

2020 Annual Report | Alzheimer's Disease Research | Macular Degeneration Research | National Glaucoma Research



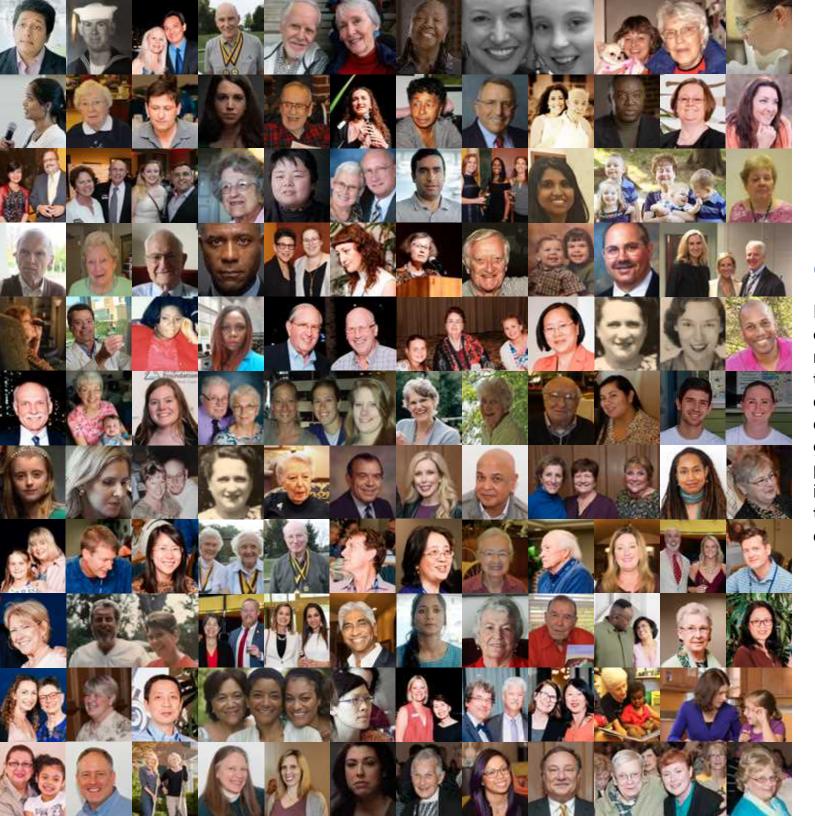
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Over 322 Million Impacted.

Which is why we'll never quit.

In 2020, an estimated 322 million people worldwide are currently living with Alzheimer's, macular degeneration and/or glaucoma. Our three scientific research programs are *Alzheimer's Disease Research*, *Macular Degeneration Research*, and *National Glaucoma Research*.



Our Mission

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

DEAR FRIENDS,

2020 has been a year of great adversity and uncertainty, and also a sharp reminder of how precious life is and how much we value both those we love and the experiences we treasure.

Our annual report is titled *This is Why*, because this year powerfully reaffirms why, at BrightFocus, we relentlessly pursue a mission of innovative science to save mind and sight, to better the quality of life for our children, grandchildren, and generations to come.

On the following pages, you will meet several of the many hundreds of researchers we have funded around the world. You will discover their "why" – what fuels their lifelong pursuit of the bold "what-if's" of scientific discovery.

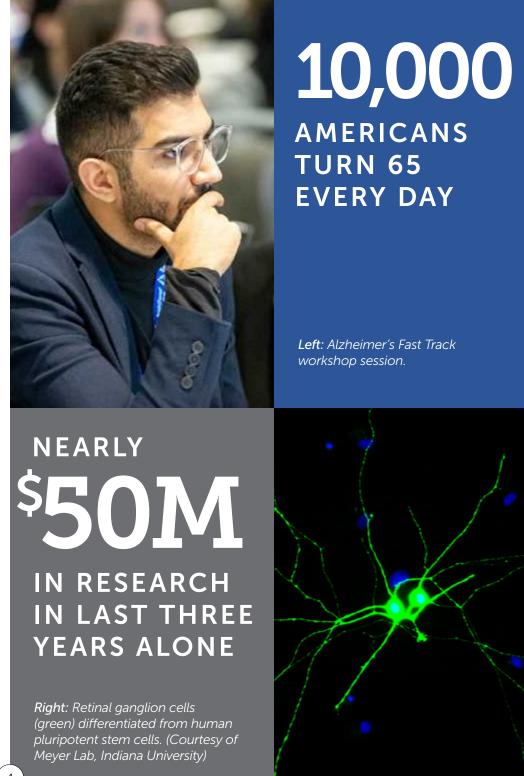
You will meet several of the many thousands of donors across the country who each year support BrightFocus and its three scientific programs: Alzheimer's Disease Research, Macular Degeneration Research, and National Glaucoma Research. Their generosity and loyalty inspire us daily, a shared belief that research equals hope.

More than ever, the need for innovative science is abundantly clear. This is why in 2020 we awarded \$17.8 million for 93 new grants, a single-year record level of support, with 70 percent going toward testing the bold ideas of early-career researchers.

We hope *This is Why* gives you a glimpse into the creativity and brilliance of the scientists we partner with, and the selfless, unyielding commitment of our donors, staff, and Board. No matter how great the challenges may seem, we fully believe there will be a day when these diseases become a thing of the past.

Stacy Pagos Haller
President and CEO

Patricia McGlothlin Stewart, CFP Chair, Board of Directors





FUNDING RESEARCH IN

25
COUNTRIES

Left: Marilyn Nadolny, one of our Donor Spotlights. (featured on page 30)



93 NEW RESEARCH GRANTS

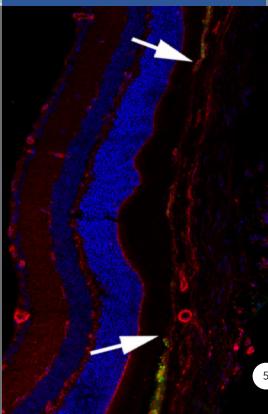
Left: Colleen McDowell, PhD, University of Wisconsin-Madison at Glaucoma Fast Track.

Below: Neurons and astrocytes. (Courtesy of Dominik Paquet, PhD, Ludwig Maximilian University of Munich, Germany)

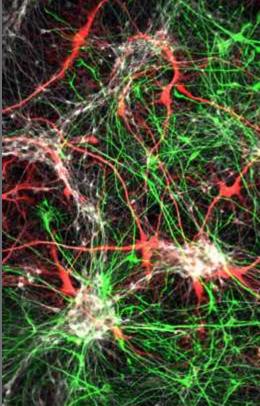
OVER **220**

RESEARCH PROJECTS

Right: A cross section of central retinal-pigmented epithelium region with atrophy, as seen by the loss of green color (between two arrows), marking retinal-pigmented epithelium cells. The optic nerve head (ONH) at the top indicates that the section is in the center. (Courtesy of Claudio Punzo, PhD, University of Massachusetts Medical School)

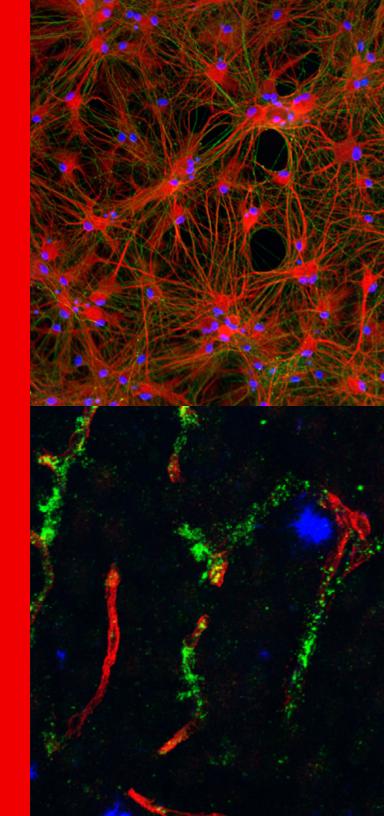


OF NEW
GRANTS WILL
TEST THE
BOLD IDEAS
OF EARLYCAREER
RESEARCHERS



Every day more than 1,300 **Americans** develop Alzheimer's disease.

