BrightFocus Foundation

Helping Scientists, Clinicians, Families and Communities Stay Strong Through Research, Partnerships, and Information

Diane Bovenkamp, PhD
Vice President, Scientific Affairs

HRA Annual Meeting
Tuesday, September 27, 2016
BrightFocus’ Initiatives

Listen

- Investigator-Initiated Research Awards for Innovative Science
- Training Grants For Young Scientists

Lead

- Symposia, Workshops, BF Fast Track “Boot Camp”
- Partnerships
- Open Access Journal
- Educational Materials
Helping Scientists, Clinicians, Families, and Communities Stay Strong:

Research
BrightFocus’ Scientific Affairs Team

Kara Summers
Scientific Program Grants Manager
BrightFocus Foundation

Diane Bovenkamp, PhD
Vice President, Scientific Affairs
BrightFocus Foundation

TBD
Director, Scientific Programs
BrightFocus Foundation
Diseases That Affect Sight and Mind

**Alzheimer’s Disease:** brain disease that causes problems with memory, thinking and behavior

- More than 5 million in U.S.; Worldwide: 46.8 million people are believed to be living with Alzheimer's disease or other dementias

**Macular Degeneration:** loss of central vision

- More than 11 million in US (2 million with advanced forms); The number of people living with macular degeneration is expected to reach 196 million worldwide by 2020.

**Glaucoma:** group of conditions—loss of side vision

- More than 3 million in US; More than 60 million in the world
BrightFocus Research Funding: Neurodegenerative Disease

Alzheimer’s Disease

The Progression of Alzheimer’s Disease

Glaucoma

Build Up of Aqueous Humor

Normal Eye

Glaucoma

Macular Degeneration

Macular Degeneration

Illustration by Bob Mooradian, provided courtesy of the BrightFocus Foundation.
What Awards Do You Offer?

- **Our vision:** help people live free from diseases of mind and sight
- We are accountable to our donors: affected families
- Investigator-initiated, high-risk research

- **Alzheimer’s Disease Research**
  - Standard: $300,000 total for 3 years
  - Postdoctoral Fellowship: $100,000 for 2 years

- **Macular Degeneration Research**
  - Standard: $160,000 total for 2 years (Postdocs can be CoPIs)

- **National Glaucoma Research**
  - Standard: $150,000 total for 2 years (Postdocs can be CoPIs)
BrightFocus Awards At-A-Glance
We Leave No Stone Unturned

55% BASIC RESEARCH GRANTS
11% CLINICAL RESEARCH GRANTS
34% TRANSLATIONAL RESEARCH GRANTS
Diseases Have No Borders... Neither Do BrightFocus Awards

Blue Dot = Since Inception (22 Locations)

Red Circle = 6 Locations for FY16:
Australia (2) Canada England (ADR) Germany Ireland USA
Since Inception Funding = $163 million

FY16: Largest dollar amount given in one year for research since inception.

Total Grant Support by Year
Fiscal Year FY16

- $11.7 million in FY16 for all 3 programs
- $4.9 million in FY16 for vision research
- Application Funding Success Rates:
  - MDR=18\% (40\% from Full Invitation)
  - NGR=17\%
  - ADR=13\%
Alzheimer’s Disease Research
FY16=30 Awards
Research Covers Many Angles

FY16 ADR Award Offers CADRO/IADRP Codings

General Research Pipeline Descriptions
Macular Degeneration Research
FY16 MDR=19 awards
Photoreceptors/RPE/Choroid

John Hulleman: Genetic Manipulation of a gene for the Treatment of Malattia Leventinese and Dry Age-Related Macular Degeneration. The University of Texas Southwestern Medical Center, Dallas, TX

Biju Thomas: Studies on Functionality of IPS-RPE Transplanted in Immunodeficient RCS Rats; USC, Los Angeles, CA

Marcelo Nociari: Lipofuscin-mediated ER stress in the pathogenesis of macular degeneration.; The Cleveland Clinic Foundation, OH.

Vera Bonilha: Geographic Atrophy: Changes in the RPE and inflammatory cell populations in the region of expanding lesions. The Cleveland Clinic Foundation, OH.

