2018 NIH
Alzheimer's Disease Research Summit

Path to Treatment and Prevention

March 1–2, 2018

National Institutes of Health

Bethesda, MD

PROGRAM

National Institute on Aging

#ADSummit18

2018 NIH ALZHEIMER'S DISEASE RESEARCH SUMMIT:
PATH TO TREATMENT AND PREVENTION

SUMMIT PURPOSE AND GOALS

Background: The NIH Alzheimer's Disease (AD) Research Summits are key strategic planning meetings tied to the implementation of the first goal of the National Plan to Address Alzheimer's: to treat and prevent AD by 2025. They bring together a multi-stakeholder community—including government, industry, academia, private foundations, and patient advocates—to formulate an integrated, translational research agenda that will enable the development of effective therapies (disease-modifying and palliative) across the disease continuum for cognitive as well as neuropsychiatric symptoms of AD.

The 2012 and 2015 AD Research Summits delivered recommendations that served as the basis for developing research implementation milestones detailing specific steps and success criteria for NIH and other stakeholders toward the development of effective treatment for and prevention of AD. The milestones span the entire AD research landscape, including basic, translational, clinical, and health services research, and serve as the basis for the development of the NIH Alzheimer's Disease Bypass Budget.

Goal: The 2018 NIH AD Research Summit will build on the foundation laid by the Summits held in 2012 and 2015. It will feature progress toward achieving the AD research implementation milestones and will continue the development of an integrated, multidisciplinary research agenda necessary to enable precision medicine for AD. Key to achieving this goal is the identification of 1) resources/infrastructure and multi-stakeholder partnerships necessary to successfully implement this research agenda and 2) strategies to engage patients, caregivers, and citizens as direct partners in research.

Program Structure: The central programmatic themes of the 2018 Summit are 1) understanding disease heterogeneity; 2) enhancing research rigor, reproducibility, and translatability; and 3) enabling rapid translational learning through open science systems and incentives.

The program agenda will be organized around seven sessions:

1. Novel Mechanistic Insights into the Complex Biology and Heterogeneity of AD

2. Enabling Precision Medicine for AD

3. Translational Tools and Infrastructure for Predictive Drug Development

4. Emerging Therapeutics

5. Understanding the Impact of the Environment to Advance Disease Prevention

6. Advances in Disease Monitoring, Assessment, and Care

7. Building an Open Science Research Ecosystem to Accelerate AD Therapy Development

The program will begin with an overview of progress achieved to date, followed by three plenary lectures. Each of the seven sessions will feature up to four brief presentations, followed by a moderated discussion that will include six to nine panelists with diverse expertise. Collectively, the session speakers and panelists will highlight major advances and discuss key issues. The composition of speakers and panelists for each session will include representatives from academia, industry, federal agencies, private foundations, and public advocacy groups working on Alzheimer's and other complex diseases.

Outcome: The general program will be followed by a writing session during which a select group of experts, together with NIA/NIH staff and representatives from other U.S. AD funding agencies and members of the Advisory Council on Alzheimer's Research, Care, and Services, will discuss and help finalize the recommendations put forward by the Summit participants. These recommendations will inform research priorities and serve as the basis for updating and refining the National Alzheimer's Project Act research milestones for measuring progress toward the goal to prevent or treat AD by 2025.

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PATH TO TREATMENT AND PREVENTION

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2018 NIH ALZHEIMER'S DISEASE RESEARCH SUMMIT:
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Natcher Auditorium, NIH Campus
Bethesda, MD
March 1–2, 2018

DAY ONE: MARCH 1, 2018

7:00 a.m.–8:00 a.m.   **REGISTRATION**

8:00 a.m.–8:10 a.m.   **Opening Remarks**
Francis Collins (Director, NIH)

8:10 a.m.–8:30 a.m.   **Introduction to the Summit Program**
Eliezer Masliah (Director, Division of Neuroscience, NIA/NIH)

AD/ADRD Research Milestones Progress Report
Richard Hodes (Director, NIA/NIH)

8:30 a.m.–9:30 a.m.   **PLENARY TALKS**

The Role of Public Advocacy in the Global Fight Against Dementia
Maria Carrillo (Alzheimer's Association)

Biomedical Research in the Era of Precision Medicine:
The All of Us Initiative
Joni L. Rutter (NIH)

The Future is Now: Deconstructing Disease Complexity to Enable
Precision Medicine for AD
Eric Schadt (Icahn School of Medicine at Mount Sinai)

9:30 a.m.–11:45 a.m.   **SESSION I: Novel Mechanistic Insights into the Complex Biology**
and Heterogeneity of AD

Chairs: Nilüfer Ertekin-Taner (Mayo Clinic Florida)
Robert Bell (Pfizer)

Speakers:

Rediscovering Myelin: From Genetics to Molecular Mechanisms
Nilüfer Ertekin-Taner (Mayo Clinic Florida)

Novel Insights in the Neuroimmune Etiology of AD
Joel Dudley (Icahn School of Medicine at Mount Sinai)

Autophagy: Common Mechanisms in Aging, Cancer, and Alzheimer's
Ana Maria Cuervo (Albert Einstein College of Medicine)

Structural Diversity of Pathogenic Proteins: Implications for Therapy Development
Robert Tycko (NIDDK/NIH)

Panelists:

Marco Colonna (Washington University)

Carol A. Colton (Duke University)

Elizabeth Bradshaw (Columbia University)

Stuart Lipton (Scripps Research Institute; University of California, San Diego)

Lennart Mucke (Gladstone Institute of Neurological Disease)

Gabriela Chiosis (Memorial Sloan Kettering Cancer Center)

Benjamin Wolozin (Boston University)

Ben Readhead (Arizona State University)

Robert Bell (Pfizer)

Moderated Discussion: 11:15 a.m.–11:45 a.m.

11:45 a.m.–12:45 p.m.   **LUNCH**

12:45 p.m.–2:45 p.m.   **SESSION II: Enabling Precision Medicine for AD**

Chairs: David Bennett (Rush University)

Rima Kaddurah-Daouk (Duke University)

Speakers:

Integrative Metabolomics: From Target Discovery to Disease Subclassification
Matthias Arnold (Institute of Bioinformatics and Systems Biology)

Integrative Proteomics for Novel Target and Biomarker Discovery
Nick Seyfried (Emory University)

Translational Epidemiology of Diverse Cohorts
Rachel Whitmer (University of California, San Francisco)

AD Genetics in the Era of Precision Medicine: Signals from Global Collaborations
Cornelia van Duijn (Erasmus University)

Panelists:

Liana G. Apostolova (Indiana University)

Nicole Schupf (Columbia University)

Mariet Allen (Mayo Clinic Florida)

Nir Barzilai (Albert Einstein College of Medicine)

Catherine Kaczorowski (Jackson Laboratory)

Chris Gaiteri (Rush University)

Sean C. Bendall (Stanford University)

Moderated Discussion: 2:15 p.m.–2:45 p.m.

2:45 p.m.–4:45 p.m.   **SESSION III: Translational Tools and Infrastructure for Predictive Drug Development**

Chairs: David Collier (Eli Lilly and Company)

Allan Levey (Emory University)

Speakers:

MODEL-AD Consortium: Infrastructure for Next-Generation Animal Models Development and Preclinical Efficacy Testing
Greg Carter (Jackson Laboratory)

Infrastructure and Recruitment for Next-Generation Clinical Trials
Laurie Ryan (NIA/NIH)

Deploying QSP Models for Precision Medicine: From Target Validation to Clinical Trial Design
Cynthia J. Musante (Pfizer)

Panelists:

Gerard Schellenberg (University of Pennsylvania)

Nathan Price (Institute for Systems Biology)

Joel Dudley (Icahn School of Medicine at Mount Sinai)

Opher Gileadi (University of Oxford)

Jacob Hooker (Massachusetts General Hospital)

Valentina Fossati (New York Stem Cell Foundation Research Institute)

Lorenzo Refolo (NIA/NIH)

Moderated Discussion: 4:15 p.m.–4:45 p.m.

4:45 p.m.–5:45 p.m.   **SESSION IV: Emerging Therapeutics, Part I**

Chairs: Kalpana Merchant (Chaperone Therapeutics)
Rachelle Doody (Roche)

Speakers:

Neurotrophic Modulators as a Therapeutic for AD
Frank Longo (Stanford University)

Neuroregenerative Therapeutics for AD
Roberta Diaz Brinton (University of Arizona)

PDE4 Inhibitors for MCI and AD
Mark Gurney (Tetra Discovery Partners)

Reinvigorating the Industry Pipeline Through Precompetitive Partnerships
David Collier (Eli Lilly and Company)

5:45 p.m.   **DAY ONE ADJOURNS**

DAY TWO: MARCH 2, 2018

7:00 a.m.–8:00 a.m.　　**REGISTRATION**

8:00 a.m.–9:30 a.m.　　**SESSION IV: Emerging Therapeutics, Part II**

Chairs: Kalpana Merchant (Chaperone Therapeutics)
　　　　　　Rachelle Doody (Roche)

Panelists:
Mark Tuszynski (University of California, San Diego)
Linda J. Van Eldik (University of Kentucky)
Daniel Martin Watterson (Northwestern University)
Steven Wagner (University of California, San Diego)
Michela Gallagher (Johns Hopkins University)
Rong Xu (Case Western Reserve University)
Marina Sirota (University of California, San Francisco)
Kalpana Merchant (Chaperone Therapeutics)

Moderated Discussion: 8:45 a.m.–9:30 a.m.

9:30 a.m.–12:00 p.m.　　**SESSION V: Understanding the Impact of the Environment to Advance Disease Prevention**

Chairs: Laura Baker (Wake Forest School of Medicine)
　　　　　　Chirag Patel (Harvard Medical School)

Speakers:

Translating Knowledge About Socioeconomic Risk Factors into Disease Prevention
Jennifer Manly (Columbia University)

The Circadian Etiology of AD
Andrew Lim (University of Toronto)

Measuring the Impact of Chemical Pollutants on the Brain Across the Lifespan
Kelly M. Bakulski (University of Michigan)

Multimodal Lifestyle Interventions: What Nonpharmacologic Interventions Tell Us About Disease Mechanisms
Laura Baker (Wake Forest School of Medicine)

Panelists:

Mariana G. Figueiro (Rensselaer Polytechnic Institute)

Andrew J. Saykin (Indiana University)

Rong Xu (Case Western Reserve University)

Martha Clare Morris (Rush University)

Aliza P. Wingo (Emory University)

Noam Beckmann (Icahn School of Medicine at Mount Sinai)

Gayathri J. Dowling (NIDA/NIH)

Sumitra Muralidhar (U.S. Department of Veterans Affairs)

Moderated Discussion: 11:15 a.m.–12:00 p.m.

12:00 p.m.–1:00 p.m.	**LUNCH**
1:00 p.m.–3:15 p.m.	**SESSION VI: Advances in Disease Monitoring, Assessment, and Care**

Chairs: Rhoda Au (Boston University)

Magali Haas (Cohen Veterans Bioscience)

Speakers:

eHealth Tools to Quantify Brain Health Across the Disease Trajectory
Rhoda Au (Boston University)

Digital Tools for Sleep Monitoring and Optimization
Daniela Brunner (Early Signal)

Revolutionizing In-Home Disease Monitoring: The CART Initiative
Jeffrey Kaye (Oregon Health & Science University)

New Directions in Research on Care: Report from the AD Care Summit
Laura N. Gitlin (Johns Hopkins University)

Panelists:

Hiroko H. Dodge (Oregon Health & Science University; University of Michigan)

Larsson Omberg (Sage Bionetworks)

Dorothy Farrar-Edwards (University of Wisconsin, Madison)

Meryl Comer (Geoffrey Beene Foundation Alzheimer's Initiative)

Stephen Friend (Sage Bionetworks)

Moderated Discussion: 2:45 p.m.–3:15 p.m.