In 2020, BrightFocus awarded more than \$11 million in funding for 53 new Alzheimer's research grants.



5.8 million

people live with Alzheimer's in the United States today and by 2050 there will be close to

15 million.





Above left: Alzheimer's Fast Track® workshop session. **Above right:** Alzheimer's Fast Track Co-chairs (left to right): Harry Steinbusch, PhD; Cynthia Lemere, PhD; Stacy Pagos Haller; Diane Bovenkamp, PhD; and Frank LaFerla, PhD.

Incubator for Promising Researchers

Nearly 90 scientists from across the globe attended the latest BrightFocus Alzheimer's Fast Track® workshop in October 2019. Bringing together preeminent Alzheimer's disease experts with graduate students, postdoctoral fellows or other early career scientists, they reviewed the latest discoveries and research directions and fostered new

collaborations to accelerate progress toward treatments and cures.

"Alzheimer's Fast Track is an immersive learning opportunity specifically created for scientists who are starting or contemplating a career in Alzheimer's research," said Diane Bovenkamp, PhD, BrightFocus Vice President, Scientific Affairs.

Page 6 top: This 3-D "Alzheimer's-in-a-dish" collection of blue, green and red brain nerve cells is for studying the causes of protein clumping or nerve cell death. (Courtesy of Dominik Paquet, PhD, Ludwig Maximilian University of Munich, Germany)

Page 6 bottom: Reducing the excitability of brain neurons with a repurposed drug may reduce amyloid-beta deposits in Alzheimer's (nerve cells in green, blood cells in red and amyloid plaques in green). (Courtesy of Shannon Macauley, PhD, Wake Forest University)



In pre-pandemic days, Dr. Patrick Kehoe takes the podium at a scientific conference in Japan. His groundbreaking BrightFocus-funded research is among the first to examine biological links between Alzheimer's and hypertension, with relevance to COVID-19.

Groundbreaking Insights Into Alzheimer's and Hypertension

Patrick Kehoe, PhD, Gestetner Professor of Translational Dementia Research at the University of Bristol, UK, a current Alzheimer's Disease Research grantee, is exploring molecular links between hypertension and Alzheimer's, and whether some existing drugs could be repurposed as Alzheimer's treatments.

His findings, published in early 2020, were viewed in an even broader light than might have been imagined because of their potential relevance to the COVID-19 disease process and treatments being developed.



Kristine Yaffe, MD, University of California, San Francisco being interviewed by Richard Lui, MSNBC on World Alzheimer's Day.

Marking World Alzheimer's Day

Appearing on an MSNBC program, University of California, San Francisco researcher and former Alzheimer's Disease Research grantee, Kristine Yaffe, MD, joined MSNBC anchor Richard Lui on a segment to mark World Alzheimer's Day. She shared key scientific findings of the increased dementia risk for military veterans who sustained traumatic brain injury.

Dr. Yaffe sees patients and conducts research through her roles as a UCSF professor and chief of Geriatric Psychiatry and director of the Memory Evaluation Clinic at the San Francisco Veterans Affairs Medical Center.



Virginia M.Y. Lee, PhD, University of Pennsylvania.

Renowned Alzheimer's Researcher Wins "The Oscars of Science"

University of Pennsylvania professor Virginia M.Y. Lee, PhD, who helped develop and guide BrightFocus Foundation's Alzheimer's Disease Research program, won a 2020 *Breakthrough Prize in Life Sciences*. The prize, known as the "The Oscars of Science," recognizes her research leading to new avenues for potential drug discovery and development.



"BODY WEIGHT LOSS IS A COMMON FEATURE OF ALZHEIMER'S DISEASE THAT WORSENS AS ALZHEIMER'S PROGRESSES."

Guided by his Grandmother's Experience

Makoto Ishii, MD, PhD, of Weill Cornell Medicine, is shedding new light on why Alzheimer's can lead to weight loss, particularly early in the course of the disease.

Ishii is running a clinical trial analyzing blood and spinal fluid samples from cognitively healthy volunteers who have the earliest pathological signs of Alzheimer's and comparing those samples to healthy individuals who lack Alzheimer's pathology. Through his research, Ishii hopes to explore new avenues for developing better diagnosis and treatment of the disease.

He has seen the awful impact of Alzheimer's up close. When watching the progression of his grandmother's disease, he not only noticed her loss of identity and independence, but also that she shed a significant amount of weight despite eating what appeared to be her normal amount of food.

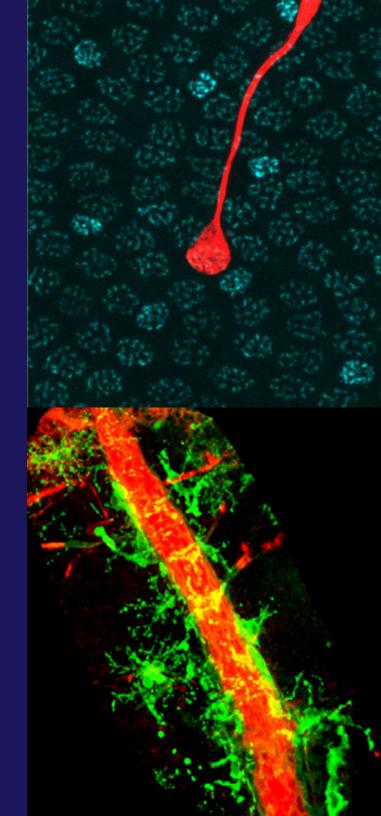
"As a grandson, I feel at times helpless as my grandmother's dementia continues to worsen," said Ishii. "As a clinician-scientist, I see the potential advances we can make by exploring clinical observations that can help solve the complexities of Alzheimer's disease."

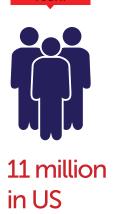
Ishii began his connection to BrightFocus by attending *Alzheimer's Fast Track*, its signature program to identify and train the most promising early-career scientists in the field.

Grateful for a grant from the foundation's Alzheimer's Disease Research program, he aims to make, "a broader contribution to the large community of clinicians, research scientists, tireless family caregivers, and most importantly to the patients like his grandmother, who are all battling this devastating disease."

Age-related Macular Degeneration is a leading cause of irreversible vision loss in the United States, and for Caucasians over age 40, it is the leading cause of blindness.

In 2020, BrightFocus awarded \$3.5 million in funding for 22 new macular degeneration research grants.







BY 2050



Sharing Guidance with Families

Our free, monthly telephone call-in series, *BrightFocus Chats,* features the latest news and advice for those living with vision loss. Researchers, clinicians, and low vision specialists share their tips and answer questions from participants via phone or online. The *Chats* are archived at <u>BrightFocus.org</u>.

A recent telephone discussion featured Michael B. Gorin, MD, PhD, an ophthalmologist from UCLA devoted to research and clinical care of hereditary retinal disorders, especially age-related macular degeneration, retinal dystrophies and other medical retinal conditions.

Noting both patients' questions and concerns, as well as changes in vision care during the pandemic, Dr. Gorin cautioned, "It is very important that we do not lose ground in maintaining your sight going forward."

