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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

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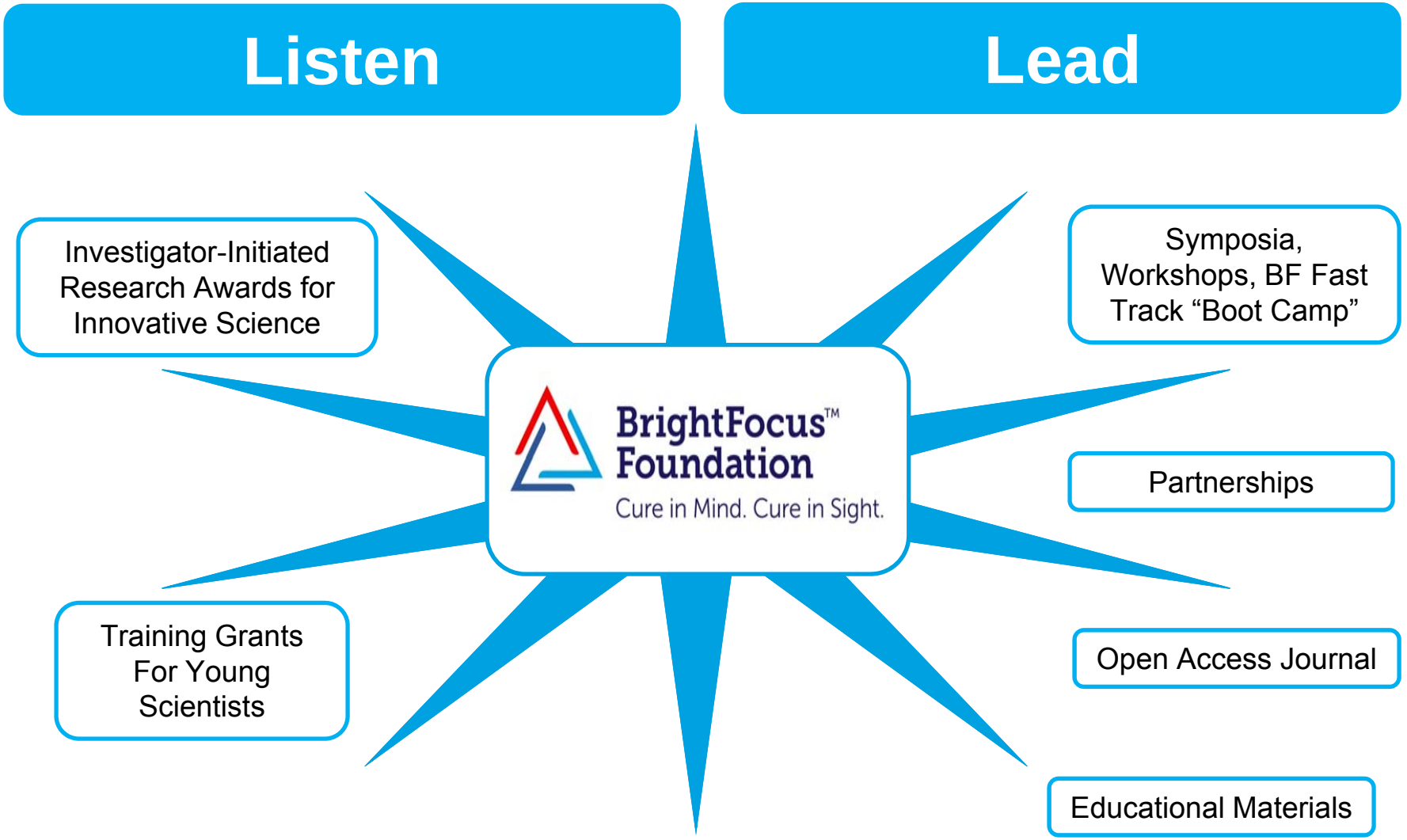
BrightFocus' Initiatives



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Helping Scientists, Clinicians, Families, and Communities Stay Strong:

Research

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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

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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

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BrightFocus Research Funding: Neurodegenerative Disease

