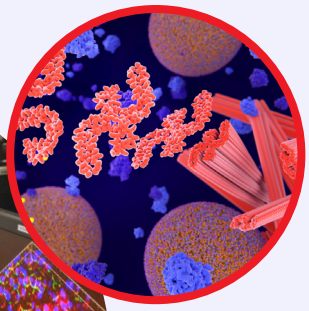
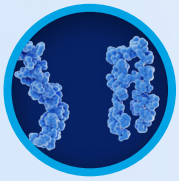
BrightFocus® Foundation

Cure in Mind. Cure in Sight.

Alzheimer's Disease Research
Macular Degeneration Research
National Glaucoma Research





Today's investments, **tomorrow's breakthroughs.**

2024 ANNUAL REPORT

Message from Leadership

Dear Friend,

As BrightFocus Foundation enters its fifth decade, we remain steadfast in our commitment to serve the 335 million individuals and families worldwide suffering from age-related diseases with no cure. This past year has seen groundbreaking research and the development of new treatments, all made possible by the unwavering support of our donors.

A cornerstone of our success has been our continued investment in research, with a focus on supporting early investigative ideas. This year, we awarded more than $10 million in new research grants, fueling innovative projects that hold great promise to slow the progression of, treat, and ultimately cure Alzheimer's disease, macular degeneration, and glaucoma. We are especially proud of this historic year for funding female and diverse scientists, empowering a wide range of brilliant minds to lead the charge across eye and brain research.

Another way we show our commitment to promising, early-career scientists is through travel awards. This year, we supported over 150 researchers in sharing their findings and collaborating globally to accelerate discovery. These travel awards reflect our belief that cures for these diseases require a broad spectrum of perspectives and findings.

This past year has seen groundbreaking research and the development of new treatments, all made possible by the unwavering support of our donors.

Educating the public about these diseases of sight and mind is another key aspect of our mission. We have seen remarkable growth in our outreach efforts, particularly through our Zoom In on Dementia & Alzheimer's and BrightFocus Macular and Glaucoma Chats programs. These initiatives have allowed us to connect with more people than ever before, spreading awareness, sharing vital information, and offering support to those affected by these diseases.

We are deeply grateful for the support and dedication of our 630,000+ donors across the country who believe that today's investments in research represent tomorrow's breakthroughs. Together, we are planting roots for a future where all people can age free from diseases of mind and sight.

Thank you for standing with us.

With hope and gratitude,

Stacy Pagos Haller
President and CEO

Patricia McGlothlin Stewart, CFP
Chair, Board of Directors

Mission

BrightFocus funds exceptional scientific research worldwide to defeat Alzheimer's disease, macular degeneration, and glaucoma and provides expert information on these heartbreaking diseases.

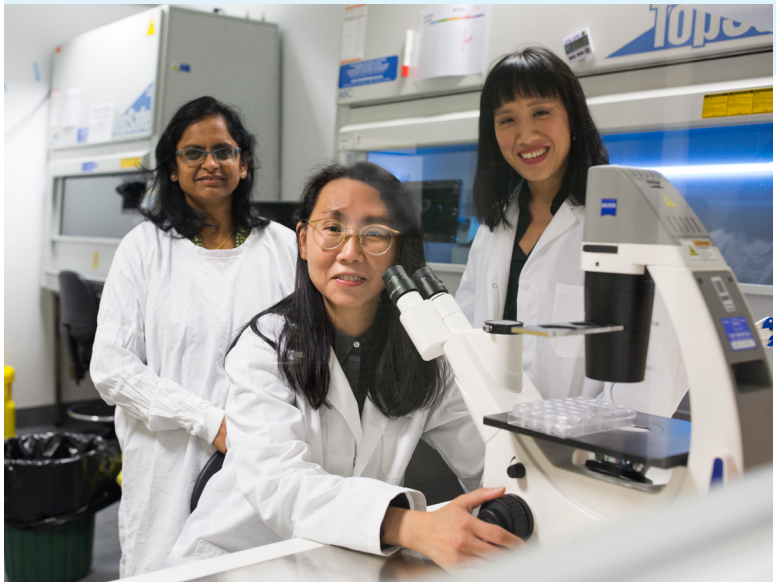
Vision

A world where all people age free from diseases of mind and sight.

Contents

Our Impact

Thanks to our early support, most of the researchers we fund go on to receive government and industry grants that, on average, are 10 times larger than their original BrightFocus award, **a 1,000% return on investment**.



BrightFocus advances groundbreaking mind and sight research across the globe. Through our signature programs—Alzheimer's Disease Research, Macular Degeneration Research, and National Glaucoma Research—we invest in bold, innovative science that will find the cures for these heartbreaking diseases.

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

Since our founding more than 50 years ago, we've funded the boldest research and what-if ideas to get us closer to cures, resulting in the novel treatments and diagnostic tools in use today. We also share the latest research findings and trusted expert information on treatments, healthy living, risk reduction, and more to inform and empower individuals and families impacted by neurodegenerative diseases.

BrightFocus is currently supporting:

More than
$55 million
in active research grants

666
researchers

202
active research projects

Our investigators

107
global institutions

83
cities

Across
15
countries

Since inception

6,385
scientists supported across 25 countries

Nearly
$300 million
in research grants awarded

**as of July 3, 2024*

Innovative Research Leads to Breakthroughs

Alzheimer's disease, the most common form of dementia, is an irreversible degeneration of the brain that causes disruptions in memory, cognition, personality, and other functions that interfere with everyday activities and eventually leads to death from complete brain failure.

Our Alzheimer's Disease Research grants leave no stone unturned, exploring the full range of scientific paths toward better treatments and ultimately a cure for a disease that affects more than 55 million people worldwide.

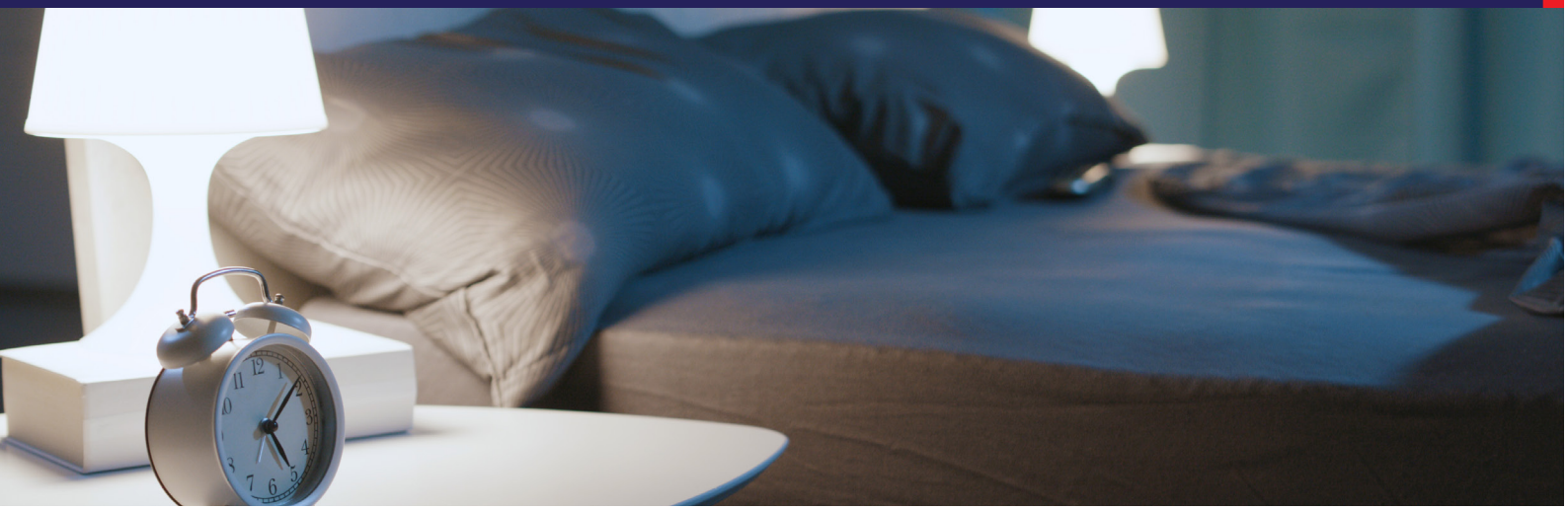
Thanks to the generous support of our donors, we've awarded more than $180 million in Alzheimer's Disease Research grants to date to better understand and cure this devastating disease.