Page 10 top: Shown in red is a cone photoreceptor on an array of other cone terminals, responsible for high-definition central vision, the kind lost in macular degeneration. (Courtesy of Mrinalini Hoon, PhD and Raunak Sinha, PhD, University of Wisconsin) Page 10 bottom: Inflammation is a major player in AMD, where fragile, leaky blood vessels damage retinal cells. Here, immune cells (green) interact with blood vessels (red) in an animal retina. (Courtesy of David Alvarez, PhD Harvard Medical School, and Ye Sun, MD, PhD)



Michael B. Gorin, MD, PhD, UCLA, shared tips on vision care during the pandemic with Chat listeners.



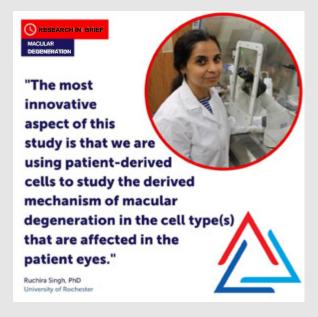


Diane Bovenkamp, PhD, BrightFocus Vice President, Scientific Affairs, at the podium during the Geroscience Summit 2019.

BrightFocus Takes Leadership Role at Geroscience Summit

Diane Bovenkamp, PhD, BrightFocus Vice President, Scientific Affairs, addressed the third NIH Geroscience Summit on how the field of geroscience (the relationship between aging and most age-related diseases) intersects with the mission of improving health and well-being in later years, and advancing cures for diseases of aging, specifically of mind and sight. "What's really relevant for today's geroscience summit is that age is the number one risk factor for Alzheimer's, macular degeneration, and glaucoma," said Bovenkamp. "Time lost is vision lost and cognition lost."

An action plan for moving forward on personalized medicine, preventive medicine and diseasebased research will be published in the future.



BrightFocus grantees' discoveries are shared with the world on our social media channels.



Take 5 is a new feature on our website that reveals the personal side of our grantees and expert contributors.



Working Toward a New Treatment for AMD

"I WOULD
LIKE TO SAY
A MASSIVE
THANK YOU FOR
GIVING ME THE
OPPORTUNITY
TO DO THE
RESEARCH THAT
I LOVE DOING."

A professor at the Institute of Neurosciences at Trinity College Dublin, Sarah Doyle, PhD, focuses her research on investigating the role of inflammation in advanced forms of age-related macular degeneration (AMD), a leading cause of blindness.

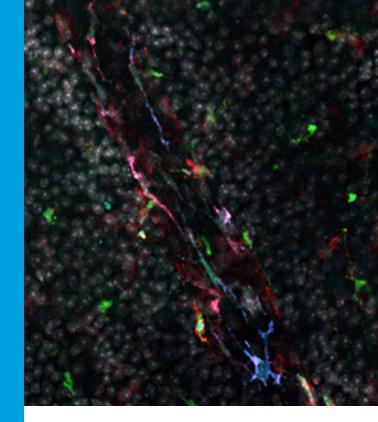
According to Doyle, "The more we understand about the disease processes underlying AMD, the better we'll be to contribute to new treatments. Our work on a therapeutic for wet AMD continues, and we are hopeful that our research can lead to a new way for treating this condition."

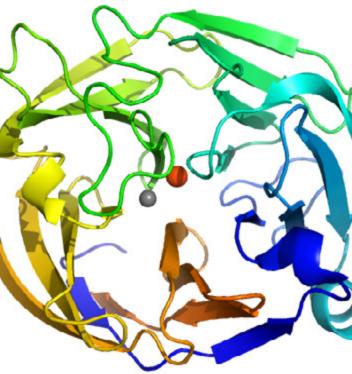
Doyle serves as one of the world's experts in AMD as a reviewer on the BrightFocus Macular Degeneration Research Scientific Review Committee. She has served as an investigator and co-investigator on past-BrightFocus projects.

The support of Macular Degeneration Research, a BrightFocus program, has been key to her research. "I would like to say a massive thank you for giving me the opportunity to do the research that I love doing," said Doyle. "I can't imagine what it would be like to lose my sight... to be able to help people keep their sight would be amazing."

Glaucoma is the second leading cause of irreversible blindness worldwide, and shows increased risk for Hispanics and African Americans according to the World Health Organization.

In 2020, BrightFocus awarded more than \$3 million in funding for 18 new glaucoma research grants.





Today, more than **3 million** Americans have glaucoma. By 2050, it is estimated that the number will double to

6 million people





Forum for Rising Researchers

BrightFocus held its second Glaucoma Fast Track[™] to accelerate the fight for a cure by investing in promising young scientists in the field of vision research.

The Glaucoma Fast Track featured world-renowned glaucoma experts who are known for their research

and/or clinical expertise, as well as their mentoring skills. Together, they reviewed the latest discoveries and research directions, and inspired new thinking and interdisciplinary approaches in the search for cures.

Page 14 top: Gene therapy is being explored as a way to rebalance immune factors in the eye that could protect against glaucoma. In this animal model showing neurons (white), microglia (green), and varied gene expression (multicolored), it's shown some success. (Courtesy of Alejandra Bosco, PhD, University of Utah). **Page 14 bottom:** A BrightFocus-funded team was first to unveil the 3D structure of myocilin, a protein linked to inherited forms of glaucoma, to shed light on how it becomes misshapen through genetic miscoding. (Courtesy of Raquel Lieberman, PhD, Georgia Institute of Technology)

Above left and center:

Glaucoma Fast Track™ attendees at the Emory Conference Center.

Above right: Jessica Cooke Bailey, PhD, Case Western Reserve University School of Medicine is interviewed by Richard Lui. MSNBC.



BrightFocus Town Hall on Challenges of COVID-19 and Older Adults

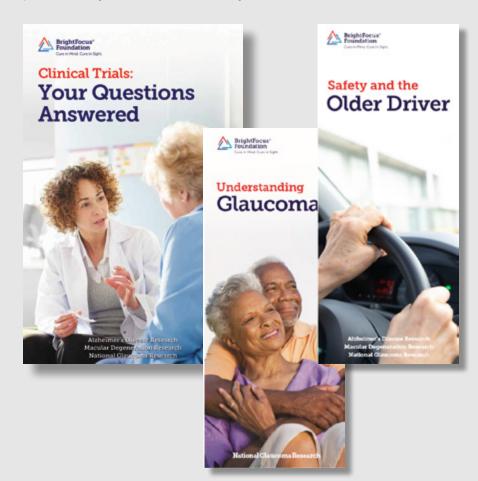
BrightFocus held a virtual town hall on *COVID-19* and *Older Adults* to address topics like long-distance caregiving, tele-health, social isolation and anxiety disproportionately affecting aging adults. The program featured guests Scott Kaiser, MD, a noted geriatrician and Chief

Innovative Officer with the Motion Picture & Television Fund, and Art Taylor, CEO of the Better Business Bureau's Wise Giving Alliance, and moderator Cecilia Arradaza, a leading health and science communicator and Executive Director, Strategy, Wondros.

Resources for Families

Resources for families to better understand, manage and engage with loved ones who are impacted by diseases of mind and sight, are available free for download at BrightFocus.org or upon request by email to info@brightfocus.org.

BrightFocus also has a trial finder tool on our website, powered by *Antidote*, to identify local clinical trials.





SHE SEES HER
WORK AS A "WAY
TO HONOR MY
GRANDFATHER...
AN OPHTHALMOLOGIST WHO
PROVIDED EYE
TREATMENT TO
ABORIGINAL
AUSTRALIANS."

