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Cure in Mind. Cure in Sight.

BrightFocus Foundation: Cure In Mind. Cure In Sight.

Diane Bovenkamp, PhD
Vice President of Scientific Affairs
September 25, 2019

Health Research Alliance Annual Meeting

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- **Vision: A world free from diseases of mind and sight.**
- **Mission: BrightFocus funds exceptional scientific research worldwide to defeat Alzheimer's disease, macular degeneration, and glaucoma and provides expert information on these heartbreaking diseases.**
- **History: We were founded in 1973 and known until February 1, 2013 as the American Health Assistance Foundation (AHAF).**
- **Awarded more than $206 million for more than 1500 awards since inception**

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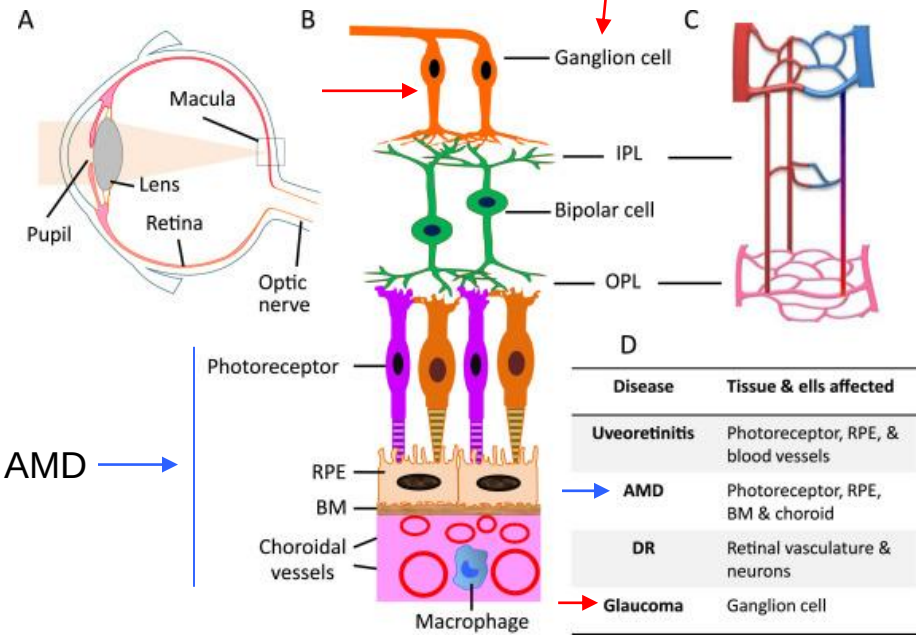
Cells Affected in Diseases of Mind and Sight

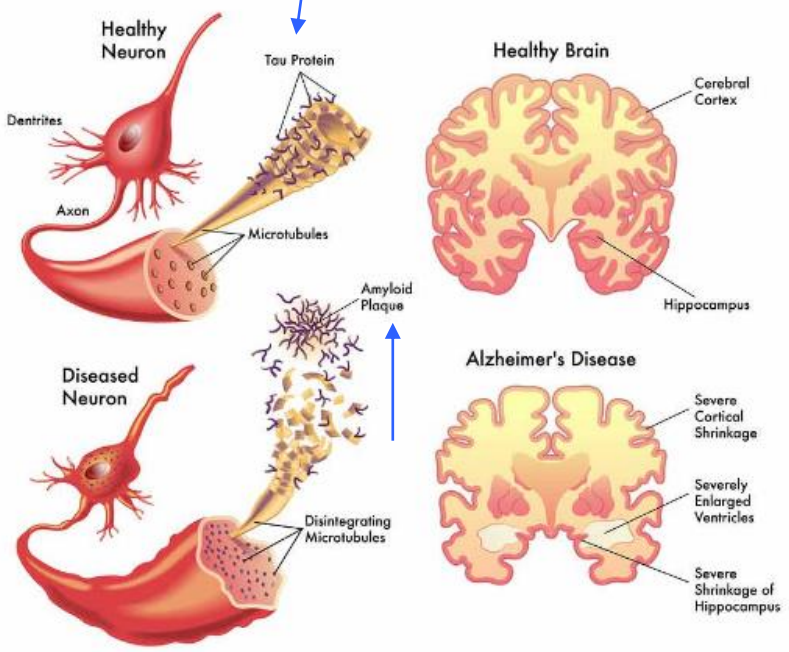
Glaucoma

Alzheimer's and Related Dementias



D

Disease	Tissue & ells affected
Uveoretinitis	Photoreceptor, RPE, & blood vessels
AMD	Photoreceptor, RPE, BM & choroid
DR	Retinal vasculature & neurons
Glaucoma	Ganglion cell