Read about a few of the research breakthroughs you helped make possible over the last year.

In 2024, Alzheimer's Disease Research invested:

More than
$30 million
in active research grants

Funding
112
total projects



RESEARCH SPOTLIGHT

Researchers Uncover Link Between Sleep and Alzheimer's Disease Onset

Maxime van Egroo, PhD

People with Alzheimer's disease often have difficulty sleeping. Now, researchers have evidence that monitoring sleep can help identify those who are at risk for the disease.

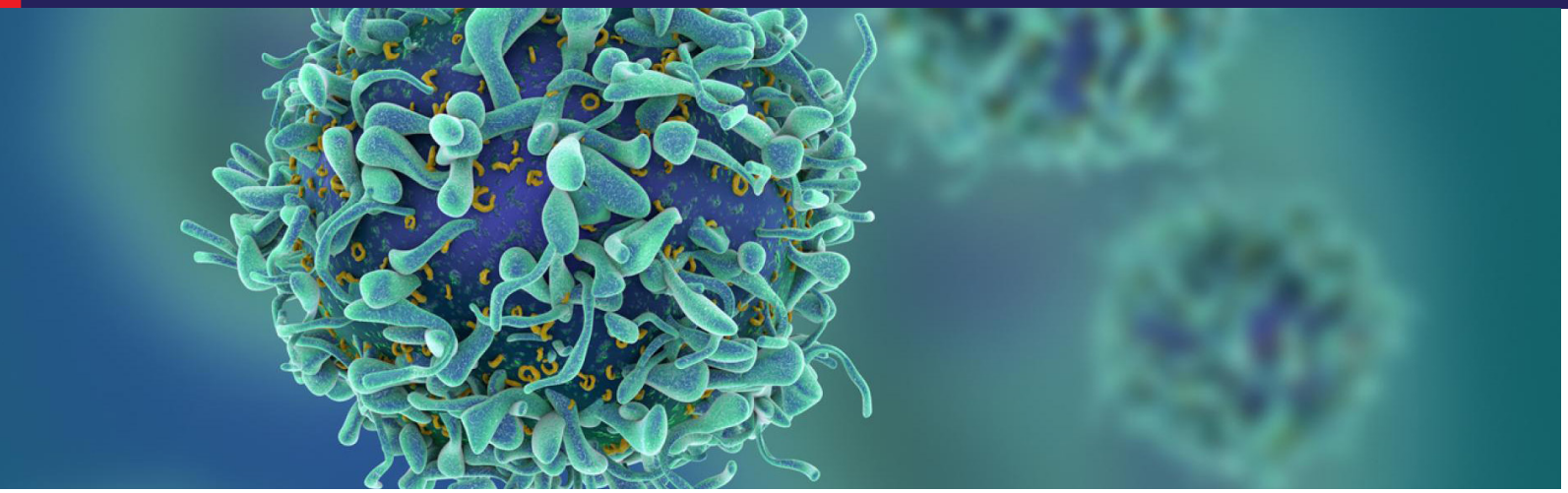
A team led by Alzheimer's Disease Research-funded investigator **Maxime van Egroo, PhD**, during his postdoctoral fellowship under **Heidi Jacobs, PhD**, at Maastricht University in the Netherlands, found that damage to a brain area called the locus coeruleus is closely associated with sleep disruption prior to cognitive decline in Alzheimer's disease.

Dr. van Egroo's team collected data from an observational study of 388 volunteers aged 60 and older who underwent yearly medical testing and donated their brains to research after death. Researchers looked at their performance on cognitive tests and measurements of 24-hour rest-activity patterns. Brain studies looked for signs of degeneration in the locus coeruleus and the presence of Alzheimer's tau tangles and amyloid plaques.

The researchers discovered that 25% of participants showed degeneration of their locus coeruleus, which appeared more severe in those diagnosed with Alzheimer's. These participants showed a more fragmented rest-activity pattern, which is also observed in people with Alzheimer's. Study results also showed a direct link between fragmented sleep patterns and locus coeruleus degeneration.

The study's authors suggested that these results support a strategy for monitoring patterns of rest and activity in older people. Everyday activity monitors may be used by doctors as notification devices for further diagnostic testing, as they currently are used to monitor changes in heart function and blood pressure.

The researchers concluded that doing so could help clinicians identify people at greatest risk of developing Alzheimer's and guide preventive strategies.



RESEARCH SPOTLIGHT

Study Finds Changes to Blood Immune Cells in Alzheimer's Disease

Immune genes associated with higher Alzheimer's risk may also be vulnerable to changes caused by individual lifestyle factors and behaviors, according to a recent study published in Neuron. The research team behind the study hopes their findings will eventually lead to new therapeutic targets.

Lead investigator **David Gate, PhD**, an Alzheimer's Disease Research grant recipient and assistant professor of neurology at Northwestern University, and his research team investigated immune cells in the blood of individuals with Alzheimer's disease.

They found that immune cells showed modifications driven by a person's behavior or environment, called epigenetic changes. These occur to the packaging that surrounds DNA inside a cell. The cell's DNA can become altered when the packaging is left open—a common sign of epigenetic changes.

Through their research, they uncovered that the immune cell genes most impacted by these changes are also known risk factors for Alzheimer's. For example, one gene whose protein is thought to facilitate T-cell entry into the brain was particularly vulnerable to epigenetic changes. The researchers point to environmental factors or viral infection as possible instigators behind the modified genes.

"Altogether, these findings indicate that immune function in Alzheimer's patients is significantly altered," Dr. Gate said. "It could be that environmental factors, like pollutants or infections that a person has in their lifetime, cause these epigenetic changes."

As a next step, Dr. Gate and his team will use postmortem brain tissue samples and sophisticated molecular tools to determine if T-cells appear in the same places as misfolded proteins in Alzheimer's. This could provide further evidence of a relationship between peripheral inflammation and Alzheimer's pathology.

David Gate, PhD

Image: A digital rendering of a T-cell, one of the immune cells to show epigenetic, or noninherited, changes in Alzheimer's disease.

RESEARCH SPOTLIGHT

Cognitively Healthy Centenarians Offer Clues to Alzheimer's Resistance

Henne Holstege, PhD

A recent Alzheimer's Disease Research-funded study uncovered a link between long-term cognitive health and several genetic variations that are linked to Alzheimer's risk. The researchers found that cognitively healthy centenarians are enriched with gene variants that help protect the brain from amyloid plaques and other hallmarks of the disease. Findings from this study could uncover specific genetic variants or resilience-associated pathways that can be targeted to help prevent cognitive decline in those at risk of developing Alzheimer's.

The research team was led by Alzheimer's Disease Research grant recipient **Henne Holstege, PhD**, of Amsterdam University Medical Center. Dr. Holstege's team studied 6,747 people, about one-third of whom had been diagnosed with Alzheimer's. They sought to determine the prevalence of 86 known Alzheimer's-related single nucleotide polymorphisms—or genetic variants—in cognitively healthy centenarians. They focused on different versions, or alleles, of Alzheimer's-associated variants.

"Cognitively healthy centenarians have a lower frequency of almost all risk-increasing alleles and a higher frequency of protective alleles," the researchers concluded.

Specifically, centenarians who resist Alzheimer's have significantly lower levels of three risk alleles, plus significantly higher levels of four protective alleles than do age-matched controls. The seven key alleles are critical to maintaining immune system responses and waste clearance mechanisms that effectively process and recycle toxic proteins like amyloid and tau.

Cognitively healthy centenarians showed amyloid plaques in many regions, but these did not result in Alzheimer's disease. This suggests that protective alleles process amyloid in a way that prevents it from accumulating in the brain.

The team's findings are part of Dr. Holstege's overall mission to unlock the genetic processes that drive Alzheimer's, in the hopes of improving the search for new treatments and, in the future, predicting those at risk of the disease long before they develop symptoms.

