

Alzheimer's Disease Genetics Consortium

ADGC

Alzheimer's Disease Sequencing Project

ADSP

National Institute on Aging Genetics of Alzheimer's Disease

Storage site

NIAGADS

Partners:

National Alzheimer Coordinating Center – NACC

National Cell Repository for Alzheimer's Disease - NCRAD



ADGC Cohorts

Cohort	Cases	Controls
ADC1	1,549	512
ADC2	727	156
ADC3	894	586
ADC4	304	377
ADC5	286	505
ADC6	213	338
ADC7	500	790
ADC8	1,061	1,597

ADCs
5,534cases
4,861 controls

IGAP

Consortium	Cases	Controls
ADGC	15,988	16,949
CHARGE	2,137	13,474
EADI	2,240	6,631
GERAD	3,177	7,277
Totals	23,542	44,331



ADGC Major Project

Rare Variant GWAS

Previous analysis – impute to HapMap, MAF \sim > 2%

Impute to 1,000 Genomes – MAF to 0.1% to 1.5%

Validate by Sanger sequencing

Replicate in 19,000 subjects from IGAP

Exome Chip

8,158 Cases, 6,703 Controls

Replicate in 10,000 IGAP samples

Transethnic analysis

Caucasian

African American

Asian

Caribbean Hispanic



Recent ADGC Publications

1. Beecham et al. (2014) Genome-wide association meta-analysis of neuropathologic features of Alzheimer's disease and related dementias. *PLOS Genetics* **10**, (9)
2. Barral et al. (2014) Common genetic variants on 6q24 associated with exceptional episodic memory performance in the elderly. *JAMA Neurology* (in press).
3. Wetzel-Smith et al. (2014) A rare mutation in *UNC5C* predisposes to Alzheimer's disease and increases neuronal cell death. *Nat. Med.* **20**, 1452-1457
4. Wang et al. , (2015) Rarity of the Alzheimer's disease-protective APP A673T variant in the United States. *JAMA Neurol.* 72, 209-216.
5. Jun et al. (2015) A novel Alzheimer disease locus located near the gene encoding tau protein. *Molecular Psychiatry* (in press).
6. Desikan et al. (2015) Genetic overlap between Alzheimer's disease and Parkinson's disease at the *MAPT* locus. *Molecular Psychiatry*
7. Hohman et al. (2015) Global and Local Ancestry Effects on Alzheimer's Disease Risk. *Alzheimer's & Dementia*
8. Desikan et al. (2015) Polygenic overlap between C-reactive protein, plasma lipids and Alzheimer's disease. *Circulation* (in press).

56 publications

7 submitted/under review



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Alzheimer's Disease Sequencing Project (ADSP)

Whole exome sequencing:

5,000 unrelated cases: 4,220 from the ADGC
2,430 from ADC's

5,000 elderly normal controls: 3,240 from the ADGC
840 from the ADC's

1,000 cases from multiplex families – one/family

Whole-genome sequencing

Replication

All sequencing completed

QC in process

VCF files (genotypes) available by June

Data Access – all subjects

SNP array data – all subjects/studies

Published data sets: NIAGADS

Most recent data: SAG process

3 page application to ADGC

imputed 1000 Genome data

ADSP Sequence data

dbGaP – all data, de-identified

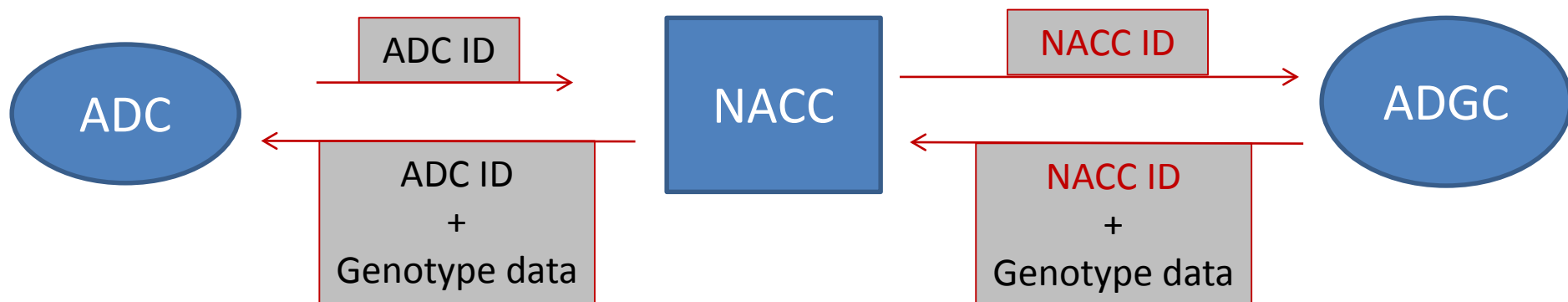
embargoed (publication) until August 2015



