NIH Alzheimer's Disease Centers Panel Recommendations

In June, 2017 "NIA engaged leading experts from academia, industry and non-profit foundations, working in Alzheimer's and other complex diseases, in a strategic planning process to help ensure that the next generation of AD Centers is poised to accomplish the goals of the *National Alzheimer's Plan*."

https://www.nia.nih.gov/news/expert-panel-offers-transformative-recommendations-nih-alzheimers-research-centers

NIH ADC Panel Recommendations

Outline a roadmap for the Alzheimer's Disease Centers Program to improve the chances of achieving the goal of successful development of more effective approaches to prevention, diagnosis, and therapy for people with dementia and their families.

Focus Topics:

A. Gaps in disease mechanisms and risks
B. Clinical research capacities
C. **Maximize value of neuropathology expertise across ADCs**
D. Translational research
E. Cross-ADC interactions/networking
F. Interactions beyond the ADC network
G. Infrastructural supports to enable prior recommendations
H. Further development of training programs

https://www.nia.nih.gov/sites/default/files/2017-06/ADC%20PANEL%20RECOMMENDATIONS%20FINAL%20June%202017.pdf

Panel Statement on Neuropathology

”Autopsy continues to be an **invaluable component** of ADC activities, providing a **national resource** for expertise in the pathology of neurodegenerative diseases. Postmortem examination remains the **gold standard** by which to: confirm diagnostic criteria and clinical diagnoses, understand the prevalence of dementia subtypes including those with mixed pathologies, validate imaging and biofluid biomarkers, evaluate therapeutic response, and identify the major therapeutic targets for AD and ADRDs.”

Areas of Emphasis (my interpretation)

- Case Selection, Diversity, and Prioritization
- Tissue, Data, and Resource Sharing
- Diagnostic and Precision Neuropathology
- Biomarkers and Therapeutics
- Education and Training

Case Selection, Diversity, and Prioritization

- Improve autopsy consent processes for research broadly to help achieve diversity
- Maximize post-mortem rates
  - **Support outreach and education efforts to promote value of brain donation**
  - **Protocols to ensure consented subjects undergo autopsy (in place)**
- Prioritize clinically well-characterized research participants and those of particular interest
  - **Yes**
- Expand opportunities for autopsies beyond UDS and clinical core participants when they facilitate AD and ADRD research.
  - **Site specific**

Tissue, Data, and Resource Sharing

- Establish transparent guidelines for acceptance, retention, and sharing of tissue and data for research purposes to eliminate barriers and facilitate broad access to samples for research.
  - **Site Specific**
  - **National guidelines?**

- Augment approaches to increase autopsy material from cognitively normal individuals
- Assess scientific value of late stage brains in freezers, both current and future. Develop a protocol for addressing any excesses, while maintaining those that are of value to other researchers.
  - **Site Specific**