Accelerating Breakthroughs in Macular Degeneration Research

We invest in groundbreaking research to better understand the root causes of and prevention strategies for macular degeneration, the **leading cause of blindness** in people over age 50 worldwide.

With generous donor support, Macular Degeneration Research has awarded nearly $53 million to date to fund critical research on the disease's causes and potential prevention, treatment, and cure. **Read about some of the research breakthroughs you helped make possible over the last year.**

In 2024, Macular Degeneration Research invested:

Nearly
$16 million
in active research grants

Funding
49
total projects

RESEARCH SPOTLIGHT

How Does Blood Flow Drive Macular Degeneration?

Albert Gonzales, PhD

Blood flow tells a story about the unique needs and functions of the body's tissues. And with one of the highest rates of blood flow in the body, it's clear that the choroid—the part of the eye that supplies oxygen and nutrients to and helps remove waste materials from the retina—plays a key role in healthy vision.

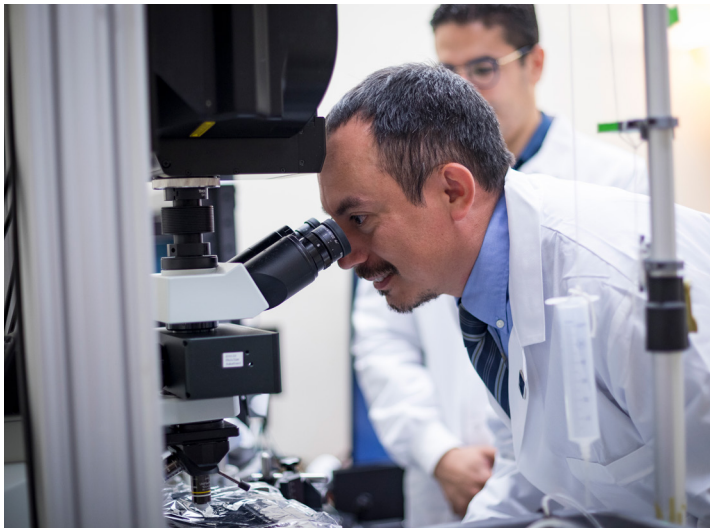
Macular Degeneration Research grant recipient **Albert Gonzales, PhD**, an assistant professor at the University of Nevada, Reno School of Medicine, is exploring choroidal blood flow to explain macular degeneration and open new avenues of treatment for vision loss. Blood reaches the choroid through tiny vessels called capillaries. Previously, researchers thought blood flowed through these capillaries passively, like water seeping downhill. Dr. Gonzales challenged that notion, showing capillaries in the brain and retina adjust blood flow to actively respond to cells' energy needs.

"We aim to demonstrate that the capillary network has the remarkable ability to actively sense and respond to the needs and environment of tissues," he explained.

Dr. Gonzales believes these flow-regulation mechanisms are essential for eye health. He's examining how choroidal blood flow fluctuates with a new experimental model of the mouse eye. His initial results suggest certain wavelengths of light reduce blood flow in the choroid and encourage cells to clear waste. Conditions like macular degeneration could impact this process.

"Our research could offer fresh perspectives on the development of macular degeneration," he said.

Ultimately, this work could bring about a drug that treats macular degeneration through the vascular system. Dr. Gonzales explained, "With more people, effort, and scientific capabilities, we can push for discoveries faster, with hopes that the best ideas rise to the top."



"With more people, effort, and scientific capabilities, we can push for discoveries faster, with hopes that the best ideas rise to the top."

Albert Gonzales, PhD

RESEARCH SPOTLIGHT

Adult Stem Cell Research Could Uncover New Treatments for Dry Macular Degeneration

Understanding the early events associated with age-related macular degeneration (AMD) is key to treating it, and patient-derived stem cells are an essential tool for researchers. These malleable cells give researchers the ability to study models of the eye and screen for small molecules with therapeutic potential.

Macular Degeneration Research grant recipient **Srinivasa R. Sripathi, PhD**, director of the Henderson Ocular Stem Cell Laboratory at the Retina Foundation of the Southwest, is using this technique to advance our knowledge of AMD. By growing stem cells from an individual's blood sample, he's converting them to retinal pigment epithelium (RPE) cells that are then used to generate AMD models. This allows him to understand the loss of RPE cells with the goal of developing personalized treatments for the condition.

Dr. Sripathi's lab is investigating drugs to prevent harmful changes in the RPE and help cells survive exposure to stressors such as cigarette smoke, blue light, and toxic by-products of the visual cycle. He is also studying important components of biological pathways involved in these changes using CRISPR, an advanced gene-editing technique. Through this research, he's begun to identify drugs that reverse signs of AMD in his stem cell model.

In the future, he aims to study stem cells from patients with different genetic risks for AMD to better understand how environmental and genetic factors interact so that doctors can one day prescribe personalized treatments for AMD. This innovative method of using stem cell-derived RPE cells with CRISPR gene editing will allow Dr. Sripathi to observe harmful changes in RPE cells while also testing potential treatments and monitoring the cells' health.

"I am grateful to BrightFocus Foundation donors for their generous grant support," Dr. Sripathi said. "The grant is critically important to spark vision research. It will give me tremendous support to establish new AMD research at the Retina Foundation of the Southwest."

Srinivasa R. Sripathi, PhD

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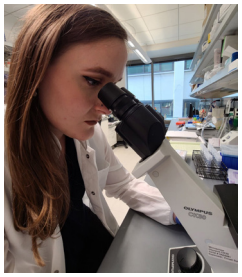
RESEARCH SPOTLIGHT

What "Junk DNA" Could Reveal About Macular Degeneration



Leah VandenBosch, PhD

Many view DNA as a recipe book for all the body's proteins, but by some estimates, this so-called coding DNA only accounts for about 2% of DNA. The rest, called noncoding DNA, doesn't directly correspond to making proteins but still contains valuable information. Once thought of as "junk DNA," researchers now believe noncoding DNA has important functions, such as turning genes on and off, protecting chromosomes, and organizing genetic material during cell division.

Macular Degeneration Research grant recipient **Leah VandenBosch, PhD**, a postdoctoral fellow at Seattle Children's Research Institute, is investigating how changes in noncoding DNA could predict the development of age-related macular degeneration (AMD). She's using genetic information to train machine learning models that mimic different types of retinal cells, including the retinal pigment epithelium (RPE) cells that are involved in AMD. Her goal is to use these models to predict how genetic variations in noncoding DNA affect retinal cells.

Dr. VandenBosch's project uses advanced methods such as machine learning, miniorgans grown from cells, and DNA sequencing to understand how genes are regulated in the retina. The models she creates will help identify which noncoding DNA variations may contribute to AMD, a currently underresearched area. Her research will help prioritize which genetic variations to study further that can be useful as a reference in genetic testing for AMD.

Dr. VandenBosch's research will help prioritize which genetic variations to study further that can be useful as a reference in genetic testing for AMD.

Ultimately, she hopes to develop sophisticated models that can accurately predict how subtle variations in noncoding DNA affect AMD. This means that new genetic variations found in people with AMD can be quickly analyzed to see if they cause the disease, potentially accelerating the development of new treatments and expediting personalized treatments for those living with or at risk of developing AMD.

Unraveling the Mysteries of Glaucoma

National Glaucoma Research, one of the world's premier nonprofit funders of research on glaucoma, has invested nearly $51 million to date in scientific grants exploring root causes, prevention strategies, and treatments for glaucoma, a group of eye diseases that can damage the optic nerve and result in vision loss and blindness.

National Glaucoma Research-funded scientists are advancing new and innovative ways of detecting, preventing, and curing this "sneak thief of sight," which impacts 80 million people worldwide.

Explore a few of the scientific breakthroughs you helped make possible over the last year.

In 2024, National Glaucoma Research invested:

Nearly
$8 million
in active research grants

Funding
39
total projects

RESEARCH SPOTLIGHT

Breakthrough Discovery Reveals New Pathway to Lowering Eye Pressure

Myoungsup Sim, PhD

The findings from a first-of-its-kind study funded by National Glaucoma Research can help improve current glaucoma drugs and lead to the development of new treatments.