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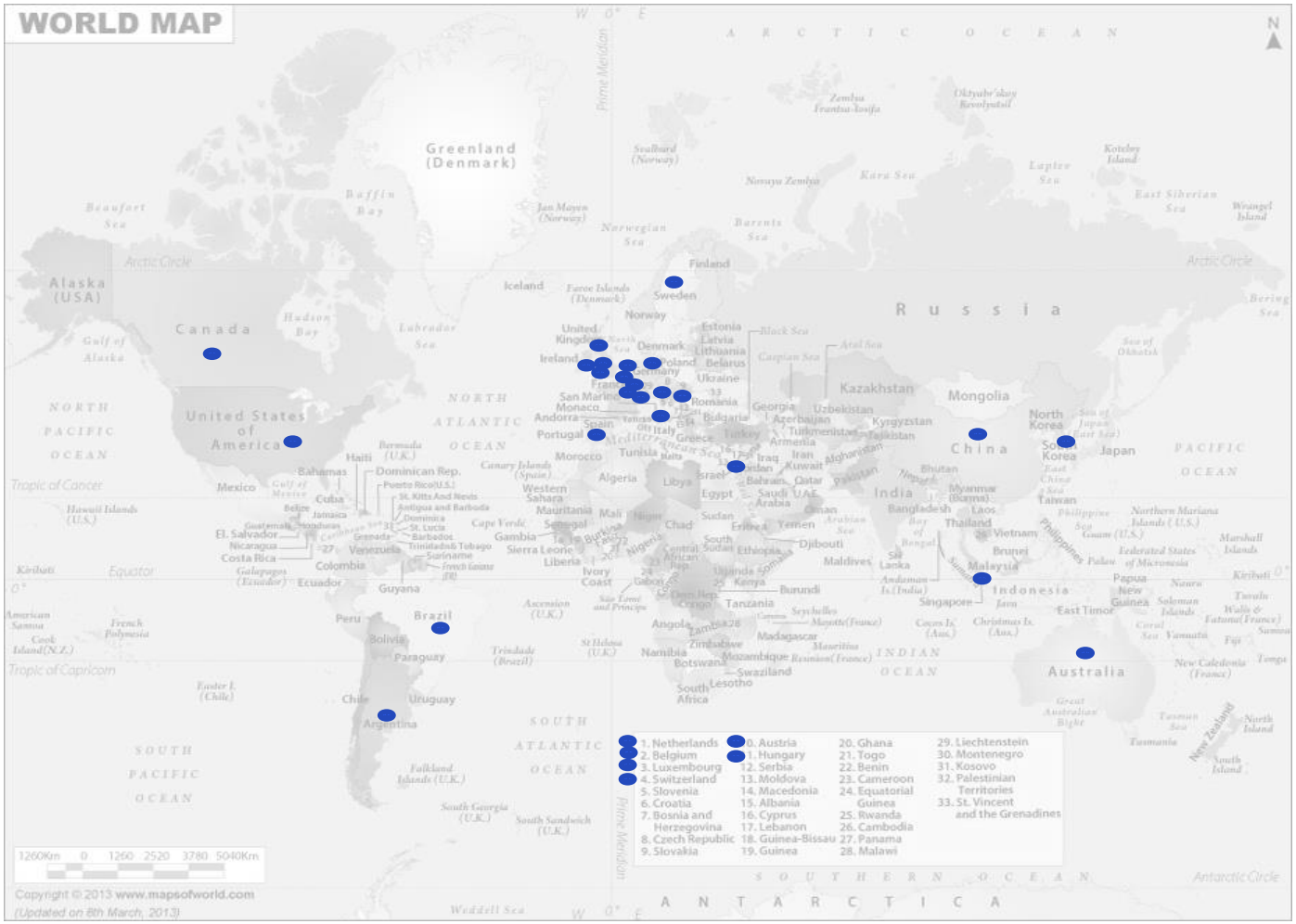
Diseases Have No Borders...
Neither Do BrightFocus Awards



Blue Dot= Since Inception (24 Locations)

