National Cell Repository for Alzheimer Disease (NCRAD)

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Overall Goal of NCRAD

- NCRAD and NACC goal is to bank a sample from EVERYONE seen at an ADC!
  - Centralize samples at NCRAD to facilitate research
  - Centralized phenotyping at NACC to facilitate research

NCRAD-ADC-NACC-ADGC Initiatives

- Initiatives with the ADGC
  - Phase I: Autopsy confirmed AD and controls
    - Send brain tissue or DNA
  - Phase II: Everyone with a UDS
    - Send DNA or buffy coat
  - Blood Eligible List: Subset of Phase II
    - Possible & Probable AD and controls
    - Send in blood samples

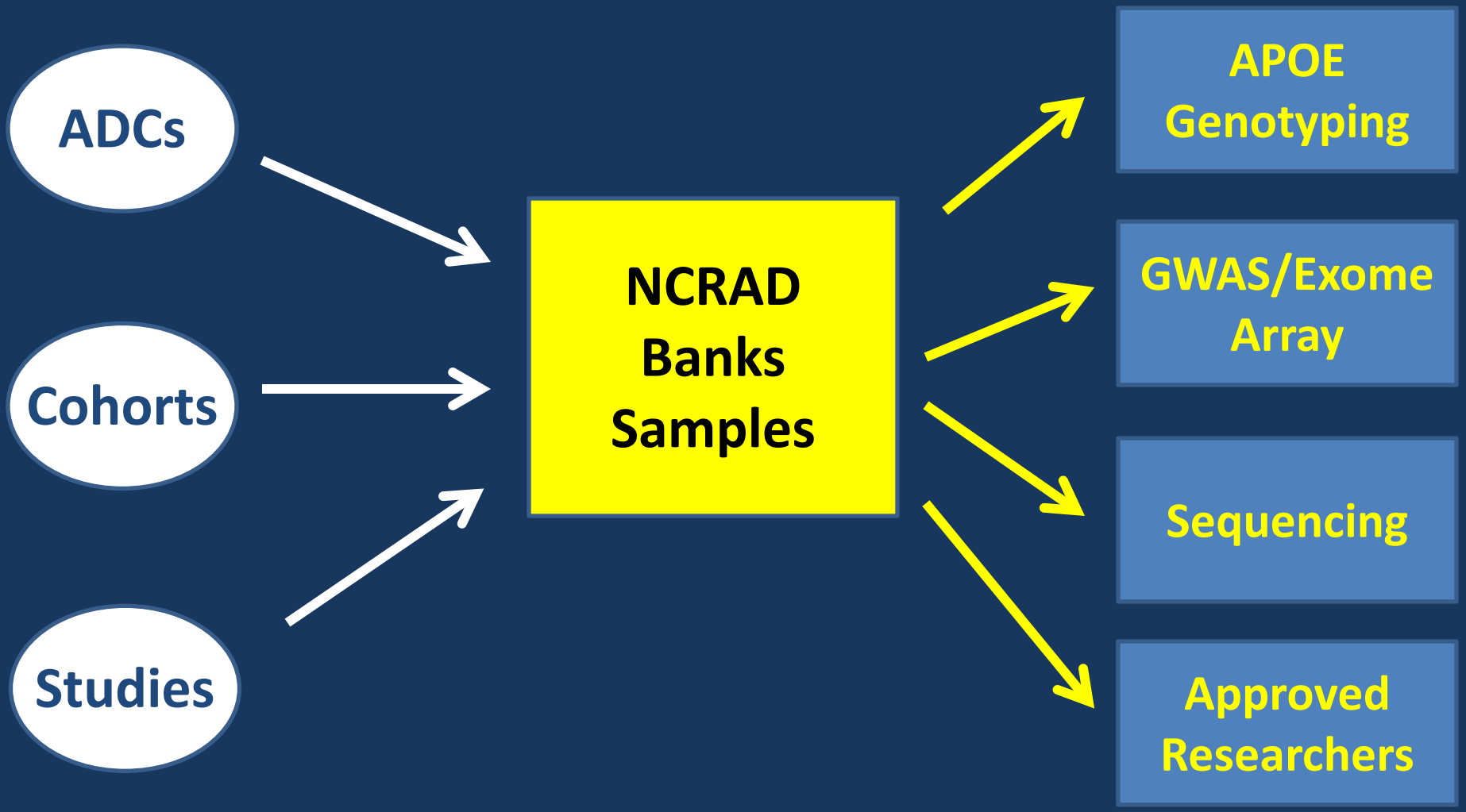
Updated site specific lists available at the NACC website