National Glaucoma Research grant recipients **Myoungsup Sim, PhD**, and **Paloma B. Liton, PhD**, of Duke University and colleagues found that cellular activity within Schlemm's canal could help lower eye pressure. They reported their study results in the journal Autophagy Reports.

Schlemm's canal is a ring-shaped vessel that circles the cornea. It acts, in part, as a gatekeeper to maintain the correct amount of fluid in the eyes and regulate eye pressure. In glaucoma, the optic nerve at the back of the eye becomes damaged from too much pressure within the eye. In most cases, this damage is related to increased eye pressure caused by a buildup of fluid called aqueous humor.

In healthy eyes, a balance exists between the fluid made in the eye and the fluid that leaves the eye. With glaucoma, however, the outflow of aqueous humor becomes blocked and builds up in the eye, creating high pressure that can harm the optic nerve. To leave the eye, excess aqueous humor flows through spongy tissue called the trabecular meshwork and into Schlemm's canal.

The study identified a new mechanism in which waste removal, called autophagy, is activated in the canal and used to maintain a pressure balance in the eye. These findings can help advance and improve current glaucoma drugs and provide a more complete understanding of how autophagy regulates eye pressure. Future studies will tease apart the mechanisms involved in autophagy within Schlemm's canal.

> These findings can help advance and improve current glaucoma drugs and provide a more complete understanding of how autophagy (waste recycling) regulates eye pressure
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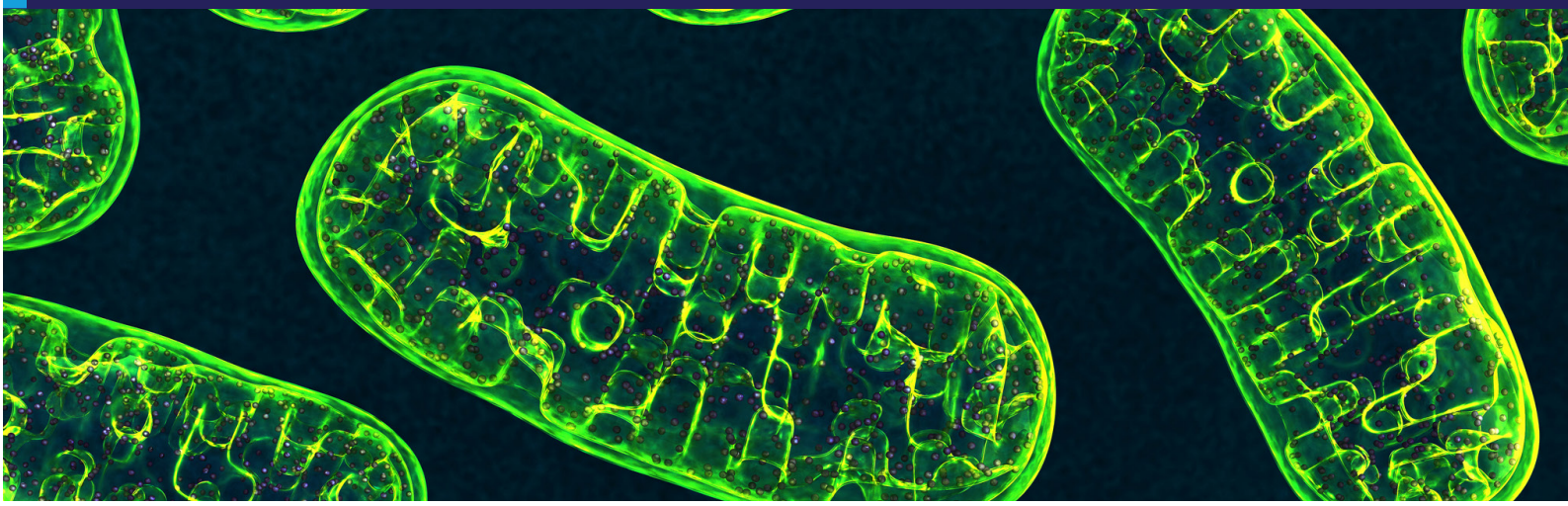


RESEARCH SPOTLIGHT

Experimental Drug Could Improve Vision in Glaucoma

Adriana Di Polo, PhD

In glaucoma, problems with mitochondria—a source of cell energy—can lead to damage in the neurons that carry visual information from the eyes to the brain, resulting in vision loss and blindness.

National Glaucoma Research grant recipient **Adriana Di Polo, PhD**, in collaboration with Mitochon Pharmaceuticals, is researching the use of experimental small-molecule drugs to prevent mitochondria-related damage in these neurons, known as retinal ganglion cells.

"Retinal ganglion cells are particularly vulnerable to deficits in mitochondria, as evidenced by known mitochondrial-related disorders that affect the eye," explained Dr. Di Polo and her colleagues.

Neurons can be divided into three areas: a message-receiving end, a long hallway called an axon, and a message-sending end. In glaucoma, the movement of mitochondria along the axons of retinal ganglion cells is disrupted, leaving the axons depleted of energy. Glaucoma also leads to a buildup of calcium in retinal ganglion cells, which further damages or kills the cell.

The small-molecule drugs Dr. Di Polo and her team are testing prevent calcium from building up in the liquid part of the cell. They also stop the production of damaging by-products, known as free radicals, within the mitochondria. The research team is also testing to see if these small-molecule drugs can enhance the function of mitochondria in retinal ganglion cells and promote the survival of the cells. If this research is successful, it could lead to clinical trials of these drugs as a treatment for glaucoma.

> If this research is successful, it could lead to clinical trials of these drugs as a treatment for glaucoma.

Image: A 3D illustration of mitochondria.

RESEARCH SPOTLIGHT

Health Disparities in Visual Field Testing Highlight the Need for Equitable Glaucoma Care

Joel S. Schuman, MD

Regular visual field testing is critical for diagnosing and monitoring whether someone's glaucoma is remaining stable or worsening. But research shows that this important test is being administered less frequently to Blacks than whites, despite Blacks being at higher risk of blindness from glaucoma than whites.

To help understand this inequity in glaucoma care, a research team led by National Glaucoma Research grant recipient **Joel S. Schuman, MD**, examined medical records for over 2,600 adults diagnosed with glaucoma who received visual field testing. They found that Blacks had the worst disease severity at their first visit, noting that this "would typically warrant increased test frequency in conventional clinical practice." Yet their findings showed that Blacks diagnosed with glaucoma underwent visual field testing less often per office visit compared to white people.

This suggests that Blacks with severe glaucoma are not being tested frequently enough, which could delay the detection of disease progression and appropriate treatment. The disparity in testing frequency is compounded by the higher risk of blindness in Blacks with glaucoma compared to whites.

The research shows the need for ongoing efforts to promote equitable glaucoma care, given that Black people, who are more prone to a severe form of the disease, are not being tested frequently or early enough. The researchers noted, "Diagnosing glaucoma at its earliest stages makes it possible to minimize avoidable vision loss and structural damage to the optic nerve."

The research shows the need for ongoing efforts to promote equitable glaucoma care, given that Black people, who are more prone to a severe form of the disease, are not being tested frequently or early enough.

Expanding Impact Across the Globe

Age-related brain and vision diseases have no borders, and neither does our work. As one of the only research funders with no citizenship requirements for scientists, we foster cross-border collaborations to unlock future discoveries and deepen collective expertise.