3:15 p.m.–3:30 p.m.   **BREAK**

3:30 p.m.–5:30 p.m.   **SESSION VII: Building an Open Science Research Ecosystem to Accelerate AD Therapy Development**

Chairs: Lara Mangravite (Sage Bionetworks)

Eric M. Reiman (Banner Alzheimer's Institute)

Speakers:

Accelerating Reproducible and Translatable Discovery Research Through Open Science
Lara Mangravite (Sage Bionetworks)

Why We Need Open Drug Discovery for AD
Aled Edwards (University of Toronto)

Liberating Clinical Trials Data to Enable Translational Learning
Eric M. Reiman (Banner Alzheimer's Institute)

Panelists:

Magali Haas (Cohen Veterans Bioscience)

Richard Wilder (Bill & Melinda Gates Foundation)

Stuart Buck (Laura and John Arnold Foundation)

Kevin Da Silva (Nature Publishing Group)

Jessica Polka (ASAPbio)

Giorgio A. Ascoli (George Mason University)

Katja Brose (Chan Zuckerberg Initiative)

Scott Hayton (bgC3)

Suzana Petanceska (NIA/NIH)

Moderated Discussion: 4:45 p.m.–5:30 p.m.

5:30 p.m.   **MEETING ADJOURNS**

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Participant Biographies

MARIET ALLEN

Dr. Allen is Assistant Professor of Neuroscience at the Mayo Clinic Florida. She received a bachelor's degree in biochemistry from the University of Leeds and a PhD in human genetics from the University of Edinburgh. Her research is primarily focused on the role of genetics and transcriptomics in AD and related dementias, with a particular interest in the use of quantitative endophenotypes. Dr. Allen co-leads the M²OVE-AD molecular profiling working group, and she is a contributing participant in the Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD) consortium.

LIANA G. APOSTOLOVA

Dr. Apostolova is the Barbara and Peer Baekgaard Professor of Alzheimer's Disease Research at Indiana University School of Medicine. She is a prolific researcher focused on the early symptomatic and presymptomatic stages of AD and on the development and validation of sensitive imaging and genetic biomarkers for AD and other dementing disorders. Dr. Apostolova is the Lead Principal Investigator of the recently funded Longitudinal Early-Onset Alzheimer's Disease Study (LEADS), which will study people with early-onset, sporadic AD and age-matched controls recruited at 14 sites across the United States.

MATTHIAS ARNOLD

Dr. Arnold studied bioinformatics at two universities, Ludwig-Maximilians University and Technical University Munich. During his PhD studies at Helmholtz Center Munich (HMGU), he specialized in integrative functional annotation of human genetic variants across "omics" layers. In several genetic studies, he contributed to building the first large-scale mappings of genetic influences on the human metabolome and proteome. In 2016, he joined the AD Metabolomics Consortium (ADMC) within the Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD) and M²OVE-AD initiatives. Currently, he is assembling a team for computational neurobiology at the Institute of Bioinformatics and Systems Biology at HMGU and supports the ADMC informatics team as adjunct assistant professor at Duke University.

GIORGIO A. ASCOLI

Dr. Ascoli received a PhD in biochemistry and neuroscience from the Scuola Normale Superiore of Pisa, Italy, and continued his research at the National Institutes of Health in Bethesda, MD, to investigate protein structure and binding in the nervous system. He moved to George Mason University in 1997, where he is University Professor in the Bioengineering Department and Neuroscience Program. He is also Director of the Center for Neural Informatics, Structures, and Plasticity and founding Editor-in-Chief of the journal *Neuroinformatics*. Dr. Ascoli fervently promotes data and knowledge sharing via NeuroMorpho.org, Hippocampome.org, and related initiatives.

RHODA AU

Dr. Au is Professor of Anatomy and Neurobiology, Neurology, and Epidemiology at Boston University's Schools of Medicine and Public Health. Since 1990, she has conducted research related to cognitive aging and dementia for the Framingham Heart Study. Recently she integrated digital technology into the cognitive assessment process to identify digital biomarkers as surrogate indices for more expensive and invasive fluid and imaging biomarkers. In addition, she uses "big data" analytics to identify novel AD pathways and treatments. Dr. Au is also building multisector ecosystems to generate solutions that move the focus on precision medicine to one centered more broadly on precision health.

LAURA BAKER

Dr. Baker is Associate Director of the NIH-funded Alzheimer's Disease Center at the Wake Forest School of Medicine. She has conducted research for the past 15 years focused on lifestyle interventions to protect brain health and prevent cognitive decline in older adults at increased risk for dementia. She currently leads four large national clinical studies, three of which are randomized clinical trials involving lifestyle modification. Dr. Baker serves on the National Institute on Aging/Alzheimer's Association National Strategy for Alzheimer's Disease Clinical Research Recruitment & Participation Taskforce; she leads efforts to develop strategies for recruitment and retention at the local level as part of this initiative.

KELLY M. BAKULSKI

Dr. Bakulski is Research Assistant Professor in the Department of Epidemiology at the University of Michigan. Her degree is in environmental health sciences, and she completed a postdoctoral fellowship in genetic and epigenetic epidemiology. Dr. Bakulski's research goal is to understand the etiologies of neurological disorders, including Alzheimer's. She investigates the integration of environmental exposures and genetic risk on cognitive function in aging populations.

NIR BARZILAI

Dr. Barzilai is Director of the Institute for Aging Research at the Albert Einstein College of Medicine and Director of the Glenn Center for the Biology of Human Aging and the Nathan Shock Center of Excellence in Biology of Aging. He is the Ingeborg and Ira Leon Rennert Professor of Aging Research, Professor of Medicine and Molecular Genetics, and a member of the Diabetes Research Center, Divisions of Endocrinology and Geriatrics. Dr. Barzilai's interests focus on several basic mechanisms in the biology of aging, including the biological effects of nutrients on extending life and the genetic determinants of lifespan. He has discovered several longevity genes in humans and, through support from a National Institutes of Health grant, is further characterizing the phenotype and genotype of humans with exceptional longevity. He has received grant support from the National Institute on Aging, American Federation for Aging Research, and the Ellison Medical Foundation.

NOAM BECKMANN

Dr. Beckmann is a postdoctoral fellow in Dr. Eric Schadt's laboratory at the Icahn School of Medicine at Mount Sinai, where he also completed his PhD. His main focus is on using computational tools to model complex traits and diseases, with applications ranging from AD biology to the molecular effects of meditation and vacation. Previously, he worked in the genetics department of the CHUV (hospital of Lausanne, Switzerland), where he studied large CNVs. Earlier, he graduated with a master's degree in life sciences and technology from the École Polytechnique Fédéral de Lausanne and completed his master's thesis at the Salk Institute.

ROBERT BELL

Dr. Bell received a PhD in pathology, studying vascular dysfunction in AD under Dr. Berislav Zlokovic at the University of Rochester. He completed a postdoctorate in cardiovascular biology and held a Research Assistant Professor position in the University of Rochester Neurosurgery Department. He joined Pfizer's Neuroscience Research Unit in 2012 and created a lab focused on vascular targets in central nervous system (CNS) disorders and drug delivery across the blood-brain barrier. In 2017, Dr. Bell joined the Rare Disease Research Unit. His group focuses on developing novel gene-therapy vectors and understanding molecular mechanisms that regulate AAV trafficking and biodistribution in the CNS and peripheral tissues.

SEAN C. BENDALL

Dr. Bendall is Assistant Professor in the Department of Pathology at the Stanford University School of Medicine. His research specialty is the development and application of single-cell proteomic tools for the investigation of human systems. This includes pioneering single-cell CyTOF mass cytometry and multiplexed ion beam imaging (MIBI). Dr. Bendall's work in mass cytometry analysis has provided an unparalleled granularity of understanding in multiple facets of human hematopoiesis and immunology. His lab continues to unravel the nature of both healthy and dysfunctional early human hematopoietic immune cell biology, as well as the phenotypic landscape of cognitive decline in the human brain using single-cell proteomic analysis. His work has been recognized by numerous awards, including the Damon Runyon Cancer Research Foundation "Breakthrough Scientist" Award, the International Society for the Advancement of Cytometry President's Award of Excellence, and the NIH Common Fund "New Innovator" Award.

DAVID BENNETT

Dr. Bennett directs the Rush Alzheimer's Disease Center at Rush University Medical Center, Chicago. He is Principal Investigator of the Religious Orders Study and the Rush Memory and Aging Project. His studies have enrolled thousands of older adults, all of whom are organ donors. He has linked a wide range of risk factors to the development of common diseases of aging. He has also generated a multilevel brain "omics" resource (genomics, epigenomics, transcriptomics, proteomics, and metabolomics) that feeds a computational pipeline for novel drug target discovery for several neurodegenerative diseases. He has more than 700 peer-reviewed publications.

ELIZABETH BRADSHAW

Dr. Bradshaw recently joined the Center for Translational and Computational Neuroimmunology at Columbia University. A main focus of her work has been understanding the role of the human innate immune system in complex neurodegenerative diseases such as Alzheimer's and Parkinson's. Interestingly, genetic studies of AD directly implicate the involvement of the innate immune system. In Parkinson's disease, the genetic modulation of the immune system is still being uncovered. One of Dr. Bradshaw's major research interests is the translation of findings from these studies to molecular outcomes and, potentially, therapeutically targetable molecules in innate immune cells.

ROBERTA DIAZ BRINTON

Dr. Brinton is Director of the Center for Innovation in Brain Science at the University of Arizona, where she is Professor of Pharmacology and Neurology in the College of Medicine. Dr. Brinton is an internationally recognized leader in Alzheimer's discovery, translational, and clinical research for the development of therapeutics to prevent, delay, and treat AD. She has published more than 200 scientific articles and holds multiple patents. Outcomes of her research have appeared in more than 100 global media outlets. Dr. Brinton has received multiple awards, including the Presidential Citizens Medal, Alzheimer's Drug Discovery Foundation Scientist of the Year, and the National Institute on Aging MERIT Award.

KATJA BROSE

Dr. Brose is a Science Program Officer at the Chan Zuckerberg Initiative (CZI), whose goals are to support basic science and technology that will make it possible to cure, prevent, or manage all diseases by the end of the century. Before joining CZI, she was part of the editorial team at Cell Press, where she was Editor-in-Chief of *Neuron* and a Publishing Director at Cell Press-Elsevier. She earned her undergraduate degree in 1990 from Brown University, with a double concentration in biology and European history. She received her PhD in biochemistry from the University of California, San Francisco. Her graduate work focused on axon guidance mechanisms in the developing spinal cord in Dr. Marc Tessier-Lavigne's laboratory.

DANIELA BRUNNER

Dr. Brunner is Founder and President of Early Signal. She has worked on the validation of developmental, psychiatric, and neurodegenerative disease models for the last 20 years. A major focus of her work has been the establishment and automatization of preclinical behavioral tests and novel high-throughput preclinical platforms, using computer vision and machine learning algorithms to comb behavioral signatures for phenotyping, drug screening, and systems biology approaches. As Senior Vice President of Behavioral R&D at PsychoGenics, she was in charge of large projects focused on back-translation of anti-smoking cessation medication, preclinical cognitive assessment, and studies in neurodegeneration, psychiatry, and autism. As head of Early Signal, Dr. Brunner directs the development of an analytical system that integrates human behavioral and "omics" readouts for health care and monitoring in rare disorders, connecting genomic information with behavioral domains, especially those passively captured with wearable sensors.

STUART BUCK

Dr. Buck is Vice President of Research at the Laura and John Arnold Foundation, where he advises the Board and programmatic teams on the Foundation's overall research agenda as well as external research investments. He holds a PhD in education policy from the University of Arkansas, a JD with honors from Harvard Law School, and bachelor's and master's degrees in music performance from the University of Georgia. Dr. Buck serves on the boards of the Harvard Multi-Regional Clinical Trials Center and the Houston Education Research Consortium, and he is a technical advisor to the Veterans Health Administration's Partnered Evidence-Based Policy Resource Center.

