ADRC Directors meetings
National Institute on Aging
Virtual
May 1, 2020

"NIA Division of Neuroscience Update"

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NIA-NIH
Some NIA-AD Research Priorities

- Greater integration among basic, preclinical, and clinical AD programs
- Early detection and diagnosis
- National Strategy to enhance recruitment for AD clinical studies
- Enhance clinical trials pipeline
  - “More shots on goal”

DATA SHARING
The ADRC’s are critical at interacting with NIA consortia to promote data, biospecimens and models sharing for AD/ADRD research.
Trends in NIA-funded AD Drug Discovery and Preclinical Drug Development Projects - by therapeutic target -
Trends in NIA-funded Projects on the **Molecular/Cellular Mechanisms of AD** by main research topic:

- 2015
  - 1. Amyloid beta
  - 3. Presenilin Biology
  - 5. Other Proteinopathies
  - 7. Circuits and Synapses
  - 9. Immunity and Inflammation
  - 11. Vascular Etiology
  - 13. Molecular Mechanisms of Neuroprotection...
  - 15. Sleep and Circadian Rhythm
  - 18. Other Pathogenic Mechanisms

- 2016
- 2017
- 2018
- 2019

**Fiscal Years**

- 2. Tau
- 4. ApoE and Lipid Neurobiology
- 6. Autophagy, Endocytosis and Membrane Trafficking
- 8. Cell Death
- 10. Metabolism and Bioenergetics
- 12. Neuroendocrine Mechanisms
- 14. Gut-Brain Axis and Microbiome
- 16. Environmental Mediated Factors
Understanding AD in the context of Aging

Proteinopathy

HIV-1, HHV, other pathogens

Aging

Proteostasis
Mitochondria
Inflammation
Endosomes
Growth Factors
Epigenetics
DNA damage
Senescent cells
Immune surveillance

Abeta
Tau
Synuclein
TDP43
Others

Synapse damage

Neurodegeneration
Neurogenesis in Aging and AD/ADRD (workshop)

Oscillatory gene expression in aging and AD/ADRD (FOA)

Transposable elements, viruses, aging and AD/ADRD (workshop)

Glial cell plasticity in Aging and AD/ADRD (FOA)

Cell senescence in Aging and AD/ADRD (FOA)

New workshops and FOA’s in Aging related cellular and molecular mechanisms in AD/ADRD FY2019 and 2020
Session I. Neurogenesis in the Adult Human Brain.
• Hippocampal neurogenesis linked cognitive deficits and AD
• Solving human neurogenesis in vivo toward therapy of brain disorders

Session II. Regulation of Neurogenesis in the Aging Brain.
• Regulation of neural stem cell aging with single cell
• Enhanced plasticity of new neurons in the hippocampus
• Blood-borne regulators of the hippocampal neurogenic niche

Session III. Functional Significance of Adult Neurogenesis.
• Blood: at the interface of aging and adult neurogenesis
• Re-engineering and Rejuvenating aging memory circuits
• Harnessing Neurogenesis to Improve Pattern Separation in Aging
New or renewed U19 Centers for data and resource sharing to bolster collaborations in AD/ADRD research

Center for α-synuclein strains in AD/ADRD
(J. Trojanowsky)

A Platform for cell type level interrogation of AD/ADRD
(Ed Lein)

Next Generation Proteomics in AD/ADRD
(M. MacCoss)

Longitudinal Fronto temporal lobar degeneration
ALL-FTD
(B. Boeve)

DIAN
BIOCARD

DIAN
Dominantly Inherited Alzheimer Network

ALLFTD
ARTFL LEFFTDS Longitudinal Fronto-temporal Lobar Degeneration
U19 Center: A platform for cell type-level transcriptomic, epigenomic and spatial interrogation of Alzheimer’s disease

Project 1: University of Washington
Neuropathology, case selection, biostatistics
ADRC Neuropathology Kaiser ACT Study
Tom Grabowski Dirk Keene Eric Larson

Tissue Specimens

Project 2
Single nucleus -omics
Allen Institute

Project 3
Spatial -omics
Allen Institute

Data Core
Allen Institute
Specimen metadata
Neuropath images
snRNA-Seq
snATAC-Seq/CH3ome
Spatial mapping
Data visualization
Data integration
Taxonomy mapping
Search & mining tools

Admin Core
Coordination, reporting
Allen Institute: Ed Lein, Mike Hawrylycz

NIH National Institute on Aging
Center for cell type-level interrogation of AD Goals

• **Improved methods for single cell –omics and spatial histological techniques.**

• **Optimize, standardize and scale cutting-edge single cell genomics technologies for aged brain tissues from AD.**

• **Define the topographic, cell type- and molecular profile of Alzheimer’s disease using a combination of single nucleus transcriptomics and epigenomics and spatial transcriptomics.**

• **Create an Alzheimer's Disease data resource integrated with similar large-scale efforts in neurotypical brain.**
Elucidate mechanisms of pathological aSyn-mediated neurodegeneration in AD+aSyn versus pure AD (AD-aSyn) compared with LBD as a function of aging and accumulations of aSyn aggregates as well as tau, Aβ and TDP-43 co-pathologies that influence different clinical manifestations of these disorders.