Among this year's grants, **24%** were awarded to scientists at leading institutions outside the U.S. in **15 countries.**

BrightFocus Research Grants by Country

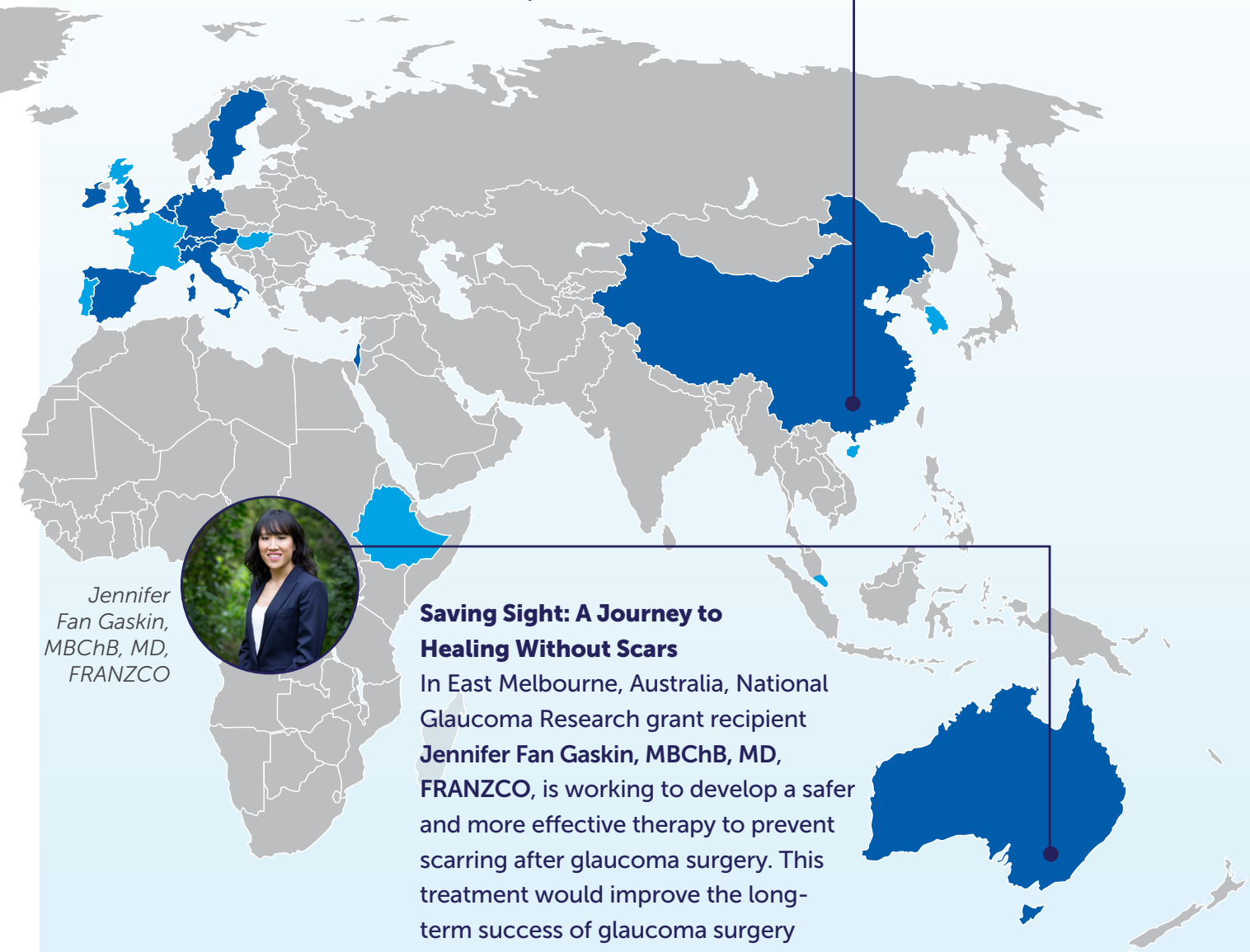
Yali Jia, PhD

Imaging Tiny Blood Vessels in the Eye for Markers of Age-Related Macular Degeneration
Here in the States in Oregon, Macular Degeneration Research grant recipient **Yali Jia, PhD**, and her team are developing a specialized instrument to image blood flow in the eye that may show changes before other signs of age-related macular degeneration (AMD) occur. The imaging tool could facilitate even earlier detection of AMD, allowing for treatment that could preserve remaining vision.

The Effects of Peripheral APOE2 on Alzheimer's Disease Pathology and Pathways

In Hong Kong, Alzheimer's Disease Research grant recipient **Guojun Bu, PhD**, is investigating the protective effect of the *APOE2* gene using new model systems and advanced technologies. Outcomes from these studies will provide new insight into how the *APOE* gene can be targeted for Alzheimer's therapies.

Guojun Bu, PhD



Jennifer Fan Gaskin, MBChB, MD, FRANZCO

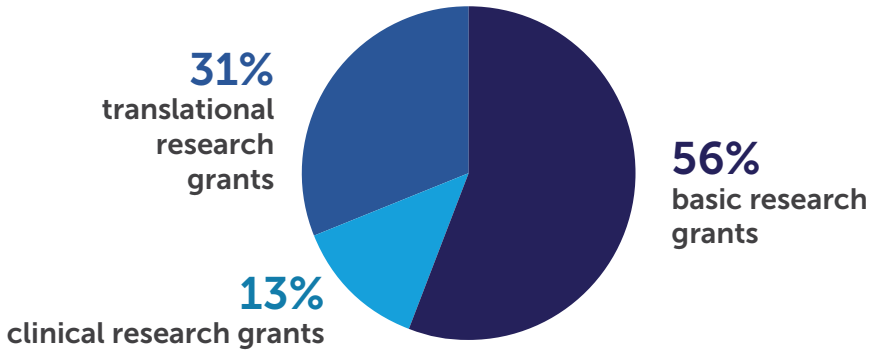
Saving Sight: A Journey to Healing Without Scars

In East Melbourne, Australia, National Glaucoma Research grant recipient **Jennifer Fan Gaskin, MBChB, MD, FRANZCO**, is working to develop a safer and more effective therapy to prevent scarring after glaucoma surgery. This treatment would improve the long-term success of glaucoma surgery and enhance the quality of life for individuals with glaucoma worldwide.

2024 Grant Awards

BrightFocus 2024 Grants at a Glance

*as of July 3, 2024



Basic
Research that aims to better understand how a disease occurs 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 to the bedside by testing potential treatments.

2024 Research Grants

Alzheimer's Disease Research

The Effect of Alzheimer's Disease on Neurons Across the Sleep-Wake Cycle
Md. Joynal Abedin, PhD
Massachusetts General Hospital

The Effects of Peripheral APOE2 on Alzheimer's Disease Pathology and Pathways
Guojun Bu, PhD
Hong Kong University of Science and Technology (China)

Understanding Alzheimer's Risk and Immune Health in Heart Disease
Brittany Butts, PhD
Emory University
Co-Principal Investigator: Whitney Wharton, PhD

Neurostimulation to Improve Depression and Memory in Dementia
Davide Cappon, PhD
Hebrew Rehabilitation Center

Shining a Light on How Early Tau-Related Brain Changes Affect Memory Loss
Martin J. Dahl, PhD
Max Planck Institute for Human Development (Germany)

The Role of the Immune System in Driving Cognitive Decline
Hannah Ennerfelt, PhD
Stanford University

Identifying New Memory and Brain Markers for Early Alzheimer's Disease
Helena Gellersen, PhD
German Center for Neurodegenerative Diseases (Germany)

Identifying the Mechanisms That Underlie Tau Aggregation and Neurotoxicity
Sarah Kaufman, MD, PhD
University of California, San Francisco
Recipient, Dr. Edward H. Koo Postdoctoral Fellowship Award for Alzheimer's Disease Research

Does Alzheimer's Disease Accelerate Brain Aging?
María Llorens-Martín, PhD
Spanish National Research Council (Spain)

Decoding Alzheimer's Disease Genomes With Deep Learning
Tatsuhiko Naito, MD, PhD
Icahn School of Medicine at Mount Sinai

Uncovering How Gene Regulators Protect Neurons Against Alzheimer's
Raffaella Nativio, PhD
Imperial College of Science, Technology, and Medicine (UK)

Progranulin as a Potential Therapeutic Target for Alzheimer's Disease
Andrew D. Nguyen, PhD
Saint Louis University
Co-Principal Investigator: Susan Farr, PhD

The Role of the Brain Vascular-Immune Processes in Alzheimer's Disease
Julie Ottoy, PhD
Sunnybrook Research Institute (Canada)

The Role of Immune Cells' Interaction in Alzheimer's Disease Pathology
Emanuela Pasciuto, PhD
Flanders Institute for Biotechnology (Belgium)

Characterizing Factors That Induce Waste Clearance in Microglia
Anna Podlesny-Drabiniok, PhD
Icahn School of Medicine at Mount Sinai
Co-Principal Investigator: Alison Goate, DPhil

