

NAPA Research Progress Report

NAPA Advisory Council Meeting

Richard J. Hodes, M.D.
Chair, Federal Research Subcommittee

December 2, 2013

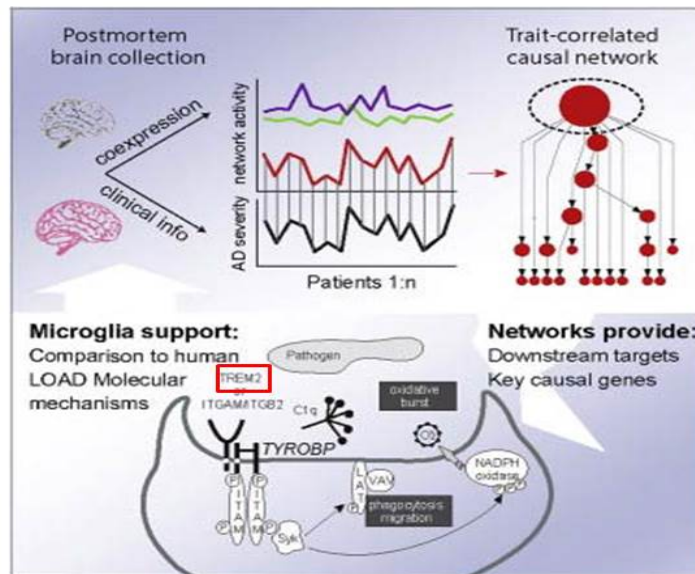


Predicted Mechanisms of LOAD GWAS Alzheimer's Disease Associated Genes

Innate immune/brain inflammatory response	Endocytosis and cellular protein trafficking including APP trafficking	Lipid transport/metabolism	Synaptic transmission	Cytoskeletal function
HLA-DRB5/ HLA-DRB1 TREM2 CR1 CLU MS4A4/MS4A6E EPHA1 INPP5D ABCA7	SORL1 PICALM BIN1 CD2AP	APOE CLU ABCA7	PTK2B MEF2C	CELF1 NME8 CASS4 FERMT2

Nature Genetics (Oct. 27, 2013)

Integrated Systems Approach Identifies Genetic Nodes and Networks in Late-Onset Alzheimer's Disease



Bin Zhang et al, Cell 153:707, 2013

2013 RFA: Interdisciplinary Approach to Identification and Validation of Novel Therapeutic Targets for AD

- **Supports interdisciplinary and integrative research focused on identification and preclinical validation of novel targets for AD treatment and prevention**
 - Encourages the pursuit of paradigm-shifting biological and therapeutic hypotheses and promotes the creation of new translational teams
 - Encourages the use of network-based approaches, such as systems biology and systems pharmacology to gain understanding of the molecular and physiological context within which potential therapeutic targets operate

Identification and Validation of Novel Therapeutic Targets for Alzheimer's Disease, RFA-AG-13-013: <http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-13-013.html>

2013 RFA: Interdisciplinary Approach to Identification and Validation of Novel Therapeutic Targets for AD

- **U01-A Systems Approach to Targeting Innate Immunity in Alzheimer's** –
Dr. Todd Golde, University of Florida, and Colleagues
- **U01-Pathway Discovery, Validation and Compound Identification for Alzheimer's Disease** –
Drs. Philip De Jager, Brigham and Women's Hospital, Broad Institute, Harvard University, Boston, and David Bennett, Rush University Medical School, Chicago
- **U01-Integrative Biology Approach to Complexity of Alzheimer's Disease** –
Dr. Eric Schadt of Icahn School of Medicine at Mount Sinai, New York City, and Team of investigators

2013 RFA: Alzheimer's Disease Prevention Trials

- Phase II or Phase III clinical trials testing pharmacological (small molecules and biologics) and non-pharmacological interventions, in cognitively normal individuals at-risk for AD (e.g., individuals at risk genetically, older adults positive for biomarker evidence of Alzheimer's disease pathology) or in individuals with MCI using a combination of biomarkers (fluid and imaging) and cognitive measures as outcomes.

AD Prevention Trials, RFA-AG-13-015:
<http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-13-015.htm>

2013 RFA: Alzheimer's Disease Prevention Trials*

- **UF1 - The Alzheimer's Prevention Initiative APOE4 Trial** – Drs. Eric Reiman and Pierre Tariot, Banner Alzheimer's Institute, Phoenix, and Co-investigators
- **U01 – Stimulating the Innate Immune System to Prevent Alzheimer's** – Dr. Ted Ashburn, Sanofi Aventis, Cambridge, Mass., in partnership with Baylor College of Medicine, Houston, Texas

Not supported from RFA, but part of FY 2013 AD Funds:

- **U01 -The Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU) Trial** – Dr. Randall Bateman, Washington University, St. Louis, MO, and Co-investigators

2013 RFA: Alzheimer's Disease Phase I Clinical Trials

- Provide support for first-in-human studies for promising AD therapeutics.
- Evaluate the metabolic and pharmacological actions of drugs, including biologics in humans.

