow passage of transplanted cells. If successful, the method will offer a controlled, targeted way to create this passage for cells while causing the least disruption to important structures of the eye.

Cell-to-Cell Communication in Health and Disease

Michael Risner, PhD | Vanderbilt University Medical Center
Co-Principal Investigator: David Calkins, PhD

Using high-resolution microscopy, researchers will track the movement of mitochondria between cells through tubes connecting different cell types. The team is exploring possible backup pathways that may activate when stress interferes with this mitochondrial transfer. The findings will add to our understanding of the metabolic interaction between healthy and stressed cells in the context of cell transplantation for the treatment of glaucoma.

Investigating Autophagy in Nitric Oxide Production to Control Eye Pressure

Myoungsup Sim, PhD | Duke University School of Medicine

Several studies have shown that nitric oxide (NO) lowers eye pressure. However, most of the NO-based drugs have failed to be approved by the FDA due to challenges related to the delivery of NO, suggesting that regulation of the cells' own NO production could represent a better strategy for glaucoma treatment. Researchers will investigate how to regulate endogenous NO production to improve the current NO-based glaucoma therapy.

Developing Communication Strategies for Genetic Risk Testing in Glaucoma

Emmanuelle Souzeau, PhD | The Flinders University of South Australia (Australia)
Mentor: Jamie E. Craig, DPhil, FRANZCO

Polygenic risk scores (PRS) for glaucoma make genetic testing an ideal strategy to identify at-risk individuals who can benefit from early management to reduce preventable blindness. However, the current lack in reporting strategies to efficiently communicate PRS to patients impedes the implementation of testing in clinical practice. Researchers aim to develop the first patient-friendly reports and assess delivery methods for risk communication of PRS for glaucoma, which will ultimately benefit at-risk individuals globally.

Predicting and Detecting Glaucoma Progression with New Imaging

Zhichao Wu, PhD | Centre for Eye Research (Australia)
Co-Principal Investigators: Xavier Hadoux, PhD, Peter van Wijngaarden, MBBS, PhD, Flora Hui, PhD & Keith Martin, DM, FRANZCO

Injured retinal ganglion cells (RGCs) undergo changes that result in important retinal changes before RGC loss occurs. Researchers will use a powerful imaging technique to detect these changes. The aim is to address the urgent need for more effective tools to predict and detect progression to prevent irreversible vision loss from glaucoma.

Harnessing Artificial Intelligence to Improve Glaucoma Clinical Trials

Jithin Yohannan, MD, MPH | Johns Hopkins University School of Medicine

Researchers will deploy artificial intelligence to make glaucoma-related clinical trial enrollment and follow-up more efficient. Tools will be developed that can screen for patients who are a good fit for the repeated tests most trials entail and are at high risk for disease progression. The findings are expected to make clinical trials of new glaucoma therapies faster and less costly, translating into quicker assessment and approval of candidate treatments for glaucoma.

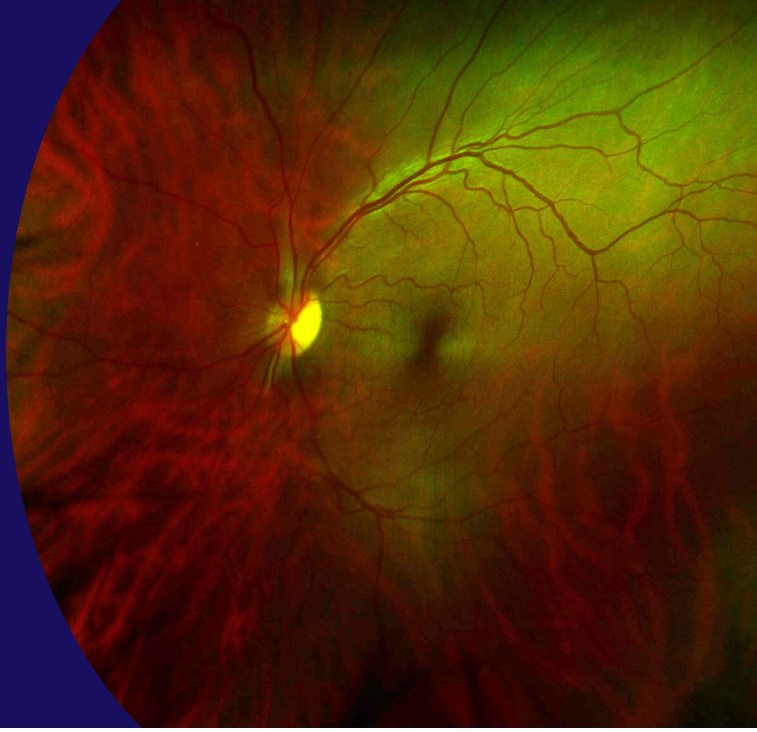
Validation of Novel OCT-Based Imaging Tools for Noninvasive Monitoring