Evaluating the Role of the TDP-43 Protein in Alzheimer's Disease Pathogenesis
Mercedes Prudencio, PhD
Mayo Clinic Jacksonville
Co-Principal Investigator: Yongjie Zhang, PhD

Unlocking Tau's Secrets: Human Brain Cells in the Mouse Brain
Wenhui Qu, PhD
Weill Cornell Medicine

Staging Alzheimer's Disease Using Blood Samples
Gemma Salvadó, PhD
Lund University (Sweden)

The Role of the Immune System in Alzheimer's Disease
Paula Sanchez-Molina, PhD
Oregon Health & Science University

Understanding Tau Seeds: The Role of Protein Clumps on Membranes in Alzheimer's Disease
Sankalp Shukla, PhD
University of California, Berkeley

Increase of ADAM10 Protein Expression in the Brain as an Alzheimer's Disease Therapeutic
Jaehong Suh, PhD
Massachusetts General Hospital

Study of a Novel Genetic Risk Factor for Alzheimer's Disease
Giuseppina Tesco, MD, PhD
Tufts University
Recipient, Alzheimer's Disease Research Distinguished Investigator Award

Oxysterols in Innate and Adaptive Immunity in a Tauopathy Mouse Model
Danira Toral-Rios, PhD
Washington University in St. Louis

2024 Grant Awards

Macular Degeneration Research

Investigating AMD-Like Disease in Animal Models
Brittany Carr, PhD
University of Alberta (Canada)

Exosomes and Autophagy: Suspicious Partners in Drusen Biogenesis and AMD
Miguel Flores-Bellver, PhD
University of Colorado Anschutz Medical Campus
Recipient, Dr. Joe G. Hollyfield New Investigator Award for Macular Degeneration Research

Storing Fat in the Eye: A Pathway for Tackling AMD
John Han, PhD
University of Michigan Medical Center
Recipient, Helen Juanita Reed Award for Macular Degeneration Research

The Generation of Cone Photoreceptor Outer Segments
Heike Kroeger, PhD
University of Georgia

The Novel Role of an Intracellular Nuclear Receptor in AMD Pathogenesis
Neetu Kushwah, PhD
Boston Children's Hospital

Innovative Night Vision Tests for Age-Related Macular Degeneration
Maximilian Pfau, MD
Institute of Molecular and Clinical Ophthalmology Basel (Switzerland)

Development of a Transplant-Independent Therapy for RPE Dysfunction
Shintaro Shirahama, MD, PhD
Schepens Eye Research Institute of Massachusetts Eye and Ear

Exploring How NRF2 Protein Reduces RPE Cell Damage by Cigarette Smoke
Krishna Singh, PhD
Johns Hopkins University School of Medicine
Recipient, Elizabeth Anderson Award for Macular Degeneration Research

Understanding Early Molecular Events in Age-Related Macular Degeneration
Sandeep Moothedath Subrahmanian, PhD
Pennsylvania State University College of Medicine

Regeneration of Cone Photoreceptors in the Human Retina
Juliette Wohlschlegel, PhD
University of Washington

National Glaucoma Research

Saving Sight: A Journey to Healing Without Scars
Jennifer Fan Gaskin, MBChB, MD, FRANZCO
Centre for Eye Research Australia (Australia)
Co-Principal Investigators: Elsa Chan, PhD & Roy Kong, PhD

How the Microenvironment Affects Schlemm's Canal Cell Behavior
Samuel Herberg, PhD
SUNY Upstate Medical University
Recipient, Dr. Douglas H. Johnson Award for Glaucoma Research

The Role of Microtubules in Glaucomatous Schlemm's Canal Mechanobiology
Haiyan Li, PhD
Georgia Institute of Technology

The Impact of Glaucoma on Light-Mediated Mood and Sleep Disorders
Xiaorong Liu, PhD
University of Virginia
Co-Principal Investigator: Ignacio Provencio, PhD

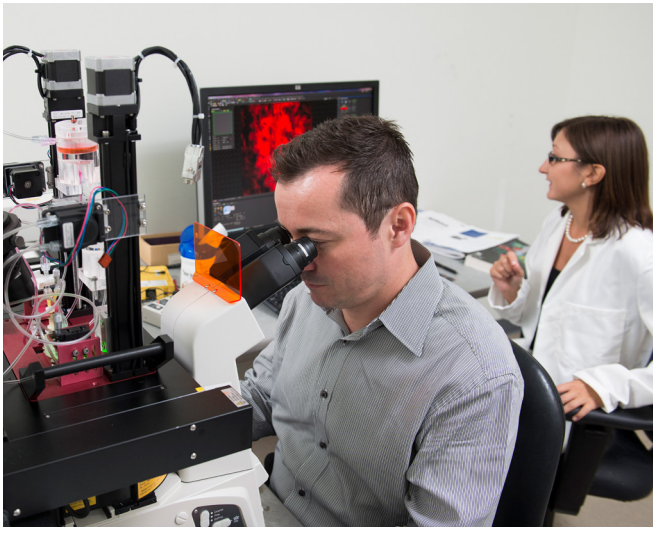
IOP-Related Gene Responses in the Optic Nerve Head and Trabecular Meshwork
Diana C. Lozano, PhD
Oregon Health & Science University
Co-Principal Investigator: Kate Keller, PhD

Retinal Ganglion Cell Axon Degeneration in a 3D Microfluidic Hydrogel Model
Shruti Patil, PhD
Indiana University

Pressure-Induced Axon Damage and Its Link to Glaucoma-Related Vision Loss
Bingrui Wang, PhD
University of Pittsburgh

Understanding How Variants in LOXL1 Affect Pseudoexfoliation Glaucoma Risk
Hannah Youngblood, PhD
Georgia Institute of Technology
Recipient, Thomas R. Lee Award for Glaucoma Research

Why Certain Retina Ganglion Cells Stay Strong in Glaucoma
Mengya Zhao, PhD
University of California, San Francisco



All grants will be awarded pending conclusion of contract negotiations.

Explore the Research

Special Thanks to Donors Supporting Ongoing Awards

Alzheimer's Disease Research

Revealing Early Biomarkers in Alzheimer's
Uri Ashery, PhD
Tel Aviv University (Israel)
Co-Principal Investigator: Shahar Alon, PhD,
Bar-Ilan University (Israel)
This award is supported by the Luminescence Foundation.

The Impact of Midlife Cardiovascular Health on Brain's Well-Being
Marta Cortes-Canteli, PhD
Spanish National Centre for Cardiovascular Research (Spain)
Co-Principal Investigators: Valentine Fuster, PhD & Juan Domingo Gispert, PhD
This award is supported by the Sephardic Foundation on Aging.

A Novel Test for Alzheimer's Based on DNA Circulating in Blood
Yuval Dor, PhD
Hebrew University of Jerusalem (Israel)
This award is supported by the Sephardic Foundation on Aging.

Macular Degeneration Research

Regenerative Response in Spiny Mice
Manas R. Biswal, PhD
University of South Florida
This award is supported by the Free Family Foundation.

Identifying FDA Approved Drugs to Reverse Dry AMD
Steffi Daniel, PhD
University of Minnesota, Twin Cities
This award is supported by the Ivan Bowen Family Foundation.