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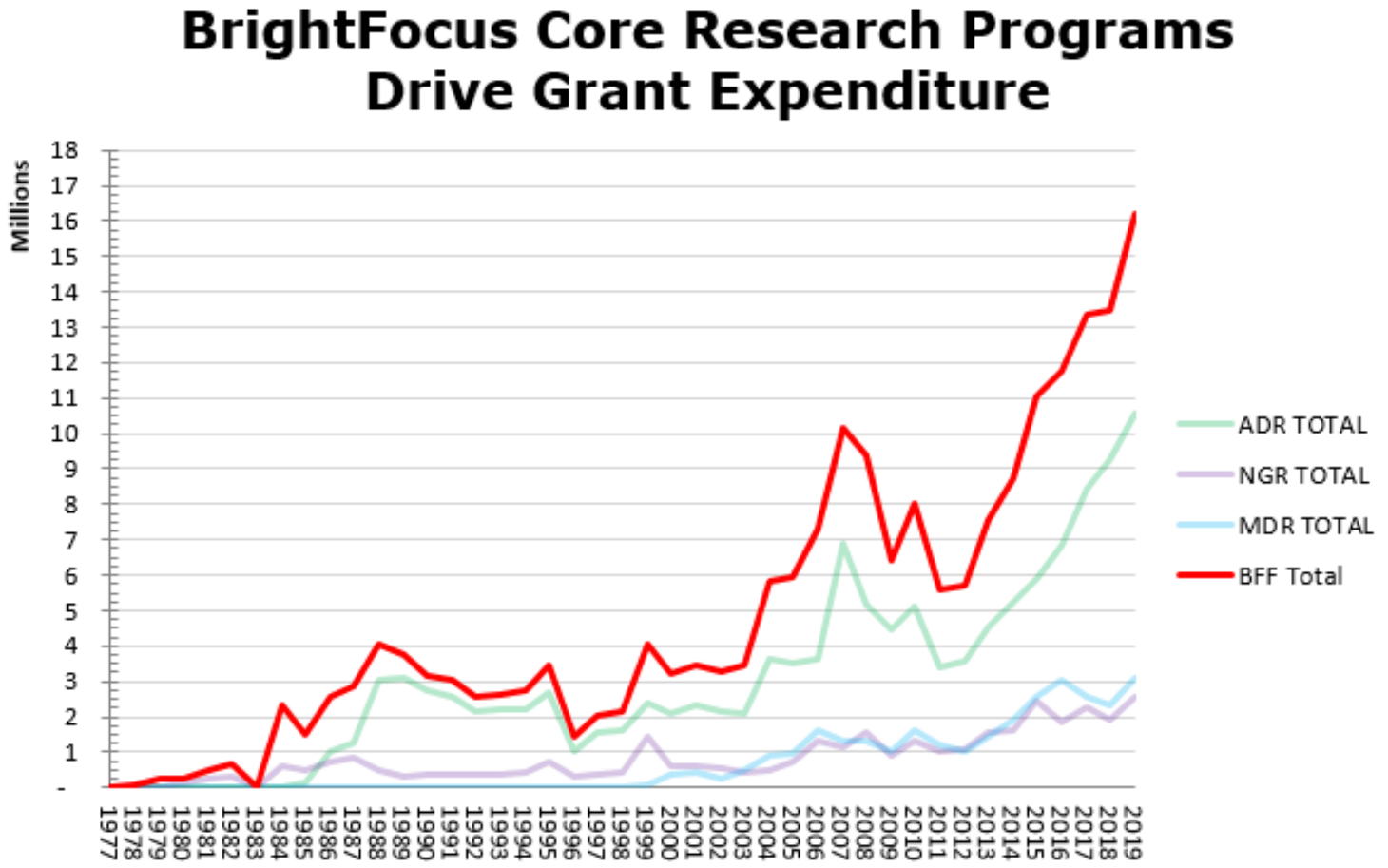
FY19 Research Funding Sets New Record High (8 Consecutive Years!)



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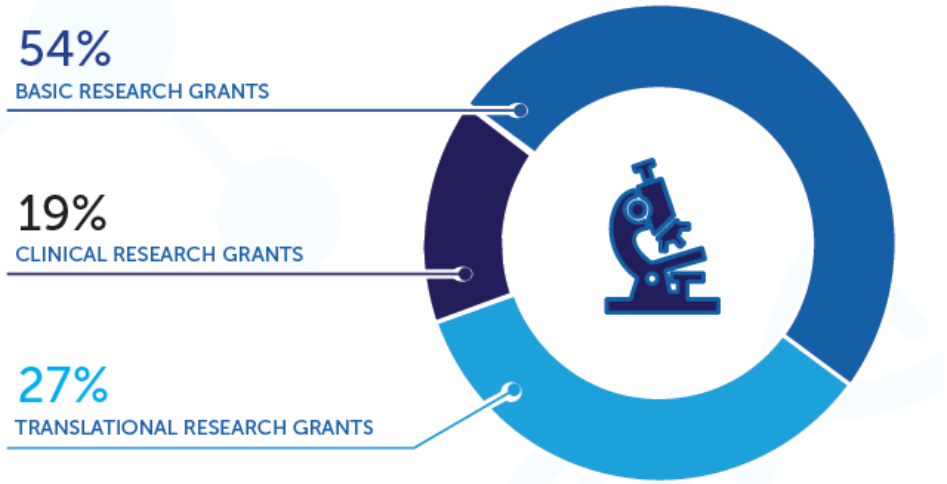
Awards In a Nutshell

- **Fiscal Year 2019:**
  - **$16.2 Million**
  - **76 New Awards**
  - **13% International**
  - **40 Cities Worldwide**
  - **17 US States**



- **Currently Active (Total) Portfolio:**
  - ✓ **Nearly 200 awards**
  - ✓ **More than $45 million**
  - ✓ **12 Countries (Australia, Austria, Canada, China (Fujian Sheng and Hong Kong), England, France, Germany, Italy, Netherlands, Spain, Sweden, USA)**

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BrightFocus Awards

- **Investigator-initiated, high-risk/high-reward research**
- **International (no citizenship or country requirements)**
- **$100,000 per year**

- **Alzheimer's Disease Research**
  - Standard: $300,000 total for 3 years
  - Postdoctoral Fellowship: $200,000 for 2 years
- **Macular Degeneration Research**
  - Standard: $200,000 total for 2 years (Postdocs can be CoPIs)
- **National Glaucoma Research**
  - Standard: $200,000 total for 2 years (Postdocs can be CoPIs)