Provide standardized PFF’s derived from human brains, animal models, expertise.
RESOURCES

Training

A key goal of the Penn U19 Center is to train the next generation of AD/HD investigators and provide a solid foundation for career enhancement.

We will provide 10 days of the pre-fund (PF) to remote investigators, some of whom may elect to visit our U19 Center to learn best practices for AD/HD and the PF7 generation and simulation of brain-derived AD/HD and LBD flies, as well as best practices for injection of pathological tau and adopt the basis of care.

To learn more about training opportunities offered by the Penn U19 team, contact:

(999) 999-9999

More information (drop down)

A sample training itinerary:

Visit the University of Pennsylvania for a 3-day training experience

- Visit hands-on in the lab alongside a member of the U10 research team
- Network with other AD/HD investigators for potential collaborative opportunities
- Meet regularly with other Penn Medicine investigators also working in AD/HD research at Penn

FAQ

Who is eligible for training?

Eligibility criteria are as follows:

- Are travel and accommodations covered?

No. The trainee is responsible for all costs including travel and accommodations. However, when possible, we may be able to provide recommendations and/or assistance in booking a nearby stay.

Data Sharing

A unique AD/HD-like resource component of this U19 is the use of procedures we developed over the past 20 years to share biologicals obtained through this U19 Center and from prior collections of CSF, plasma, serum, DNA/RNA and brain samples from AD and LBD patients who have been followed through NIH-funded programs.

To obtain biosamples, investigators must have an active IRB approval for their studies involving human tissues. This IRB approval must accompany the request form below, which must be completed and signed by the requesting principal investigator.

Download the Biosample Request Form here. (download link)

Please send your Request Form and IRB Approval to:

Kevin Davis
davensk@upenn.edu
215-349-9099 (fax)

If you have questions or need further assistance in completing the above form to request a biosample, please contact:

Kevin Davis
davensk@upenn.edu
215-349-9099

Download the full U10 Overview Here

ABOUT CORES PROJECTS RESOURCES NEWS

CONTACT

NATIONAL INSTITUTE ON AGING (NIA) PENN U19
Center On Alpha-synuclein Strains In Alzheimer Disease & Related Dementias

NIH National Institute on Aging
New FOA’s and U19 Center for investigating the cross talk between pathogens and AD/ADRD research

- Infectious etiology of AD/ADRD (NOT-AG-19-012)
- COVID-19 NIA NOSI (NOT-AG-20-022)
- HIV, brain aging and AD/ADRD (RFA AG18-023)
- Microbiome in Aging brain and AD/ADRD (U19)
Coronaviruses and the CNS

Neurological complications in SARS-CoV-2
• Dizziness, headache, impaired consciousness, CVD, ataxia, epilepsy
• Hyposmia, hypogeusia, hypopsia, neuralgia

Evidence for Coronaviruses in the CNS
• Detection of SARS-CoV-1 in CSF and CNS
• Axonal and olfactory transport of Coronaviruses
• Acute necrotizing encephalitis and meningitis in MERS, SARS-CoV-1 and 2
• Infection of maccs and neurons by CoV OC43

Association of Coronaviruses with neurological disease
• Parkinson’s disease
  • HCoV RNA in CSF (Christallo 1997)
  • HCoV 229E and OC43 RNA in brain (Arbour 2007)
• Multiple Sclerosis
  • Virus in CSF (Tanaka 1976), Virus in brain (Burks 1980)
  • Epidemiological association with HCoV293 URI (Hovanec 1983)
Notice of Special Interest (NOSI): NIA Availability of Administrative Supplements and Revision Supplements on COVID-19

**Notice Number:** NOT-AG-20-022

**Key Dates**
- **Release Date:** April 2, 2020
- **First Available Due Date:** April 06, 2020
- **Expiration Date:** May 01, 2021

**Related Announcements**
- PA-18-591 Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp Clinical Trial Optional)
- PA-18-935 Urgent Competitive Revision to Existing NIH Grants and Cooperative Agreements (Urgent Supplement - Clinical Trial Optional)
- NOT-AG-20-031

**Division of Neuroscience**
- Studies of neurological and neurocognitive symptoms with COVID-19
- Studies of mechanisms underlying SARS-CoV-2 pathology
- Studies aimed at discover and development of BBB penetrant anti-SARS-CoV-2 drugs
- Development of computational and informatics methods for multimodal COVID-19 diagnosis

- Include “**NOT-AG-20-022**” (without quotation marks) in the Agency Routing Identifier field **(box 4B)** of the SF424 R&R form.

- The project period will generally be **limited to 1 year**. Project periods up to 2 years will be considered only with strong justification.
Concept Approvals:
https://www.nia.nih.gov/approved-concepts

General FOAs:
https://www.nia.nih.gov/research/funding

Alzheimer’s Disease and Related Dementias FOAs:
http://www.nia.nih.gov/AD-FOAs

Follow our “Inside NIA” blog:
https://www.nia.nih.gov/research/blog