Francesco Giorgianni: In vitro and in vivo studies of a gene as a possible key role player in drusen biogenesis-Increasing stress resistance: a new strategy for AMD. The University of Tennessee Health Science Center, Memphis, TN

Jeffrey Gross: A Zebrafish Model of AMD: A Novel Approach to Identify Factors That Facilitate RPE Regeneration and Functional Restoration; University of Pittsburgh, PA

Robyn Guymer: Failure to remove debris: defective mechanisms may play a role in the pathogenesis of AMD. Centre for Eye Research Australia, The University of Melbourne, Australia

Debasish Sinha: Modulating lysosomal function in RPE as a novel therapeutic approach for the treatment of AMD. Johns Hopkins University, Baltimore, MD

Jianhai Du: NAD metabolism in normal and disease-specific human RPE cells. West Virginia University, Morgantown, WV

Patrick Daugherty: Antibody specificity repertoire characterization in age-related macular degeneration. University of California, Santa Barbara, CA

Petr Baranov: Indirect photoreceptor neuroprotection through small molecule-induced growth factors; Schepens Eye Institute/MEEI, Boston, MA

Brian Ballios: Bioengineered stem cell-derived cone photoreceptor therapy; University of Toronto, Canada

Zhihong Hu: Automated Multimodal Detection and Analysis of Geographic Atrophy; Doheny Eye Institute, Los Angeles, CA

Kip Connor: Lipid regulators of choroidal neovascularization. Schepens Eye Institute/MEEI, Boston, MA

Kaustabh Ghosh: Micromechanical Determinants of Choriocapillaris Dysfunction in AMD Pathogenesis; University of California, Riverside

Maria Valeria Canto-Soler: A novel 3D human mini-retina model for early AMD; Johns Hopkins University, Baltimore, MD

Sarah Doyle: The role of Toll/IL-1 receptor (TIR)-signalling ‘checkpoint’ regulators in the pathobiology of AMD; Trinity College Dublin, Ireland

Paul Baird: Identifying gene pathways that delineate the two late stage types of disease in age-related macular degeneration. Centre for Eye Research Australia, The University of Melbourne, Australia

Malia Edwards: Retinal glial changes in AMD. Johns Hopkins University, Baltimore, MD
National Glaucoma Research
FY16=13 Awards
Front and Back of the Eye

Gillian McLellan: TGF-B and glaucoma progression in a spontaneous model
University of Wisconsin, Madison, WI

Yvonne Ou: Retinal synapse disassembly in glaucoma
UCSF, San Francisco, CA

Xiuqian Mu: Generation of retinal ganglion cells by reprogramming
SUNY Buffalo, NY

Kevin Chan: Widespread Structural and Functional Brain Changes and Visuomotor Impairments in Glaucoma
University of Pittsburgh, PA

Meredith Gregory-Ksander: The NLRP3 inflammasome as a new target in glaucoma
Schepens Eye Institute/MEEI, Boston, MA

Daniel Sun: Do we need optic nerve head astrocytes to become reactive in glaucoma?
Schepens Eye Institute/MEEI, Boston, MA

Shahid Husain: Pro-inflammatory Cytokines Regulation by HIF-1α in Glaucoma
Medical University of South Carolina, SC

Crawford Downs: Continuous Telemetric Measurement and Chronic Control of Cerebrospinal Fluid Pressure
University of Alabama at Birmingham, AB

Yutao Liu: miR-182 and TM Dysfunction in High Tension Glaucoma
Georgia Regents University, Augusta, GA

Xiuqian Mu: Generation of retinal ganglion cells by reprogramming
SUNY Buffalo, NY

Shahid Husain: Pro-inflammatory Cytokines Regulation by HIF-1α in Glaucoma
Medical University of South Carolina, SC

Crawford Downs: Continuous Telemetric Measurement and Chronic Control of Cerebrospinal Fluid Pressure
University of Alabama at Birmingham, AB

Yvonne Ou: Retinal synapse disassembly in glaucoma
UCSF, San Francisco, CA

Yvonne Ou: Retinal synapse disassembly in glaucoma
UCSF, San Francisco, CA

Raquel Lieberman: Identification of myocilin posttranslational modifications and binding partners under static and glaucoma-relevant mechanical stretch
Georgia Institute of Technology, Atlanta, GA

Audrey Bernstein: Autophagic Dysfunction in Exfoliation Glaucoma
Icahn School of Medicine, Mount Sinai University, New York, NY

Rudolf Fuchshofer: Role of non-coding RNAs in outflow resistance dysregulation; University of Regensburg, Germany

Haiyan Gong: Cell-cell interaction in giant vacuole/pore formation
Boston University, Boston, MA
Helping Scientists, Clinicians, Families, and Communities Stay Strong:

Partnerships
AD/PD 2017 Pre-Meeting Satellite: Common Features of Neurodegenerative Diseases: Exploring the Brain-Eye Connection