NeuroBiobank: Overview and opportunities for collaboration with ADC NP cores

Anna Taylor, PhD PROGRAM DIRECTOR, NIH NEUROBIOBANK, NINDS

Tissue, Data, and Resource Sharing

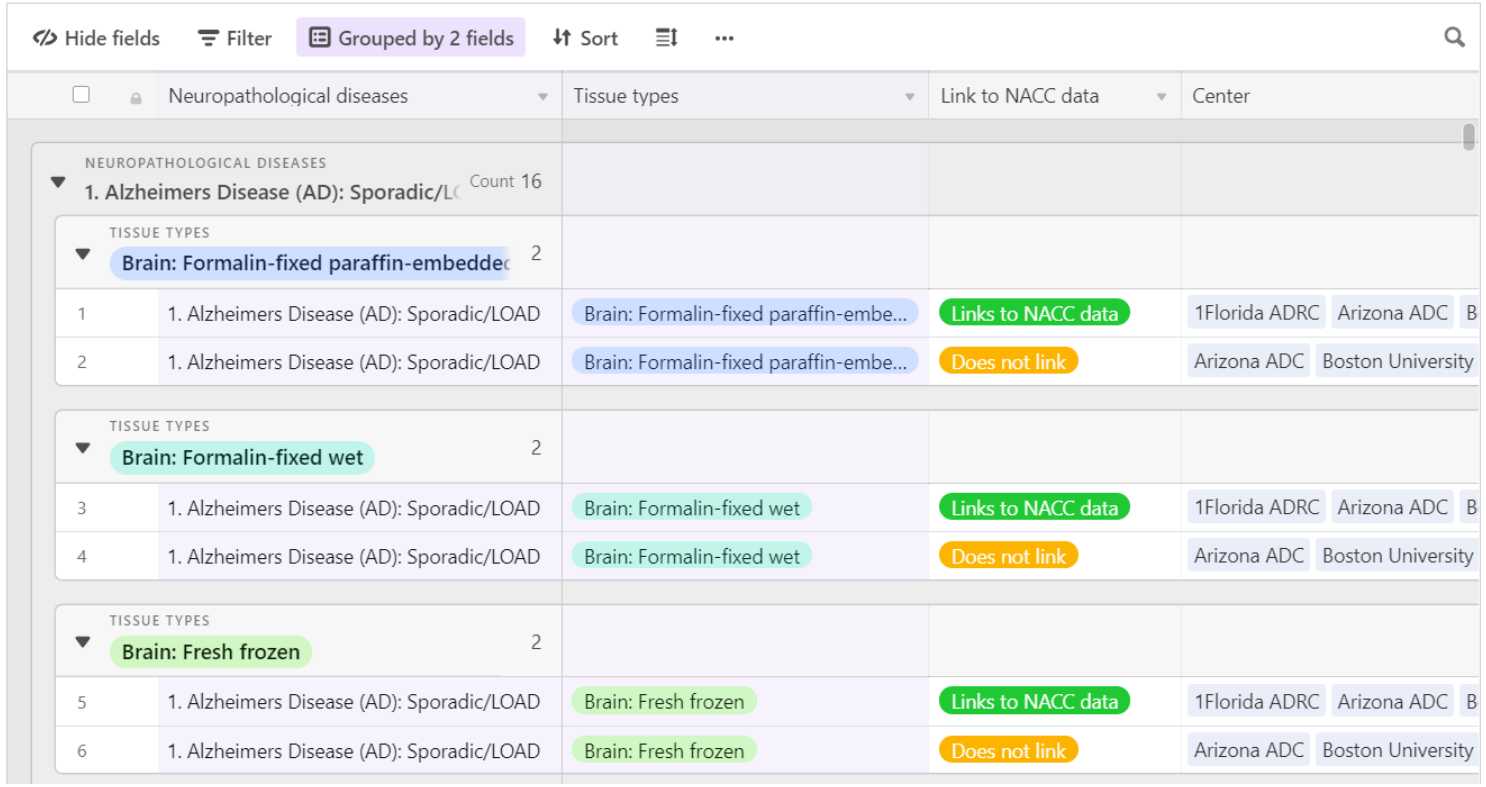
- Build through NACC a central, publicly interfacing database registry of all stored and banked autopsy materials related to ADC research participants

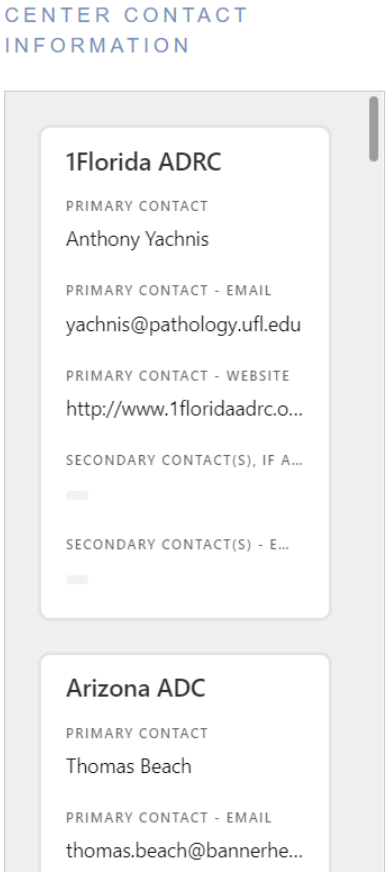
- Survey availability across the ADC network and NACC to identify gaps in available autopsy material from cognitively normal individuals with useful prior clinical characterization.