Unlocking the Genetics of Glaucoma in Africa

Working to save sight, National Glaucoma Research is supporting Kathryn Burdon, PhD, of Australia's University of Tazmania and Girum Gessesse, MD, of Ethiopia's St. Paul's Hospital Millennium Medical College to expand our scientific understanding of glaucoma in Africa.

The majority of glaucoma research has studied white populations in Europe and in the United States. Now, with this upcoming study, scientists will examine the genetic variants of African populations in hopes of better meeting the needs of those at a higher risk of vision loss, while also reducing the medication burden for those at lower risk. Their work will begin by focusing on patients in Ethiopia, and then broaden by comparing their research findings with other studies of African populations.

"Although Sub-Saharan Africa is with the highest prevalence of glaucoma with particularly

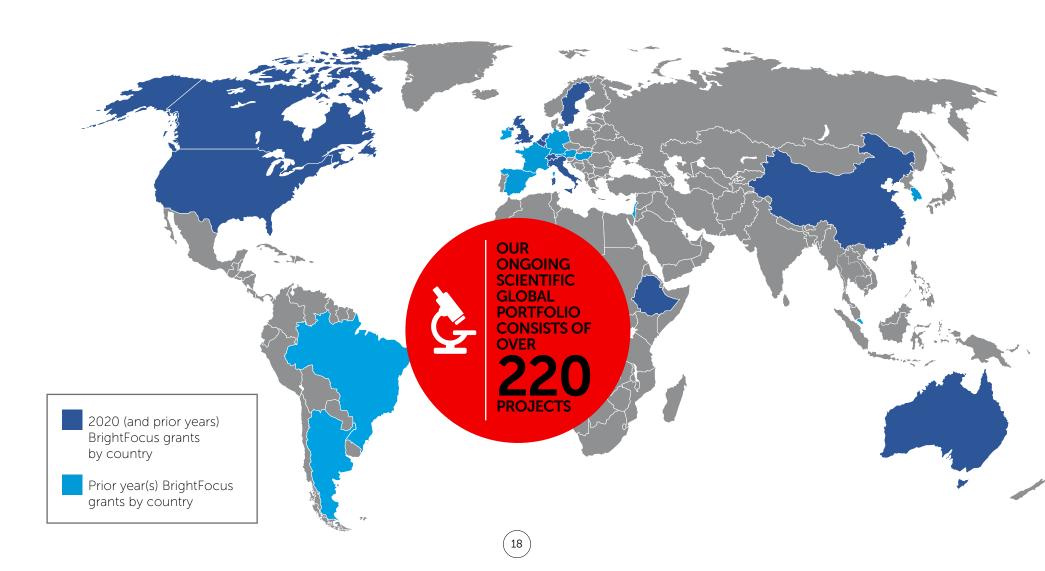
worse outcome, research undertakings on the disease are very limited in the region. We need to do much more," said Gessesse. "Research on glaucoma is very important for better understanding of the clinical, epidemiological and genetic nature of the disease, for evidence-based decision-making in our clinic work, and also for planning and policy making by the government."

Burdon credits her grandfather for her inspiration. "He was an ophthalmologist who provided eye treatment to Aboriginal Australians to ensure they got the care they needed. When the opportunity came up to do a PhD in the genetics of eye disease, it seemed like the perfect way to combine my interests and honor the earlier work of my grandfather preventing blindness. I still strive towards this goal every day."

These new research awards that were offered total

more than \$17.8 million

in 2020, part of our ongoing scientific portfolio of over 220 projects, nearly \$50 million investment in research worldwide in the past three years alone.



2020 BrightFocus Grants at a Glance

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

TRANSLATIONAL – Research to move findings from the lab bench to the "bedside" by testing potential treatments.

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

51%
BASIC RESEARCH GRANTS

31%
TRANSLATIONAL RESEARCH GRANTS

18%
CLINICAL RESEARCH GRANTS

Alzheimer's Disease Research

Studying the Role of a Novel Innate Immunity Pathway in Inducing Brain Inflammation and Damage in Alzheimer's Disease

Sadaf Amin, PhD

WEILL CORNELL MEDICINE Fellowship Mentor: Li Gan, PhD

Understanding the Beneficial Role of Sleep in Cognitive Deficits

Christelle Anaclet, PhD UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL

Co-Principal Investigator: Heinrigh Gompf, PhD

Washing Alzheimer's Disease Off the Brain

Michele Cavallari, MD, PhD
HARVARD MEDICAL SCHOOL
& BRIGHAM AND WOMEN'S
HOSPITAL

Nanobodies Stabilizing
Fragile Molecular Machines
to Lower the Production
of Toxic Amyloid-Beta in
Alzheimer's Disease

Lucía Chávez-Gutiérrez, PhD VLAAMS INSTITUUT VOOR BIOTECHNOLOGIE (VIB), (BELGIUM) Examining How the TREM2 R47H Mutation Effects Microglial Lipid Content and the Interactions Between Human Microglia and Alzheimer's Disease Pathology Within the Brain

Christel Claes, PhD
UNIVERSITY OF CALIFORNIA,
IRVINE
Fellowship Mentor:
Mathew Blurton-Jones, PhD

Gene Correction as a Therapy for Frontotemporal Dementia (FTD) and Amyotrophic Lateral Sclerosis (ALS) Caused by the C9orf72 Mutation

Claire Clelland, MD, PhD
UNIVERSITY OF CALIFORNIA,
SAN FRANCISCO
Fellowship Primary Mentor:
Bruce Conklin, MD
UNIVERSITY OF CALIFORNIA,
SAN FRANCISCO/GLADSTONE
INSTITUTES
Fellowship Co-Mentor: Li Gan,
PhD
WEIL CORNELL MEDICINE

Is Hexokinase 2 a Molecular Link Between TREM2 Signaling and Microglial Activity in Alzheimer Disease?

Juan Codocedo, PhD INDIANA UNIVERSITY Fellowship Mentor: Gary Landreth, PhD The Role of Chemical Messenger Signaling in Removing Alzheimer's Pathology From the Brain

Scott Counts, MD
MICHIGAN STATE UNIVERSITY
Co-Principal Investigator:
Roxana Carare, MD, PhD
UNIVERSITY OF
SOUTHAMPTON (ENGLAND)

Protecting Brain Cells from Death using Lipid Metabolic Drugs as a New Treatment for Alzheimer's Disease

Simone Crivelli, PhD
UNIVERSITY OF KENTUCKY
Fellowship Mentor:
Erhard Bieberich, PhD
UNIVERSITY OF KENTUCKY
Fellowship Co-Mentor:
Pilar Martinez-Martinez, PhD
MAASTRICHT UNIVERSITY,
(THE NETHERLANDS)

Co-principal investigator and fellowship mentor institutions are listed if different than the PI.

Note: All grants will be awarded pending conclusion of contract negotiations.