MARIA CARRILLO

Dr. Carrillo is Chief Science Officer, Medical and Scientific Relations, at the Alzheimer's Association. She has a wide range of responsibilities, including oversight of the Association's grant-making process and communication of scientific findings within and outside of the organization. Dr. Carrillo directly manages several Alzheimer's Association initiatives, including the Research Roundtable, the World-Wide Alzheimer's Disease Neuroimaging Initiative, and the Global Alzheimer's Association Interactive Network. She is co-author of the National Institute on Aging–Alzheimer's Association revised criteria for the diagnosis of Alzheimer's and the Appropriate Use Criteria for Amyloid Imaging. Dr. Carrillo was the Alzheimer's Expert Scientific Consultant for the 2014 movie "Still Alice." In 2016, Dr. Carrillo joined the Governing Board of the Global Brain Health Institute, which supports a new generation of leaders to translate research evidence into effective policy and practice. In 2016, she also became a member of the Research Committee for the American Heart Association.

GREG CARTER

Dr. Carter is Associate Professor at The Jackson Laboratory, where he combines genetic, genomic, imaging, and other data resources to understand the causes and progression of AD. As a lead investigator for the Model Organism Development and Evaluation for Late-Onset Alzheimer's Disease (MODEL-AD) consortium, he is primarily focused on creating new animal models that develop neurodegenerative disease at advanced age. These models are being used to dissect the genetics, genomics, and neuropathology of late-onset Alzheimer's and to provide vital models for preclinical testing of candidate therapeutics.

GABRIELA CHIOSIS

Dr. Chiosis received her graduate training at Columbia University in New York and joined the Memorial Sloan Kettering Cancer Center in 1998, first as a fellow and, since 2005, as a faculty member. She has authored more than 130 scientific articles, holds more than 250 patents and patent applications on the discovery of compounds as therapeutic agents or diagnostics in human medicine, and serves as a reviewer for scientific magazines and on scientific panels. She is also a co-founder of Samus Therapeutics and serves on its Board of Managers. Novel compounds and diagnostics discovered by Dr. Chiosis's lab are currently in clinical evaluation for AD and cancer.

DAVID COLLIER

Dr. Collier joined Eli Lilly and Company in April 2012 as a Research Fellow and leader of the Neuroscience Genetics group in Erl Wood, UK. His role is to apply molecular genetics, bioinformatics, and network biology to neurodegeneration and pain disorders to discover and advance novel drug targets. He serves as the Eli Lilly representative on several public-private research consortia, including the Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD), the Brainseq Consortium, and the IMI2 projects PHAGO (phagocytosis) and IMPRIND (protein misfolding). Dr. Collier is also a Visiting Professor at the King's College London Institute of Psychiatry, Psychology, and Neuroscience. Before joining Eli Lilly, Dr. Collier was Professor of Neuropsychiatric Genetics at the Institute of Psychiatry, where he worked on the genetics of complex disorders using genome-wide association and copy number variants analysis.

MARCO COLONNA

Dr. Colonna is Professor of Pathology and Immunology at the Washington University School of Medicine. Prior to that, he was a member of the Basel Institute for Immunology in Basel, Switzerland. His research accomplishments encompass identification and characterization of the Killer cell Ig-like receptors and HLA-C polymorphisms as their inhibitory ligands, as well as the discovery of the LILR and TREM inhibitory and activating receptor families. Through analysis of the cellular distribution of these receptors, he identified plasmacytoid dendritic cells as source of IFN-a/b in antiviral responses and innate lymphoid cells that produce IL-22 in mucosae. His current areas of research include lymphoid cells in mucosal immunity, plasmacytoid dendritic cells in host defense and autoimmunity, and innate immunoreceptors in AD.

CAROL A. COLTON

Dr. Colton is Professor in the Department of Neurology at Duke University. She has received the Alzheimer's Drug Discovery Foundation's Harrington Scholar award and the Alzheimer's Association Zenith award. Her work has been continually supported by NIH grants since 2000. Dr. Colton was among the first scientists to study microglia, the brain's immune cell, and has developed multiple mouse models that recapitulate immune responses similar to those found in humans with disease. Her recent work demonstrates complex immune changes in AD, connecting these changes to metabolic stress in the brain and opening new avenues of AD research.

MERYL COMER

Ms. Comer is President and CEO of the Geoffrey Beene Foundation Alzheimer's Initiative, which promotes early diagnosis, virtual innovation challenges, and mobile health technologies. A co-founder of WomenAgainstAlzheimer's and the Global Alliance on Women's Brain Health, Ms. Comer is the recipient of the 2016 BrightFocus Public Advocacy Award, 2015 Lauder Alzheimer's Drug Discovery Fund "Great Ladies" Award, and 2014 Wertheim Global Medical Leadership Award. In 2012, she led the formation of the 21st Century BrainTrust® (21CBT), a nonprofit partnership to advance mobile technologies to promote brain health. She is also Co-Principal Investigator for the Patient-Centered Outcomes Research Institute's Alzheimer's Patient/Caregiver Research Network in partnership with the Mayo Clinic, Brain Health Registry, and USAgainstAlzheimer's Networks. One hundred percent of proceeds from her *New York Times* bestseller book, *Slow Dancing with a Stranger*, supports Alzheimer's research.
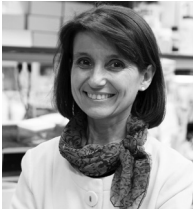
ANA MARIA CUERVO

Dr. Cuervo is the Robert and Renee Belfer Chair for the Study of Neurodegenerative Diseases and Professor in the Departments of Developmental and Molecular Biology and of Medicine at the Albert Einstein College of Medicine, as well as Co-Director of the Einstein Institute for Aging Research. She obtained her MD and PhD in biochemistry and molecular biology from the University of Valencia (Spain) and received postdoctoral training at Tufts University, Boston. In 2002, she started her laboratory at the Albert Einstein College of Medicine, where her group is interested in understanding how altered proteins can be eliminated from the cells through the lysosomal system (autophagy) and how malfunction of autophagy in aging is linked to age-related disorders, including neurodegenerative and metabolic diseases.

KEVIN DA SILVA

Dr. Da Silva has been the Chief Editor of *Nature Neuroscience* since 2016. He received his PhD in neuroscience in the Department of Laboratory Medicine and Pathobiology at the University of Toronto, where he studied AD vaccines with JoAnne McLaurin. He continued his work on neurodegenerative disease as a postdoctoral fellow at Sunnybrook Research Institute, investigating neurogenesis and cholinergic neuron degeneration in AD. He joined *Nature Medicine* as a manuscript editor in 2009. He has handled manuscripts related to neuroscience, immunology, and stem cells.

HIROKO H. DODGE

Dr. Dodge is Professor of Neurology and has been simultaneously directing two NIH-funded Alzheimer's Disease Center Data Cores at Oregon Health & Science University and the University of Michigan. Her practical applications of complex statistical models to epidemiological data and digital biomarkers are recognized by the dementia research community. Along with her strong quantitative background, she has been the Principal Investigator for National Institute on Aging-funded behavioral intervention trials examining whether social interactions through modern technology (e.g., web cam and Internet) can enhance cognitive reserve. Her projects target socially isolated seniors, who rarely get involved in trials despite their high risk of cognitive decline.

RACHELLE DOODY

Dr. Doody is the Global Head of Neurodegeneration and AD Franchise Head in Product Development, Neuroscience, at Roche and Genentech. Prior to joining the company in 2016, Dr. Doody was the Effie Marie Cain Chair in Alzheimer's Disease Research at the Baylor College of Medicine, where she founded and directed the Alzheimer's Disease and Memory Disorders Center for 27 years. Dr. Doody has published more than 200 original research articles dealing with the diagnosis and treatment of AD and related neurodegenerative disorders. She has served on the steering committees for the NIH-funded Alzheimer's Disease Cooperative Study and Alzheimer's Disease Neuroimaging Initiative and on the executive committee of the Alzheimer's Therapeutic Research Institute. Dr. Doody was the Principal Investigator for the Phase II and III development of donepezil (Aricept), the most widely used AD therapy globally. As a practicing neurologist, Dr. Doody was elected to Best Doctors in America from 1996 to 2016.

GAYATHRI J. DOWLING

Dr. Dowling is Director of the National Institute on Drug Abuse (NIDA) Adolescent Brain and Cognitive Development program, the largest long-term study of brain development and child health in the United States. Dr. Dowling served as Deputy Director of the Office of Science Policy, Engagement, Education, and Communications at the National Heart, Lung, and Blood Institute and as Chief of Science Policy at NIDA. She has also served as a Program Director at the National Institute of Neurological Disorders and Stroke and as a Scientific Review Administrator at the National Institute of Mental Health. Dr. Dowling earned a PhD in neurobiology from the University of California at Davis, where she studied the developing nervous system and subsequently conducted research at the Parkinson's Institute. Along with publishing multiple scientific papers and a range of multimedia products, Dr. Dowling has earned numerous awards and widespread recognition for her work.

JOEL DUDLEY

Dr. Dudley is Associate Professor of Genetics and Genomic Sciences and Director of the Institute for Next-Generation Healthcare at the Icahn School of Medicine at Mount Sinai. Prior to Mount Sinai, he held positions as Co-Founder and Director of Informatics at NuMedii, Inc. and Consulting Professor of Systems Medicine in the Department of Pediatrics at Stanford University. His work focuses on developing and applying methods to integrate the digital universe of information to build better predictive models of disease, drug response, digital health, and scientific wellness. His work has been featured in the *Wall Street Journal, Scientific American, MIT Technology Review*, CNBC, and other popular media outlets. Dr. Dudley received a bachelor's degree in microbiology from Arizona State University and master's and doctorate degrees in biomedical informatics from the Stanford University School of Medicine.

ALED EDWARDS

Dr. Edwards is Director of the Structural Genomics Consortium, an international, open science, public-private partnership that focuses on creating knowledge and reagents for human proteins that are relatively understudied. These reagents include highly characterized chemical inhibitors, protein structures, and recombinant antibodies. Dr. Edwards is on the faculty at the University of Toronto, as well as at Oxford University and McGill University. His interests are in open science, open drug discovery, and science reproducibility.

NILÜFER ERTEKIN-TANER

Dr. Ertekin-Taner is Professor of Neurology and Neuroscience at Mayo Clinic Florida. She received her medical degree from Hacettepe University in Turkey and her doctorate degree from the Mayo Graduate School. She completed her neurology residency at the Mayo Clinic in Rochester, MN, and a behavioral neurology fellowship at Mayo Clinic Florida. Dr. Ertekin-Taner's laboratory aims to identify novel therapeutic targets and biomarkers for Alzheimer's and related neurodegenerative diseases through an integrative approach combining biological, clinical, and large-scale multi-omics data. Dr. Ertekin-Taner is the Principal Investigator for numerous NIH and foundation grants and serves as Principal Investigator on the Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD) and M^{2}OVE-AD consortia.

DOROTHY FARRAR-EDWARDS

Dr. Farrar-Edwards is Professor of Medicine and Kinesiology at the University of Wisconsin, Madison. She currently leads the Outreach, Recruitment, and Education and Minority Recruitment Cores of the Wisconsin Alzheimer's Disease Research Center. In addition, she directs the University of Wisconsin Collaborative Center for Health Equity. Her research focuses on increasing participation of under-represented groups in clinical trials and studies requesting biospecimens.

MARIANA G. FIGUEIRO

Dr. Figueiro is Director of the Lighting Research Center and Professor of Architecture and Biological Sciences at Rensselaer Polytechnic Institute, in Troy, NY. Dr. Figueiro is well known for her research on the effects of light on human health, circadian photobiology, and lighting for older adults, including using light to improve sleep, behavior, and mood in people with AD. She is a Fellow of the Illuminating Engineering Society and is the author of more than 80 scientific articles. Dr. Figueiro has brought attention to the significance of light and health as a topic of public interest through a recent TEDMED talk.

VALENTINA FOSSATI

Dr. Fossati is a Senior Investigator at the New York Stem Cell Foundation Research Institute, an independent, nonprofit laboratory, where she focuses on advancing translational science models and preclinical studies of neurodegenerative and neuroinflammatory disorders, utilizing human iPSC-derived brain cells. Dr. Fossati established highly reproducible protocols to generate oligodendrocytes, astrocytes, microglia, and neuronal cell types. She is developing human disease relevant culture systems to identify and target the key pathogenic mechanisms leading to neurodegeneration and/or demyelination in progressive multiple sclerosis, AD, and other disorders of the central nervous system.