Glaucoma

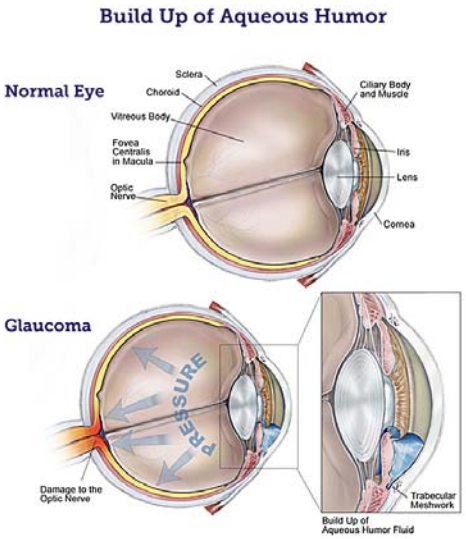

Illustration by Bob Morreale, provided courtesy of the BrightFocus Foundation

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Alzheimer's Disease

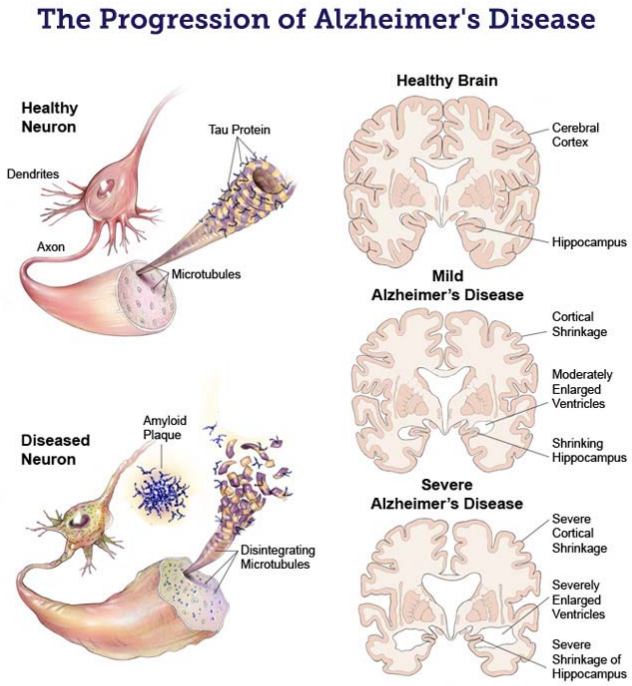

Illustration by Bob Morreale, provided courtesy of the BrightFocus Foundation

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Macular Degeneration

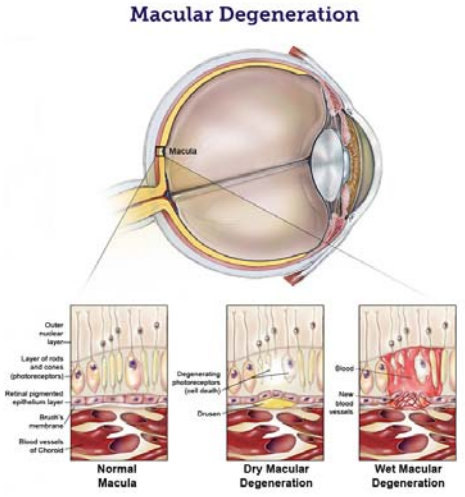

Illustration by Bob Morreale, provided courtesy of the BrightFocus Foundation

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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)