Improving Cognitive Function in Alzheimer's Disease Therapy Using a Combinatorial Approach of Reducing Disease Progression and Increasing Memory

Brati Das, PhD
UNIVERSITY OF
CONNECTICUT HEALTH
CENTER
Fellowship Mentor:
Riqiang Yan, PhD

Mitochondrial Calcium Deregulation and Memory Loss in Alzheimer's Disease

Heng Du, MD, PhD
THE UNIVERSITY OF TEXAS AT
DALLAS

Identifying Therapeutic Targets and Biomarkers to Facilitate a Meaningful Therapy and a Pre-Symptomatic Alzheimer's Diagnostic

Mark Ebbert, PhD
MAYO CLINIC, JACKSONVILLE

Testing New Markers of Brain Function that May be Sensitive to Early Signs of Alzheimer's Disease in Older Adults Who Still Have Normal Cognition

Peter Fried, PhD

BETH ISRAEL DEACONESS

MEDICAL CENTER &

HARVARD MEDICAL SCHOOL

Understanding ApoE

Carl Frieden, PhD WASHINGTON UNIVERSITY IN ST. LOUIS

Evaluating the Role of Immune Cells in the Brain and a Related Protein, TREM2, on Alzheimer's Disease Pathology

Maud Gratuze, PhD
WASHINGTON UNIVERSITY IN
ST. LOUIS
Fellowship Mentor:
David M. Holtzman, MD

Identifying Aging and Alzheimer's Disease-Related Protein Changes in Skin Cells, Blood and Spinal Fluid That Can be Used as Markers of Disease or Therapeutic Targets

Chadwick Hales, MD, PhD EMORY UNIVERSITY

Unraveling the Biological Overlap of Alzheimer's Disease and Dementia with Lewy Bodies

Lenora Higginbotham, MD EMORY UNIVERSITY Fellowship Co-Mentor: Allan Levey, MD, PhD Fellowship Co-Mentor: Nicholas Seyfried, PhD

Co-principal investigator and fellowship mentor institutions are listed if different than the PI.

Investigating Coordinated Removal of Old and Synthesis of New Materials in Neurons and How These Processes are Disrupted in FTD

Sarah Hill, PhD

NATIONAL INSTITUTES OF
HEALTH/NINDS
Fellowship Co-Mentor:
Michael Ward, MD, PhD
Fellowship Co-Mentor:
Jennifer Lippincott-Swartz,
PhD
JANELIA RESEARCH CAMPUS,
HHMI

The Role of Signaling Factors That Modulate Immune and Metabolic Function in Alzheimer's Disease

Makoto Ishii, MD, PhD WEILL CORNELL MEDICINE

A Simple Blood Test to Identify Individuals at Risk of Developing Alzheimer's Disease

Thomas Karikari, PhD UNIVERSITY OF GOTHENBURG, (SWEDEN) Fellowship Mentor: Kaj Blennow, MD, PhD Fellowship Co-Mentor: Henrik Zetterberg, MD, PhD

Using OCTA Eye Imaging of Retinal Blood Vessels As Biomarker of Vascular Cognitive Impairment and Dementia

Amir Kashani, MD, PhD UNIVERSITY OF SOUTHERN CALIFORNIA, ROSKI EYE INSTITUTE

Non-Neuronal Contribution to Alzheimer's Disease

Ksenia Kastanenka, PhD MASSACHUSETTS GENERAL HOSPITAL & HARVARD MEDICAL SCHOOL

The Impact of the Exercise Hormone Irisin on Astrocytes in Alzheimer's Disease

Eunhee Kim, PhD
MASSACHUSETTS GENERAL
HOSPITAL & HARVARD
MEDICAL SCHOOL
Fellowship Mentor: Rudolph E.
Tanzi, PhD

Twisting Away Toxic Proteins in Alzheimer's Disease

John Koren, PhD UNIVERSITY OF FLORIDA, GAINESVILLE

A New Way to Measure How the Brain Uses Ketones as Fuel in Alzheimer's Disease

Lydia Le Page, DPhil, MChem UNIVERSITY OF CALIFORNIA, SAN FRANCISCO Fellowship Co-Mentor: Myriam Chaumeil, PhD Fellowship Co-Mentor: Ken Nakamura, MD, PhD

Circadian Regulation, Autonomic Function, and Alzheimer's Disease

Peng Li, PhD
BRIGHAM AND WOMEN'S
HOSPITAL & HARVARD
MEDICAL SCHOOL

Explore the Impacts of APOE Genotype Switching From apoE4 to apoE2 in the Periphery (Liver and Bloodstream) for Alzheimer's Disease Therapy

Chia-Chen Liu, PhD MAYO CLINIC, JACKSONVILLE

A New Method to Determine Alzheimer's and Parkinson's Toxins in the Lipid-Enriched Environment

Jinghui Luo, PhD
PAUL SCHERRER INSTITUTE
(PSI), (SWITZERLAND)

Targeting Blood Vessel Excitability to Reduce Tau Pathology in Alzhiemer's Disease

Shannon Macauley-Rambach, PhD
WAKE FOREST UNIVERSITY

Finding Aberrant Glial and Neuronal Dysfunctions that Promote Neurodegeneration in Alzheimer's Disease and Related Dementia

Elise Marsan, PhD UNIVERSITY OF CALIFORNIA, SAN FRANCISCO Fellowship Mentor: Eric L. Huang, MD, PhD Fellowship Co-Mentor: Arnold Kriegstein, MD, PhD

Identifying Groups of Alzheimer's Disease Patients with Slower Disease Progression

Justin Miller, PhD
BRIGHAM YOUNG
UNIVERSITY
Fellowship Mentor:
John S. K. Kauwe, PhD

Gene Changes in Individual Cells Assessed Across the Progression of Alzheimer's Disease

Michael Miller, MD, PhD
BRIGHAM AND WOMEN'S
HOSPITAL & HARVARD
MEDICAL SCHOOL
Fellowship Mentor:
Christopher Walsh, MD, PhD
BOSTON CHILDREN'S
HOSPITAL & HARVARD
MEDICAL SCHOOL

Validation of a Biomarker That Could Identify a Subset of Frontotemporal Dementia and Alzheimer's Disease Patients

Sarah Pickles, PhD MAYO CLINIC, JACKSONVILLE Fellowship Mentor: Leonard Petrucelli, PhD

A New Method That Uses the 3D Structure of the Human Genome to Identify the Genetic Basis of Alzheimer's Disease

Ivana Quiroga, PhD UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL Fellowship Mentor: Douglas Phanstiel, PhD

Investigating How Genetic Risk Contributes to Cerebrovascular Damage in Alzheimer's and Dementia

Alaina Reagan, PhD
THE JACKSON LABORATORY
Fellowship Mentor:
Gareth Howell, PhD

Using Astrocyte Factors to Prevent Synaptic Alterations in Alzheimer's Disease

Isabel Salas, PhD THE SALK INSTITUTE FOR BIOLOGICAL STUDIES Fellowship Mentor: Nicola Allen, PhD

Deciphering the Alzheimer's Disease Glyco-Code

Manveen Sethi, PhD BOSTON UNIVERSITY Fellowship Mentor: Joseph Zaia, PhD

Role of Platelet-Derived Factors in Ameliorating Alzheimer's Disease Pathology

Saul Villeda, PhD UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

Understanding the Role of Lysosome in Brain Function and Alzheimer's Disease

Shuo Wang, PhD
BAYLOR COLLEGE OF
MEDICINE
Fellowship Mentor:
Hui Zheng, PhD

Development of Synthetic Gene Feedback Circuits to Prevent Tau Aggregation

Benjamin Wolozin, MD, PhD

BOSTON UNIVERSITY Co-Principal Investigator: Ahmad Khalil, PhD

A Novel Way to Expand Human-Derived Pathogenic Tau Seeds in a Cell Free System

Hong Xu, PhD UNIVERSITY OF PENNSYLVANIA Fellowship Mentor: Virginia M.Y. Lee, PhD

Study Vascular Dysfunction of Cerebral Perforating Arteries in the Pathogenesis of VCID/AD

Lirong Yan, PhD

This grant is made possible in part by support from Alzheimer's Los Angeles UNIVERSITY OF SOUTHERN CALIFORNIA