STEPHEN FRIEND

Dr. Friend is a scientist, physician, social entrepreneur, and Chairman of Sage Bionetworks. His breakthrough approaches all have at their center a desire to change how we work and why we do what we do. These approaches include the first discovery of a cancer susceptibility gene in the 1980s at Harvard and MIT, prototyping how knowns can be used to query unknowns at the startup Rosetta Inpharmatics, discovery efforts in oncology at Merck, and founding and leading the nonprofit Sage Bionetworks. Dr. Friend has also been involved with the Resilience Project (2014) and ResearchKit Apps (2015- 2017). He was a member of the Health Special Projects Team at Apple. He is now interested in how devices can nurture the desires of individuals to navigate toward health by asking fundamental questions about how to do individual assessments and how to provide them in ways that allow one to act on suggestions.

CHRIS GAITERI

Dr. Gaiteri loves networks. He uses them to help answer biological and social questions, for instance, identifying biological processes behind major depression and AD and predicting collaboration and trust between humans. Recently he has examined meta-network interactions between molecular systems and brain connectivity to understand how they both impact AD. Dr. Gaiteri works at the Rush University Alzheimer's Disease Center in Chicago.

MICHELA GALLAGHER

Dr. Gallagher's scientific work has focused on individual differences, including age-related memory impairment and conditions in the aging brain of individuals with preserved cognition. Her work in the past few years has focused on a clinical research program in older adults with a form of mild cognitive impairment that is transitional between normal aging and dementia caused by AD. She is leading a pivotal trial of a novel therapeutic approach in this prodromal phase of AD aimed at preventing or slowing progression to clinical dementia.

OPHER GILEADI

Dr. Gileadi obtained his bachelor's degree and PhD at Hebrew University in Jerusalem, followed by a postdoctoral fellowship at Stanford University, where he focused on the transcription machinery in yeast. With his own group at the Weizmann Institute, he continued to investigate gene regulation in yeast. Since 2004, Dr. Gileadi has been at the Structural Genomics Consortium at the University of Oxford, supervising a pipeline of protein production and crystallization of novel human proteins. The group, which has specialized in the structural and chemical biology of DNA repair proteins, is expanding to include proteins involved in neurodegeneration and psychiatric disorders.

LAURA N. GITLIN

Dr. Gitlin, an applied research sociologist, is the Isabel Hampton Robb Distinguished Professor at the Johns Hopkins University School of Nursing and founding director, Center for Innovative Care in Aging. Starting Feb. 1, 2018, she is Distinguished Professor and Dean of the College of Nursing and Health Professions at Drexel University. Dr. Gitlin is nationally and internationally recognized for her programs of research that apply a social ecological perspective and person- and family-directed approach to address clinical symptoms of dementia, enhance quality of life, and support aging in place. Many of her proven programs are being implemented worldwide.

MARK GURNEY

Dr. Gurney is the Chairman and CEO of Tetra Discovery Partners, Inc. Tetra is developing BPN14770, a negative allosteric modulator of phosphodiesterase-4D, for the treatment of AD and other dementias, psychiatric disease, and neurodevelopmental disorders, including fragile X syndrome. BPN14770 uniquely targets the biology of the synapse to improve learning and memory, with the potential to slow AD progression. Dr. Gurney has authored 117 peer-reviewed scientific articles that have been cited more than 21,000 times and holds 36 issued patents. He earned a PhD in neuroscience from the California Institute of Technology and an MBA from the Kellogg Graduate School of Management at Northwestern University.

MAGALI HAAS

Dr. Haas is Chair, CEO, and President of Cohen Veterans Bioscience, a nonprofit brain research organization based in Cambridge, MA, whose mission is to fast-track diagnostics and therapeutics for brain disorders. Dr. Haas has more than 15 years of pharmaceutical executive experience, predominantly at Johnson & Johnson (J&J), where she assumed broad, end-to-end development leadership roles in early- and late-stage clinical development, translational medicine, diagnostics, and integrative solutions. Her entrepreneurial spirit led her to spin out her own nonprofit from J&J in 2012, originally called Orion Bionetworks, while also serving as founding Chief Science and Technology Officer for One Mind for Research. Dr. Haas earned her bachelor's degree in bioengineering from the University of Pennsylvania, master's degree in biomedical engineering from Rutgers University, and MD and PhD in neuroscience with distinction from the Albert Einstein College of Medicine.

SCOTT HAYTON

Dr. Hayton is a Director of Special Projects with bgC3, the private office of Bill Gates. Prior to joining bgC3, Scott was a management consultant with McKinsey and Company, where he advised neurology clients on product strategy, digital marketing, and big data. Scott earned his PhD in neuroscience from Queen's University in Canada and was a postdoctoral fellow at Stanford University School of Medicine.

JACOB HOOKER

Dr. Hooker is the Phyllis and Jerome Lyle Rappaport MGH Research Scholar and Associate Neuroscientist at Massachusetts General Hospital. He is an Associate Professor in Radiology at Harvard Medical School and Director of Radiochemistry at the Martinos Center for Biomedical Imaging. The mission of Dr. Hooker's lab is to accelerate the study of the living human brain and nervous system through the development and application of molecular imaging agents. The lab has developed and patented several imaging technologies for neuroscience, including a first-in-class radiotracer for neuroepigenetic imaging

CATHERINE KACZOROWSKI

Dr. Kaczorowski earned her PhD in neuroscience from Northwestern University and completed postdoctoral training in biotechnology and bioengineering at the Medical College of Wisconsin. In October 2017, she joined the faculty of The Jackson Laboratory, where her lab is using advanced research strategies that she developed with her team to identify the genetic, molecular, cellular, and neuronal network mechanisms underlying normal aging and resilience to AD. In addition to their utility in the discovery of novel drug targets, the approaches and tools they recently developed are enabling rapid, mouse-to-human translational validation on a scale that far surpasses what had been previously achievable.

RIMA KADDURAH-DAOUK

Dr. Kaddurah-Daouk is a Professor in the Departments of Medicine and Psychiatry at the Duke University Medical Center and a member of the Duke Institute of Brain Sciences. She co-founded the Metabolomics Society as well as Metabolon, a leading biotechnology company that has played a central role in development and application of metabolomics in the medical field. With significant funding from NIH, she has established and led three national consortia with more than 150 scientists from 30-plus academic institutions: the Pharmacometabolomics Research Network, the Mood Disorder Precision Medicine Consortium, and the Alzheimer's Disease Metabolomics Consortium. Within these consortia, mathematicians, engineers, clinicians, geneticists, biochemists, and molecular biologists are working collaboratively to create a biochemical map for Alzheimer's that can enable discovery of new drugs. Dr. Kaddurah-Daouk is one of the principal investigators in the Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD) and M^{2}OVE-AD open-science consortia.

JEFFREY KAYE

Dr. Kaye is the Layton Endowed Professor of Neurology and Biomedical Engineering at Oregon Health & Science University (OHSU). He directs the Layton Aging and Alzheimer's Disease Center and ORCATECH (Oregon Center for Aging and Technology) at OHSU. He leads several longitudinal studies, including: *Intelligent Systems for Detection of Aging Changes* (ISAAC), *ORCATECH Life Laboratory, Ambient Independence Measures for Guiding Care Transitions*, and the *Collaborative Aging Research Using Technology* (CART) *Initiative*, all using pervasive computing and sensing technologies for assessments and interventions. Dr. Kaye serves on many national and international panels and boards in the fields of geriatrics, neurology, and technology and is an author of more than 400 scientific publications.

ALLAN LEVEY

Dr. Levey is Professor and Chair of the Department of Neurology at the Emory University School of Medicine and Director of Emory's Alzheimer's Disease Research Center. He is a cognitive neurologist and neuroscientist with research interests spanning basic, translational, and clinical science for AD and related neurodegenerative diseases. He leads one of the programs in the Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD), focusing on proteomics discovery of novel therapeutic targets and biomarkers. Dr. Levey also serves on the federal Advisory Council on Alzheimer's Research, Care, and Services.

ANDREW LIM

Dr. Lim is Assistant Professor of Neurology at the University of Toronto and a neurologist at Sunnybrook Health Sciences Centre in Toronto. His research program focuses on understanding the contribution of disordered sleep and circadian biology to neurodegenerative diseases, especially Alzheimer's.

STUART LIPTON

Dr. Lipton, a neurologist and neuroscientist, is a renowned expert in dementia. In addition to running a basic-science laboratory as Co-Director of the Neuroscience Translational Center at the Scripps Research Institute, he has an active clinical neurology practice at the University of California, San Diego. Dr. Lipton completed his PhD thesis research with John Dowling at Harvard University, followed by a clinical neurology residency with Norman Geschwind and postdoctoral fellowship with Torsten Wiesel. He was on the Harvard faculty for more than 20 years before moving to La Jolla, CA, in 2000. Dr. Lipton is best known for developing the FDA-approved Alzheimer's drug memantine (Namenda®) and for co-discovering the post-translational redox modification S-nitrosylation, the GluN3 NMDAR subunit family, and the neurogenic transcription factor MEF2C. Dr. Lipton's honors include the Ernst Jung Prize in Medicine, elected fellow of the American Association for the Advancement of Science, and an NIH Director's (DP1) Grant Award.

FRANK LONGO

Dr. Longo is Professor and Chairman of the Department of Neurology at Stanford University. Following neurology training at the University of California, San Francisco, he and his team pioneered the development of small-molecule ligands that modulate neurodegenerative disease mechanisms. He is the founder of PharmatrophiX, a company focused on commercial development. Dr. Longo has had the unusual experience of advancing a program from basic mechanism discovery through preclinical trials, human phase I safety testing, and now into a phase IIa AD trial. He is the 2015 recipient of the Melvin R. Goodes Prize for Excellence in Alzheimer's Drug Discovery from the Alzheimer's Drug Discovery Foundation.

LARA MANGRAVITE

Dr. Mangravite is President of Sage Bionetworks, an organization focused on the development and implementation of practices for large-scale, collaborative biomedical research. Previously, she served as Director of the systems biology research group at Sage Bionetworks, focusing on the application of collaborative approaches to advance understanding of disease biology and treatment outcomes at a systems level, with the goal of improving clinical care. Dr. Mangravite obtained a bachelor's degree in physics from Pennsylvania State University and a PhD in pharmaceutical chemistry from the University of California, San Francisco. She completed a postdoctoral fellowship in cardiovascular pharmacogenomics at the Children's Hospital Oakland Research Institute.

JENNIFER MANLY

Dr. Manly is Associate Professor of Neuropsychology in Neurology at the Taub Institute for Research in Alzheimer's Disease and the Aging Brain at Columbia University. Her research focuses on mechanisms of disparities in cognitive aging and AD. She received early career awards from the Society for Clinical Neuropsychology and the National Academy of Neuropsychology, received the Tony Wong Diversity Award for Outstanding Mentorship, and is an American Psychological Association Fellow. She served on the Alzheimer's Association Medical and Scientific Research Board and the federal Advisory Council on Alzheimer's Research, Care, and Services.

KALPANA MERCHANT

Dr. Merchant has deep expertise in the neurobiology of chronic neurodegenerative and psychiatric disorders. From 1993 to 2014, she held scientific and strategic leadership and management roles in the U.S. pharmaceutical industry. She retired from Eli Lilly and Company as Chief Scientific Officer for Tailored Therapeutics–Neuroscience. Since March 2014, Dr. Merchant has provided advisory and consulting services to nonprofit institutions and startup pharmaceutical/biotechnology companies. She serves on the Advisory Council for the National Center for Advancing Translational Services and the NIH Cures Acceleration Network Review Board. She is also an advisor to the Michael J. Fox Foundation for Parkinson's Research and a member of the Wellcome Trust Review Board. Dr. Merchant received her PhD in neuropharmacology from the University of Utah in 1989 and completed a postdoctoral fellowship at the University of Washington.

MARTHA CLARE MORRIS

Dr. Morris is Professor and Director of the Rush Institute for Healthy Aging and the MIND Center for Brain Health at Rush University in Chicago. She received her doctoral degree in epidemiology from the Harvard School of Public Health. She has more than 25 years of experience studying risk factors for AD and cognitive decline and has published findings on the relations of diet patterns and nutrients to these conditions. Dr. Morris is the lead creator of the MIND diet and is Principal Investigator of a multi-center randomized clinical trial of the MIND diet to prevent AD.