UF1- Allopregnanolone Regenerative Therapeutic for MCI/Alzheimer's: Dose Finding Phase 1 –

Drs. Roberta Brinton and Lon Schneider, University of Southern California, Los Angeles

AD Phase I Clinical Trials, RFA-AG-13-016:

<http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-13-016.htm>

MAY 1-2
2013



ALZHEIMER'S DISEASE-RELATED DEMENTIAS: Research Challenges and Opportunities

Sponsored by the
National Institute of Neurological Disorders and Stroke
in cooperation with:

- National Institute on Aging
- Alliance for Aging Research, ACT-AD
- Alzheimer's Association
- Association for Frontotemporal Degeneration
- USAgainst Alzheimer's

www.ninds.nih.gov/ADRelatedDementias2013

CONFERENCE

• **Goals**

- Each topic area presents rationale for prioritized research recommendations and timelines
- Provoke discussion among group experts
- Solicit feedback and opinions from audience

• **Outcomes**

- 567 registrants: 322 in-person, > 200 on-line
- Lively 2-day public session with many comments
 - Culminated with “open mike” and review of all suggested revisions
- Closed session to plan post-conference work

EXECUTIVE SUMMARY - Overall

TOPIC AREA	FOCUS AREA (number of prioritized research recommendations)			
	1. Multiple etiology dementias (MED)	Differential Diagnosis (3)		Epidemiology (3)
2. Health disparities (HD)	Recruitment (4)		Advancing Treatment and Prevention Strategies (4)	
3. Lewy body dementias (LBD)	1. Establish longitudinal cohorts with common measures, culminating in autopsy studies. (2)	2. Discover disease mechanisms through brain mapping and genetics (2)	3. Develop and validate biological and imaging biomarkers (2)	4. Model disease processes to develop potential symptomatic and disease modifying therapies (2)
4. Frontotemporal dementia and other tauopathies (FTD)	Basic Science: Pathogenesis and Toxicity (4)		Clinical Science: Discovery, tools, and cohorts (4)	
5. Vascular contributions to AD/DRD - focus on small vessel disease and AD/vascular interactions (VAS)	Basic Mechanisms and Experimental Models (3)		Human-Based Studies (3)	

EXECUTIVE SUMMARY – Overlap

- **Although ordering of priorities and timelines differed, several recs applied across AD/DRD (and AD)**
 - **Fundamental research to fill critical knowledge gaps**
 - **Training and education to ensure durable progress**
 - **Improved diagnostics**
 - **Optimized repositories**
 - **All recommendations within HD**
 - **Culmination of research in effective interventions**



Alzheimer's Disease Summit: The Path to 2025

November 6 - 7, 2013

The New York Academy of Sciences

Presented by The New York Academy of Sciences,
National Institute on Aging/NIH and the Global
CEO Initiative on Alzheimer's Disease



Alzheimer's Disease Summit: The Path to 2025

Primary Goal: To convene leading industry, academic, and government stakeholders in discussions regarding how to prevent and effectively treat Alzheimer's by 2025:

- Coordinating with governmental efforts to build research resources
- Reengineering our current drug development and evaluation systems
- Identifying innovative technologies and financing models

Outcome: To comprise a research agenda that will delineate the pathways needed to effectively treat and prevent Alzheimer's disease by 2025.

www.nyas.org/pathto2025

UK Hosts the First G8 Dementia Summit on December 11, 2013

Host: The Right Honorable Jeremy Hunt MP

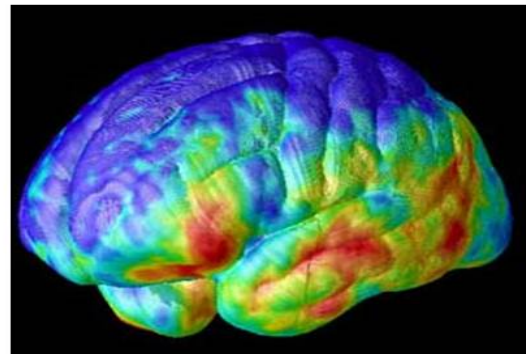
Participating Countries:

Canada
France
Germany
Italy
Japan
Russia
USA
United Kingdom

<https://www.gov.uk/government/news/uk-to-host-g8-dementia-summit>

SAVE THE DATE

Alzheimer's Disease Research Summit 2015



February 9-11, 2015
National Institutes of Health
U.S. Department of Health & Human Services
Bethesda, MD