Fingerprinting *In Vivo* and *In Vitro* Prion Strains

Hyunjun Yang, PhD
UNIVERSITY OF CALIFORNIA,
SAN FRANCISCO
Fellowship Mentor:
William DeGrado, PhD
Fellowship Co-Mentor:
Carlo Condello, PhD

Macular Degeneration Research

Engineered Eye Tissue Models to Analyze Mechanisms of Age-related Vision Loss

Kapil Bharti, PhD NATIONAL INSTITUTES OF HEALTH/ NEI Co-Principal Investigator: Eric Nguyen, PhD

A New Therapeutic Strategy to Treat AMD

Sabrina Carrella, PhD FONDAZIONE TELETHON, ROMA, (ITALY) Co-Principial Investigator: Alessia Indrieri, PhD UNIVERSITY OF NAPLES FEDERICO II. (ITALY)

A Novel Method for Modeling AMD in a Dish

Jennifer Chao, MD, PhD UNIVERSITY OF WASHINGTON

Discovery of New Methods to Regenerate Cone Photoreceptors

Mark Emerson, PhD
THE CITY COLLEGE OF NEW
YORK, CITY UNIVERSITY OF
NEW YORK

Understanding the Role of Support Cells, known as Glia in Geographic Atrophy

Malia Edwards, PhD

This grant was made possible in part by the support of the Victor and Anna Mae Charitable Foundation WILMER EYE INSTITUTE, JOHNS HOPKINS MEDICINE

Examining the Role of Choroidal Blood Flow in AMD

Bradley Gelfand, PhD
UNIVERSITY OF VIRGINIA

Targeting Proline Metabolism in AMD

Jianhai Du, PhD
WEST VIRGINIA UNIVERSITY
RESEARCH CORPORATION
Co-Principal Investigator:
Deborah Ferrington, PhD
UNIVERSITY OF MINNESOTA

Immune Cell Specific DNA Modifications and Gene Expression in AMD

Willard Freeman, PhD
OKLAHOMA MEDICAL
RESEARCH FOUNDATION
Co-Principal Investigator:
Ana J Chucair-Flliott, PhD

Exploring the Role of Gut Bacteria in Early AMD

Christopher Hammond, MD, MRCP, FRCOphth KING'S COLLEGE LONDON (UNITED KINGDOM)

The Gut Bacteria and AMD in Aging Women

Amy Millen, PhD UNIVERSITY OF NEW YORK AT BUFFALO

Generating Precision Model for AMD Research

Jurgen Naggert, PhD
THE JACKSON LABORATORY

Elucidating How Smoking Causes Advanced AMD

Claudio Punzo, PhD UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOI

Profiling of Immune Cell Subtypes in AMD Patients and Controls

Philip Ruzycki, PhD

This award is made possible by support from The Ivan Bowen Family Foundation. WASHINGTON UNIVERSITY IN SAINT LOUIS Co-Principial Investigator:

Role of Lipids (Deposits) in Causing Dry AMD

Rajendra Apte, MD, PhD

Dorota Skowronska-Krawczyk, PhD

The Elizabeth Anderson Award UNIVERSITY OF CALIFORNIA, IRVINE Co-Principal Investigator: Daniel Chao, MD, PhD UNIVERSITY OF CALIFORNIA, SAN DIFGO

A Novel Method for Treating Wet AMD Reversibly with Single Intraocular Injection

Shushen Wang, PhD
TULANE UNIVERSITY
Co-Principal Investigator:
Bo Yu. PhD

Development of Gene Editing as a Permanent Cure for Wet AMD

Glenn Yiu, MD, PhDUNIVERSITY OF CALIFORNIA,
DAVIS

National Glaucoma Research

Cell Replacement in Glaucoma: Making Mature Retinal Ganglion Cells

Petr Baranov, MD, PhD SCHEPENS EYE RESEARCH INSTITUTE, MASSACHUSETTS EYE AND EAR AND HARVARD MEDICAL SCHOOL

A Dietary Supplement in Treatment of Glaucoma

Jeffrey Boatright, PhD EMORY UNIVERSITY Co-Principal Investigator: Ying Li, MD, PhD

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)

A Novel Use of Specialized Pro-resolving Mediators to Treat Glaucoma

Kin-Sang Cho, PhD SCHEPENS EYE RESEARCH INSTITUTE, MASSACHUSETTS EYE AND EAR AND HARVARD MEDICAL SCHOOL,

Preventing Vision Loss by Helping Doctors Predict and Treat Exfoliation Syndrome in Patients

Karen Curtin, PhD UNIVERSITY OF UTAH Co-Principal Investigator: Barbara M. Wirostko, MD

Regulation of APBB2 Gene Expression and How it Influences Risk for Glaucoma

John Fingert, MD, PhD UNIVERSITY OF IOWA

Using Electric Fields to Regenerate the Optic Nerve

Kimberly Gokoffski, MD, PhD
Dr. Douglas H. Johnson Award
UNIVERSITY OF SOUTHERN
CALIFORNIA EYE INSTITUTE

Identifying Factors that Protect Ganglion Cells from Death after Optic Nerve Injury

Jeffrey Gross, PhD UNIVERSITY OF PITTSBURGH

Determine the Genetic Element on Human Chromosome 9 that Increases Risk for Glaucoma

Gareth Howell, PhD
THE JACKSON LABORATORY

A Novel Tool for Seeing Neuron Cells in the Eyes of Glaucoma Models

Yali Jia, PhD
OREGON HEALTH AND
SCIENCE UNIVERSITY
Co-Principal Investigator:
Shaohua Pi, PhD

Defining the Importance of Extrinsic Signalling in Glaucoma Neurodegeneration

Richard Libby, PhD Thomas R. Lee Award UNIVERSITY OF ROCHESTER MEDICAL CENTER

Insights into Genetic Risk Factors and Biological Consequences in a Naturally Occurring Glaucoma Model

Amanda Melin, PhD
UNIVERSITY OF CALGARY
(CANADA)
Co-Principal Investigator:
James Higham, PhD
NEW YORK UNIVERSITY

Astrocytes Regulate the Health and Degeneration of Retinal Ganglion Cells in Glaucoma Neurodegeneration

Jason Meyer, PhD INDIANA UNIVERSITY

A Novel Model Enabling Identification of Strategies for Replacing Lost Cells and Restoring Vision in Glaucoma Patients

Jeff Mumm, PhD WILMER EYE INSTITUTE, JOHNS HOPKINS MEDICINE

Investigating Risk Factors for Primary Open-angle Glaucoma in People of African Descent

Alberta Thiadens, MD, PhD ERASMUS MEDICAL CENTER, ROTTERDAM, (THE NETHERLANDS) Co-Principal Investigator: Caroline C.W. Klaver, MD, PhD

Direct Observation and Manipulation of Energy Regulation in Retinal Neurons During Glaucoma

Philip Williams, PhD WASHINGTON UNIVERSITY IN ST. LOUIS

Identifying Which Retinal Ganglion Cell Types Die Earlier in Glaucoma

Siamak Yousefi, PhD
UNIVERSITY OF TENNESSEE

Co-principal investigator and fellowship mentor institutions are listed if different than the Pl.

Special Thanks to Donors Supporting Ongoing Awards

ALZHEIMER'S DISEASE RESEARCH

Investigating Neuropeptides as Biomarkers and Novel Therapeutics for Alzheimer's Disease

Becky Carlyle, PhD

This grant is made possible by the support from The Luminescence Foundation, Inc.