LENNART MUCKE

Dr. Mucke directs the Gladstone Institute of Neurological Disease and is the Joseph B. Martin Distinguished Professor of Neuroscience and Professor of Neurology at the University of California, San Francisco. He uses experimental models of AD to identify pathogenic mechanisms and develop strategies to counteract neurological decline. He has received the Potamkin Prize, MetLife Foundation Award, Kalid Iqbal Lifetime Achievement Award, Zenith Award, American Pacesetter Award, and MERIT award. He chairs the Senate of the German Center for Neurodegenerative Diseases and has served on the National Advisory Council on Aging of NIH and the Scientific and Medical Advisory Council of the Alzheimer's Association.

SUMITRA MURALIDHAR

Dr. Muralidhar is Program Director for the U.S. Department of Veterans Affairs' (VA) Million Veteran Program (MVP) in the Office of Research and Development (ORD). In this role, she oversees the development of policy and infrastructure for enrolling at least 1 million veterans in a longitudinal cohort collecting genetic, clinical, lifestyle, and military-exposure data for future research, as well as the policy for data use and conduct of science. She served as ORD's liaison to the White House Precision Medicine Initiative under President Obama and continues to represent ORD/MVP in the federal interagency group on precision medicine. Dr. Muralidhar also serves as the designated federal officer for the VA's Genomic Medicine Program Advisory Committee, which advises the VA Secretary on the development and implementation of research and clinical arms within the Veterans Health Administration.

CYNTHIA J. MUSANTE

Dr. Musante is a Research Fellow and Head of the Quantitative Systems Pharmacology (QSP) Lab in Pfizer's Internal Medicine Research Unit in Cambridge, MA. She received her PhD in applied mathematics from North Carolina State University and has more than 17 years of experience in QSP modeling. Dr. Musante currently serves as Co-Chair of the IQ Consortium Clinical Pharmacology QSP Working Group and as Treasurer and a member of the Board of Directors of the International Society of Pharmacometrics (ISoP). She was the inaugural Chair of ISoP's QSP Special Interest Group.

LARSSON OMBERG

Dr. Omberg is Vice President of Systems Biology at Sage Bionetworks and oversees a research agenda that focuses both on genomics and mobile health. The group focuses heavily on using open and team-based science to get a large number of external partners to collaborate on data-intensive problems. Dr. Omberg has a background in computational biology and has been developing computational methods for genomics analysis and disease modeling. He obtained a PhD in physics from the University of Texas at Austin and completed a postdoctoral fellowship in computational biology and biostatistics at Cornell University.

CHIRAG PATEL

Dr. Patel's long-term research goal is to address problems in human health and disease by developing computational and bioinformatics methods to reason over high-throughput information spanning molecules to populations. Dr. Patel's group focuses on computational strategies to efficiently and reproducibly uncover the complex interaction between the exposome, genome, and phenome toward development of new tools for disease diagnosis and therapy. He trained in biomedical informatics at Stanford University. Prior to graduate work, he was a software engineer in the biotechnology industry. Dr. Patel is Assistant Professor of Biomedical Informatics at Harvard Medical School, where he teaches introductory courses in data science, is a mentor to three postdoctoral associates, and advises three PhD students.

SUZANA PETANCESKA

Dr. Petanceska is a Senior Advisor for strategic development and partnerships and a Program Director for systems biology and systems pharmacology in the Division of Neuroscience at the National Institute on Aging (NIA). During her tenure at NIA, she has overseen and developed a number of research portfolios and innovative programs in basic and translational research for AD. Her recent program development efforts have focused on developing systems biology and systems pharmacology capabilities for AD research and drug development within an open-science framework. Dr. Petanceska was instrumental in the development of NIA's AD Translational Research Program and leads NIA's open-science, systems biology programs for target and biomarker discovery: the Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD) Target Discovery and Preclinical Validation Project and the M^{2}OVE-AD and Resilience Consortia.

JESSICA POLKA

Dr. Polka is Director of ASAPbio, a biologist-driven project to promote transparency and innovation in life sciences communication. Before becoming a visiting scholar at the Whitehead Institute, she performed postdoctoral research in the Department of Systems Biology at Harvard Medical School, following a PhD in biochemistry from the University of California, San Francisco. Dr. Polka serves as President of the board of directors of Future of Research, a steering committee member of Rescuing Biomedical Research, a member of the NAS Next Generation Researchers Initiative, and a member of the American Society for Cell Biology's public policy committee.

NATHAN PRICE

Dr. Price is Professor and Associate Director of the Institute for Systems Biology in Seattle, WA, where he co-leads the Hood-Price Lab for Systems Biomedicine. He is the recipient of the NIH Howard Temin Pathway to Independence Award, National Science Foundation CAREER award, Roy J. Carver Charitable Trust young investigator award, "Tomorrow's PIs" by *Genome Technology*, Camille Dreyfus Teacher-Scholar Award, and Grace A. Goldsmith Award. He serves on advisory boards for Roche (personalized medicine), Habit, Trelys, Novo Nordisk Foundation Center for Biosustainability, Providence St. Joseph Health, *Science Translational Medicine*, and *Cell Systems*. He is Co-Founder and on the Board of Directors of Arivale.

BEN READHEAD

Dr. Readhead is an Australian-born medical practitioner who is passionate about innovation in the life sciences, with a focus on the application of bioinformatics to improve patient care. He is currently Assistant Professor at the Arizona State University– Banner Neurodegenerative Disease Research Center, where a key goal is to generate a comprehensive public atlas cataloging single-cell transcriptomic, genetic, proteomic, and epigenetic perturbations associated with AD across multiple regions and cell types within the brain. This resource will enable the construction of cell-specific networks that can be leveraged by the research community to identify novel molecular drivers of disease and to prioritize high-value therapeutic targets.

LORENZO REFOLO

Dr. Refolo is Director of Alzheimer 's Disease Drug Discovery and Development at the National Institute on Aging (NIA). Prior to joining NIH, he was the Scientific Director at the Institute for the Study of Aging, where he created and managed a large portfolio of Alzheimer's drug discovery programs. In 2005, Dr. Refolo joined NIH as a Program Director at the National Institute of Neurological Disorders and Stroke, overseeing a portfolio of basic, clinical, and translational research on AD and other neurodegenerative diseases. During his tenure at NIA, Dr. Refolo has developed a number of new translational programs focused on enabling predictive drug development for AD, including the MODEL-AD Consortium and AlzPED.

ERIC M. REIMAN

Dr. Reiman is Executive Director of the Banner Alzheimer's Institute, CEO of Banner Research, Professor of Psychiatry at the University of Arizona, University Professor of Neuroscience at Arizona State University, Clinical Director of Neurogenomics at the Translational Genomics Research Institute (TGen), and Director of the Arizona Alzheimer's Consortium. He is an author of more than 300 publications, Principal Investigator of several NIH grants, leader of the Alzheimer's Prevention Initiative, and recipient of the Potamkin Prize for his contributions to the study of preclinical AD and the accelerated evaluation of Alzheimer's prevention therapies.

JONI L. RUTTER

Dr. Rutter is Director of Scientific Programs for the *All of Us* research program at NIH, leading the scientific development and implementation of a large national cohort to advance precision medicine research. Previously, Dr. Rutter was the Director of the Division of Neuroscience and Behavior at the National Institute on Drug Abuse. She received her PhD from Dartmouth Medical School and trained at the National Cancer Institute. Her scientific interests include integrating genetic principles with environmental influences to inform more deeply our understanding of how individual and societal factors impact health and disease.

LAURIE RYAN

Dr. Ryan is Chief of the Dementias of Aging Branch in the Division of Neuroscience at the National Institute on Aging (NIA). She oversees the development, coordination, and implementation of NIA's basic and clinical AD research program. Dr. Ryan also directs the AD clinical trials research portfolio and focuses on pharmacologic treatment and management of mild cognitive impairment, AD, and other dementias of aging to slow their course, to treat and manage their cognitive and behavioral manifestations, and, ultimately, to delay their onset and prevent them. Prior to joining NIH, Dr. Ryan served as Assistant Director for Research and Senior Neuropsychologist for the national Defense and Veterans Brain Injury Center, where she was responsible for overseeing clinical research development and implementation, with a focus on clinical trials.

ANDREW J. SAYKIN

Dr. Saykin is the Raymond C. Beeler Professor of Radiology and Imaging Sciences and Professor of Medical and Molecular Genetics at Indiana University (IU) School of Medicine, where he serves as Director of the Indiana Alzheimer Disease Center and the IU Center for Neuroimaging. Dr. Saykin leads the ADNI Genetics Core and participates in multiple AD consortia. His research focuses on the integration of multimodal brain imaging and multi-omics methods for early detection of AD and for identification of disease mechanisms and potential therapeutic targets. He is the founding Editor-in-Chief of *Brain Imaging and Behavior*, a Springer-Nature journal.

ERIC SCHADT

Dr. Schadt is Dean for Precision Medicine at the Icahn School of Medicine at Mount Sinai and CEO of Sema4, a spinout, next-generation health information company of the Mount Sinai Health System that provides advanced genomic testing and merges big-data analytics with clinical diagnostics. He was previously the founding Director of the Icahn Institute for Genomics and Multiscale Biology and Chair of the Department of Genetics and Genomics Sciences at the Icahn School of Medicine at Mount Sinai. His work combines supercomputing and advanced computational modeling with diverse biological data to understand the relationship between genes, gene products, other molecular features such as cells, organs, organisms, and communities and their impact on complex human traits such as disease.

GERARD SCHELLENBERG

Dr. Schellenberg is a leading expert on genetics and gene sequencing with specialties in neuropathology, immunobiology, and experimental pathology. His career has focused on applying advanced genome technology to the problem of finding the underlying causes of human diseases. He co-leads the Alzheimer's Disease Sequencing Project and is Co-Director of the Genomics Center of Alzheimer's Disease at the University of Pennsylvania. Dr. Schellenberg was instrumental in discovering genes for early-onset AD and identified the gene for Werner's Syndrome, a premature aging disorder. His current research focuses on the genetics of neurodegenerative disorders, with a major emphasis on AD, but he also works on different forms of frontotemporal lobar degeneration, as well as Guam amyotrophic lateral sclerosis/parkinsonism dementia complex. He has received numerous awards and honors, including the Potamkin Prize for Alzheimer's Disease Research.

NICOLE SCHUPF

Dr. Schupf is Professor of Epidemiology at the Columbia University Medical Center. She directs studies of aging and AD in adults with Down syndrome and shared genetic susceptibility to Down syndrome and AD in mothers of adults with Down syndrome. Dr. Schupf's recent work focuses on understanding the relationship between estrogen deficiency, apolipoprotein E genotype, and age at onset of AD in women with Down syndrome, and on examining blood-based preclinical proteomic biomarkers of age at onset and risk for the development of dementia.

NICK SEYFRIED

Dr. Seyfried's research focuses on the integration of proteomics, transcriptomics, and systems biology to tackle fundamental questions related to the pathogenesis of AD and other neurodegenerative disorders. His team utilizes high-resolution liquid chromatography coupled to tandem mass spectrometry to identify and quantify proteins and post-translational modifications in human brain, plasma, and cerebrospinal fluid. As part of the Accelerating Medicines Partnership for Alzheimer's Disease (AMP-AD) consortium, Dr. Seyfried and his team leverage the strengths of a national team of collaborating investigators to nominate new drug targets and biomarkers for AD.

MARINA SIROTA

Dr. Sirota is Assistant Professor at the Institute for Computational Health Sciences at the University of California, San Francisco. Prior to that, she was the Lead Research Scientist in the Division of Systems Medicine at Stanford University. She has also worked as a Senior Research Scientist at Pfizer, where she focused on developing precision medicine strategies in drug discovery. Her research interests lie in developing computational integrative methods and applying these approaches in the context of disease diagnostics and therapeutics. Dr. Sirota's research experience in translational bioinformatics spans 10 years, during which she has co-authored nearly 40 scientific publications in a number of high-impact journals, including *Nature Communications, JCI, PLoS Computational Biology*, and *Science Translational Medicine*. Her laboratory is funded by NIH, Pfizer, March of Dimes, and the Burroughs Wellcome Fund.