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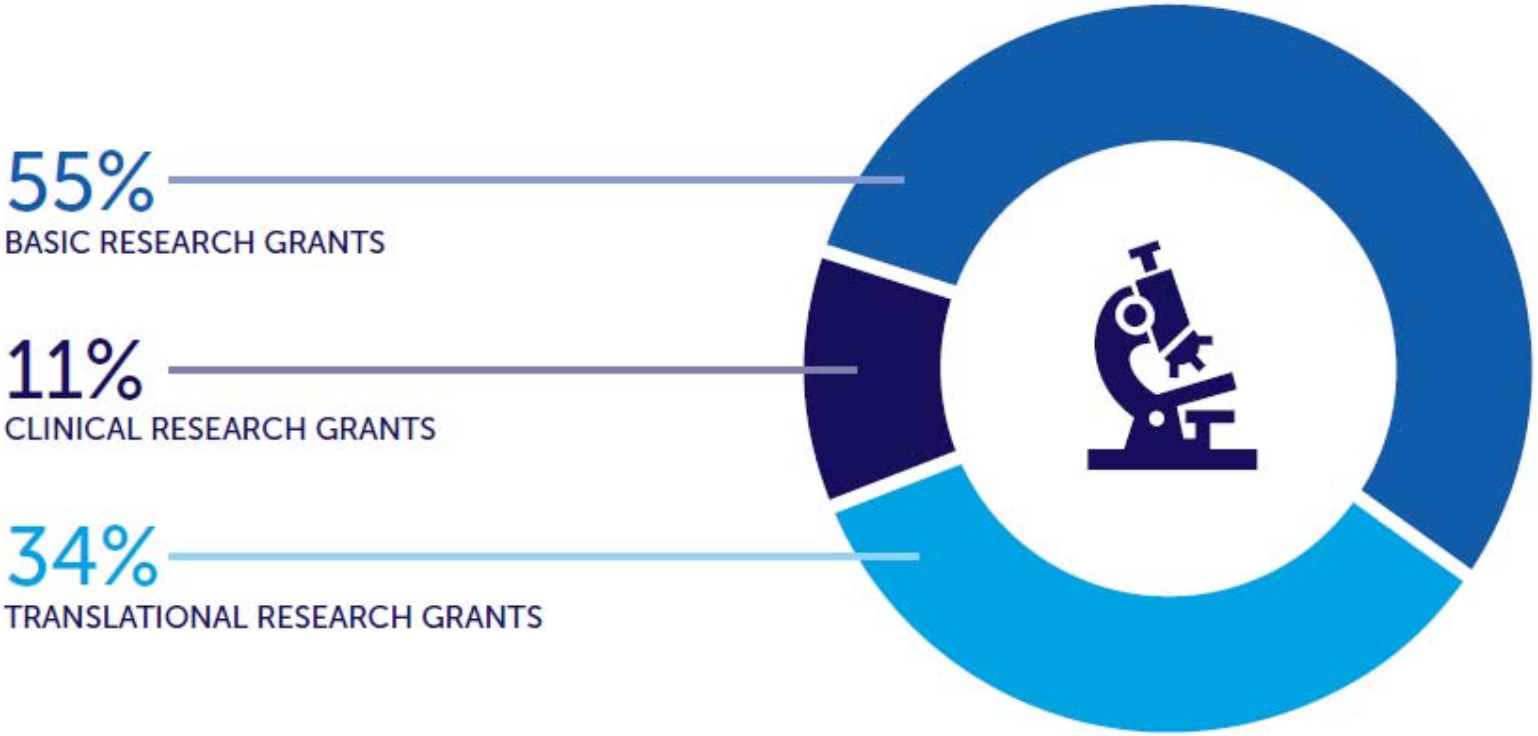
BrightFocus Awards At-A-Glance

