National Cell Repository for Alzheimer Disease

Tatiana Foroud, Ph.D.

Indiana University School of Medicine

NCRAD
The National Cell Repository for Alzheimer's Disease

NCRAD History

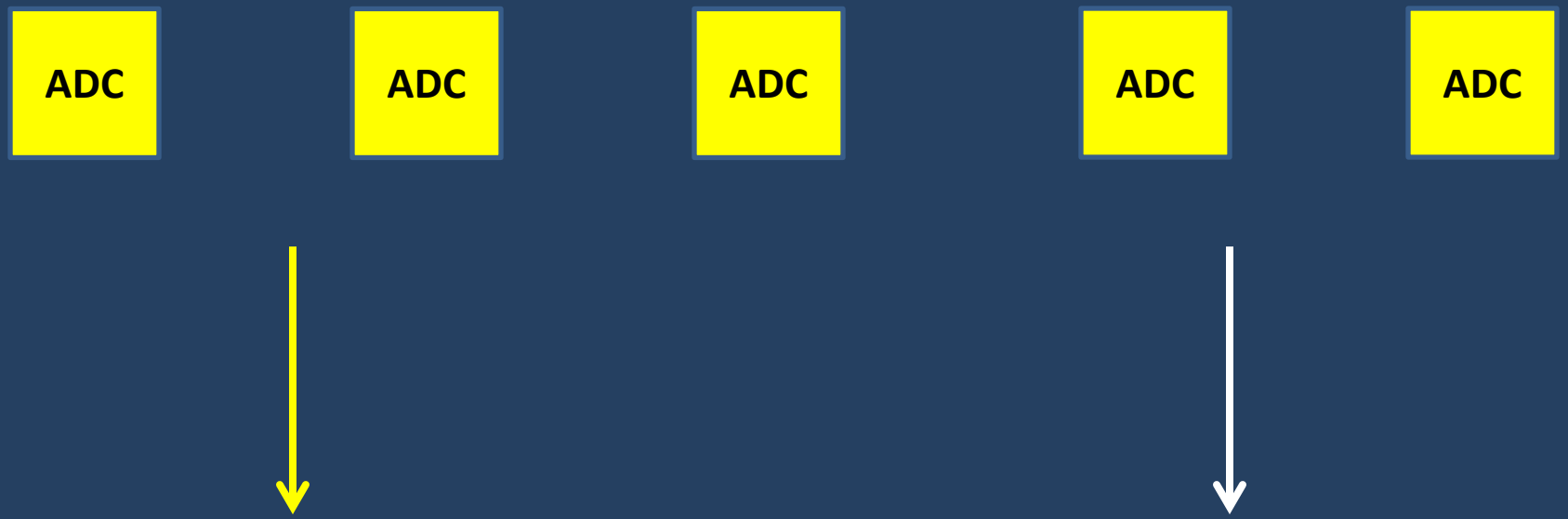
- Established in 1990 as part of the Indiana Alzheimer Disease Center
  - Called the 'Indiana Cell Bank'
- In 2002, NCRAD was established
  - Removed from the Indiana Alzheimer Disease Center and awarded as an independent grant
- Original PI was P. Michael Conneally

NCRAD
The National Cell Repository for Alzheimer's Disease

NCRAD Update

- The mission of NCRAD is to bank samples that are then distributed to dementia researchers
- Initially, banked DNA and lymphoblastoid cell lines
- More recently, expanded to also store
  - Plasma
  - Serum
  - Brain tissue (for DNA extraction)
  - RNA (from blood)

Why am I here?



Data collected from subjects enrolled in the ADC are captured on the UDS and submitted to NACC for central storage