MARK TUSZYNSKI

Dr. Tuszynski is Professor of Neurosciences at the University of California, San Diego (UCSD), and Founding Director of the UCSD Translational Neuroscience Institute. He received his undergraduate and MD degrees from the University of Minnesota, clinical training in neurology at Cornell University Medical Center, and a PhD in neuroscience at UCSD. Dr. Tuszynski's research focuses on central nervous system plasticity in animal models of learning, AD, spinal cord injury, and peripheral nerve injury. He investigates nervous system growth factors, stem cells, tools of gene delivery, and bioengineering approaches in many of these studies. In 2001, Dr. Tuszynski began the first human clinical trial of gene therapy to treat an adult human neurodegenerative disease, testing the effects of nerve growth factor gene delivery in patients with early AD. He has won 21 research awards and has authored more than 200 scientific and medical publications.

ROBERT TYCKO

Dr. Tycko is a Senior Investigator in the Laboratory of Chemical Physics of the National Institute of Diabetes and Digestive and Kidney Diseases at NIH. His research focuses on the development of solid-state nuclear magnetic resonance techniques and on their application to structural problems in biology and biophysics. Beginning in 2000, Dr. Tycko's lab developed the first experimentally based molecular structural models for amyloid fibrils formed by the amyloid-β (Aβ) peptide. An important finding was that Aβ can form multiple distinct fibril structures, with potentially different biological effects, depending on details of fibril growth conditions. Recent work investigates Aß fibril structures that develop in the brain tissue of people with AD.

CORNELIA VAN DUIJN

Dr. van Duijn is Professor of Genetic Epidemiology at the Erasmus University Medical Center and Professor of Translational Epidemiology at the University of Leiden. For more than 25 years, her work has focused on discovering genes involved in age-related disorders, including AD, glaucoma, dyslipidemia, and hypertension. She has been a leading figure in various international genome-wide association consortia, including the International Genetics of Alzheimer's Disease Project and the Alzheimer's Disease Sequencing Project (ADSP). At present, she combines genomics research with high-throughput metabolomics in large-scale epidemiological biobanks and organ-on-chip models to translate findings to prevention and care.

LINDA J. VAN ELDIK

Dr. Van Eldik is Director of the Sanders-Brown Center on Aging and the National Institute on Aging (NIA)-funded Alzheimer's Disease Center at the University of Kentucky, Co-Director of the Kentucky Neuroscience Institute, and Professor of Neuroscience. Her research program, currently funded by NIA, National Institute of Neurological Disorders and Stroke, and the Alzheimer's Association, focuses on dysregulated neuroinflammation in central nervous system disorders. She earned her PhD in microbiology/immunology from Duke University and completed postdoctoral work in virology and cell biology at Rockefeller University. Dr. Van Eldik has also served on the faculty at Vanderbilt University and Northwestern University, where she was Co-Director of the Center for Drug Discovery and Chemical Biology, and Associate Director of the Alzheimer's Disease Center.

STEVEN WAGNER

Dr. Wagner is Professor in the Department of Neurosciences at the University of California, San Diego. He spent 25 years in the biopharmaceutical industry and academia, studying translational neuroscience of AD. He led the team that discovered the first potent gamma-secretase modulators (GSMs) and for the first time purified to homogeneity the gamma-secretase enzyme complex ultimately responsible for generating amyloid β. He was awarded a Blueprint Neurotherapeutics U01 grant to optimize and develop GSMs for the treatment and/or prevention of AD. He is also a member of the Cure Alzheimer's Fund Research Consortium and the Scientific Advisory Board for the Alzheimer's Association's C4C.

DANIEL MARTIN WATTERSON

Dr. Watterson is the John G. Searle Professor at Northwestern University and Professor of Pharmacology in its Feinberg School of Medicine. His research focuses on elucidation and molecular characterization of signal transduction pathways, the study of their role in pathophysiology, and the development of novel molecular probes to attenuate pathophysiology progression. Previous academic positions include Professor of Pharmacology and HHMI Investigator at Vanderbilt University School of Medicine, and Associate Professor and Mellon Fellow at Rockefeller University.

RACHEL WHITMER

Dr. Whitmer is a Senior Scientist at the Kaiser Permanente Northern California Division of Research, Director of the Population Based Research Program in Brain Aging, and Associate Professor of Epidemiology and Biostatistics at the University of California, San Francisco. For more than 15 years, she has directed a research program investigating life-course population level risk and protective factors for AD, dementia, and cognitive impairment. Dr. Whitmer is Principal Investigator of: *SOLID* (Study of Longevity and Cognitive Aging in Diabetes), a cohort study of 1,100 older adults with diabetes; *KHANDLE* (Kaiser Healthy Aging and Diverse Life Experiences Study), a multiethnic study of dementia incidence in 1,800 elderly adults; Kaiser *STAR* (Study of Healthy Aging in African Americans), a cohort of 700 middle-aged and older African Americans; and *Life After 90*, a cohort of ethnic minority oldest-old individuals.

RICHARD WILDER

Mr. Wilder is Associate General Counsel in the Global Health Program at the Bill & Melinda Gates Foundation and has cross-foundation leadership roles on emerging issues of open access, data, and science. His career has focused on the law and policy of intellectual property and trade, as well as global health and development in sectors spanning corporate, law firm, the United Nations, and the U.S. government. Mr. Wilder has taught law and speaks and writes often in the field of international and intellectual property law. Mr. Wilder is qualified in both engineering and law.

ALIZA P. WINGO

Dr. Wingo is Assistant Professor of Psychiatry at Emory University and a psychiatrist at the U.S. Department of Veterans Affairs Medical Center in Atlanta. She studies the genetic basis of depression and anxiety, resiliency, and psychological well-being. Additionally, Dr. Wingo investigates the molecular mechanisms underlying the detrimental effects of depression and the protective effects of psychological well-being on dementia risks. As an early-stage investigator, Dr. Wingo has received an American Psychiatric Association research fellowship award, a NARSAD Young Investigator award, and a VA Career Development Award. She recently received three federal grants to pursue these lines of inquiry and hopes to contribute to efforts in the prevention and early detection of dementia.

BENJAMIN WOLOZIN

Dr. Wolozin is Professor of Pharmacology, Neurology, and Neuroscience at the Boston University School of Medicine. His research investigates the pathophysiology of neurodegenerative diseases. The current work of the Wolozin lab addresses the roles of regulated protein aggregation, phase separation, and membrane-less organelles on proteostasis, RNA metabolism, neuronal function, and neurodegeneration. Investigating the biology of RNA granules (with a particular focus on stress granules), provides a theoretical framework for understanding the biology of neurodegenerative disease, as well as new directions for therapeutic intervention for tauopathies and other neurodegenerative diseases.

RONG XU

Dr. Xu is Associate Professor of Biomedical Informatics in the Department of Population and Quantitative Health Sciences at Case Western Reserve University. Dr. Xu earned her bachelor's degree in biology from Peking University, master's degree in computer science, and PhD in biomedical informatics from Stanford University. Dr. Xu is conducting cutting-edge research in the field of biomedical informatics. As evidence of her creativity and innovation, Dr. Xu recently received the NIH Director's New Innovator Award (2014), Landon-AACR Innovator Award for Cancer Prevention Research (2015), and American Medical Informatics Association New Investigator Award (2016).

2018 NIH ALZHEIMER'S DISEASE RESEARCH SUMMIT:
PATH TO TREATMENT AND PREVENTION

Helpful Links and Resources

Alzheimer's Disease and Related Dementias (AD+ADRD) Research Implementation Milestones Database

www.nia.nih.gov/research/milestones

The AD+ADRD Research Implementation Milestones Database is a web-based tool for tracking funding initiatives and activities developed by the National Institutes of Health (NIH) and other funding organizations supporting AD+ADRD. The purpose of this data resource is to facilitate strategic coordination and collaborations among funding organizations to maximize the public health impact of the collective investment in AD+ADRD research.

The milestones represent a research framework detailing specific steps and success criteria for NIH and other stakeholders toward the development of effective treatments for AD+ADRD. They were developed based on recommendations from the Strategic Research Planning Summits—the 2012 and 2015 NIH AD Research Summits and the 2013 and 2016 NIH ADRD Research Summits—put forward by more than 200 leading academic and industry experts, innovators, and public advocates. (For recommendations, see pages 31–41 in this program.) The milestones span the entire AD+ADRD research landscape, including basic, translational, clinical, and health services research, and serve as the basis for the development of the NIH Alzheimer's Disease Bypass Budget (*www.nia.nih.gov/bypass-budget*).

Active AD+ADRD Funding Opportunity Announcements (FOAs)

NIH, in addition to welcoming investigator-initiated proposals, offers a range of directed funding opportunities for AD+ADRD. A list of currently active FOAs is available on the National Institute on Aging (NIA) website at *www.nia.nih.gov/ad-foas*.

NIH also invites applications through its small-business programs. NIA is offering funding to develop and commercialize products addressing aging and aging-related diseases and conditions, Alzheimer's disease and related dementias, and the special problems and needs of older Americans. Products of interest include, but are not limited to, tools for clinical care of people with Alzheimer's disease, specific and standardized tests for diagnosing dementia, assistive technologies for people with AD+ADRD, and more. The list of small business funding opportunities for AD and ADRD can be accessed at *www.nia.nih.gov/research/nia-small-business-funding-opportunities*.

Recommendations from the 2012 NIH AD Research Summit

Overarching Themes

Several overarching and transformative concepts were identified by Summit participants as critical to achieving success in Alzheimer's disease (AD) therapy development, and these emerged repeatedly among the themes brought forward by the different workgroups:

- Recognize the heterogeneity and the multifactorial nature of the disease.
- Employ new research paradigms such as systems biology and network pharmacology.
- Enable rapid and extensive sharing of data, disease models, and biological specimens.
- Build new multidisciplinary translational teams and create virtual and real spaces where these teams can operate.
- Develop strategies to overcome intellectual property barriers to AD drug development.
- Develop new public-private partnerships.
- Establish a National Institutional Review Board for AD clinical research.

Specific recommendations are presented here:

Session 1: Interdisciplinary Approach to Discovering and Validating the Next Generation of Therapeutic Targets for Alzheimer's Disease

A. Intensify scientific efforts to deepen the understanding of the complex pathobiology of AD and diversify target identification to better address the multifactorial nature of the disease. These efforts should include the use of systems biology approaches and tools, as well as cutting-edge stem cell technology.

B. Develop a better systems-level understanding of how the many discoveries that have already been made (e.g., genetic, pathological, biochemical, radiological, neuropsychological) and the contributory factors that have already been identified (e.g., Aβ, tau, apoE4, α-synuclein, TDP-43, aging, proteostasis failure, mediators of inflammation, comorbidities) are related mechanistically.

C. Facilitate the conversion of existing genetic information into mechanistic insights and therapeutic advances and continue to generate new genetic data using exome and genomic sequencing approaches to identify rare genetic variants of large functional effect.

D. Generate new experimental models (e.g., different animal species, human induced pluripotent stem [iPS] cells, in silico models) that better simulate the multifactorial etiology of AD and use these models to identify modulators of disease pathways and to assess combination treatments which may be required to defeat this disease. Ensure that these new tools and models are freely shared.

E. Develop *in vivo* imaging agents (tracers for PET scans) to assess target engagement and the burden of brain pathology to enable successful drug development for existing and new therapeutic targets.

F. Develop robust biomarkers that can feasibly be obtained in large cohorts of volunteers, including metabolic signatures to develop and validate diagnostic, prognostic, and surrogate biomarkers for AD and biomarkers for disease subtypes.

G. Establish links among peripheral biochemical changes (e.g., blood-based markers) and imaging and cerebrospinal fluid changes to identify and validate peripheral biomarkers of disease.

H. Enable rapid sharing of new data via web-based resources with the capacity to store large and diverse datasets (such as data about clinical phenotypes, genetics, epigenetics, proteomics, and metabolomics) that can be used for testing different models or hypotheses at the computational level.