We Leave No Stone Unturned



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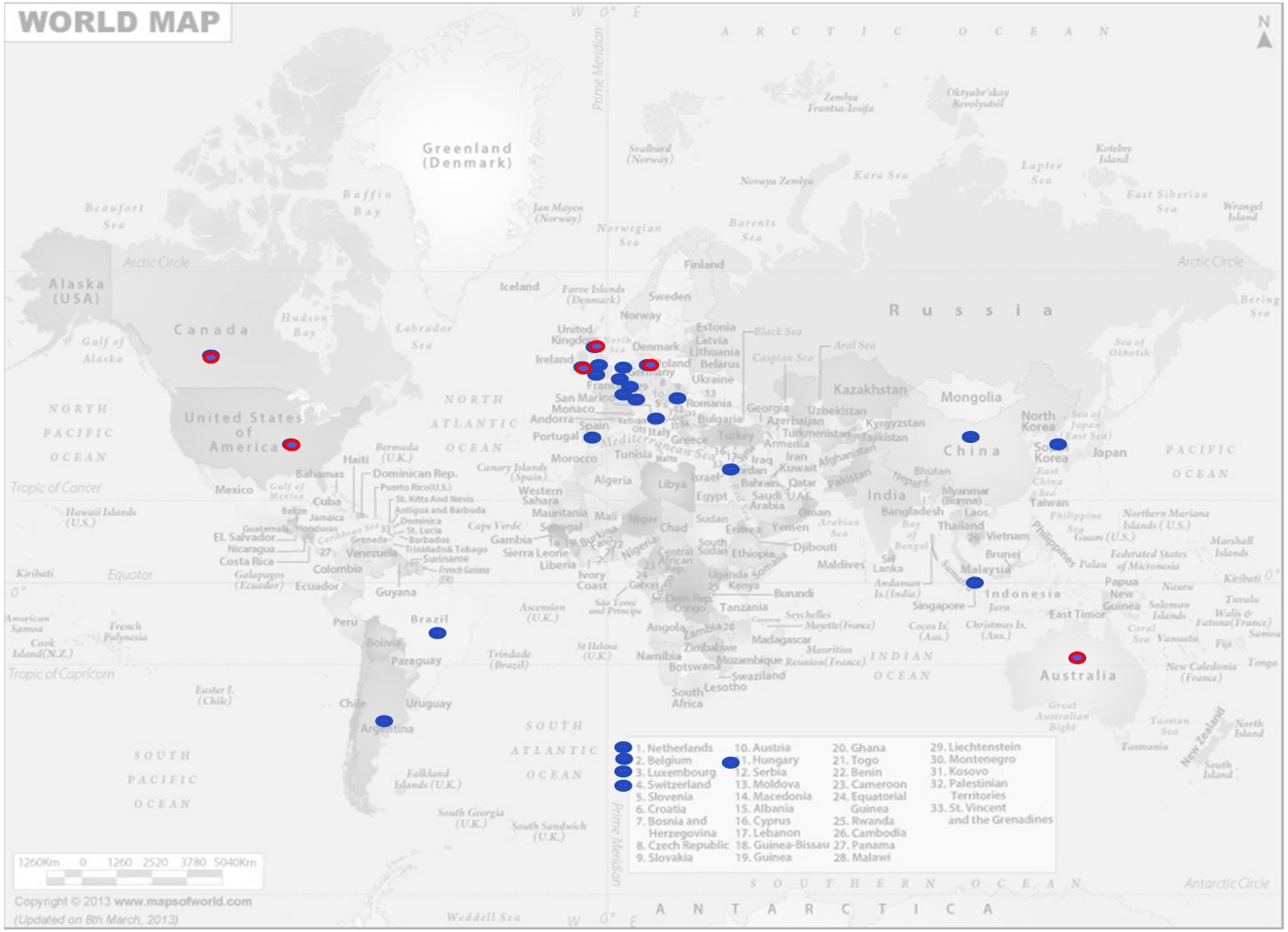
Diseases Have No Borders… Neither Do BrightFocus Awards



Blue Dot= Since Inception (22 Locations)

Red Circle = 6 Locations for FY16:
Australia (2)
Canada
England (ADR)
Germany
Ireland
USA