- Determine which ADCs have biospecimens that may be available for sharing

Tissue, Data, and Resource Sharing

NACC Neuropathology and Biospecimen Resource Locator Tool





Demo during NACC session, Sat. 1:30pm

Tissue, Data, and Resource Sharing

- Establish mechanisms for digital slide scanning and electronic image sharing/analysis of neuropathologically characterized tissue sections.
  - **Accessibility to neuropathological specimens for research**
  - **Standardization of diagnostic neuropathology protocols**
  - **Neuropathology training**
  - **Work in progress**

- For all autopsy cases facilitate DNA extraction and collection of biosamples for storage through NCRAD when this is not already available through existing processes.
  - **Yes**

- Establish and publicize a cost structure for neuropathology services that allows other ADCs, non-ADC research programs and families access to their neuropathology expertise.
  - **Site specific**

Diagnostic and Precision Neuropathology

Enhance opportunities to describe the co-occurrence of neurodegenerative and other pathologies from preclinical asymptomatic stages to dementia and death.

- **Case selection/Diagnostic strategies/Incorporate new pathologies**

TDP-43 pathologies and HS-related disorders in the elderly

Peter Nelson, MD, PhD NP CORE LEADER, UNIVERSITY OF KENTUCKY

Develop new measures of risk, tapping into constructs that are currently measured poorly or incompletely, e.g., lifespan exposures, cognitive reserve/resilience, sleep, daily function, etc.

- **Broad applications depending on cohort and characterization**

Neurodegenerative disease transmissibility

Ermias Belay, MD NATIONAL CENTER FOR EMERGING AND ZOONOTIC INFECTIOUS DISEASES, CENTERS FOR DISEASE CONTROL AND PREVENTION

Matthew Frosch, MD, PhD NP CORE LEADER, MASSACHUSETTS ADRC

Diagnostic and Precision Neuropathology

Encourage application of novel innovations in quantitative neuropathology technologies/methods of assessment as they develop, beyond the standard diagnostic approach.

- **Site Specific**
- **Diverse applications/assays/systems**
  - **NP Core Leader Career Development Awardees**
- **“Living biobank” approaches (iPSC)**

Neuropathology keynote: A molecular and cellular paradigm for understanding human brain function and dysfunction

Ed Lein, PhD INVESTIGATOR, ALLEN BRAIN INSTITUTE

Biomarkers and Therapeutics

- Continually evolve standard protocols of assessment and tissue banking in parallel with advancing clinical and biomarker research
- Modify prioritized regions for anatomical sampling to match ROIs based on emerging PET targets/specific therapeutic targets
  - **Site specific**
  - **NP UDS updates**
  - **Other updates/consensus criteria**

- Establish interactions with therapeutic trial sponsors to obtain autopsy tissue from therapeutic studies
  - **Site specific**
  - **Centralized coordination**

Education and Training

Create opportunities for the training of neuropathologists in the sub-field of neurodegenerative disease research.

- **ADC NP Core Leader Career Development Award Program**
  - **15 awardees from 2015-2017**
- **Pilots/Development Project grants**
- **Site specific opportunities/initiatives**
- **Local NP fellowship program integration**

Summary

- NP Cores are already meeting many recommendations of the NIA ADC Panel already in site specific ways and through collaborations

- Opportunities exist to further address recommendations in partnership with NIA

FINAL AGENDA

NP Core Leaders Meeting

6:30 **Neurodegenerative disease transmissibility**

Ermias Belay, MD NATIONAL CENTER FOR EMERGING AND ZOONOTIC INFECTIOUS DISEASES, CENTERS FOR DISEASE CONTROL AND PREVENTION

Matthew Frosch, MD, PhD NP CORE LEADER, MASSACHUSETTS ADRC

7:15 **Neuropathology keynote: A molecular and cellular paradigm for understanding human brain function and dysfunction**

Ed Lein, PhD INVESTIGATOR, ALLEN BRAIN INSTITUTE

8:15 **TDP-43 pathologies and HS-related disorders in the elderly**

Peter Nelson, MD, PhD NP CORE LEADER, UNIVERSITY OF KENTUCKY

8:30 **NeuroBiobank: Overview and opportunities for collaboration with ADC NP cores**

Anna Taylor, PhD PROGRAM DIRECTOR, NIH NEUROBIOBANK, NINDS

9:00 **Adjourn**