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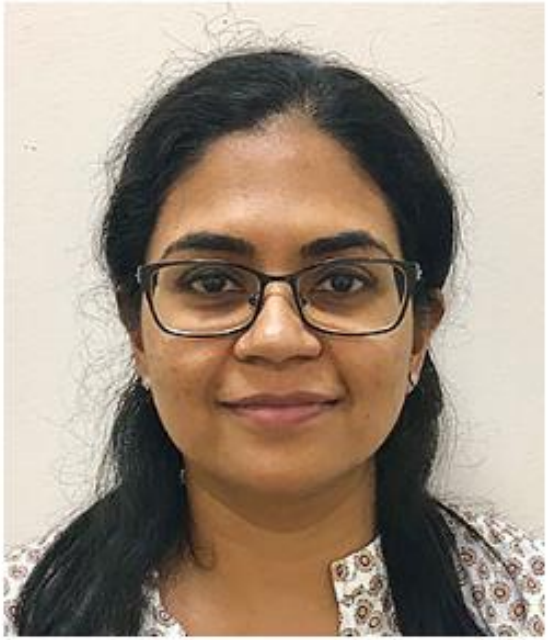
BrightFocus Scientific Affairs At Health Research Alliance

Keith Whitaker, PhD

Director of Scientific Programs, Neuroscience (ADR)



Preeti Subramanian, PhD

Director of Scientific Programs, Vision Science (MDR, NGR)

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Web Resources For Each Award

A New Method to Measure Tau Kinetics in Humans with Alzheimer's Disease

Randall Bateman, MD
Washington University (St. Louis, MO)

YEAR AWARDED: 2014
GRANT DURATION: October 1, 2014 to September 30, 2017
DISEASE: Alzheimer's
AWARD AMOUNT: $250,000
GRANT REFERENCE ID: A2014344S
AWARD TYPE: Standard
AWARD REGION: US Midwestern

This grant is made possible by a bequest from the Estate of David and Annagel Ballard (The Ballard/Herwin Alzheimer's Research Fund).

Stable Isotope Labeling Kinetics of Human Tau in Alzheimer's Disease

SUMMARY
In Alzheimer's disease, and amyloid protein called tau is increased in the brain and fluid that surrounds the brain. It is unclear why it is increased. Is this due to increased production or impaired clearance? How much is production or clearance altered? Can drugs be developed that can correct abnormal tau production or clearance? These questions can now be answered and the answers will give drugs that target tau a better chance of working against Alzheimer's disease.

DETAILS
We have developed stable isotope labeling kinetics (SILK) methods to study the kinetics of proteins in the human central nervous system (CNS). With a tau SILK method, we will label participants with stable isotope amino acids and measure the amount of labeled tau that the brain produces over time. By measuring labeled tau, we will calculate how fast the brain produces tau and clears it away. In Aim 1, we will label young normal participants to study tau kinetics in a normal physiological state. In Aim 2, we will label participants with AD and age-matched cognitively normal controls to answer the question, do tau kinetics change in AD?

The past few decades of AD research have focused on amyloid-beta as the cause of AD, but today more evidence indicates that tau protein plays central roles in AD. Tau is mostly an intracellular protein but is also secreted as extracellular protein in normal conditions, and in increased amounts in AD. The SILK method that we pioneered is uniquely able to measure production and clearance of tau in humans. We believe our study elucidating the kinetics of tau in the human CNS will provide the first measures of why tau is increased in AD (i.e., through increased production versus impaired clearance).

Tau is an important biomarker of AD. Our study elucidating human CNS tau kinetics will enable better designs for prevention and treatment of AD in the future. Specifically, understanding why tau increases in AD will allow for better development of tau-targeted treatments. Our study will also greatly advance the understanding of basic tau biology.

First published on: Wednesday, July 9, 2014

Understanding the Earliest Steps of Optic Nerve Cell Death in Glaucoma

Yvonne Ou, MD
University of California, San Francisco

YEAR AWARDED: 2016
GRANT DURATION: July 1, 2016 to June 30, 2018
DISEASE: Glaucoma
AWARD AMOUNT: $150,000
GRANT REFERENCE ID: G2016004
AWARD TYPE: Standard
AWARD REGION: US Northwestern

The Douglas H. Johnson Award for Glaucoma Research.

Retinal Synapse Disassembly in Glaucoma

SUMMARY
In glaucoma, the cells of the optic nerve die and that can lead to blindness. Although we know that optic nerve cells are injured in glaucoma, we do not yet understand the steps between optic nerve cell injury and death. A detailed understanding of the earliest changes that occur will allow us to design treatments that can rescue these injured optic nerve cells before irreversible cell death occurs.

DETAILS
Our goal is to understand the earliest steps of injury to the optic nerve cell, or retinal ganglion cell (RGC), in glaucoma. In glaucoma, the cells of the optic nerve die and can lead to blindness. Although we know that these RGCs are injured in glaucoma, we do not yet understand the steps between optic nerve cell injury and death; nor do we know whether other cell types in the retina are also affected by elevated intraocular pressure. A detailed understanding of the earliest changes that occur will allow us to design treatments that can rescue these injured optic nerve cells before irreversible cell death occurs.