Robert Zawadzki, PhD | University of California, Davis
Co-Principal Investigator: Pengfei Zhang, PhD

Novel treatments focused on restoring vision in glaucoma using gene or stem cell therapies would benefit from developing cellular resolution in vivo imaging tools, which could offer sensitivity and specificity beyond current clinical tests. To achieve that, researchers plan to develop and validate a novel structural and functional extension of optical coherence tomography (OCT), so-called temporal speckle analysis OCT (TSA-OCT), for basic science research.

Because it often has no early symptoms, **half of people living with glaucoma may not even be aware they have the disease.**

Protecting & Regenerating the Optic Nerve



***Above**: Photographic scan of a retina, with the optic nerve in the middle.*

Unlike most cells in the body, which repair themselves, the nerve cells providing our vision don't regrow once damaged. National Glaucoma Research is supporting research into ways of protecting cells threatened by advancing glaucoma and regenerating those cells after vision loss.

The focus of these efforts is to replace and reconnect retinal ganglion cells (RGCs), the nerve cells that make up the optic nerve and carry visual signals over axons, long threadlike tails extending from the eye to the brain. This is a sophisticated undertaking, given how RGCs are wired into the brain.

Another focus is to develop neuroprotective drugs and therapies that will help nourish and support fragile RGCs to ensure their long-term viability.

A Dietary Supplement in the Treatment of Glaucoma

Jeffrey Boatright, PhD | Emory University
Co-Principal Investigator: Ying Li, MD, PhD

Mitochondria are the energy factories of cells. The mitochondria of retinal ganglion cells (RGCs) lose function with age, probably due to age-related loss of nicotinamide adenine dinucleotide (NAD+), an enzyme cofactor needed for energy production, making the cells more susceptible to damage. The goal of this study is to test whether systemic delivery of the NAD+ precursor nicotinamide riboside, a dietary supplement, increases retinal NAD+ and protects RGCs in glaucoma models.

Treating Immune-Mediated Glaucomatous Neural Degeneration Using Specialized Proresolving Mediators

Kinsang Cho, PhD | The Schepens Eye Research Institute

The goal of this study is to identify a novel molecule that would suppress the immune inflammation and lead to protecting the retinal ganglion cells from death and preserving vision. This work will identify potent specialized proresolving mediators that would suppress neuroinflammation and investigate its neuroprotection effect in mouse models of glaucoma. The findings will shed light on the development of a novel approach to treat glaucoma.

Boosting Neuronal Energy to Improve Vision in Glaucoma

Adriana Di Polo, PhD | University of Montreal Hospital Center (Canada)

Researchers will test the effects of small molecules that can clear potentially damaging calcium buildup from retinal ganglion cells and keep the cells' mitochondria healthy and functioning efficiently. The small molecules are "mitochondrial uncouplers" because they uncouple mitochondrial processes that normally lead to production of damaging byproducts. If mitochondrial uncouplers show potential benefit, the project is expected to open the door to clinical trials of these drugs in glaucoma.

Preserving the Eye's Vision by Neuroprotecting Retinal Cells

Marco Feligioni, PhD | Fondazione EBRI Rita Levi-Montalcini (Italy)

Neuroprotection is an unmet medical need. This project aims to investigate the properties of a new drug to protect against degeneration of retinal ganglion cells. Researchers will investigate the interaction of a pair of proteins previously implicated in damage to these cells. They will also use a mouse model to test whether a specific molecule they have identified can prevent these effects.

Using Electric Fields to Regenerate the Optic Nerve

Kimberly Gokoffski, MD, PhD | University of Southern California Roski Eye Institute

This project uses electrical stimulation to direct neuron growth so that healthy neurons that have been injected into diseased eyes can form new connections with the brain and restore vision. Researchers will also use genetic approaches to examine how this technology could interact with genetic manipulations to produce even greater benefits. This work will be pivotal in propelling the development of a device that can help restore vision in people blinded by advanced glaucoma.