MASSACHUSETTS GENERAL HOSPITAL

Towards New Stimulation Methods to Correct Memory in Alzheimer's Disease

Arjun Masurkar, MD, PhD

This grant made possible in part by the support of the Ping Y. Tai Foundation.
NEW YORK UNIVERSITY

A New Method to Assess Cellular Dysfunction in Alzheimer's Using Human Neurons

Jessica Young, PhD

This grant made possible in part by the support of the Jerome Jacobson Foundation. UNIVERSITY OF WASHINGTON, SCHOOL OF MEDICINE

A Novel Approach for Memory Improvement in Alzheimer's Disease

Ying Juan Zhao, PhD.

This grant made possible by the support of the J. T. Tai Foundation. XIAMEN UNIVERSITY

MACULAR DEGENERATION RESEARCH

A Novel Negative Immune Regulator to Control Wet AMD

Ye Sun. MD. PhD

This grant is made possible by the support of Dr. H. James and Carole Free. BOSTON CHILDREN'S HOSPITAL AND HARVARD MEDICAL SCHOOL

BrightFocus scientists shared research highlights at special movie screening



During a virtual
BrightFocus at-home
movie night, Dr. Amir
Kashani, University of
Southern California,
Roski Eye Institute
discussed his innovative
new research to develop
retinal scans to identify
early signs of vascular
contributions to
cognitive dementia, one
of the leading causes of
memory loss.



Dr. Yvonne Ou of the University of California, San Francisco explained the importance of glaucoma research in helping save sight for millions around the world

Our world class scientific review committees

comprised of renowned leaders in their fields, recommend new research opportunities for BrightFocus to advance our goal of defeating Alzheimer's, macular degeneration, and glaucoma.









BrightFocus grantees have received numerous prestigious awards over the years.

The following experts have served on each committee within the preceding five years:

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I OUIS

Hui Zheng, PhDBAYLOR COLLEGE OF
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BrightFocus works closely with nonprofit and corporate partners on issues of common concern.

As a respected member of broad coalitions, we communicate with key policymakers and elected officials on the importance of research funding and caregiving support.













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The Nancy Peery Marriott Foundation













From here, For here,







Global Network for Alzheimer's

BrightFocus has worked with partners worldwide to advance research and provide public awareness of Alzheimer's disease including:

Belgium

Stichting Alzheimer Onderzoek

France

Fondation Vancre Alzheimer

Germany

Alzheimer Forschung Initiative e.V.

The Netherlands

Alzheimer Nederland

BrightFocus thanks our donors for their generosity toward our three scientific and public awareness programs:

Alzheimer's Disease Research, Macular Degeneration Research, and National Glaucoma Research. 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 important and needed to help us find a cure.

Sowing the Seeds of Scientific Progress

BrightFocus-funded researchers often go on to receive awards

TEN TIMES GREATER

from NIH and other sources, a

1,000% return

on our early investment.



TOGETHER FOR MIND, SIGHT & MUSIC

LINDA RONSTADT: THE SOUND OF MY VOICE

AT-HOME MOVIE NIGHT WITH



A FREE VIRTUAL EVENT
ONE WEEK ONLY
Starts June 4 at 7:00 p.m. EST

TO WATCH, VISIT: BRIGHTFOCUS.ORG/MOVIE





Together for Mind, Sight & Music

BrightFocus provided a free special screening of the award-winning documentary, *Linda Ronstadt: The Sound of My Voice*. The movie follows the life and career of one of the world's best-selling artists as she embraced genres spanning rock, country, operetta and Latin, and paved the way to become an iconic female pioneer in the male-dominated music world. Ronstadt was forced to retire early due to a neurodegenerative disease.

Prior to the movie, four BrightFocus-funded scientists shared highlights from their ongoing research and progress toward ending diseases of mind and sight.



Stacy Pagos Haller, BrightFocus President and CEO, and James Keach, filmmaker, PCH Films, share a message on the importance of the research for the cure of diseases of mind and sight.

Investing in a Cure | Donor Spotlight



Ed and Marilyn Nadolny.

"RESEARCH IS SO
IMPORTANT TO
FIND SOME WAY TO
ELIMINATE AND SLOW
DOWN ALZHEIMER'S
DISEASE."

BrightFocus donors often have special connections to the scientific research programs they support. We are honored to share four of those stories with you.

A Commitment to Help Future Generations

For Marilyn Nadolny of The Villages, Florida, Alzheimer's is personal. Her husband Ed, of nearly 60 years, suffered from the disease for 14 years.

Marilyn supports Alzheimer's Disease Research, a program of BrightFocus Foundation to help make the difference for other families. "Research is so important to find some way to eliminate and slow down Alzheimer's disease," said Marilyn Nadolny. "It is so just devastating to families." Ed was a repair specialist who could fix anything. His career spanned decades – working at top technology companies like Smith Corona and Sun International before joining the Broward County School Board.

Marilyn, Ed and their family enjoyed the outdoors and were longtime campers. "Our plans to travel across the country got wiped out, and we had to sell our motorhome," Marilyn said. "Later on, Ed, who was no longer driving, went missing for two days.

Four generations of the Nadolny family.

He headed south until he couldn't drive any further – he had reached Key West! It was truly a miracle that he was able to return home safely as the police were in the driveway with me discussing next steps in their statewide search."

The Nadolny family now spans four generations with Marilyn, two children, five grandchildren and one great grandchild. "I just hope that the research can find a cure, so the disease won't have the same impact on my children or my grandchildren," Marilyn added.







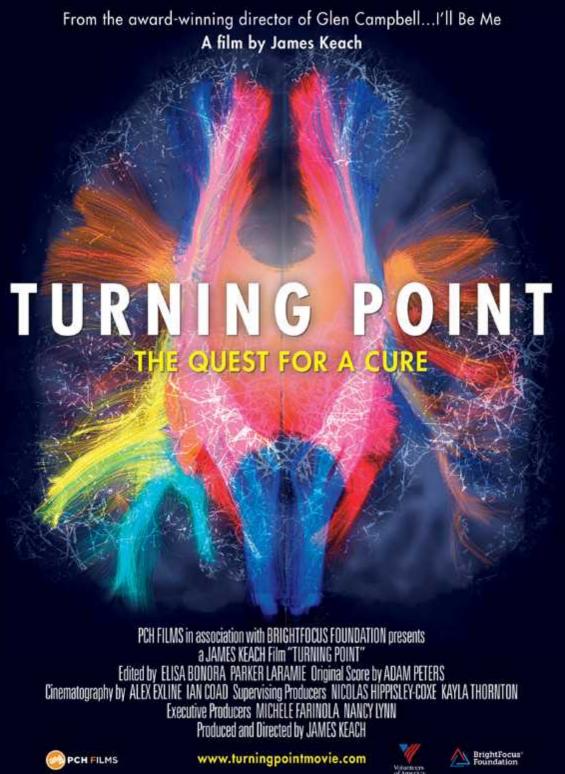
Turning Point Film Continues to Captivate Audiences

BrightFocus is proud to serve as presentation partner for *Turning Point*, a documentary that captures the drama and personal dedication of researchers who are pursuing drug breakthroughs to make Alzheimer's a distant memory. Directed and produced by award-winning filmmaker James Keach, the film has been screened over 130 times worldwide since its festival premiere in 2018.

Turning Point was recently released on VOD (video on demand) platforms and is now available to watch at home. For more information, visit <u>brightfocus.org</u>.

BrightFocus also works on the RACERS initiative, in partnership with Gates Ventures, the National Institute on Aging, and the Health Resources and Services Administration, to help health care providers learn about early detection and diagnosis of cognitive impairment/ Alzheimer's/related dementias. The film has been screened for medical associations and schools of health professionals nationwide.