Our laboratory is focused on how RGCs degenerate in glaucoma in order to improve diagnosis and treatment of this disease. The retina is composed of multiple layers of interconnecting nerve cells, with the RGC being the final "output" nerve cell, or neuron, that transmits all of the light information received by the retina to the brain where it is processed. We are identifying some of the earliest changes in the retina, specifically at the synapses, which connect RGCs with their partners. Synapses are the connections where information from one neuron passes to another. In the case of the RGC, it receives information via synapses from bipolar cells, another type of neuron. A second goal of this project is to understand whether the bipolar cells are responding to elevated eye pressure and altering their synapses in response. Finally, recent studies have highlighted the importance of components of the immune system, specifically complement, in tagging these damaged synapses for elimination. We will study whether these components are increased in the

Investigating How Loss of an "Off Switch" for Inflammation Contributes to AMD

Sarah Doyle, PhD
Trinity College Dublin (Dublin, Ireland)

YEAR AWARDED: 2016
GRANT DURATION: July 1, 2016 to June 30, 2018
DISEASE: Macular Degeneration
AWARD AMOUNT: $150,000
GRANT REFERENCE ID: M2016030
AWARD TYPE: Standard
AWARD REGION: International

The Role of Toll/IL-1 Receptor (TIR)-Signalling "Checkpoint" Regulators in Pathobiology of AMD

SUMMARY
The inflammatory response is needed to take care of all the tissues that make up our body to keep us in working order. However inflammation is a double-edged sword: too much can cause damage to the surrounding tissues, and too little can be ineffective at inducing healing. To overcome this problem, the inflammatory response has evolved so that once a pro-inflammatory response is generated, it promotes the expression of chemicals that provide feedback and switch off inflammation by inhibiting the very pro-inflammatory signals that generated them; in this way, the process of inflammation programs its own end. Age-related macular degeneration (AMD) has elements that indicate that the inflammatory response is uncontrolled and persistent when low-level inflammation is observed. Our research question asks whether this active process of switching off the inflammatory response is lost in people with AMD.

DETAILS
My lab aims to understand the underlying mechanisms that are the driving forces behind age-related macular degeneration (AMD) so that we can prevent macular degeneration in future generations and stop its progression in those currently suffering with this blinding disease. The overarching goal of this proposal is to investigate the contribution that "negative-regulators" of toll-like receptors (TLRs) play in the pathogenesis of AMD.

TLRs are critical sensors of danger used by our immune system. First we will analyze expression levels of a range of negative-regulators of TLRs in our circulating immune cells and in the retinae of AMD and healthy donors. Second, we will analyze the impact of a pro-inflammatory or anti-inflammatory state on negative regulators of TLRs. Third, we will investigate the role of negative-regulators of TLRs in the eye's ability to protect itself from overt inflammation. Finally we will analyze a role for negative regulators of

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Diversified Portfolio

Blood Test for Alzheimer's

BrightFocus-funded Alzheimer's Test Gets Encouraging Sign from FDA

Silk ABeta Spot Test

Philip Verghese, PhD
C2N Diagnostics (St. Louis, MO)

C2N Diagnostics

YEAR AWARDED: 2016
GRANT DURATION:
May 1, 2016 to April 30, 2018
DISEASE: Alzheimer's
AWARD AMOUNT: $750,000
GRANT REFERENCE ID: CA2016636
AWARD TYPE: Other
AWARD REGION: US Midwestern

CO-PRINCIPAL INVESTIGATORS

Joel Braunstein, MD, MBA
C2N Diagnostics (St. Louis, MO)

A BrightFocus-funded project to develop a blood-based screening test for Alzheimer's disease has turned a major corner toward reaching the marketplace, with the U.S. Food and Drug Administration (FDA) giving it a "Breakthrough Device" designation which may accelerate this promising diagnostic tool's approval for use in healthcare settings.

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Clinical Risk Algorithm for Alzheimer's in Early Midlife/Sex-based Differences

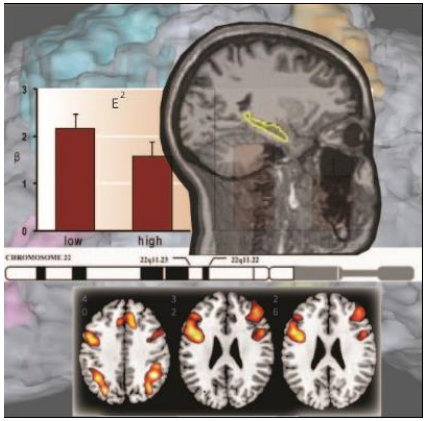
Midlife Biomarkers of Alzheimer's Disease Risk and Impact of Sex Differences

