

# National Glaucoma Research Current Grantees

Glaucoma is the second leading cause of blindness worldwide, according to the World Health Organization, affecting 60.5 million in 2010. As people live longer, this number may increase to almost 80 million by 2020. More than three million Americans are living with glaucoma, 2.7 million of whom—aged 40 and older—are affected by its most common type, open-angle glaucoma. In the United States, glaucoma is a leading cause of blindness among African Americans and Hispanics.

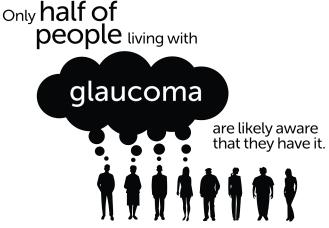
Since inception, National Glaucoma Research (NGR) has awarded almost \$31 million to support research projects on the causes and potential prevention and treatment of this disease.

NGR funds investigator-initiated research topics, allowing us to invest in a wide range of scientific approaches to ending glaucoma. The research projects

currently supported by NGR fall into these broad categories:



- Eyes on the Outflow Pathway
- Finding New Ways to Treat Glaucoma
- Detecting Glaucoma Early and Predicting Its Path
- Exploring the Eye-Brain Connection
- Protecting and Regenerating the Optic Nerve



#### New Knowledge about What Causes Glaucoma

Glaucoma is a group of eye diseases united under one name. Ultimately, glaucoma threatens sight by damaging the optic nerve, which is like a fiber optic cable carrying light signals from the eye to the brain. However, our knowledge of how and when glaucoma damages nerve cells remains imprecise. It's mostly linked to chronic elevated intraocular pressure (IOP) caused by the eye's inability to drain properly. There may be other factors besides IOP increases that lead to glaucoma. NGR is funding research that looks at how inflammation, oxygen deprivation, changes in the retinal blood supply (microvasculature), and other factors threaten the health of the optic nerve. New understanding will lead to new therapies.



Douglas Gould, PhD (7/1/17 - 6/30/19) University of California, San Francisco

Growth Factor Signaling in Eye Development

"We are studying genes involved in normal eye development so that we may understand how defects lead to blindness from glaucoma and other diseases, and if there are ways to intervene and prevent vision loss."

www.brightfocus.org/grant/G2017218



Meredith Gregory-Ksander, PhD (7/1/16 - 6/30/18) Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School, Boston

A New Method to Inhibit Inflammation and Prevent Glaucoma

"Our project identifies an important new regulator of inflammation in the optic nerve head and tests whether inhibiting this regulator will stop disease development and vision loss."

www.brightfocus.org/grant/G2016081 Recipient of the Thomas R. Lee Award



Shahid Husain, PhD (7/1/16 - 6/30/18) Medical University of South Carolina, Charleston

Low Oxygen Mediated Proteins Play Pathological Role in Glaucoma

"The studies in this project seek to limit the up-regulation of neurotoxic proteins to slow/halt neuronal death in glaucoma."



Krishnakumar Kizhatil, PhD (7/1/17 - 6/30/19) The Jackson Laboratory, Bar Harbor, ME

Neuronal Control of Intraocular Pressure

"The objective is to determine how neuronal control regulates aqueous humor (AQH) outflow and intraocular pressure (IOP)."

www.brightfocus.org/grant/G2017152



Xiugian Mu, MD, PhD (7/1/16 - 6/30/18) University at Buffalo, The State University of New York Generating Retinal Ganglion Cells in a Dish to Study and Treat Glaucoma

"This proposal aims to improve existing procedures and establish new ones to generate retinal ganglion cells, the cells affected in glaucoma, in a petri dish. The cells thus produced will be used to study the reasons causing glaucoma, to screen for drugs to treat it, and to develop new therapeutic strategies."

www.brightfocus.org/grant/G2016024



Thao Nguyen, PhD (7/1/15 - 12/30/17) Johns Hopkins University, Baltimore, MD

Measuring the Effects of Structure on the Deformation of the Optic Nerve

"This project investigates the biomechanical environment of the human optic nerve head as it is affected by intraocular pressure (IOP) with the goal of understanding the connection between IOP and glaucoma."

www.brightfocus.org/grant/G2015132

This grant is made possible in part by a beguest from the Margaret Louise Rigby Trust.



Julia Richards, PhD (7/1/15 - 6/30/18) University of Michigan, Ann Arbor

Validating a New Angle-Closure Glaucoma Gene

"We will study a new angle closure glaucoma gene, MTRR, which we found by studying a large family with iris cysts. We will study the biochemical and functional changes to this protein that have been caused by the mutation."

www.brightfocus.org/grant/G2015202 Recipient of The Douglas H. Johnson Award



Daniel Sun, PhD (7/1/16 - 6/30/18) Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School, Boston

Astrocyte Reactivity in the Glaucomatous Optic Nerve Head: Beneficial or Harmful for Vision?