Neuroprotection and Neuroenhancement in Glaucoma

Jeffrey Goldberg, MD, PhD | Stanford University

The goal of this project is to evaluate safety and proof of concept for whether ciliary neurotrophic factor can enhance vision or protect against vision loss in glaucoma. In this randomized trial, researchers will evaluate the retina and optic nerve in patients using a series of biomarkers to increase the chance of detecting evidence of vision improvement or protection against vision loss.

The Role of Reactive Astrocytes in Glaucomatous Axonal Degeneration

Cátia Gomes, PhD | Indiana University Bloomington
Mentor: Jason Meyer, PhD

Reactive astrocytes are closely associated with retinal ganglion cells (RGCs) in the optic nerve head, where the initial insult to RGC axons occurs. In this study, RGCs and astrocytes will be differentiated from human pluripotent stem cells, and microfluidic platforms will be used to study the effect of toxic insults from astrocytes on RGC axons. Identifying reactive astrocyte-induced axonal degeneration pathways will allow for the development of novel therapeutic strategies.

Defining the Importance of Extrinsic Signaling in Glaucoma Neurodegeneration

Richard Libby, PhD | University of Rochester Medical Center

This work will explore the importance of extrinsic signaling in glaucomatous neurodegeneration. It builds on the work of many groups that have proposed that after an ocular hypertensive injury, glial cells (cells that support retinal neurons) transition from being helpful to being toxic to retinal ganglion cells. Specifically, researchers will test the importance of three molecules thought to turn glial cells neurotoxic after a glaucomatous injury.

Targeting Eye Immune Cells to Prevent Glaucoma-Induced Nerve Damage

Shubham Maurya, PhD | University of California, Berkeley
Mentor: Karsten Gronert, PhD

The aim of this project is to learn how microglia in the eye contribute to nerve damage in glaucoma and test molecules that might prevent it. Researchers will work with naturally occurring small molecules that may dampen the reaction of the microglia. They also will sort out how astrocytes produce these small molecules and usually keep microglia in check, highlighting potential treatment targets in glaucoma.

A Novel Model for Replacing Lost Cells and Restoring Vision in Glaucoma Patients

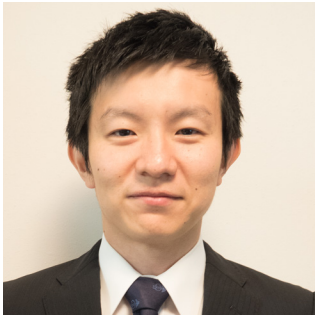
Jeff Mumm, PhD | Wilmer Eye Institute, Johns Hopkins University

Although human eyes do not normally regenerate lost retinal ganglion cells (RGCs), they retain the capacity to produce new neurons, suggesting untapped potential for RGC regeneration. Zebrafish have a natural ability to replace lost cells in the retina, including RGCs. By studying how zebrafish naturally regenerate RGCs, researchers hope to identify genes and pathways that are important for stimulating the eye's ability to repair itself and apply this knowledge toward the development of transformative regenerative therapies for glaucoma patients.

A Study to Define the Link Between Cell Adhesion and Retinal Ganglion Cell Death

Robert W. Nickells, PhD | University of Wisconsin-Madison

Cells living in a complex tissue are healthiest when they make and retain contact with other cells and with the extracellular environment. The goal of this research is to determine if loss of cell-to-cell and/or cell-to-surface contacts by retinal ganglion cells stimulates the biological pathway leading to their death after damage to the optic nerve.



Repurposing an Approved Diabetes Drug for Glaucoma

Kazuya Oikawa, PhD, BVSc | University of Wisconsin-Madison
Mentor: Gillian McLellan, BVMS, PhD, DECVO, DACVO, FARVO

For this project, researchers will repurpose an FDA-approved diabetes drug as an anti-neuroinflammatory therapy for glaucoma. The drug mimics a naturally occurring insulin-regulating hormone and targets myeloid cells, which are implicated in neuroinflammation in glaucoma. The group expects to demonstrate that this already approved drug can be repurposed to target neuroinflammation in glaucoma.