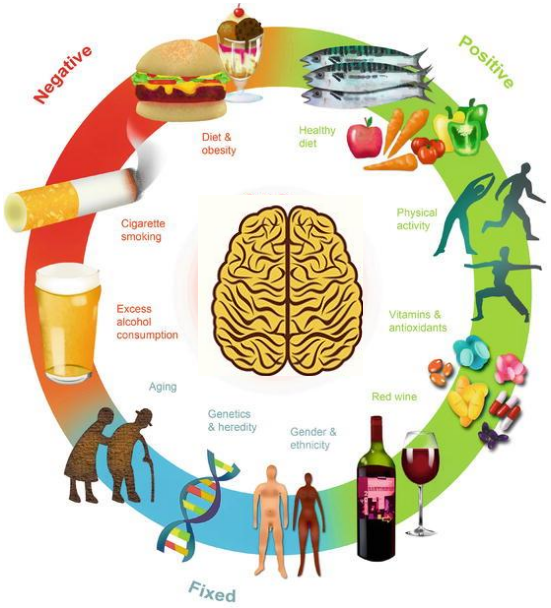
Jill M. Goldstein, PhD
Massachusetts General Hospital and Harvard Medical School (Boston, MA)

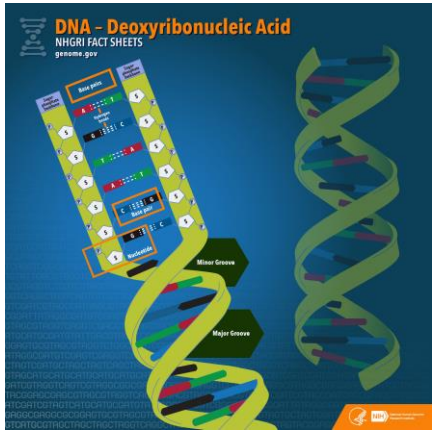
YEAR AWARDED: 2018
GRANT DURATION: March 30, 2018 to March 29, 2020
DISEASE: Alzheimer's Disease
AWARD AMOUNT: $1,112,000
GRANT REFERENCE ID: CA2018607
AWARD TYPE: Standard
AWARD REGION: US Northeastern

Clinical Neuroscience Lab for Sex Differences in the Brain

Massachusetts General Hospital







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Microbiome influences microglia phenotypes and Aβ amyloidosis in a sex-specific manner

- Hemraj Dodiya
- University of Chicago
- Mentor: Sangram S. Sisodia

Prior experiments demonstrated that perturbation of the microbiome altered amyloidosis in a sex-specific manner. The proposed experiments will cross male-microbiome into female mice and evaluate the role of microglia in the reduction of amyloidosis.

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FY19 MDR International Awardees

Paul Baird, PhD, Centre for Eye Research Australia, The University of Melbourne
Co-Principal Investigators: **Adam Kowalczyk, PhD** and **Alice Pebay, PhD**

A New Method for Prediction of the Two Advanced Types of AMD

- **High throughput computing and big data analysis** to aid our understanding and advancement of treatments for AMD; particularly the dry form.
- Identify genes that interact with each other as well as with other factors known to be involved in increased risk of AMD such as age, sex of an individual and smoking.

Zhichao Wu, PhD, *Centre for Eye Research Australia, The University of Melbourne*

New Visual Function Tests to Enable Treatment Trials of AMD

- A new and better method to measure the eye's ability to perceive different light levels in the macula
- Enables better evaluation of promising new treatments.

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Joelle Hallak, PhD, The University of Illinois, Chicago
Co-Principal Investigators: **Daniel Rubin, MD, Theodore Leng, MD, and Luis de Sisternes, PhD**

A Novel Approach to Personalized Prediction of Progression of Age-Related Macular Degeneration

- Develop a tool to predict the chances of AMD progression on a personalized, patient-by-patient basis
- Distinguishing which patients progress from an early or intermediate stage of AMD to the advanced stage will help guide patient follow-up and testing.

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FY19 NGR Awardees

Kevin Chan, PhD, New York University School of Medicine

The Role of Brain Waste Clearance System in Glaucoma

- Understand glaucoma mechanisms by determining the pathophysiological events and disease progression in the brain's visual system
- Use novel, multi-parametric magnetic resonance imaging techniques in experimental glaucoma models.

Co-recipient: The Thomas R. Lee Award for Glaucoma Research

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Eldon Geisert, PhD, Emory University

Robust Optic Nerve Regeneration: A Systems Biology Approach

- Identify genes that will increase the number of regenerating axons by at least four times and the distance the axons grow by at least three times.
- If functional recovery is to occur in humans we must increase the number of regenerating axons and their rate of growth.

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Thought Leader: Convening Experts, Developing The Next Generation

Cure in Mind, Cure in Sight – Bridging Brain and Eye Research

BrightFocus Convenes and Leads International Conference

The conference was organized by, from left, Guojun Bu, PhD (Mayo Clinic, Jacksonville); Todd Golde, MD, PhD (U Fla); Diane Bovenkamp, PhD (BrightFocus); and Adriana di Polo, PhD (U Montreal), who's not pictured here.

BrightFocus-Led Panel Examines Impact of Lifestyle on AMD and Glaucoma

Looks at Research on Role of Diet, Exercise, Vitamins

Moderating the session, from right, were: Diane Bovenkamp, PhD, Adriana Di Polo, PhD, and David Calkins, PhD.