NCRAD-ADC-NACC-ADGC Initiatives

- NCRAD obtains APOE data for samples
- ADGC generates GWAS data for some samples
- Sites can download APOE and GWAS data for their samples through the NACC website

- GWAS data for samples outside a single ADC are available through NIAGADS

NCRAD's Broader Mission



Samples Sent for GWAS

Study	# of Samples
ADCs	10,051
Chicago Healthy Aging Project (CHAP)	848
Religious Orders Study (ROS)/Memory and Aging Project (MAP)	599
Adult Changes in Thought (ACT)	401
Biomarkers for Older Controls At Risk for Dementia (Biocard)	308
Einstein Aging Study (EAS)	299
Texas Alzheimer's Research Consortium (TARC)	299
University of Miami	161
Vanderbilt University	102

Studies Facilitated by Samples in NCRAD

- GWAS studies
  - Jun et al, 2010: Meta-analysis confirms CR1, CLU and PICALM as Alzheimer disease risk loci and reveals interactions with APOE genotypes.
  - Naj et al, 2011: Common variants at MS4A4/MS4A6E, CD2AP, CD33 and EPHA1 are associated with late-onset Alzheimer's disease.
  - Reitz et al, 2013: Variants in the ATP-binding cassette transporter (ABCA7), apolipoprotein E e4, and the risk of late-onset Alzheimer disease in African Americans.