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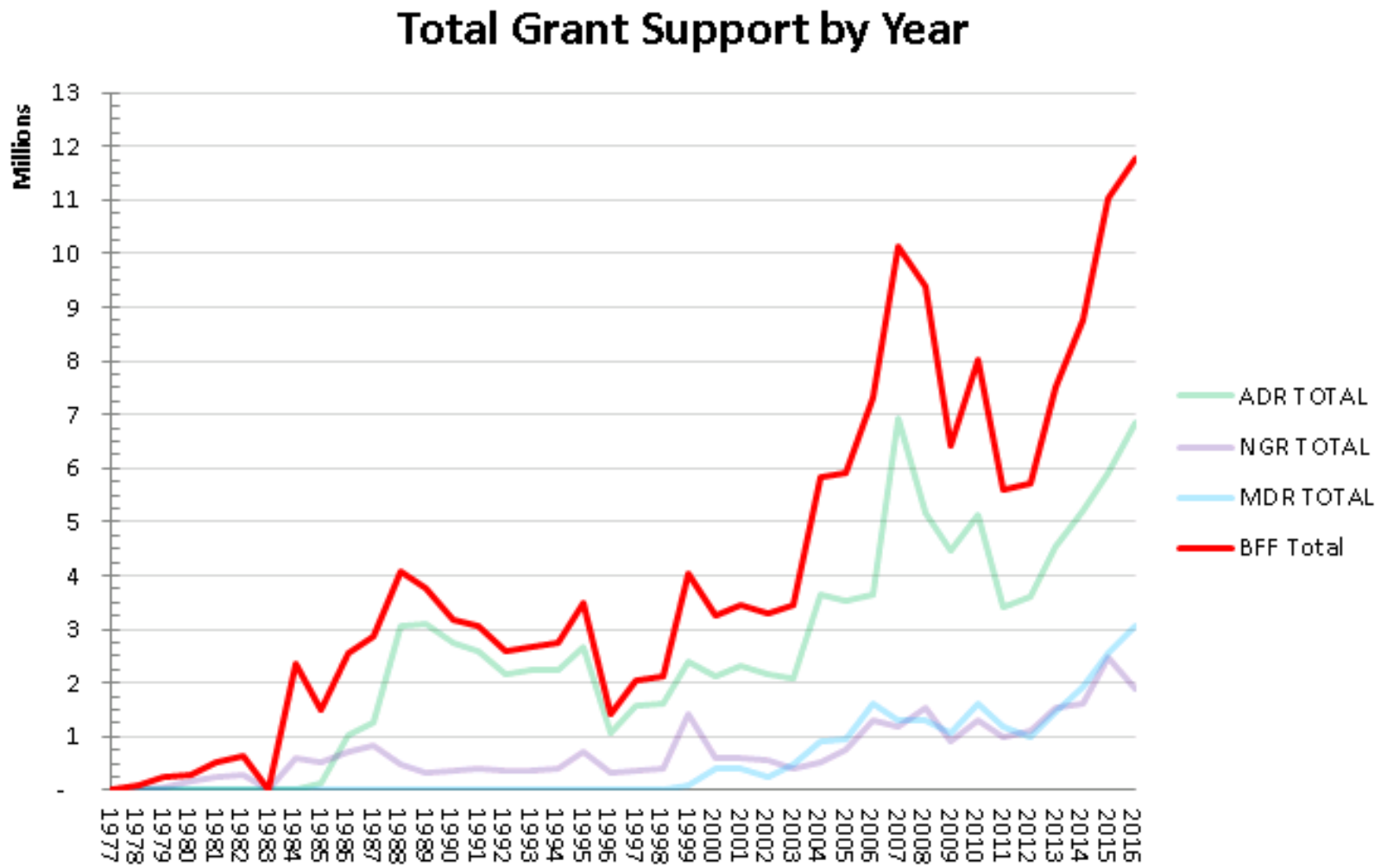
Since Inception Funding =$163 million

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



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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%