Genotype Data Access

data from specific subjects from an ADC

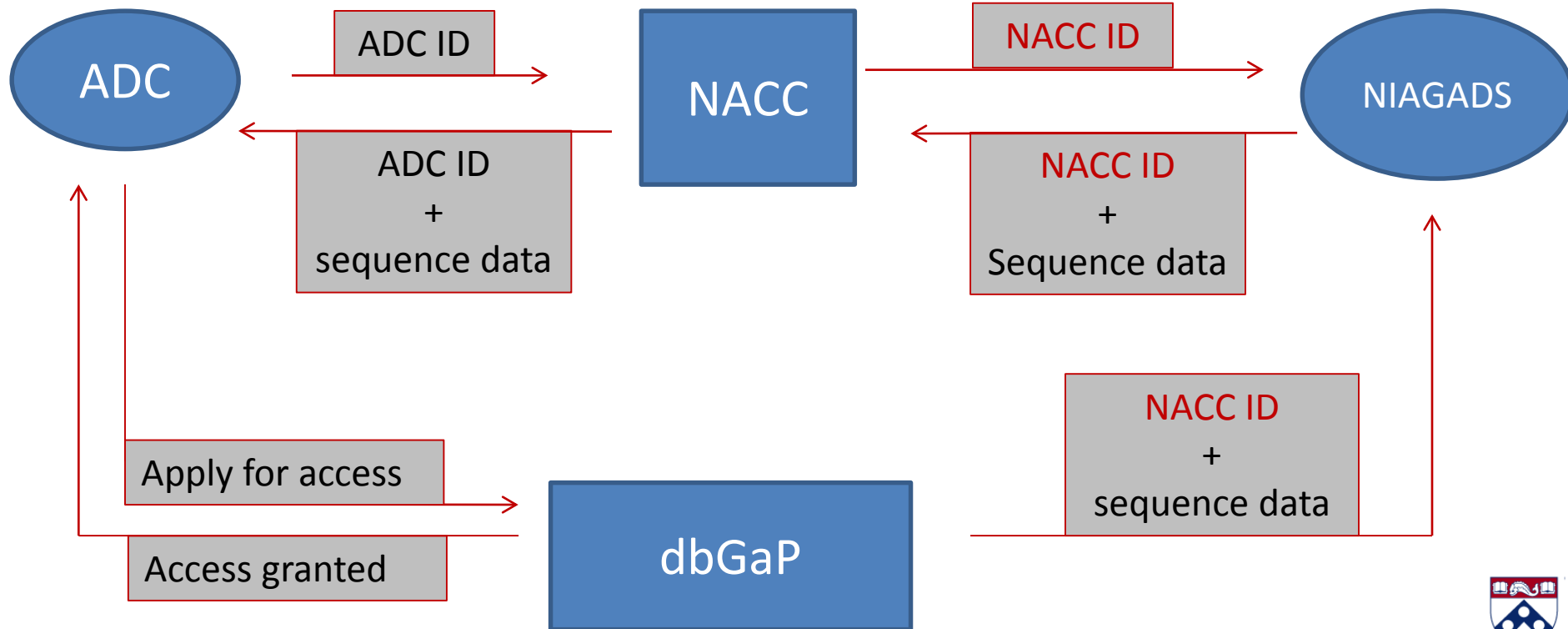
Array genotypes
APOE genotypes
Imputed genotypes



Sequence Data Access (ADSP)

data from specific subjects from an ADC

Whole genome sequence
Whole exome sequence



Alzheimer's Disease Genetics Consortium

University of Pennsylvania

Li-San Wang

Laura Cantwell

Beth Dombroski

Sherry Beecher

Familial AD

Richard Mayeux

Deborah Blacker

Clinical Group

John Morris

Debbie Tsuang

Neuropathology Group

Tom Montine

Eric Reiman

Biomarker Group

Alison Goate

Andy Saykin

Prospective Cohort Group

David Bennett

Bernadino Ghetti

Brad Hyman

Denis Evans

Eric Larson

Paul Crane

John Hardy

Ilyas Kamboh

Eric Reiman

Nilifur Taner

Julie Schneider

Steve Younkin

Denis Dickson

Charlie DeCarli

Douglas Galasko

Elaine Peskind

Neil Graff-Radford

Matthew Frosch

John Trojanowski

Vivianna Van Deelin

John Morris

Christian Reitz

NACC

Bud Kukull

Duane Beekly

NCRAD

Tatiana Foroud

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University of Miami

Peggy Pericak-Vance

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Gyungah Jun

Jacqueline Buross

Case Western

Jonathan Haines

NIA/NIH, Alzheimer's
Association