I. Enable analysis of new data before publication, using approaches such as collaborative challenges open to all citizens and scientists.

J. Maximize the use of existing infrastructure and resources (e.g., research centers, biobanks, and repositories) by publicizing their availability to researchers.

K. Facilitate the creation of new translational teams to expedite the discovery and validation of new therapeutic targets. These teams should include epidemiologists, basic research scientists, geneticists, computational biologists, medicinal chemists, pharmacologists, toxicologists, pharmacogenomics experts, clinicians, and project managers, collaborating within and across institutions.

Session 2: Challenges in Preclinical Therapy Development

A. Develop infrastructure and resources to increase the likelihood that preclinical therapeutic development efforts for AD will translate to success in the clinic by:

- Creating expert advisory committees for all aspects of preclinical and early clinical drug development to assist academic drug discovery efforts
- Establishing a network of AD preclinical therapy centers integrated with existing and proposed translational infrastructure and resources (e.g., Alzheimer's Disease Neuroimaging Initiative, Alzheimer's Disease Centers)
- Establishing an open-access resource for reviewing and publishing negative and discrepant data

B. Develop broad capabilities in quantitative and systems pharmacology to understand the impact of drugs on organisms, to predict dosing, to reduce toxicity, and to facilitate drug repurposing and the identification of combination therapies. This will require a wide collaboration among NIH Institutes, government, academia, industry, voluntary health organizations, and foundations, including the establishment of new training programs.

C. Increase the predictive power of preclinical testing in animal models by:

- Establishing a standardized and rigorous process for the development and characterization of animal models, and ensuring their maximal and rapid availability to all researchers for preclinical drug development
- Aligning the pathophysiological features of AD animal models with the corresponding stages of clinical disease using translatable biomarkers
- Establishing guidelines for rigorous preclinical testing in animal models and reporting of both positive and negative findings.

D. Provide an expedited review track for applications focused on drug discovery, preclinical, and clinical drug development for AD to mitigate difficulties with intellectual property and commercialization issues that are imposed by the current lengthy review/grant cycle at NIH. Establish multidisciplinary review panels with adequate expertise to evaluate all aspects of translational research.

Session 3: Who to Treat, When to Treat, and What Outcomes to Measure

A. Initiate treatment trials in asymptomatic, at-risk individuals (e.g., individuals at risk genetically, older adults positive for biomarkers for AD) using uniform biomarkers and cognitive outcomes, informed by data from AD trials using patients with more advanced disease.

B. Collect DNA and other biosamples from these studies to enable subsequent interrogation based on treatment response and predictors of decline in the groups receiving placebo.

C. Expand large-scale registries and natural history cohorts of healthy individuals from early midlife to late life, as well as individuals with subjective and/or objective cognitive impairment and use the data generated to inform clinical trial design. These cohorts should be population-based and should oversample under-represented ethnic minorities and groups with lower education.

D. Develop, validate, and standardize sensitive neuropsychological and other clinical and behavioral measures to detect and track the earliest clinical manifestations of AD and to predict long-term clinical and functional outcomes. These measures should be sensitive to change and capture the variability in cognitive function that may be an important predictor of treatment response.

E. Optimize biomarkers for detecting and monitoring the progression of AD and focus particularly on standardization. These biomarkers will be used to elucidate the temporal trajectories over the course of preclinical and prodromal AD, to assess the proximity to onset of clinical symptoms, and to predict long-term clinical response to treatment.

F. Develop treatments for patients with symptomatic AD and support proof-of-concept studies to validate novel targets for cognitive and neuropsychiatric symptoms across all disease stages.

G. Develop approaches to stratify and individualize treatments based on the heterogeneity of symptomatic patient populations.

H. Support broad infrastructure changes that will accelerate and improve the efficiency of prevention initiatives, including the formation of a national, centralized Institutional Review Board for multicenter Alzheimer's trials and the development of agreements for data sharing of deidentified data from both placebo and treatment arms via public databases.

Session 4: Drug Repurposing and Combination Therapy

A. Expand publicly available libraries of drugs, drug signatures, and AD tissues and publicize their availability to the Alzheimer's research community. Consider including cell-type and region-specific expression differences in the brain and periphery at varying stages of the disease, as different stages may require different drugs. Expression libraries from cognitively normal adults positive for amyloid imaging and cerebrospinal fluid Alzheimer's biomarkers and from centenarians without dementia could be used to identify AD-resistant expression signatures that correlate with specific drug signatures for prevention studies.

B. Maintain rigor in the development of repurposed drugs with respect to scientific rationale, as well as design of clinical trials. Provide adequate prior clinical trial evidence for safety in populations with or at risk for AD.

C. The optimal therapy for AD may involve the use of drug combination cocktails and require different composition of these cocktails at different stages of the illness. To facilitate the development of effective combination therapies, develop translational workgroups that include experts in network biology and network pharmacology.

D. Encourage the evaluation of drugs that simultaneously target multiple disease pathways (e.g., insulin, selective estrogen receptor modulators).

E. Develop translational groups across institutions that focus on specific therapy development efforts (e.g., apoE therapeutics, combinatorial therapeutic strategies, drug repurposing, neuropsychiatric symptoms).

Session 5: Nonpharmacological Interventions

A. Integrate epidemiological studies with mechanistic research to explore underlying pathways by which risk and protective factors contribute to the disease process.

B. Continue to identify the molecular mechanisms by which nonpharmacological interventions operate, and employ systems biology approaches to examine brain health in relation to, and in concert with, other organ systems.

C. Initiate rigorously designed clinical trials in asymptomatic and cognitively impaired older adults to establish the effectiveness of physical exercise, cognitive training, and the combination of these interventions for AD treatment and prevention.

D. Combine nonpharmacological (e.g., behavioral, lifestyle, environmental) interventions with pharmacological treatments to maximize possible therapeutic benefit. Use epidemiologic information, mechanistic research in animal models, and network analysis to inform trial design and drug selection.

E. Develop standard outcome measures to enable data comparisons across studies. These include but are not limited to ecologically valid measures of real world function, quality of life, and physical and cognitive function.

F. Pursue the science of behavioral change for successful implementation of effective nonpharmacological interventions.

G. Invest in research to develop technologies that promote prevention and treatment trials, clinical care, caregiver support, and in-home monitoring.

Session 6: New Models of Public-Private Partnerships

A. Promote and enable partnerships across all sectors involved in basic, translational, and clinical research to successfully implement an integrated translational research agenda.

B. Increase awareness of the importance and value of public-private partnerships among federal agencies, other stakeholder organizations, and the public and engage the full spectrum of the AD community in various partnership activities for the advancement of AD therapy development.

C. Enable partnerships for:

- Data sharing (with standardized ontologies and metadata)

- Creating, validating, and sharing tools for translational research (e.g., instruments and biomarkers, animal models, high-throughput screening assays, iPS cells).

- Expanding the precompetitive space using new models of public-private partnerships, such as the Arch2POCM partnership for target validation, and also for product development partnerships.

D. Develop a National Institutional Review Board for AD studies accessible to both public and private funding research organizations.

Recommendations from the 2015 NIH AD Research Summit

Overarching Themes

Several overarching and transformative concepts were identified by Summit participants as critical to achieving success in Alzheimer's disease (AD) therapy development, and these emerged repeatedly among the themes brought forward by the different workgroups:

- Understand all aspects of healthy brain aging and cognitive resilience to inform strategies for AD prevention.

- Expand the use of integrative, data-driven research approaches such as systems biology and systems pharmacology.

- Develop computational tools and infrastructure in order to enable storage, integration, and analysis of large-scale biological and other patient-relevant data.

- Leverage the use of wearable sensors and other mobile health technologies to inform discovery science as well as research on AD care.

- Support and enable open science in basic, translational, and clinical research.

- Change the academic, publishing, and funding incentives to promote collaborative, transparent, and reproducible research.

- Invest in the development of a new translational and data science workforce.

- Engage citizens, caregivers, and patients as equal partners in AD research.

Specific recommendations are presented here:

Session 1: Interdisciplinary Research to Understand the Heterogeneity and Multifactorial Etiology of Disease

A. Maximize endophenotyping of established cohorts that are genetically, epigenetically, or otherwise at risk (e.g., due to cerebrovascular, metabolic, or neuroinflammatory compromise) to fill in the gaps of large-scale human data needed to formulate testable hypotheses around AD heterogeneity, including sex differences and ethnicity phenotypes of risk.

B. Establish new cohorts for intense endophenotyping (e.g., exposome, multidimensional "omics," imaging, cognitive) that represent gender and diverse populations.

C. Maximize, optimize, and evolve the existing National Institute on Aging/National Institutes of Health (NIA/NIH) translational infrastructure and eliminate barriers to sharing, integrating, and reuse of data needed to build predictive models of disease by:

- Removing barriers to combining data from multiple sources and sharing processed data with other investigators
- Generating combined and harmonized data sets that can be shared between investigators
- Providing genetic and other patient-level data on a common-access cloud site where researchers can perform large-scale computational tasks without the need to download and store large datasets
- Providing access to sponsor-level data from clinical trials to revisit those that failed to demonstrate efficacy
- Supporting electronic consenting and other consenting models that give ownership of health care data to patients and study participants

D. Integrate AD research with neurobiology of aging and biology of aging research by developing new programs on systems biology and integrative physiology to gain a deeper understanding of the complex biology of disease.

E. Apply systems pharmacology approaches that leverage existing systems biology efforts built on human biology to construct advanced, multiscale models of diseases. Systems pharmacology efforts can be informed by the disease models to identify subnetworks relevant to aspects of disease and disease subtypes that can serve as targets for drug discovery and drug repurposing.

F. Develop the next generation of *in vivo* models based on human data to explore experimentally the biology and physiology of genetic, epigenetic, vascular, environmental, and other risk factors for Alzheimer's and related dementias.

G. Integrate new technologies such as iPSC, genome editing, optogenetics/deep brain stimulation/transmagnetic stimulation, and next-generation *in vivo* imaging to facilitate assessment and validation of findings from human studies.

H. Accept the limitations of rodent animal models and divest from using behavioral endpoints as measures of therapeutic efficacy in favor of biochemical and physiological endpoints.

I. Build translatable biomarkers that inform the level of target engagement early in the life cycle of a drug discovery project and seek to develop the widest possible therapeutic window that will support testing a full dose range in humans.

J. Develop a new translational workforce by bringing new expertise and developing new, integrative training programs (all aspects of data science, translational bioinformatics, software engineering, traditional, and emerging drug discovery disciplines, variety of geriatric specialties).

K. Develop and implement strategies/policies to improve the poor reproducibility and translatability of basic research findings. These should include changes in the reward systems in academia, funding agencies, and journals.

Session 2: Transforming AD Therapy Development: From Targets to Trials

A. Support research on the interaction among amyloid, tau, inflammation, glucose and lipid metabolism, oxidative stress, and other aspects of AD; this should include quantification of the trajectories of biochemical changes within and across these pathways and their integrative response to therapeutic perturbations.

B. Invest in comprehensive and systematic studies of wellness that go beyond genetics by using extensive molecular profiling of individuals who age successfully and the rare individuals who resist/escape AD despite having high genetic risk (E4 homozygous) or highly penetrant, deleterious mutations that cause AD (FAD mutation carriers).

C. Continue to support and expand existing efforts focused on the generation and integration of large-scale molecular, cellular, and physiologic data to construct predictive models of AD and initiate efforts to incorporate nontraditional data modalities as dimensions of health and disease, such as data collected by wearable sensors and mobile health technologies. The development of the most predictive models of AD will require open sharing of all data, results, and network models.

D. Support *in silico* and experimental target discovery and validation efforts that are fully informed by systems biology/pharmacology models and fully embrace the complexity of disease and drug action, such that networks are considered as targets and readouts of therapeutic activity.

E. Support the development of computational tools and infrastructure that enable basic and clinical researchers to query systems biology/pharmacology models from integrated perspectives supporting translational research (e.g., target-oriented and patient/subgroup oriented).

F. Support research aimed at identifying quantitative methods to assess synergy/additivity of potential therapeutics, including synergy between drugs and nonpharmacological (e.g., foods, exercise) perturbations.