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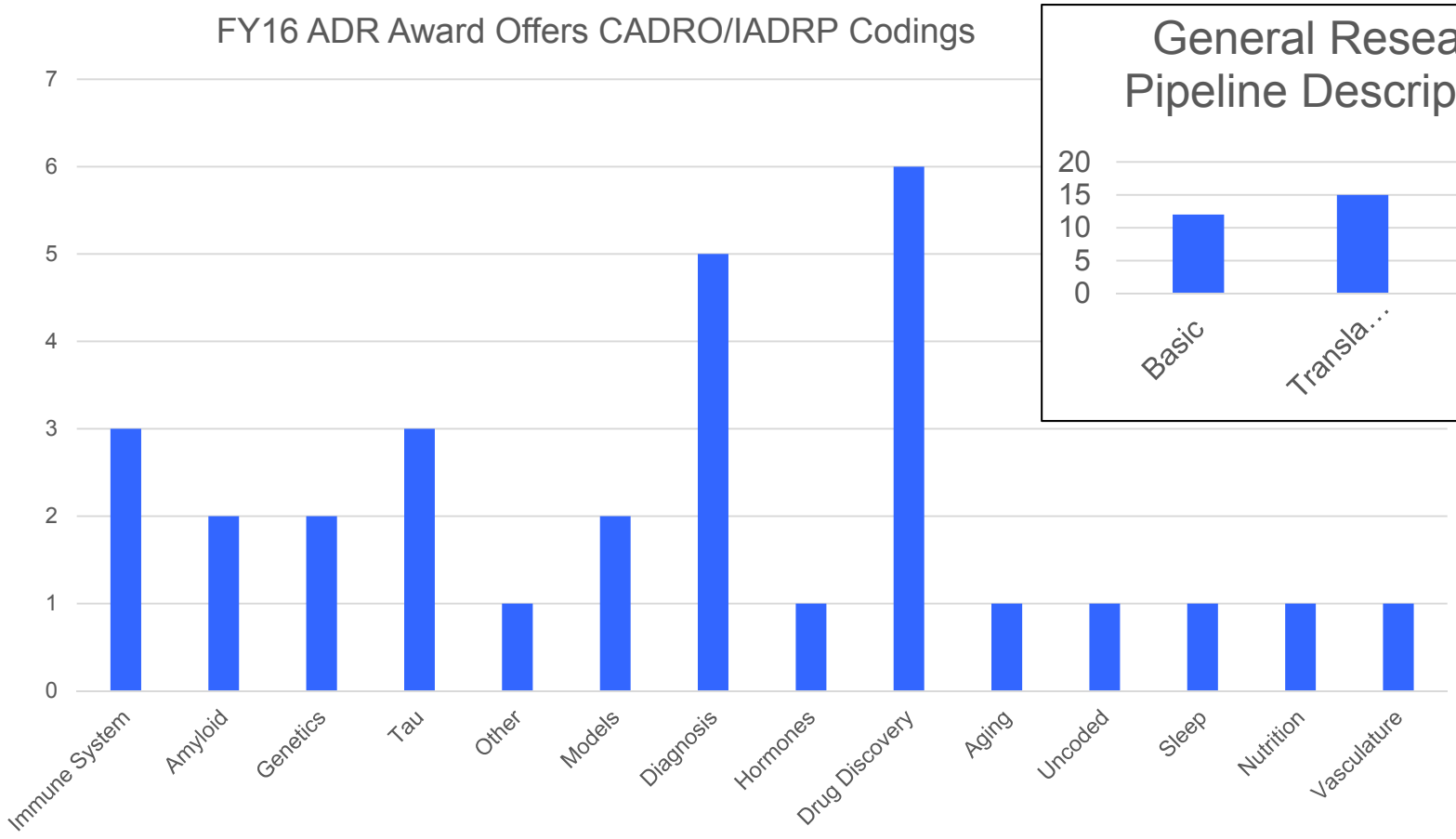
Alzheimer's Disease Research FY16=30 Awards Research Covers Many Angles



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

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

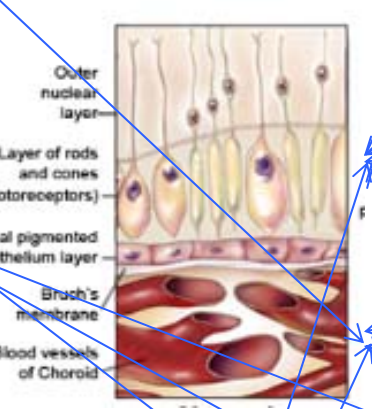
John Hulleman: Genetic Manipulation of a gene for the Treatment of Malattia Leventinese and Dry Age-Related Macular Degeneration.
The University of Texas Southwestern Medical Center, Dallas, TX

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.; Weill Cornell University, NY, NY

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



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

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

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

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

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

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

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

Malia Edwards: Retinal glial changes in AMD
Johns Hopkins University, Baltimore, MD

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National Glaucoma Research FY16=13 Awards Front and Back of the Eye