Investigating Optic Nerve Head Remodeling in Glaucoma

Babak Naghizadeh Safa, PhD | Georgia Tech Research Corporation
Mentor: Christopher Ross Ethier, PhD

Researchers will generate an accurate characterization of the mechanical properties and mechanobiology of the optic nerve head, the primary site of damage in glaucomatous optic neuropathy. They also will develop a physiologically appropriate model to study the mechanobiological response of optic nerve head cells, thought to drive characteristic changes in glaucoma. The results will eventually form the basis of a high-throughput drug discovery system, accelerating the development of future treatments for glaucoma.

Mapping the Pathways of Neurodegeneration in Glaucoma Using Artificial Intelligence

Karthik Shekhar, PhD | University of California, Berkeley

Researchers will use innovative molecular techniques, artificial intelligence approaches, and mouse models to tease apart how different cell pathways interact in cell destruction in glaucoma. Focusing on the death of retinal ganglion cells, which underlies vision loss in the disease, the team will create a detailed molecular map of how and where neurodegeneration occurs in these cells, opening the way to new treatment possibilities and use of these tools in human studies.

Hunting for Genes Controlling Optic Nerve Regeneration

Jiaxing Wang, PhD | Emory University

Researchers will seek genes that could support optic nerve regeneration and save vision. This group has found a model with enhanced regeneration response that carries such a gene and is working to identify it. Once identified, the gene will be tested to see how it alters the regeneration response. This may lead to a clinical intervention for the treatment of blindness due to optic nerve damage.

Combined Stem Cell and Trophic Factor Therapy for Glaucoma

Shaomei Wang, MD, PhD | Cedars-Sinai Medical Center

The novel approach of this study is to deliver a combined stem cell and gene therapy close to the site of disease to protect retinal ganglion cells from secondary degeneration in a model of glaucoma.

Identifying Which Retinal Ganglion Cell Types Die Earlier in Glaucoma

Siamak Yousefi, PhD | University of Tennessee, Memphis

This research team has been developing single-cell technologies to study both retinal ganglion cell (RGC) type and the early signature of glaucoma-associated cellular stress. Their aim for this work is to develop artificial intelligence approaches to identify RGC subtypes that are more susceptible to glaucoma-induced insult. Results from this study could advance our understanding of the genetic basis for glaucoma-induced RGC cell death and possible therapeutic interventions.

Glaucoma is a leading cause of irreversible blindness in the U.S. and worldwide.

Catalyzing Life-Changing Breakthroughs

For the past 50 years, BrightFocus Foundation has funded the boldest research and what-if ideas to get us closer to cures for Alzheimer's disease, macular degeneration, and glaucoma, resulting in the novel treatments and diagnostic tools in use today. We also raise awareness and empower people with these diseases and their loved ones by sharing expert resources and information.

National Glaucoma Research Milestones

National Glaucoma Research

1979

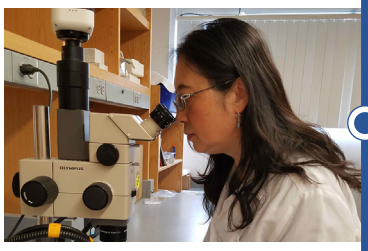
National Glaucoma Research, a program of BrightFocus Foundation, is established.

2010

Our grantees create the **first noninvasive technique to measure eye pressure**—the most important factor to consider in glaucoma. For the first time, scientists can visualize and measure how fast drainage in the front of the eye occurs without touching the eye and without any bright lights.

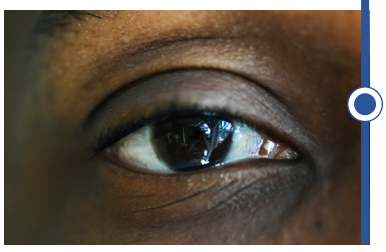
2015

We funded a **first-of-its-kind clinical trial** testing a new treatment focused on improving vision in people with glaucoma and restoring vision lost to glaucoma.



2017

The launch of Rhopressa, the first approved rho-associated protein kinase (ROCK) inhibitor, is the **first entirely new class of glaucoma medication** to become available in more than two decades. Early National Glaucoma Research-funded work proved this class of drugs could relieve eye pressure.



2021

National Glaucoma Research-funded scientists successfully reprogram cells in mice to **reverse vision loss from glaucoma**, as well as normal vision loss associated with aging. The results show strong promise for gene therapy to reprogram eye tissue to restore vision lost to glaucoma and reverse aging and age-related diseases in humans.

Explore more breakthroughs: **brightfocusbold.org/breakthroughs**

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