Above left: Stacy Pagos Haller, President and CEO, BrightFocus, joins C. Marie Taylor, President & CEO, Leadership Montgomery, at a Turning Point screening in Silver Spring, MD. Above right: James Keach, filmmaker, speaks following a Turning Point screening at the HudsonAlpha Institute in Huntsville, AL.





Alzheimer's clinical trial participant Pasquale Rocchio. (Photo courtesy of PCH Films)



Noted scientist Neil deGrasse Tyson. (Photo courtesy of PCH Films)





Sally Straus of Union receives a resolution from Freeholder Chairman Alexander Mirabella and Vice Chairman Angel G. Estrada, with State Senator Joe Cryan and former State Senator Anthony E. Russo.

(Credits: Jim Lowney/County of Union)

"HAVE A POSITIVE ATTITUDE AND DISCOVER WHAT RESOURCES ARE AVAILABLE, SUCH AS THE BRIGHTFOCUS CHATS."

The Importance of Knowledge in Saving Sight

Sally Straus of Union, New Jersey, was an office manager for a major perfume company in New York City before retiring to focus fulltime on volunteerism in her hometown. Her motto is "If it happens in Union, I am either in it, on it or know about it"

Diagnosed with wet macular degeneration in 2015, Straus has been undergoing treatment by Dr. Vinod Voleti of NJ Retina, including eye injections and taking supplements that have stabilized the progression of the disease. Her advice for those diagnosed with vision loss is, "Be prepared. Be your own advocate. Have a positive attitude and discover what resources are available, such as the BrightFocus Chats."

A supporter of Macular Degeneration Research, a program of BrightFocus Foundation, she is an active and loyal participant in the organization's monthly telephone discussions, which feature leading experts answering questions and providing helpful advice for living with vision loss. "I continue to be very impressed by the BrightFocus Chats. They are very informative and a wonderful resource. I am getting excellent care from my retina specialist, but the Chats help with my comfort level."

Straus continues her community service for the Union Public Library Board of Trustees, Union Historical Society, local Veterans alliance, and Knights of Columbus among others. In 2014, she was honored by the Union Senior Center as its inaugural Senior Citizen of the Year.



Lafayette Leopards men's basketball team defeats American University.

Defeating Alzheimer's— It Takes a Team



The Reichwein family.

Honoring his grandfather who had passed away from Alzheimer's, Lafayette College basketball player Cal Reichwein dedicated a game to supporting scientific research through BrightFocus Foundation's Alzheimer's Disease Research program. Not only did Lafayette win their game 82-70, but he raised \$4,681 for research donated by the Lafayette community.



SOMEONE DEVELOPS ALZHEIMER'S DISEASE.



The Yendall family: Carol, Rick, Wayne, Judy, Rob and Barb.

"WE ARE VERY
INTERESTED IN THE
RESEARCH—WE
DONATE WHAT WE
CAN ON LIMITED
BUDGET, AND WHAT
WE CAN GIVE, WE
GIVE GLADLY."

Moved to Action: Glaucoma's Impact on a Family

Judy and Wayne Yendall of Buffalo have long known the impact of glaucoma. The disease runs in Judy's family, affecting her grandmother, great-aunt, father and sisters. She was tested at early age and has managed her glaucoma for decades with laser surgery and eye drops.

After their son Rick was diagnosed with pigmentary glaucoma, Wayne was also tested and diagnosed with the same rare form of the disease.

Rick was a championship swimmer at Grove City College in Pennsylvania when severe eye pain took him from the school infirmary to hospitals in Pittsburgh and Boston for surgery and treatment. His disease was managed, allowing him a long career as a plastics engineer. Eventually, however, his vision declined to a point where he could no longer read the blueprints at his job. Rick, now blind, uses a special computer to stay in touch with others and is grateful for the support of his family.

Wayne has been fortunate to be able to manage his sight with eye drops, and has had both laser and cataract surgery under the care of a glaucoma specialist. He encourages others to "get your eyes checked and stay on top of your eyesight."

Judy and Wayne recently celebrated their 60th anniversary and are hopeful that scientific progress will help reverse Rick's blindness. They have been inspired by a new National Glaucoma Research project, Using Electric Fields to Regenerate the Optic Nerve, as a possible cure to reverse the damage.

"We are very interested in the research," said Judy. "We donate what we can on limited budget, and what we can give, we give gladly."



Carol Maude Pearl.

"MY HOPE IS THAT WITH ENOUGH RESOURCES, EVENTUALLY SCIENTISTS WILL BE ABLE TO COME UP WITH PREVENTION FOR THIS HORRIBLE DISEASE."

A Loving Memory

Carol Maude Pearl, lived in Odessa, Delaware for 35 years, was active in community and church activities, and was known as "our queen" and a "hostess with the mostess" by all who knew her. She opened her home each year for the Christmas in Odessa House Tour, sponsored by the Odessa Women's Club. Carol loved to dance, and her smile would light up any room.

She and David, her husband of 54 years, first met at a faculty party and both taught school for decades. In retirement, they travelled the world. The Pearl clan now includes four children, eight grandchildren and four great grandchildren.

Carol first experienced mild signs of dementia in 2012, and the disease progressed slowly at first. David became aware of Alzheimer's Disease Research (ADR), a BrightFocus program, when he attended a local session on dementia. The speaker discussed research for treatments and a cure, and that is when he began supporting the ADR program.

"I am so happy that Alzheimer's research is going on, and that there are little green shoots of progress," said David. "My hope is that with enough resources, eventually scientists will be able to come up with prevention for this horrible disease."

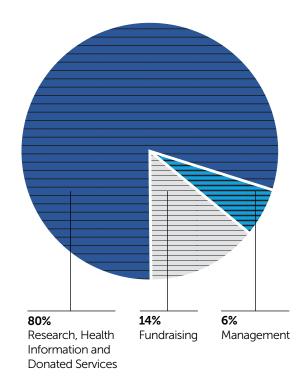
For David, supporting research was, "the only answer so the next family would not have to suffer like we did."

Carol passed away in July 2019. Her family held a celebration of her life, and David and their children light candles in her memory. David is arranging a tree memorial for Carol at BrightFocus.

Investing in hope

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 and these are included in Program Services expenses. This allowed the organization to reach millions of people with information about risk factors, treatments and caregiving.



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

CONSOLIDATED STATEMENT OF FINANCIAL POSITION As of March 31, 2020 (in thousands of dollars)	ON
ASSETS	
Cash and Investments	\$36,972
Charitable Trusts and Bequests Receivable	8,310
Rental Property	3,761
Fixed Assets, Net	3,836
Other Assets	1,109
TOTAL ASSETS	\$53,988
LIABILITIES	
Accounts Payable and Other Liabilities	\$790
Grants Payable	26,847
Charitable Gift Annuities	958
TOTAL LIABILITIES	28,595
NET ASSETS	
Without Donor Restriction	8,879
With Donor Restriction	16,514
TOTAL NET ASSETS	25,393
TOTAL LIABILITIES AND NET ASSETS	\$53,988

CONSOLIDATED STATEMENT OF ACTIVITIES For the Fiscal Year Ended March 31, 2020 (in thousands of dollars)	
SUPPORT AND REVENUE	
Contributions and Grants	\$29,868
Bequests	5,652
Donated Services	16,267
Investment Income	(1,820)
Rental & Other Income	1,338
TOTAL SUPPORT AND REVENUE	51,305
EXPENSES	
Program Services	
Research	23,155
Health Information Services	24,532
Total Program Services	47,687
Supporting Services	
Fundraising	8,055
Management and General	3,449
Total Supporting Services	11,504
TOTAL EXPENSES	59,191
CHANGE IN NET ASSETS	\$(7,886)

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