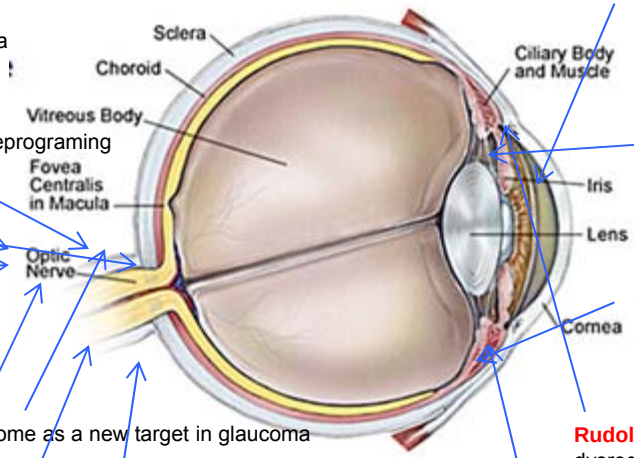
Gillian McLellan: TGF-β and glaucoma progression in a spontaneous model
University of Wisconsin, Madison, WI

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

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

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



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

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

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

Haiyan Gong: Cell-cell interaction in giant vacuole/pore formation
Boston University, 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

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Helping Scientists, Clinicians, Families, and Communities Stay Strong:

Partnerships

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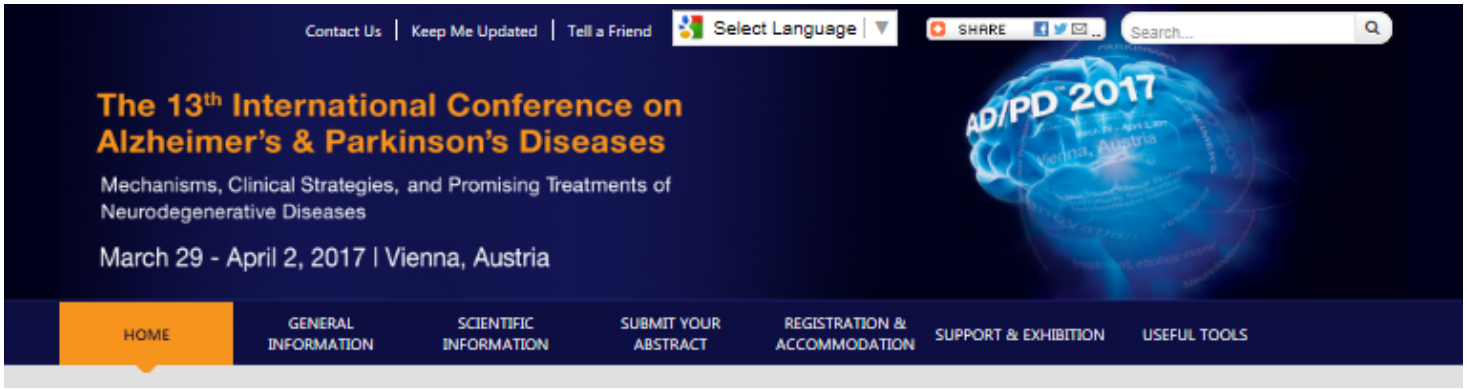
AD/PD 2017 Pre-Meeting Satellite:

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

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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)

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ISER / BrightFocus 2017 Meeting

Planning Committee Leadership:

- W. Daniel Stamer, PhD
- C. Ross Ethier, PhD
- Robert W. Nickells, PhD

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BrightFocus Alzheimer's Fast Track

(November 9-11, 2016)

BrightFocus Glaucoma Fast Track

(October 4, 2017)

Alzheimer's Fast Track

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.

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

Organized by BrightFocus Foundation, Alzheimer's Fast Track is a satellite event of the Society for Neuroscience's annual meeting, which takes place in San Diego from November 12 -16, 2016. View and download the flier.