BrightFocus Alzheimer's Fast Track 2019

BrightFocus Glaucoma Fast Track 2019

Macular Fast Track 2020

Wednesday, October 16, 2019 - 8:00 am
Friday, October 18, 2019 - 5:00 pm

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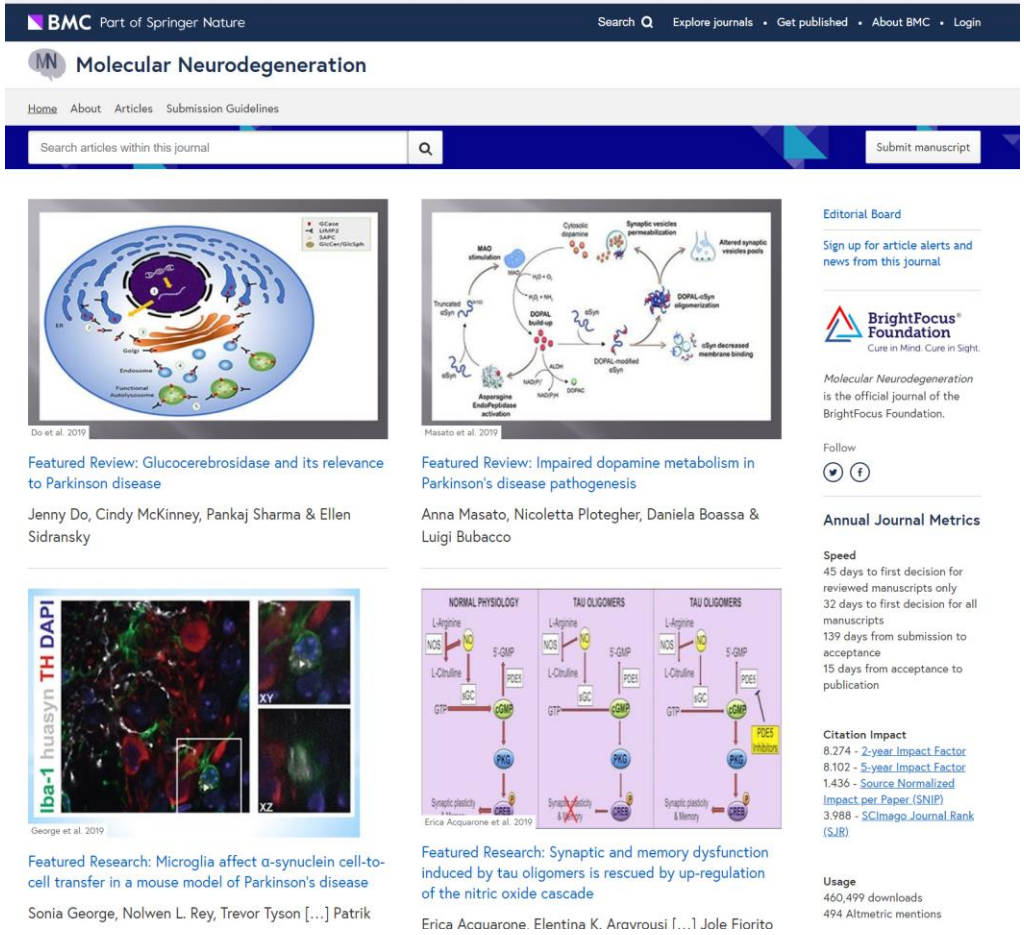
Molecular Neurodegeneration

Open Access Dissemination: Partnership with BMC/Springer Nature

Official Journal of BrightFocus



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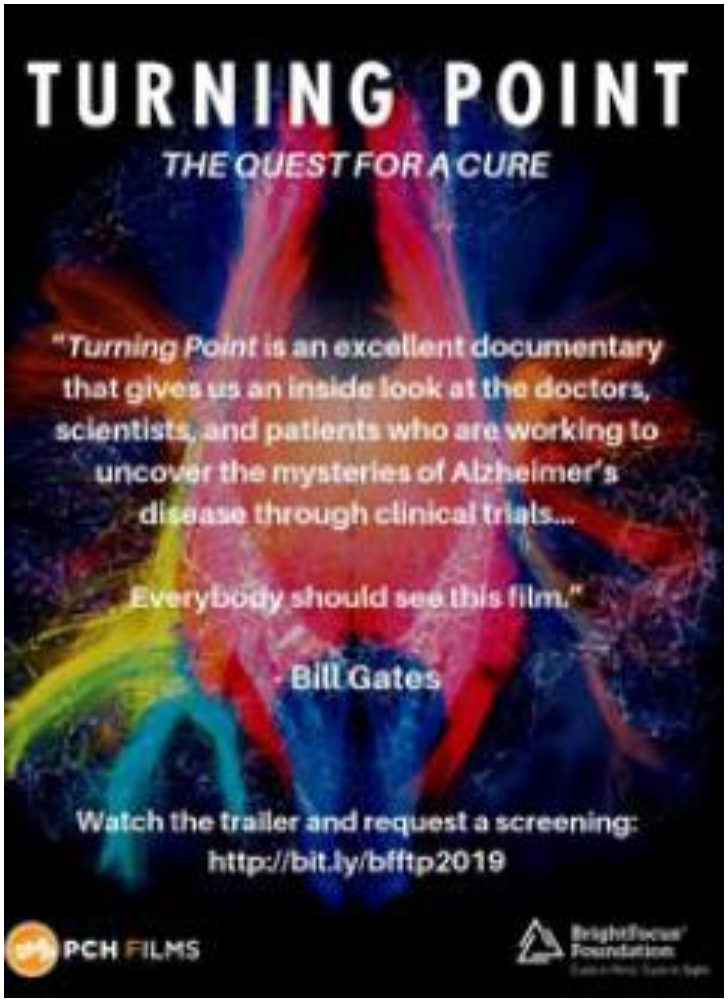
Turning Point: Inside Look At Quest For Alzheimer's Cure