Scientific Review Committees

World-Class Experts Drive Research Advancements

Composed of renowned leaders in their fields, our Scientific Review Committees recommend new research opportunities for BrightFocus to advance its goal of defeating Alzheimer's disease, macular degeneration, and glaucoma. The following experts have served on each committee within the last five years:

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Ksenia Kastanenka, PhD Massachusetts General Hospital
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Edward Koo, MD University of California, San Diego
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Gopal Thinakaran, PhD University of South Florida
Robert Vassar, PhD Northwestern University
Cheryl Wellington, PhD University of British Columbia
Donna Wilcock, PhD Indiana University School of Medicine
Benjamin Wolozin, MD, PhD Boston University
Tony Wyss-Coray, PhD Stanford Medicine
Riqiang Yan, PhD University of Connecticut School of Medicine
Na Zhao, MD, PhD Mayo Clinic Jacksonville
Xiongwei Zhu, PhD Case Western Reserve University

Macular Degeneration Research

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John D. Ash, PhD University of Pittsburgh School of Medicine
Catherine Bowes Rickman, PhD Duke University
Kristen Bowles-Johnson, OD, PhD Indiana University
Milam Brantley, MD, PhD Vanderbilt University
Karl Csaky, MD, PhD Retina Foundation of the Southwest
Itay Chowers, MD Hadassah Medical Center (Israel)
Sarah Doyle, PhD Trinity College (Ireland)
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Lois Smith, MD, PhD Boston Children's Hospital
Karl Wahlin, PhD University of California, San Diego

National Glaucoma Research

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Monica Vetter, PhD University of Utah
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Community Engagement and Outreach

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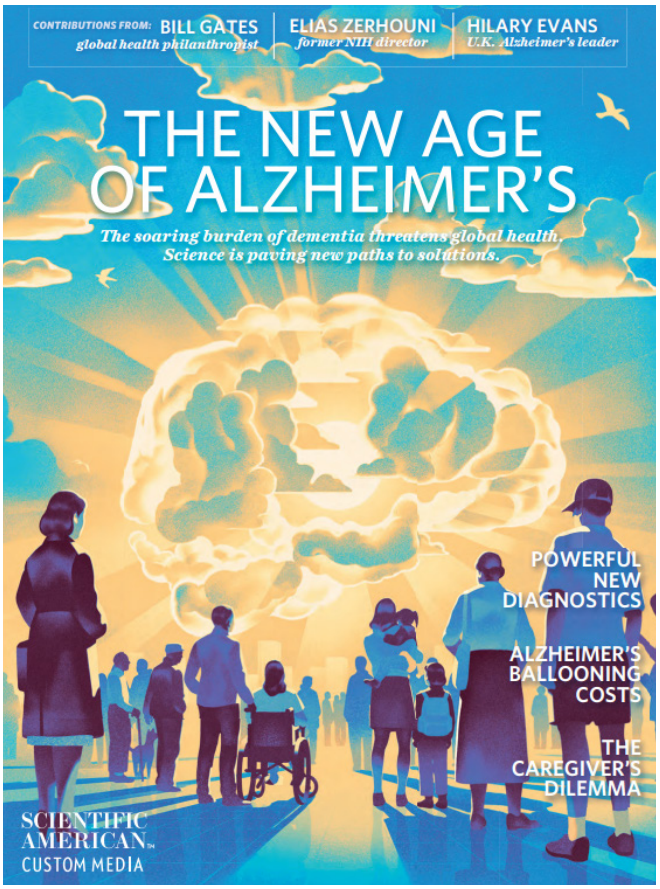
2

BrightFocus Chats

3



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Expanding Access to Free Brain and Eye Health Information

In 2023-24, BrightFocus Foundation reached hundreds of thousands of people worldwide through free public outreach and educational efforts around brain and eye health.

1. **Zoom In on Dementia & Alzheimer's**, our monthly virtual discussion series featuring world-class research scientists, captivated audiences with the latest breakthroughs and findings in the field. In 2023-24, episodes covered topics such as risk reduction, nondrug interventions, genetics, clinical trials, diagnosis, and new treatments and garnered nearly 350,000 views. Pictured: *Zoom In* host **Nancy Lynn**, senior vice president of strategic partnerships at BrightFocus, spoke with **Dr. Jeffrey Cummings**, Joy Chambers-Grundy Professor of Brain Science at the University of Nevada, Las Vegas, about the state of Alzheimer's clinical trials in 2024. Learn more at **brightfocus.org/ADZoom**.

2. **BrightFocus Chats**, our popular audio series connecting people with vision diseases to doctors and researchers, explores topics across macular degeneration and glaucoma. In 2023-24, more than 164,000 people participated in a Macular Chat or Glaucoma Chat, with topics ranging from eyedrop techniques to how artificial intelligence is being used to improve the detection of age-related eye diseases. All past episodes are available at **brightfocus.org/chats**.

Health Equity Takes Center Stage

3. BrightFocus partnered with the Davos Alzheimer's Collaborative for a special issue of *Scientific American*, **The New Age of Alzheimer's**, which reported on the advances fueling hope for ending this devastating disease. An article titled "A Grassroots Approach to Clinical Trial Diversity" featured BrightFocus' community engagement in Valdosta, Georgia, to help reverse decades of underrepresentation of people of color in clinical trials by building trust among clinicians, researchers, and members of the community.

4. On October 13, BrightFocus and the International African American Museum (IAAM) hosted "Small Miracles: A Promise Toward a Future of Health and Wellness," an in-person and live-streamed panel discussion in Charleston, South Carolina, on advancing health equity. BrightFocus' **Stacy Pagos Haller** and **Nancy Lynn** joined IAAM President and CEO **Dr. Tonya Matthews**, dementia advocate **Dr. Debra Tann**, and Medical University of South Carolina's **Dr. Marvella Ford** for a discussion on the tactics, strategies, and small miracles needed to help people within the Lowcountry—and millions across the nation—reap the benefits of today's medical breakthroughs.

Investment in Scientists

Nurturing the Next Generation of Researchers

BrightFocus is broadening access to science and fostering the next generation of rising stars. In 2023-24, we funded 159 travel fellowships to enable scientists from diverse backgrounds to attend conferences to share their research and facilitate global collaboration.

Our unique **Fast Track workshops** introduce promising new investigators to hot topics and leaders in the field, providing them with unprecedented networking opportunities and teaching them how to write a successful grant proposal.

Sarah Mattap presents her research at an Alzheimer's conference in Krakow, Poland.

"I want to thank BrightFocus Foundation for sponsoring my trip to Krakow, Poland, to attend the Global Conference of Alzheimer's Disease International. Without their generous help, I wouldn't have been able to attend and share my research papers, learn about recent developments in dementia, and create a network with other researchers in the field. **Thank you for supporting early-career researchers like me.**"

Sarah Mattap
Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia

Early-career scientists at BrightFocus' Alzheimer's Fast Track 2023 in Washington, D.C.

Partnerships

Our Valued Partners

BrightFocus works closely with nonprofit and corporate partners on issues of common concern.

Action Against AMD
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AgeWave
Alexion
Alkeus Pharmaceuticals
Alliance for Aging Research
Alzheimer's Los Angeles
Alzheon
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AOPT
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CIHR IRSC Canadian Institutes of Health Research
Dementia Friendly America
Drusolv Therapeutics
Eisai
FNIH
Gates Ventures
Genentech
GHR Foundation
tgf The Glaucoma Foundation
Glaucoma Research Foundation
Helen Keller Foundation
HFC Hilarity for Charity
ISER International Society for Eye Research
ISMND
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The Sephardic Foundation on Aging
UsAgainstAlzheimer's
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Global Alzheimer's Collaborations Foster Scientific Growth

BrightFocus has worked with partners across Western Europe to advance research and raise public awareness of Alzheimer's disease:

BELGIUM
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Alzheimer Forschung Initiative e.V.

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THE NETHERLANDS
Alzheimer Nederland

Our Supporters Make Research Possible

The support of individual donors, family foundations, and corporate partners makes our work possible. A wide range of contribution opportunities is available to accommodate resources and charitable goals. Each gift is vital in that it helps us find a cure for these diseases of mind and sight.

DONOR SPOTLIGHT Paying It Forward

Barbara Shapiro and her husband, Bernie

Barbara Shapiro is an active 85-year-old world traveler who spent her last birthday on a vacation cruise with loved ones to Athens and Istanbul. She's lived with glaucoma for the past 40 years and lost her husband, Bernie, to Alzheimer's disease in 2009. When Bernie was diagnosed with Alzheimer's, other people who had experience with it helped him understand the disease and his treatment options. He felt the drive to pay it forward and help others—and Barbara was eager to join him in this pursuit. "We were quite active," she said. "Bernie wanted to do things, and he wanted to help however he could. He was in several clinical trials for Alzheimer's. We did public speaking for Alzheimer's."

Bernie and Barbara spoke at Harvard Medical School, which hosted a multidisciplinary class to talk about Alzheimer's. They shared their firsthand experiences to help inform scientists and health care professionals about what it's like to live with this disease.

"What we stressed, and what I think is just so important, especially with Alzheimer's, is that you can't do it alone," Barbara said. "It has to be a multidisciplinary approach. It has to be as much of the community as you can involve."