Studies Facilitated by Samples in NCRAD

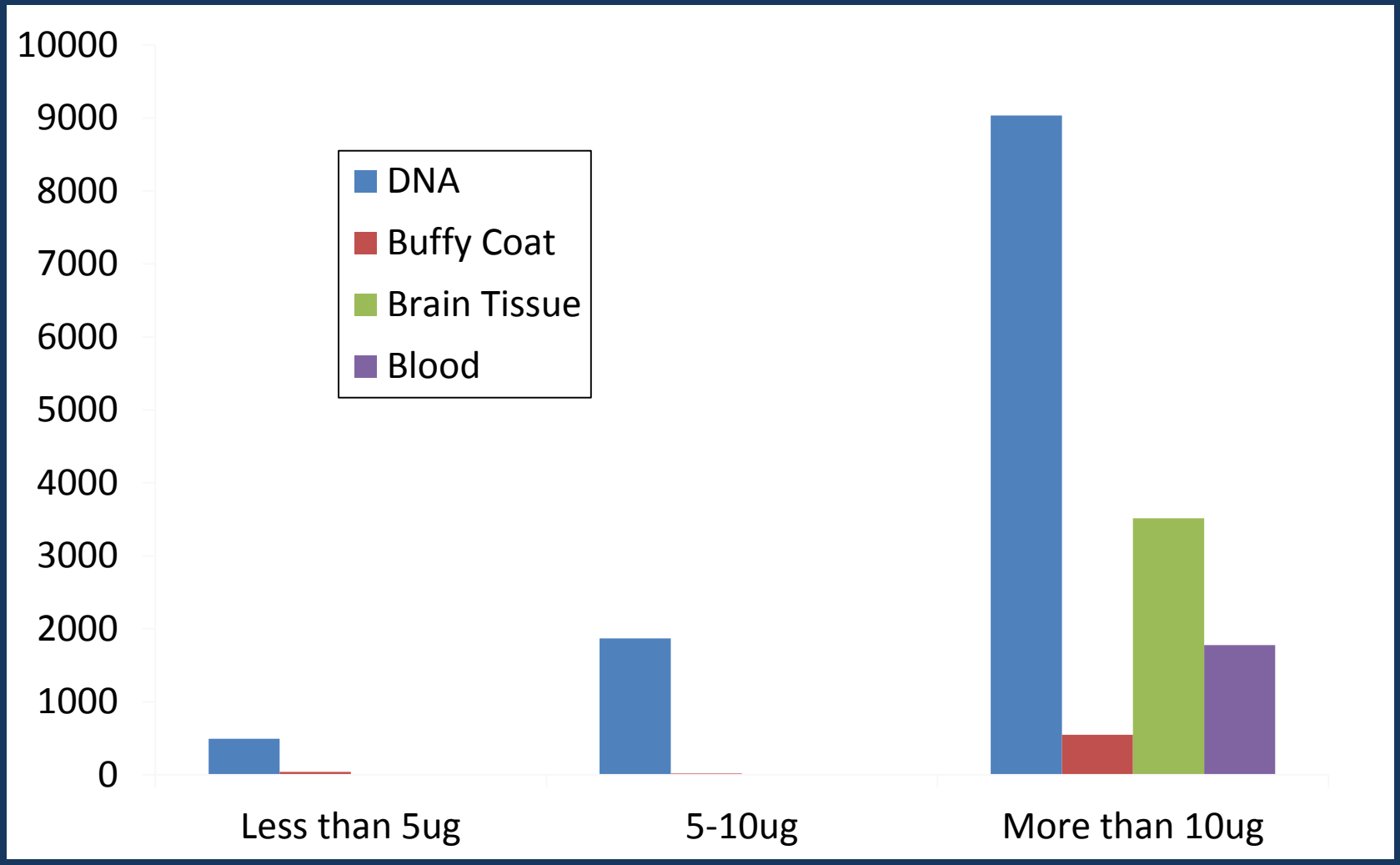
- Exome array studies
  - 4,422 AD cases
  - 2,982 controls

- Alzheimer Disease Sequencing Project (ADSP)
  - 2,430 cases and 840 control ADC samples for WES
  - TARC: 132 cases, 12 controls
  - CHAP: 27 cases, 204 controls

NCRAD Samples

- The samples from the ADCs as well as other cohort studies have been widely used in ADGC and ADSP sponsored studies
  - Very important for the research community
  - All data is made publicly available and is or will be widely used
- Challenge is that in many cases, the amount of DNA at NCRAD is now very low

NCRAD Samples



How will DNA be used in the Future?

- Anticipate more widespread studies of whole genome sequencing
  - Scope was quite limited thus far in the ADSP
- Replication of initial findings from the ADSP will require targeted sequencing in large numbers of samples
- Studies of other neurodegenerative disorders
- Biomarker and imaging genetic studies

NCRAD-ADC-NACC-ADGC Goal

- Expand the DNA available at NCRAD so that this does not become a rate-limiting step for research
  - All ADCs will receive a list of samples that are or are nearly depleted
  - Ensure a DNA sample is at NCRAD for EVERY subject seen at an ADC
- What can sites do?
  - Provide a blood sample and NCRAD will extract DNA and return 25 ug to the site
  - Send (another) aliquot of DNA

Upcoming Calls with NCRAD

- NCRAD will contact each ADC or study with samples having low remaining amounts of DNA at NCRAD
  - Conference call to review depleted or low samples
  - Identify possible solutions
- NCRAD will set up a call with any ADC interested in expanding initiatives to bank DNA from more subjects

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- Blood Eligible List: Subset of Phase II
  - Possible & Probable AD and controls
  - Send in blood samples
- Replenish samples
  - Focus on samples with < 10 ug of DNA at NCRAD
- Bank a DNA sample from EVERY ADC subject

NCRAD-ADC-NACC-ADGC