Goals:
• Co-Chairs: Guojun Bu, PhD, Adriana Di Polo, PhD, and Todd E. Golde, MD, PhD (Tuesday, March 28, 2017)
• Identify knowledge & barriers to bridging ocular neuroscience with the broader field of neurodegenerative diseases
• Provide thoughtful guidance to investigators seeking to meaningfully incorporate the idea of interdisciplinary research in their own research programs
RD Organizing Committee
John D. Ash
Robert E. Anderson
Catherine Bowes Rickman
Matthew M. LaVail
Joe G. Hollyfield
Christian Grimm

Local Organizing Committee
Nagahisa Yoshimura (Chair, Kyoto University)
Shuichi Yamamoto (Chiba University Hospital)
Akira Murakami (Juntendo University Hospital)
Yoshihiro Hotta (Hamamatsu Univ. School of Medicine)
Mineo Kondo (Mie Univ. Graduate School of Medicine)
Akihiro Ohira (Shimane University Faculty of Medicine)
Masaki Tanito (Matsue Red Cross Hospital)
ISER/BrightFocus 2017 Meeting

Planning Committee Leadership:
• W. Daniel Stamer, PhD
• C. Ross Ethier, PhD
• Robert W. Nickells, PhD
BrightFocus Alzheimer’s Fast Track
(November 9-11, 2016)
BrightFocus Glaucoma Fast Track
(October 4, 2017)

Alzheimer’s Fast Track

Co-chairs: Frank M. LaFerla, PhD, Harry M.W. Steinbusch, PhD & Cynthia A. Lemere, PhD

The Dana on Mission Bay, 1710 W Mission Bay Drive
San Diego, CA, USA

If you are a graduate student, postdoctoral fellow, or other early-stage scientist focusing on Alzheimer’s disease research, take advantage of this unique opportunity to accelerate your knowledge immersion towards becoming an expert in this exciting field.

• Connect with preeminent Alzheimer’s disease experts and fellow early-stage researchers based in the U.S. and around the world
• Participate in interactive workgroups and breakout sessions
• Engage in scientific debates

Jumpstart your career in this workshop that will offer graduate students and postdocs an immersive opportunity to learn and discuss some of the latest trends in Alzheimer’s disease research through close interaction with established leaders in the field.

http://www.brightfocus.org/event/alzheimers-fast-track
Molecular Neurodegeneration Partnership with BioMed Central

- Official Journal of BrightFocus
- Open Access
Helping Scientists, Clinicians, Families, and Communities Stay Strong:

Information/Tools
Increasing Public Awareness and Education

www.brightfocus.org
Web Page For Each Award

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

Randall Robinson, MD
Washington University (St Louis, MO)

Year Awarded: 2009
Grant Duration: July 29, 2009 - January 31, 2012
Disease: Alzheimer's
Award Amount: $200,000
Grant Reference ID: SAT36
Award Type: Standard
Award Region: US-Eastern

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

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

Details: We have developed stable isotopic labeling kinetics (SILK) to measure tau in the human central nervous system (CNS). With a tau SILK method, we will compare samples with stable isotopic amino acids and measure the amount of isotope in the brain proteins over time. By measuring labeled tau, we will calculate how fast the brain produces tau and clears it. In Aim 1 of our study, we will use normal participants to study CNS tau proteins to determine their metabolic rate. In Aim 1, we will test participants with AD and age-matched cognitively normal controls to answer the question, do CNS tau kinetics change in AD?

The past few decades of research have focused on amyloid-beta as the cause of AD, but recent evidence indicates that tau protein plays a crucial role in AD. Tau is a microtubule protein that is involved in intracellular transport and is increased in AD. The SILK method that we have developed will allow us to measure production and clearance of tau in the brain. In this study, we are using our new method to develop the kinetics of tau in the human CNS, which will provide the first values of tau in AD. With increased production and impaired clearance.

This is an important step in our understanding of AD. Our study elucidating the kinetics of tau in the human CNS will provide the first values of tau in AD, which will help us understand the significance of tau in the disease.

First published on: Wednesday, July 3, 2014

Understanding the Earliest Steps of Optic Nerve Cell Death in Glaucoma

Yvonne Wu, MD
University of California, San Francisco

Year Awarded: 2018
Grant Duration: July 2, 2018 - June 30, 2020
Disease: Glaucoma
Award Amount: $200,000
Grant Reference ID: SAT1859
Award Type: Standard
Award Region: US-Western

Rational Synapses Dysfunction in Glaucoma

SUMMARY: In glaucoma, the cells of the optic nerve die and that can lead to blindness. Although we know that optic nerves are injured in glaucoma, we do not yet understand the earliest changes that occur to design treatments that can reverse these injuries. Early changes before irreversible cell death occurs.