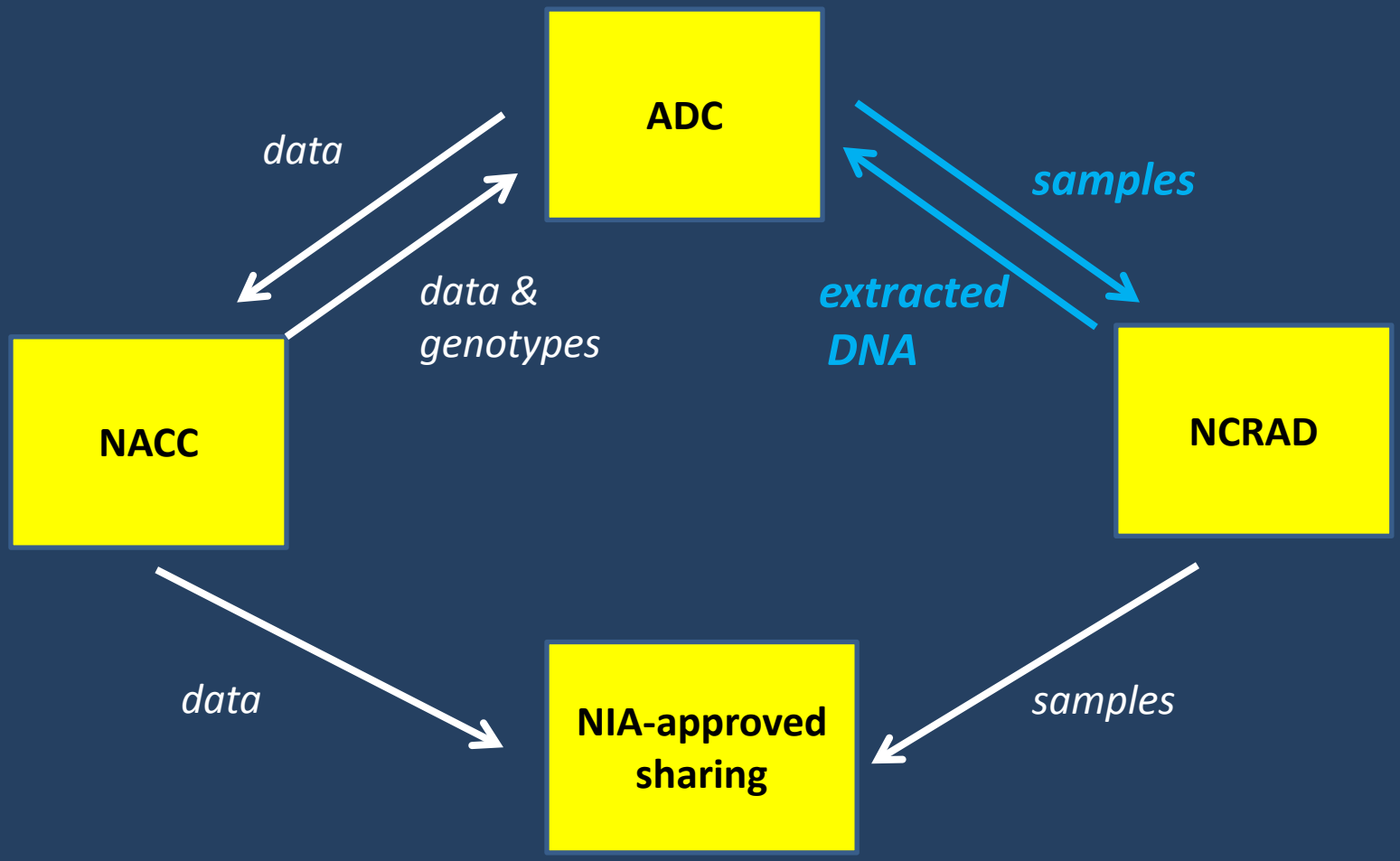
Uniform biological samples are not being collected from these well characterized subjects

No central storage of samples

Alzheimer Disease Genetics Consortium (ADGC)

- The ADGC has provided a framework that has helped us to begin to tackle this problem
  - Currently, DNA can be transferred to NCRAD for any subject with UDS data
  - Currently, blood can be sent to NCRAD for DNA extraction for any subject on the Blood Lists
    - ADGC provides funds to NACC for reimbursement to sites
  - Not all subjects are on the Blood Lists
    - Leaves a hole that includes many valuable samples
      - MCI
      - Early onset AD
      - FTD