http://www.brightfocus.org/event/alzheimers-fast-track

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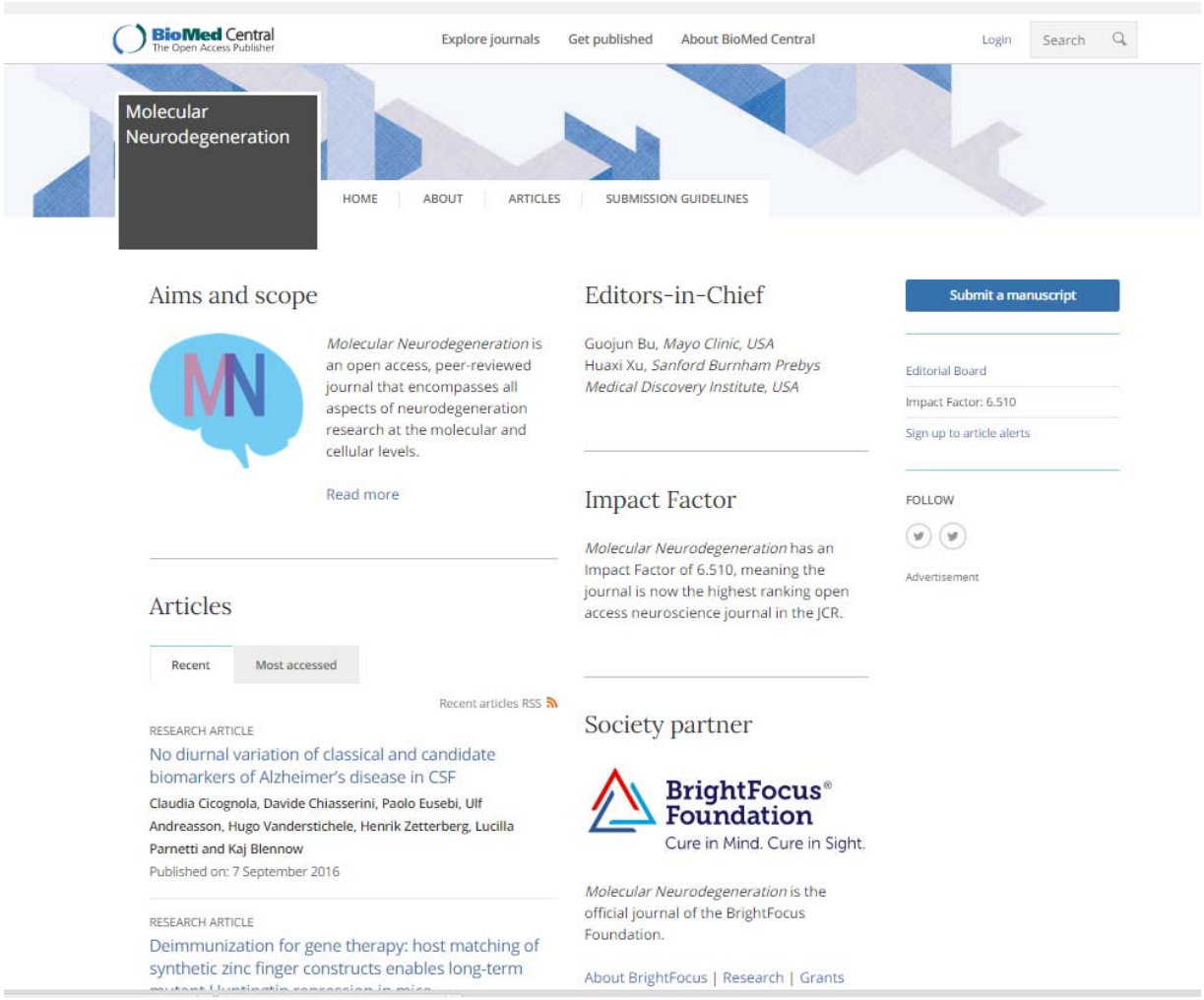
Molecular Neurodegeneration

Partnership with BioMed Central

- Official Journal of BrightFocus
- Open Access



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Information/Tools

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Increasing Public Awareness and Education

www.brightfocus.org

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Web Page 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 Annajel Ballard (The Ballard/Marvin 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: G2016054
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

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 retinas 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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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.

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Research and Tools to Better Understand and Support Caregivers

www.health-ebrainstudy.org

Launched July 26, 2016

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BrightFocus Leadership

Stacy Pagos Haller
President and CEO

Diane Bovenkamp, PhD
Vice President, Scientific Affairs

Michael Buckley
Vice President, Public Affairs

R. Brian Elderton
Sr. Vice President, Development

Nancy Lynn
Sr. Vice President, Strategic Partnerships

David Marks
Vice President, Finance and Administration