"My research focuses on better understanding the role that a type of supporting cell, called astrocytes, plays in the biological process of glaucoma, primarily whether they help to slow down the vision loss in glaucoma or make it worse."

www.brightfocus.org/grant/G2016137

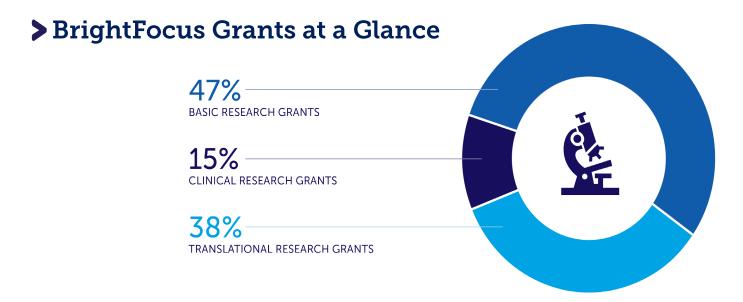


Linda Zangwill, PhD (7/1/17 - 6/30/19) University of California, San Diego

The Role of Vascular Factors in Glaucoma

"The goal is to investigate whether changes in the retinal blood supply (microvasculature) precede or follow the death of cells in a layer in the optic nerve head."

www.brightfocus.org/grant/G2017122



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.

# Eyes on the Outflow Pathway

Elevated intraocular pressure (IOP) is present in most forms of glaucoma. This happens when the fluid that constantly bathes the front of the eye, called agueous humor, gets backed up. Normally it drains through a spongy tissue known as the trabecular meshwork (TM), which is the eye's main drainage channel. However, outflow can be affected by factors such as volume and quality of fluid; TM stiffness (20 times higher in individuals with glaucoma than in normal eyes); other changes to TM tissue, such as reduced pore formation; and possibly cellular signaling. NGR researchers are studying what goes wrong with the TM and other parts of the eye's drainage system, and looking for ways to restore its function.



Rudolf Fuchshofer, PhD (7/1/16 - 6/30/18) University of Regensburg, Germany

Identifying Underlying Pressure-Control Mechanisms in Glaucoma

"The understanding of the functional role of microRNAs will be an important step toward restoring the homeostatic balance of the outflow regulation in the glaucomatous tissues and will lead to new therapies."

www.brightfocus.org/grant/G2016076



Haiyan Gong, MD, PhD (7/1/16 - 6/30/18) Boston University School of Medicine, Massachusetts

Mechanism of Decreased Giant Vacuole and Pore Formation in Glaucoma Using a Novel Method

"We propose to study two types of cellular interactions in the cells that line Schlemm's canal using a newly developed, advanced 3D electron microscopy technology."

www.brightfocus.org/grant/G2016099



Raguel Lieberman, PhD (7/1/16 - 6/30/18) Georgia Institute of Technology, Atlanta

Mechanism of Decreased Giant Vacuole and Pore Formation in Glaucoma Using a Novel Method

"We propose to study two types of cellular interactions in the cells that line Schlemm's canal using a newly developed, advanced 3D electron microscopy technology."



Yutao Liu, MD, PhD (7/1/16 - 6/30/18) Augusta University Research Institute, Georgia.

Identifying New Drug Targets to Lower Eye Pressure Via Outflow

"The purpose of this project is to study how a short RNA molecule known as miR-182 may affect the outflow of aqueous humor, which is the clear liquid circulating in the front part of human eyes to bathe its lens and other delicate tissue."

www.brightfocus.org/grant/G2016023



Vijay Krishna Raghunathan, PhD (7/1/15 - 6/30/18) University of Houston, Texas

Effects of Glucocorticoids on Trabecular Meshwork Mechanics and Composition

"In the proposed study, we will determine whether treatment with steroids alters cellular and matrix structure, composition, biomechanical attributes, and function."

www.brightfocus.org/grant/G2015078

# Finding New Ways to Treat Glaucoma

Numerous therapies exist to lower IOP effectively; however, the bulk of them (eyedrops) require skill and consistency to achieve results. Easier methods are needed, as well as new therapies to address other underlying causes of glaucoma besides IOP. NGR grantees are working to develop drugs and gene therapies that protect against nerve cell injury and death, and against abnormal proteins that misfold and/or clump together, blocking the outflow pathway.