Barbara's perspective on a community approach to Alzheimer's applies to emotional well-being, too. Having a sense of community is important to families affected by Alzheimer's who often benefit from joining support groups where they can meet others in a similar situation and understand that they are not alone in their experiences. "It's a wonderful mechanism for all involved," she said.

Barbara felt this sense of community with Bernie's Alzheimer's diagnosis, yet when she was diagnosed with glaucoma, she discovered that there wasn't the same level of community support for the disease. Her experience with glaucoma has been "a solitary journey with just me and my physician." Driven by her personal experiences, Barbara has donated to Alzheimer's Disease Research and National Glaucoma Research for the past 10 years. She wants to support research that can help her, and others currently impacted by these diseases, as well as those who might be affected in the future. "Sponsoring innovation is what is needed. For many years, we've been looking at both glaucoma and Alzheimer's in a much narrower focus than we are now," she said.

BrightFocus Foundation is also working to find a cure for age-related macular degeneration, a neurodegenerative disease that Barbara's daughter-in-law was diagnosed with just this year. Barbara said she supports BrightFocus research programs specifically because "they use so many different disciplines, both medical and scientific, to look at these diseases, which I think is very important." She added, **"This is an organization that I feel confident uses the money that is donated in a very positive way. It has done a lot of good and is funding scientists on the cutting edge."**

DONOR SPOTLIGHT

From the Classroom to Caregiving

Janet Tussing

Janet Tussing feels her calling is to help others lead a better life. She has dedicated her life to helping others, as demonstrated by her 34 years as a schoolteacher, by her position as a trustee and charter member of her church, and by being a caregiver to her loved ones. This calling, coupled with seeing her own family members suffer from age-related diseases, is what inspires her to support two BrightFocus Foundation programs, Macular Degeneration Research and Alzheimer's Disease Research.

Janet's parents were also educators—her mother was a schoolteacher and her father was a school principal. When her mother was diagnosed with macular degeneration in 2000, Janet decided to help take care of her. She felt it was part of her obligation to improve her parents' quality of life and follow their example of caring for others. "My mother always tried to take better care of [other] people than herself," she said. Her mother's journey started with cataract surgery, after which, the family believed, she would begin to see more clearly. And she did—for a short time. "She had three days that she felt and saw really nice colors and could read. She was so delighted," said Janet. "Then about three days later, she got the diagnosis that it was really a severe case of macular degeneration."

Janet has seen the effects that vision loss can have on a person's life not only with her mother but also with her brother, who regularly receives eye injections for macular edema. She donates to Macular Degeneration Research as a part of her mission to help people have better vision and a better life. Janet believes strongly in the power of research to help those living with vision loss. "If you have macular degeneration, all the things you've enjoyed during your life are gone," she said. "You can't read. My mother loved reading and she taught third grade, so she really enjoyed that."

Janet's mother passed away in 2005 at the age of 90. Janet also served in a caregiving role for her husband, who was diagnosed with Alzheimer's disease. To help others affected by this disease, Janet donates to Alzheimer's Disease Research in the hope of finding a cure. For Janet, help can come by means of providing valuable information (e.g., knowing the first steps to take after a diagnosis) or through research (e.g., supporting better treatments).

She remarked, **"I've watched many people who are having problems. I think that anything we can do to help them see or think better is how we all should help. We enjoy our life and people with macular degeneration or Alzheimer's need help too. Please donate at brightfocus.org."**

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Financial Highlights

BrightFocus is a nonprofit organization designated under Section 501(c)(3) of the Internal Revenue Code. All contributions to BrightFocus and its programs are tax deductible to the extent allowed by law. The Foundation is supported entirely by voluntary private contributions.

BrightFocus received in-kind donations to expand public health information outreach; these are included in Program Services expenses, which have allowed the organization to reach millions of people with information about risk factors, treatments, and caregiving.

BRIGHTFOCUS FOUNDATION AND SUBSIDIARIES

CONSOLIDATED STATEMENT OF FINANCIAL POSITION 2024

As of March 31, 2024 (in thousands of dollars)

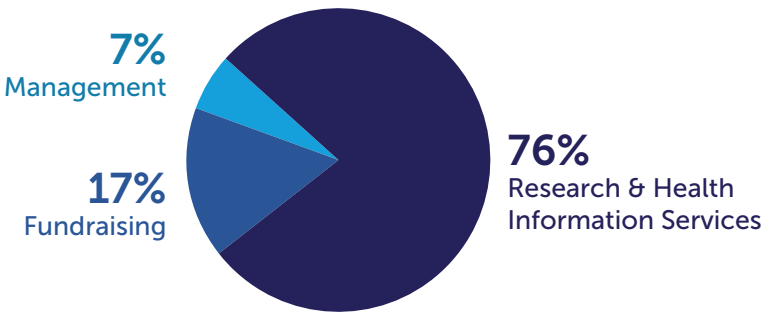
ASSETS	
Cash and Investments	$48,368
Charitable Trusts and Bequests Receivable	$5,245
Rental Property	$3,594
Fixed Assets, Net	$4,253
Other Assets	$2,005
TOTAL ASSETS	$63,465
LIABILITIES	
Accounts Payable and Other Liabilities	$2,718
Grants Payable	$24,992
Outanding Line of Credit	$9,000
Charitable Gift Annuities	$536
TOTAL LIABILITIES	$37,246
NET ASSETS	
Without Donor Restriction	$12,271
With Donor Restriction	$13,948
TOTAL NET ASSETS	$26,219
TOTAL LIABILITIES AND NET ASSETS	$63,465

CONSOLIDATED STATEMENT OF ACTIVITIES

For the Fiscal Year Ended March 31, 2024

(in thousands of dollars)

SUPPORT AND REVENUE	
Contributions and Grants	$35,399
Bequests	$7,724
Donated Services	$24,714
Investment Income	$4,334
Rental & Other Income	$1,273
TOTAL SUPPORT AND REVENUE	$73,444
EXPENSES	
Program Services	
Health Information Services	$36,919
Research	$16,726
Total Program Services	$53,645
Supporting Services	
Fundraising	$12,201
Management and General	$4,941
Total Supporting Services	$17,142
TOTAL EXPENSES	$70,787
CHANGE IN NET ASSETS	$2,657



A complete copy of financial statements audited by Marcum, LLP, is available upon request from BrightFocus Foundation, 22512 Gateway Center Drive, Clarksburg, MD, 20871, or at ***brightfocus.org****.*

"I am profoundly grateful to the BrightFocus donors, whose generous support and unwavering commitment to research make this critical work possible. Their contributions fuel our efforts and inspire hope, driving us to continue our mission with renewed vigor and determination. **Thank you for believing in the power of science to change lives.**"

Gemma Salvadó, PhD
Alzheimer's Disease Research Grant Recipient

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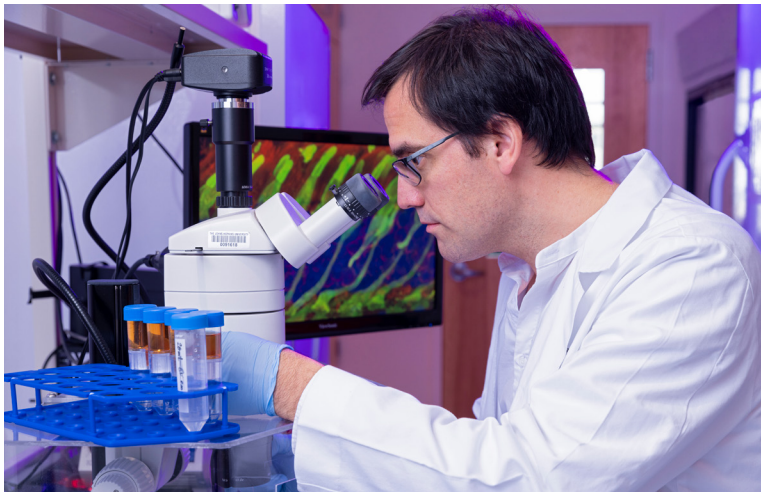

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Alzheimer's Disease Research

Macular Degeneration Research

National Glaucoma Research

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