G. Leverage the network concept of drug targets and the power of phenotypic screening to advance rational drug repurposing and data-driven development of drug combinations based on the ability of single or multiple therapeutic agents to perturb entire molecular networks away from disease states in cell-based and/or animal models.

H. Develop cost-effective, high-throughput methods to isolate different neural and glial cells for "omics" profiling, drug screening, and other studies and improved iPSC protocols for relevant cell types, and invest in more sophisticated and relevant human-based models such as organoid systems.

I. Develop robust quantitative biomarkers that can be used to provide information on specific aspects of the disease process and to measure the extent of perturbation of the disease process introduced by therapeutic interventions during preclinical testing and early-phase clinical trials. These efforts should include:

- Development of translatable biomarkers indicative of incipient disease (i.e., ocular, olfactory)
- Development of biomarkers for detection and tracking of synaptic dysfunction and synaptic response to treatment in freely behaving animals and in humans
- Discovery and validation of translatable pharmacodynamics biomarkers for a variety of therapeutic targets

J. Invest in the development of clinical tools needed to characterize disease progression to make available sensitive quantitative outcome measures across all stages of AD to efficiently evaluate meaningful clinical impact of therapies.

K. Enable the adoption of formal failure analysis as a routine approach in preclinical and clinical drug development to accelerate translational learning. This requires access to study data and biosamples and resources for data hosting and curation.

L. Expand existing and create new educational and training resources in traditional and emerging drug discovery disciplines for academic researchers, and develop research programs that bring academic and industry experts together.

Session 3: New Strategies for Prevention

A. Provide resources to liberate publicly funded data into the public domain and ensure their adequate curation to maximize usability.

B. Enhance the potential of community-based cohort studies to generate multiple types of molecular and physiological measurements that can be used for systems biology and gene-environment studies by:

- Incorporating technologies such as actigraphy and other passive devices to collect precise quantitative data to serve as endophenotypes

- Including assessments of how other aging physiologic systems interact with the brain (e.g., cardiac, pulmonary, renal, vascular, metabolic, circadian rhythm)

- Expanding the types of cross-sectional and longitudinal ante- and post-mortem biospecimen data collection needed to generate multiple layers of "omics" data

C. To accelerate the identification of genomic variants and other risk and protective factors that contribute to the heterogeneity and multifactorial etiology of dementia, develop cohorts with participants of African, Native American, Asian, and mixed ancestry, e.g., Latinos as well as younger cohorts (midlife and younger).

D. Apply an ecological perspective to better understand how lifestyle factors can impact risk of cognitive impairment and AD. Such a perspective should span physical, behavioral, social, and environmental levels and elucidate interactions among behavioral and contextual variables that can influence risk.

E. Employ a lifespan approach to study the epigenomic changes during vulnerable periods/ physiological transition states to understand the mechanisms of protective and risk factors. This will require development of methods to circumvent issues of cellular heterogeneity.

F. Invest in research aimed at:

- Testing the therapeutic potential of epigenetic regulators as therapeutic targets for treatment and prevention

- Characterizing the extent to which molecular (epi)genomic and transcriptomic variation identified in peripheral tissues (blood, saliva, etc.) can be used as a proxy for interindividual variation manifest in the brain

G. Create research programs aimed at understanding the (epi)genetics and the complex biology of cognitive resilience, especially in high-risk individuals such as E4/E4 and FAD mutation carriers and in individuals with exceptional longevity.

H. Intensify efforts to understand the pathological and protective roles of APOE and its pharmacogenetic effects on various pharmacological and nonpharmacological interventions.

I. Develop integrative research programs to understand how peripheral systems (in particular, immune, metabolic, microbiome) interact with the brain to impact a variety of central nervous system measures related to brain aging and the initiation and progression of neurodegenerative changes.

J. Invest in understanding the integrative physiology of sleep and elucidating the short- and long-term consequences of disrupted and optimized sleep on brain aging and AD.

K. Provide high-quality evidence to inform the selection and implementation of prevention strategies by:

- Using a range of clinical research designs (n-of-1 studies, functional challenge studies, pragmatic clinical trials, population-based cohort designs, and clinical trial/population-based cohort hybrid designs)
- Stratifying participant risk groups using dense "omics" and gene-environment interaction profiles
- Developing guidelines for defining "clinically significant" results of prevention trials
- Developing sustainable, "real-life," multisystems interventions and methods to analyze and interpret the observed changes

L. Compare the effectiveness of dissemination science methodologies to ensure that prevention strategies with high-level evidence are utilized by patients and other stakeholders to support healthy brain aging.

Session 4: Innovating Disease Monitoring, Assessment, and Care

A. Support the development of a wide range of technologies that enable in-place monitoring of individuals at all stages of the disease and integration of this information with other patient-relevant data in order to refine our understanding of disease progression and our ability to build predictive models of disease.

B. Develop a standard set of outcome measures to enable data comparisons across studies, including, but not limited to, daily physical function, home safety, quality of life, physical and cognitive function, behavioral symptoms, and caregiver-related outcomes. Ensure that all outcome measures are validated across diverse educational, linguistic, and cultural groups.

C. Improve methodologies for data capture, storage, and analysis and ensure collection of raw sensor data to enable pooling of data across studies. Sensor data collection apps and data collection server infrastructure should be built and released as open-source tools. These efforts should include the development of standards to enhance interoperability between devices and networks.

D. Initiate programs that bring together cross-disciplinary expertise (including mathematical, statistical, and software engineering experts) needed to develop innovative monitoring technologies and incentivize researchers with expertise in technology design, health literacy, and form-factor expertise, to develop more personalized technologies to serve the diverse populations of aging adults with and without AD and their caregivers.

E. Capitalize on the NIH Big Data to Knowledge Initiative and invest in training of the next generation of AD data scientists.

F. Leverage large, community-based longitudinal cohort studies to efficiently, economically, and systematically explore the use of the technologies and involve the community in the research process to spur discovery science.

G. Incorporate pervasive computing approaches in AD clinical trials to enable objective and continuous data capture of individual participants' everyday function. This will allow the assessment of intra-individual differences and significantly reduce trial sample sizes and the time required to identify efficacy signal(s).

H. Invest in research to develop new technologies that enhance the delivery of clinical care, caregiver support, and in-home monitoring.

I. Integrate mobile health (mHealth) technologies used for disease monitoring and assessment with the formal health care system and conduct clinical trials of mHealth technologies that rely on lay workers (rather than patients or families) to collect data in community settings and transmit these data to the formal health care system.

J. Conduct research that explores the barriers and facilitators of early diagnosis of dementia in primary care settings and explores disparities in diagnosis and treatment among vulnerable elders, including ethnic minorities.

K. Support research on clinical trials testing new models of care across the care continuum and across the full time-course of AD as well as research that tests effective approaches for facilitating productive care partnerships among the formal health care system, community service agencies, and family caregivers.

L. Conduct research designed to test the use of technology to overcome the workforce limitations in the care of older adults with dementia as well as in providing caregiver support and education.

Session 5: Empowering Patients, Engaging Citizens

A. Network with community leaders to build mutually beneficial relationships and create culturally tailored educational programs.

B. Increase the presence of individuals from ethnically and culturally diverse backgrounds as investigators, outreach staff, and personnel.

C. Engage primary physicians' offices serving under-represented communities as partners in participant recruitment.

D. Partner with communities to learn about how to measure meaningful impact of treatments and to determine the appropriate return of value from research participation (i.e., results, general information, failures).

E. Create synergies between federally funded programs such as PCORI and CTSAs to make community involvement less expensive and to learn from the various experiments of community engagement.

F. Bring the trials to the people (i.e., their homes, assisted living facilities, day programs) and leverage emerging technologies for data collection (mobile health applications, electronic medical records).

G. Use existing and invest in new crowd-powered medical research platforms that educate the public while accelerating data collection and analysis.

H. Develop methods and policies for data collection and sharing that empower participant control such as:

- Electronic consent forms that provide an option for broad sharing of deidentified data
- Improved access to data for participants and recast of complex data into forms consumable by nonspecialists

I. Align enabling technologies with policy to streamline and innovate data sharing and patient consent.

Session 6: Enabling Partnerships for Open Innovation

A. Create partnerships among funding agencies to enforce and incentivize rapid and broad sharing of data to enable open, reproducible, and translatable research. Open sharing of data must go beyond the distribution of raw data to support the sharing of efforts in data integration, repository development and maintenance, and consortia-led science.

B. Academic institutions, funding agencies, and journals should develop incentives for researchers (particularly early-career investigators) to participate in large-scale collaborative science by adopting alternative recognition and attribution methods such as:

- Microattribution (similar to the use of GitHub in software engineering)
- Use of alphabetical author lists associated with detailed acknowledgement of individual contributions within the text of the manuscript
- Developing new metrics for recruitment and career advancement purposes that recognize the importance of scientific contribution to shared-science programs

C. Develop innovative partnerships for next-generation research to incentivize students and early-career investigators to adopt a collaborative approach to research through the use of targeted small funding schemes.

D. Develop precompetitive partnerships to support novel/disruptive science focusing on ideas or approaches that are outside of the mainstream for the field and tend not to fare well in traditional peer-review systems.

E. Develop partnerships where intellectual property is not an issue or is a minimal issue and is agreed upon from the start. Ensure that intellectual property is used to support innovation and bring additional investment in the field and not to block others from working in the same research space.

F. Expand the precompetitive space from target selection through clinical proof of mechanism/proof of concept to overcome the most significant hurdle in developing innovative treatments. Specifically:

- Create precompetitive partnership(s) to validate the therapeutic targets that will be delivered by the Accelerating Medicines Partnership for Alzheimer's disease (AMP-AD), as well as other pioneer targets, through clinical proof of mechanism/proof of concept.

2018 NIH ALZHEIMER'S DISEASE RESEARCH SUMMIT:
PATH TO TREATMENT AND PREVENTION

Lunch Options

Scheduled lunch breaks

Monday, March 1: 11:45 a.m.–12:45 p.m.
Tuesday, March 2: 12:00 p.m.–1:00 p.m.

Box lunch pickup

Preordered box lunches will be available at the Atrium level. Please have your purchase receipt available to claim your box lunch. All sales are final.

Where to eat

Food is NOT allowed in the auditorium. We have reserved Classroom E1/E2 for eating lunch; you may also eat in the dining room of the cafeteria upstairs or in other public areas.

Other cafeterias on campus

The Summit is being held in Building 45 (circled on the map). There is a full-service cafeteria at the top of the stairs to the left, which is open from 6:30 a.m. to 2:30 p.m. Other lunch venues include the cafeterias in Building 38A and Building 12B (circled on map), which are open from 7:00 a.m. to 2:30 p.m.
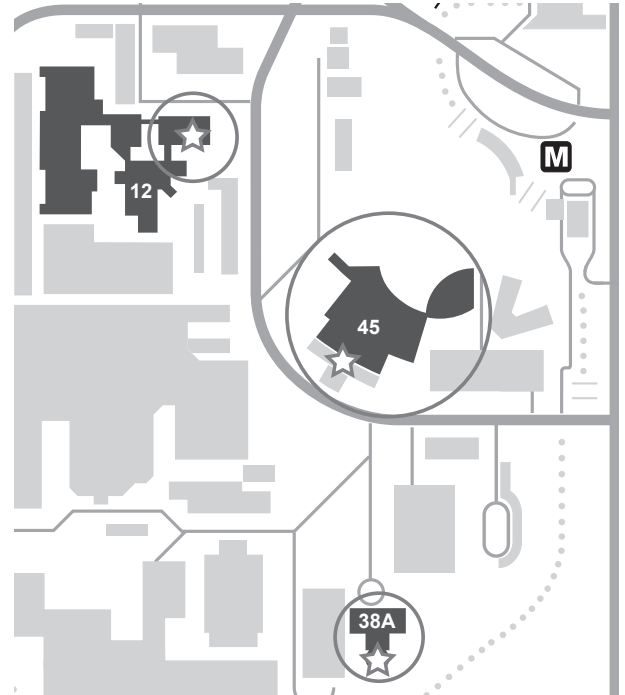
Video, Photography, Social Media Disclosure

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