Audrey Bernstein, PhD (7/1/16 - 6/30/18) SUNY Upstate Medical University, Syracuse, NY

Use of Patient-Derived Cells to Test Compounds that Will Reverse Exfoliation Glaucoma

"Our goal is to reverse the effects of exfoliation syndrome (XFS), the leading identifiable cause of open-angle glaucoma."



András Komáromy, DVM, PhD (7/1/17 - 6/30/19) Michigan State University, East Lansing

A Gene Therapy Approach to Neuroprotection in Glaucoma

"This research project will test a new form of treatment for glaucoma that uses gene therapy to protect retinal neurons and stop glaucoma from developing, even in the presence of elevated intraocular pressure (IOP)."

www.brightfocus.org/grant/G2017185



Weiming Mao, PhD (7/1/17 - 6/30/19) University of North Texas Health Science Center, Fort Worth CRISPR Interference for Glaucoma

"Our study aims to use a novel technology called CRISPR interference to correct abnormal protein modifications, with the hope of thus restoring function to the trabecular meshwork (TM) tissue that drains fluid from the eve."

www.brightfocus.org/grant/G2017151



Gillian McLellan, PhD (7/1/16 - 6/30/18) University of Wisconsin-Madison

A New Treatment to Protect the Optic Nerve in Glaucoma

"This research will test a promising new treatment strategy for glaucoma" patients by repurposing an existing drug to block transforming growth factor-beta (TGF- $\beta$ ) and preserve vision."

www.brightfocus.org/grant/G2016129



Derek Welsbie, MD, PhD (7/1/17 - 6/30/19) University of California, San Diego

Genome Editing to Inhibit Optic Nerve Cell Death in Glaucoma

"Our lab has been interested in developing a novel neuroprotective strategy that directly interferes with the cell death process in retinal ganglion cells."

www.brightfocus.org/grant/G2017212 Recipient of the Dr. Douglas H. Johnson Award



Gulab Zode, PhD (7/1/17 - 6/30/19) University of North Texas Health Science Center, Fort Worth Novel Treatment for Steroid and Myocilin Glaucoma

"We will test whether inhibition of molecules via a new type of drug known as an integrated stress response inhibitor (ISRIB) lowers eye pressure in mice and cultured trabecular meshwork cells."

#### **Detecting Glaucoma Early and Predicting Its Path**

Eye changes associated with glaucoma contribute to tiny blind spots, known as "visual field defects," which, if they worsen, might advance to vision loss and blindness. The chance of that, and the speed at which it happens, varies greatly from person to person. Early diagnosis is key, and much progress has been made in imaging the eye to detect the tiniest changes that may precede glaucoma. NGR grantees use these new technologies to look at individual cells (including retinal ganglion cells, which are nearly transparent and very difficult to image); changes to synapses, or connections between cells; and variations in light refracted from parts of individual neurons. Once abnormalities are confirmed, and a diagnosis is made, computerized algorithms are being designed to analyze an assortment of biometric data to better predict and track a patient's risk of progression to vision loss.



Tobias Elze, PhD (7/1/17 - 6/30/19)

Schepens Eye Research Institute, Massachusetts Eye and Ear, Harvard Medical School, Boston

Computational Investigation of Glaucoma Progression

"The aim of this project is to investigate the spatial configuration of glaucomatous visual field defects by a combination of mathematical algorithms and clinical expertise in order to to identify patterns of disease progression."

www.brightfocus.org/grant/G2017111



Brad Fortune, OD, PhD (7/1/17 - 6/30/19)
Devers Eye Institute, Portland, OR

Can Imaging Reveal Early Stage Damage to Individual Optic Nerve Fibers?

"We seek to determine whether a particular type of imaging is capable of reporting on the integrity of sub-microscopic structures within optic nerve fibers at an early stage of damage from glaucoma, preceding their complete degeneration and loss from the eye."

www.brightfocus.org/grant/G2017170 Recipient of the Thomas R. Lee Award



Guorong Li, PhD (7/1/15 - 12/30/17) Duke University Eye Center, Durham, NC

A Novel Non-Contact Method for Early Glaucoma Diagnosis and Monitoring

"The aim of this study is to understand the vibrant response of conventional outflow tissues to changes in IOP and to a conventional outflow drug, in real-time."



