Biomarker Meeting - summary

BIOFLUID BIOMARKERS, 6–8PM

6:00 pm **Introduction to inter-ADRC biomarker efforts, and progress towards an inter-ADRC project to standardize A-beta42/tau/P-tau**
Douglas Galasko, MD CO-CHAIR, BIOMARKERS WORK GROUP; CLINICAL CORE LEADER, UNIVERSITY OF CALIFORNIA, SAN DIEGO

6:20 **Roche Elecsys data from ADNI**
Leslie M. Shaw, PhD UNIVERSITY OF PENNSYLVANIA

6:37
- **Standardization of CSF biomarkers**
- **Neurofilament light chain protein (NFL) as a blood biomarker for neurodegeneration**

Kaj Blennow, MD UNIVERSITY OF GOTHENBURG

7:02 **MarkVCID: Developing best practices and biomarker harmonization**
Donna Wilcock, PhD CO-CHAIR, BIOMARKERS WORK GROUP; UNIVERSITY OF KENTUCKY

7:19 **Opportunities for an inter-ADC biomarker initiative**
Eric Reiman, MD DIRECTOR, ARIZONA ADC

7:30 **Group discussion: 30 min**

DIGITAL BIOMARKERS, 8–9PM

8:00 pm **Technology enablement of digital biomarkers for the futurization of AD research**
Rhoda Au, PhD BOSTON UNIVERSITY AND FRAMINGHAM STUDY

9:00 **Adjourn**

Opportunity

- 31 Centers with 12,000 active participants.
- Standardization, deep phenotyping, longitudinal follow-up, diversity, autopsy follow-up, and existing infrastructure and expertise.
- Potential to prospectively collect plasma on 12,000 unique subjects in 12 months.
- Existing plasma samples on > 4,000 unique individuals with autopsy-confirmed disease.
- Subset of individuals will also have CSF, MRI and PET imaging.

Is The Time Right?

- CSF Aβ and tau assays have matured with low variance and high levels of reproducibility.
- For $A\beta_{1\text{-}42}$, a standard reference material (SRM) enables accurate inter-laboratory quantification.
- CSF tau / Aβ ratios outperforms each marker alone in diagnosis and prediction in ADNI samples.
- Plasma proteins relevant to the brain, e.g., NFL provide information regarding neurodegeneration, although not specific to AD.

Inter-ADRC Project to Standardize CSF Aβ and tau

- Proposed by Galasko and colleagues to collect CSF prospectively at a subset of ADRCs with LP kits, collection and aliquoting tubes provided.
- Les Shaw will use the Roche Elecsys system to measure Aβ42 and tau.
- CSF data will be returned to the contributing ADRCs and will be deposited in NACC.
- Will provide proof-of-concept for ADRC network-wide fluid biomarker assessment.
- Will bank 1-2 mL of additional CSF and plasma at NCRAD

Opportunities to Identify Novel Biomarkers

- The model used in the MarkVCID Consortium is the harmonization and cross-site validation of novel fluid biomarkers for biomarker discovery.
- The standardized collection, aliquoting, and storage procedures across all ADRCs would provide a powerful repository of biofluids for such cross-site studies for novel AD biomarkers.
- Novel biomarker discovery will be required for ”precision medicine” in dementia. Identification of ADRD pathologies, as well as, potentially, subtypes of AD will be important.

Biomarker Vision

ADCs

- Well characterized subjects
- Longitudinal visits
- Genomic data
- Imaging on subset

Blood (**DNA**, plasma, serum, RNA, PBMC) + **CSF**

NACC

NCRAD

Central DNA resource used for APOE, GWAS, WGS

New central resource for biomarker studies

Biosample use
discovery
mature assays
Informatics

Leveraging NCRAD To Enable ADRC Biomarker Studies

Benefits:

- Large numbers of samples, collected uniformly, available in a single place
  - ADCs receive all materials for sample collection, processing and aliquoting
  - ADCs receive funding for sample collection
  - Reduced ADC burden for sample storage
  - Single MTA to facilitate sample sharing

- Data generated from the samples are made available rapidly to the ADCs and the research community
  - Initially propose key validated assays
  - Data can now be used within and across ADCs