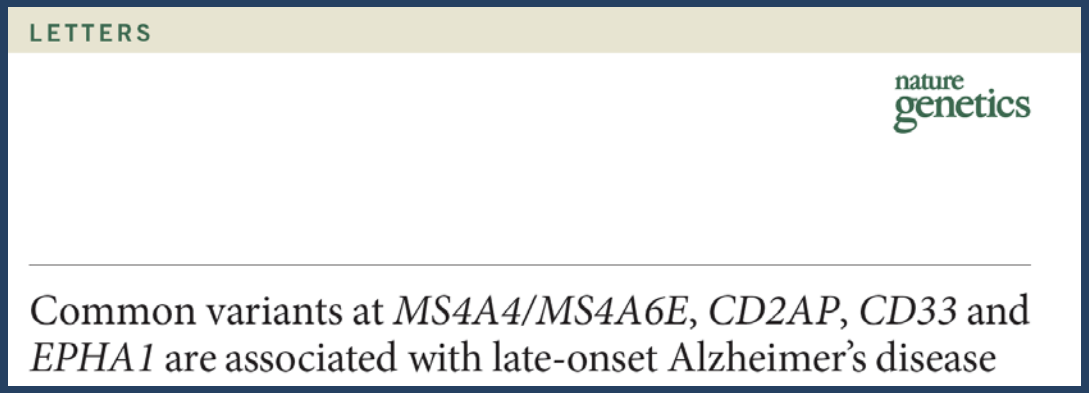
Alzheimer Disease Genetics Consortium



Study	Brief study description	# of samples (through 3/31/12)
NIA AD Genetics Initiative (LOAD Study)	Late onset AD families with ≥ 2 sampled siblings with AD and other family members; controls	**1,146 controls 5,582 family samples**
Alzheimer's Disease Neuroimaging Study (ADNI) samples	200 AD, 400 mild cognitive impairment (MCI) and 200 controls	**822 blood 707 DNA**
Amyloid Imaging VMCI and Analysis for ADNI (ADNI-GO) **And Alzheimer's Disease Neuroimaging Study (ADNI-2)**	200 newly enrolled early MCI subjects and 450-500 subjects followed up from the original ADNI project Blood samples for 550 newly enrolled normal controls, eMCI, lMCI and mild AD subjects	**477 newly enrolled 280 sampled ADNI-1 follow-ups**
Identification of Genetic Risk Factors for AD and FTD (GIFT)	AD, frontotemporal dementia and control subjects	**1477**
Genetic Epidemiology of Alzheimer's Disease in African Americans (AA Genetics Study)	Cases and controls from Non-Hispanic African Americans born in the U.S.	**1574**
Dominantly Inherited Alzheimer's Network (DIAN) Study	Adult biological offspring of an AD parent with a known mutation (APP, PS1 or PS2)	**238**
The Frontotemporal Lobar Degeneration Neuroimaging Initiative (NIFD)	Frontotemporal lobar degeneration patients and age-matched controls. Some of the individuals are or have already enrolled in the GIFT study.	**38**
Four Repeat Tauopathy Neuroimaging Initiative (4RTNI)	Subjects with corticobasal degeneration (CBD) or progressive supranuclear palsy (PSP).	**3**
Alzheimer's Disease Genetics Consortium (ADGC)	**Large consortium contributing brain tissue for DNA extraction as well as DNA aliquots**	**13,055**
University of Kentucky Controls	Control subjects who have agreed to have a blood draw but do not fit LOAD control criteria	**340**
Washington University ADRC (WU-ADRC)	All active research participants at WU-ADRC	**690**

Collaboration with the ADGC has been very productive

- The ADC samples formed a core portion of the recent GWAS meta analysis


LETTERS

nature genetics

Common variants at *MS4A4/MS4A6E*, *CD2AP*, *CD33* and *EPHA1* are associated with late-onset Alzheimer's disease

Naj et al, Nature Genetics, 2011


ORIGINAL CONTRIBUTION

ONLINE FIRST

Meta-analysis Confirms *CR1*, *CLU*, and *PICALM* as Alzheimer Disease Risk Loci and Reveals Interactions With *APOE* Genotypes

Jun et al, Annals of Neurology, 2010

We have an opportunity…

- As part of the NCRAD renewal, we have budgeted to extract DNA from blood samples in > 12,000 subjects over 5 years
  - This would allow us to receive blood from all subjects currently enrolled in the ADCs and bank DNA

How could this facilitate research?