Yvonne Ou, MD (7/1/16 - 6/30/18) University of California, San Francisco

Understanding the Earliest Steps of Optic Nerve Cell Death in Glaucoma

"Our goal is to understand the earliest steps of injury to the optic nerve cell, or retinal ganglion cell (RGC), in glaucoma."

www.brightfocus.org/grant/G2016084 Recipient of the Dr. Douglas H. Johnson Award



Ethan Rossi, PhD (7/1/17 - 6/30/19) University of Pittsburgh, Pennsylvania

Imaging Individual Cells Affected by Glaucoma

"Our goal is to understand the earliest changes to the individual cells that form the optic nerve, the retinal ganglion cells (RGCs), in patients with glaucoma."

www.brightfocus.org/grant/G2017082



Matthew Van Hook, PhD (7/1/17 - 6/30/19) Truhlsen Eye Institute, University of Nebraska Medical Center, Omaha

Effects of Elevated IOP on Ganglion-Cell Photoreceptors

"The goal of this project is to determine how the function of a neurons in the retina responsible for resetting circadian rhythms and triggering constriction of the pupil are altered at early stages of glaucoma, before irreversible degeneration of retinal ganglion cells (RGCs)."

www.brightfocus.org/grant/G2017027



**Ji Yi, PhD** (6/1/17 - 5/31/18) Boston Medical Center, Massachusetts

A New Imaging Technique to Detect Early Markers of Glaucoma

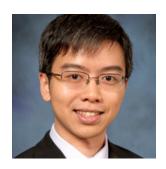
"We plan to develop a new optical imaging technology to examine the eye, which is very sensitive to early glaucoma so that we can use it for early diagnosis."





# Imaging and Exploring the Eye-Brain Connection

Glaucoma as a disease, stretches from the eye to the brain—and scientists are no longer focused solely on the eye when exploring its origins and impact. Early changes in the brain may also be indicative of glaucoma. For example, whereas pressure inside the eye (IOP) has long been thought to play a dominant role, recent work suggests that fluid pressure outside the eye, where the optic nerve enters the brain also may contribute. All of these projects will likely yield early indicators to improve glaucoma diagnosis and treatment.



Kevin Chan, PhD (7/1/16 - 6/30/18) University of Pittsburgh, Pennsylvania

Early Brain Changes and Visual and Motor Functions in Glaucoma

"The goal of the project is to understand how glaucoma may impair the brain structurally and functionally within and beyond the visual pathway, and whether the brain changes in glaucoma are associated with early vision loss or balance and mobility impairments."

www.brightfocus.org/grant/G2016030



J. Crawford Downs, PhD (7/1/16 - 6/30/18) University of Alabama at Birmingham

A Wireless System to Measure and Control Fluid Pressure Around the Optic Nerve

"We have developed a new system to wirelessly measure and record the IOP continuously in research subjects, and we now want to extend that system to measure the pressure around the nerve exiting the eye."

www.brightfocus.org/grant/G2016165



Esther G. Gonzalez, PhD (7/1/17 - 6/30/19) Krembil Research Institute at University Health Network, Toronto, Canada

Testing the Brain Structure Connecting Two Hemispheres in Glaucoma

"We plan to study the function of this brain structure in humans with glaucoma using a series of non-invasive tests."

# Protecting and Regenerating the Optic Nerve

Unlike most cells in the body, which repair themselves, the nerve cells providing our vision don't regrow once damaged. NGR is supporting research into regenerating the eye in advanced glaucoma and vision loss. The "holy grail" of these efforts is to replace and reconnect RGCs, nerve cells which make up the optic nerve and carry visual signals over long tails ("axons") extending from the eye to the brain. It's a sophisticated undertaking, given how RGCs are wired into the brain, but progress is being made in this area.



Jeffrey Goldberg, MD, PhD (7/1/15 - 12/31/19) Stanford University, California

Neuroregenerative Strategies in Glaucoma

"Dr. Goldberg is conducting a phase 2 clinical trial where he will implant into the eye a tiny device, called NT-501 encapsulated cell therapy (NT-501 ECT)."

www.brightfocus.org/grant/C2015201

This clinical trial is made possible in part by support from the Barry Friedberg and Charlotte Moss Family Foundation.



**Ephraim F. Trakhtenberg, PhD** (7/1/17 – 6/30/19) University of Connecticut Health Center, Farmington New Approach for Regenerating the Injured Optic Nerve

"We propose to identify novel biological regulators of the intrinsic ability of the retinal cells to regrow connections between the eye and the brain."

www.brightfocus.org/grant/G2017204



Fengquan Zhou, PhD (7/1/17 - 6/30/19) Johns Hopkins University, Baltimore, MD A New Approach to Optic Nerve Regeneration

"The proposed study will open a new avenue for identifying novel genes and pathways that can be manipulated to promote optic nerve regeneration."

www.brightfocus.org/grant/G2017037 This grant is made possible in part by a bequest from the Timothy Miles Charitable Trust.

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<sup>\*</sup>Note: These are the active National Glaucoma Research grants as of 7/20/2017.



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