Details: Our goal is to understand the earliest stage of injury to the optic nerve cell, or retinal ganglion cell (RGC), in glaucoma. We do not yet understand the reason for these RGC-deadly changes. Although we know that these RGCs are injured in glaucoma, we do not yet understand the reason for these changes. Early changes before irreversible cell death occurs.

Our laboratory is focused on how RGCs degenerate in glaucoma in order to understand how retina function is affected. In the retina, RGCs are composed of multiple layers of interconnected ganglion cells. With the RGCs being the "output" neurons in the retina, the retina sends 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 in the RGCs, which connect RGCs with their photoreceptors. Synapses are the connections where information from different types of neurons is transmitted. A second goal of this project is to understand how the RGCs will cause damage to the photoreceptors and how the synapses will respond. Finally, recent years have highlighted the importance of components of the immune system, specifically complement, in triggering these damaging processes. These findings will inform our understanding of the disease and help develop future treatments.

First published on: Wednesday, July 3, 2014

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

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

Year Awarded: 2018
Grant Duration: July 3, 2018 - June 30, 2020
Disease: Macular Degeneration
Award Amount: $200,000
Grant Reference ID: SAT1858
Award Type: Standard
Award Region: Ireland

The Role of TLR1/1 Receptor (TIR)-Signaling "Checkpoint" Regulators in Pathobiology of AMD

SUMMARY: The inflammatory response is needed to clear all the letters that make up our body, to keep us in working order. However, inflammation is a double-edged sword too much cause damage to the surrounding tissues and too little can be ineffective or even harmful. To overcome this problem, the inflammatory response must be regulated so that the protective inflammatory response is activated and the anti-inflammatory response is suppressed. We are studying the role of TLR1/1 in the pathobiology of AMD. Our research question asks whether the active process of switching off inflammatory responses is a loss in people with AMD.

Details: Our lab aims to understand the underlying mechanisms that are the driving forces behind age-related macular degeneration (AMD) and that we can prevent macular degeneration in future generations and stop its progression in those currently suffering with the disease. The overlying goal of this proposal is to investigate those contributions of negative regulators of Toll-like receptors (TLR) in the pathobiology of AMD.

TLRs are critical sensors of danger sensed by our immune system. First, we will analyze expression levels of a range of regulators in AMD and in the retinal AMD proliferative domain. Second, we will analyze the impact of inflammation or anti-inflammatory signaling on negative regulators of TLRs. Finally, we will analyze the role of negative regulators of
Accelerating the Development, Testing, and Dissemination of Home-Based Dementia Care Interventions

Members of the Consensus Panel

Constantine G. Lyketsos, MD, MHS  
Johns Hopkins School of Medicine

Quincy M Samus, PhD, MS  
Johns Hopkins School of Medicine

Laura Gitlin, PhD  
Johns Hopkins School of Nursing

Betty Smith Black, PhD EdS  
Johns Hopkins School of Medicine

Christopher Callahan, M.D.  
Indiana University Center for Aging Research

Deirdre Johnston, M.B.B.Ch., M.D.  
Johns Hopkins School of Medicine

Diane Bovenkamp, PhD  
BrightFocus Foundation

Helen Kales, M.D.  
University of Michigan

Nancy Hodgson, PhD, RN, FAAN  
Johns Hopkins School of Nursing

Michele Karel, PhD, ABPP  
Veterans Administration Central Office

Shari M. Ling, M.D.  
Centers for Medicare and Medicaid Services

John Jay Kenney, PhD.  
MD Department of Health & Human Services

Maï Panchal, PhD.  
LECMA, AFi, and iSAO (France)

Michael Buckley  
BrightFocus Foundation

Consensus Panel Sessions are Pre-Summit activities to inform the planned 2017 Research Summit on Care and Services for Persons with Dementia, Family Members and Caregivers. Members of the Advisory Council on Alzheimer’s Research, Care and Services recognize the value of activities such as this.
Research and Tools to Better Understand and Support Caregivers

www.health-ebrainstudy.org

Launched July 26, 2016
BrightFocus Leadership

Stacy Pagos Haller
President and CEO

R. Brian Elderton
Sr. Vice President, Development

Diane Bovenkamp, PhD
Vice President, Scientific Affairs

Nancy Lynn
Sr. Vice President, Strategic Partnerships

Michael Buckley
Vice President, Public Affairs

David Marks
Vice President, Finance and Administration