BrightFocus is the Presentation Partner Of Turning Point

Screening Requests

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RACERS

Investing in a Cure

Right: Screening of Turning Point at Emory University for patients, clinicians and caregivers to encourage participation in Alzheimer's clinical trials.

RACERS

A Partnership with Gates Ventures—RACERS Initiative

With funding from Gates Ventures, BrightFocus is working in collaboration with the National Institute on Aging to help health care providers learn, and be proactive about, early detection and diagnosis of cognitive impairment/Alzheimer's/related dementias.

With a goal of providing patients and their families the opportunity to participate in research studies, the **RACERS** project focus is to:

- **r** — **recognize** early signs of cognitive issues
- **a** — conduct or refer patient for **assessment**
- **c** — **communicate** to patient and family re: diagnosis, treatment/care options and planning, and talk about the opportunity to participate in clinical trials
- **ers** — **enroll** in **research studies** as appropriate

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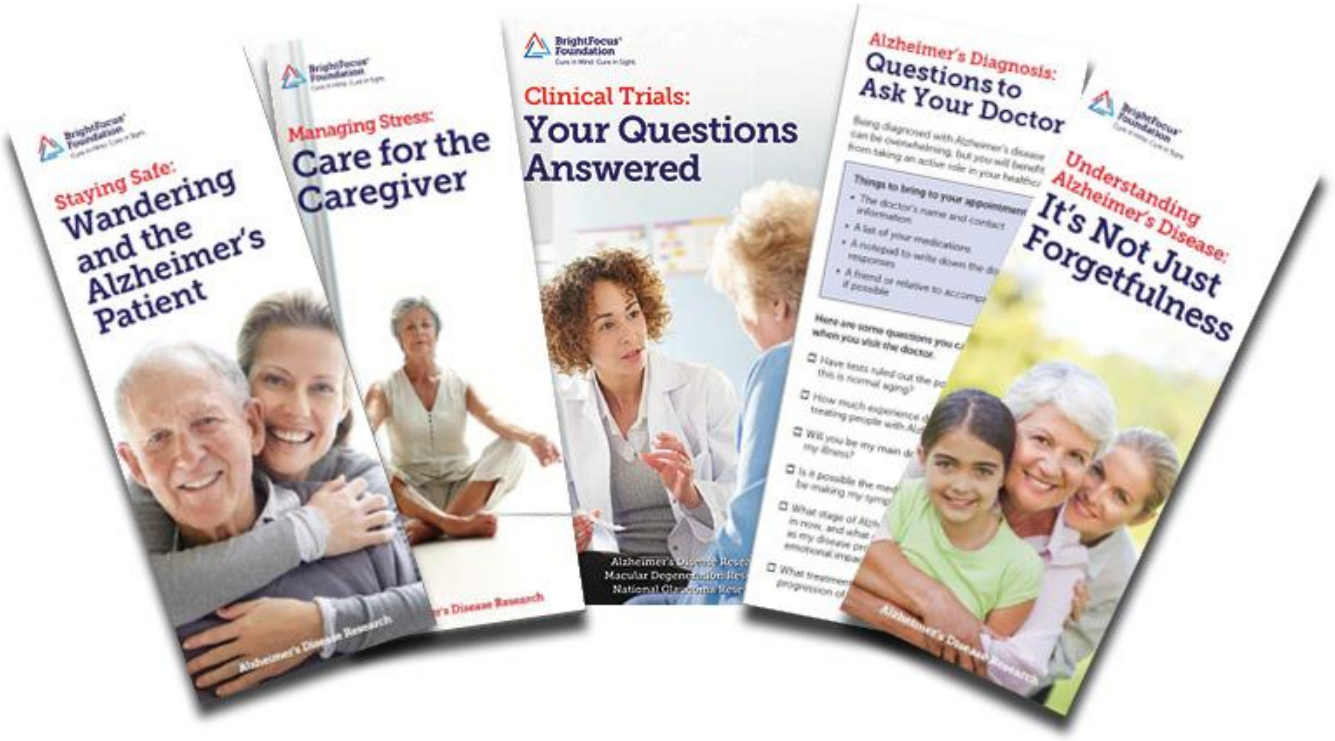
Increasing Public Awareness and Education



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Thank You