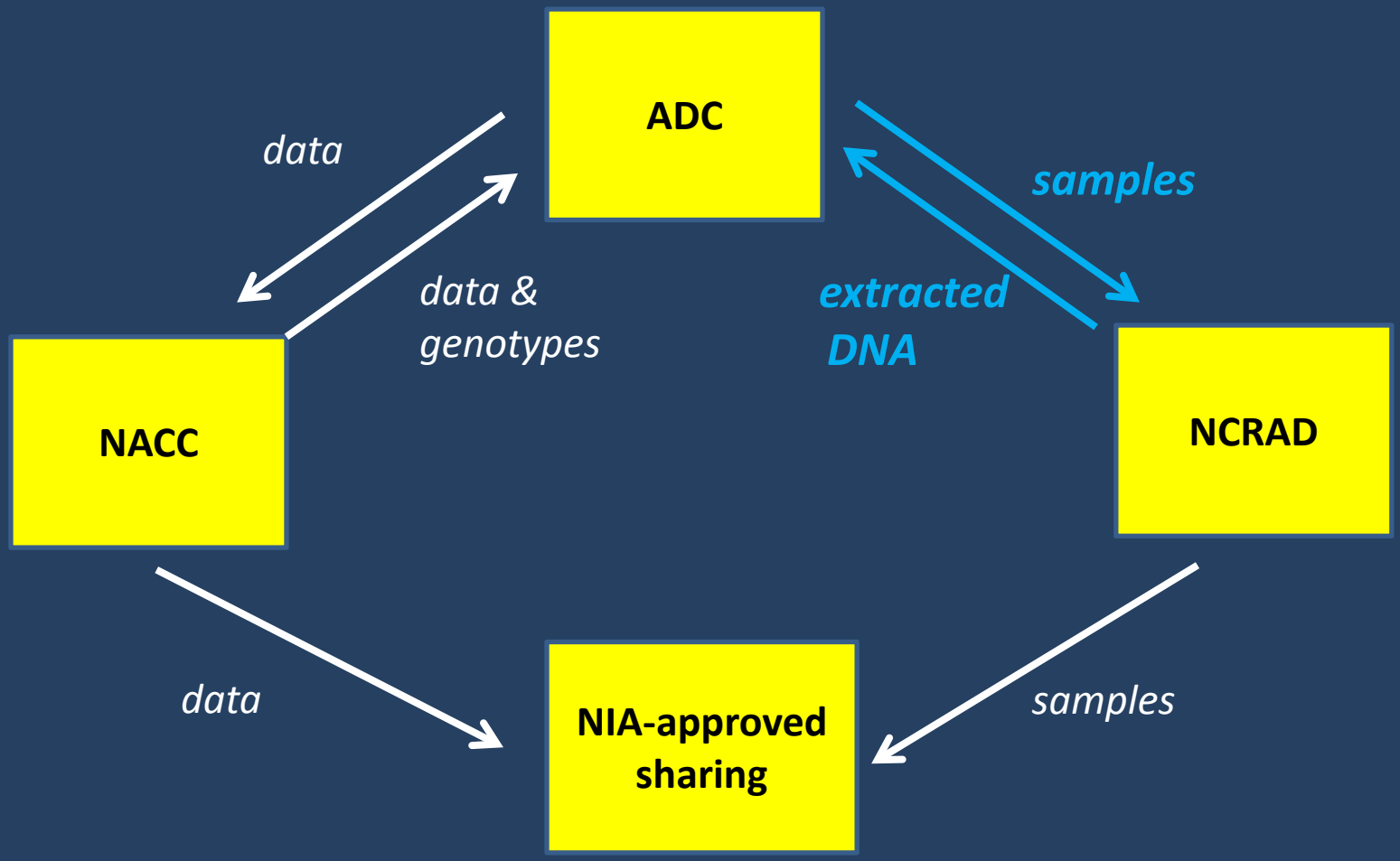
- Centers could request an aliquot of DNA from each of the subjects they contribute
  - Could be used for pilot studies at the centers
  - Could be used for new initiatives
- Having samples banked at NCRAD would allow many new studies to be initiated that could include genetic hypotheses
- Avoid having repeated requests to centers for brain tissue or transfer of DNA or blood for new studies

For some sites, it is less expensive and more convenient to use NCRAD for DNA extraction than it is to do this locally

NCRAD wants to work with centers

- NCRAD staff can work with your center and provide appropriate IRB language
- NCRAD can provide a free aliquot of DNA back to the center
- NCRAD can serve as a back-up site for samples from your center

Unique Opportunity for All



Potential NCRAD Initiative

Develop the resources for future iPS

Induced Pluripotent Stem Cells (iPS)

- Pluripotent stem cells can differentiate into most, if not all, adult cell types
  - Allows access to cell populations that may be difficult to obtain (i.e. neurons)
- Initial work has used fibroblasts or cord blood as the source of cells
- Recent work has shown that peripheral blood can also be used to generate iPS
- Differentiated cells can then be used to perform a variety of biological and functional experiments

Induced Pluripotent Stem Cells (iPS)

- The cost to develop iPS or neuronal cells is substantial
  - We want to start with focused studies obtaining samples from particular populations already of interest
- Focus initially on samples from subjects with known mutations
  - APP, PS1, PS2, Tau, GRN, c9orf72, etc.

Planning Stages

- Considering a pilot study with a few ADC sites or specific studies
- Will require modification of IC/protocol
  - To ensure that subjects understand that lines can be developed from these samples
- If sites are interested, please contact me

tforoud@iupui.edu

317-278-1291