

## Updates:

Alzheimer's Disease Genetics Consortium  
**ADGC**

Alzheimer's Disease Sequencing Project  
**ADSP**

## Partners:

National Alzheimer Coordinating Center – **NACC**

National Cell Repository for Alzheimer's Disease - **NCRAD**

National Institute on Aging Genetics of Alzheimer's Disease Storage site - **NIAGADS**

ADGC  
Cohorts

Cohort	Cases	Controls
ACT	532	1,571
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  

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10,395 total

## ADGC Major Projects – in progress

### Exome Chip

8,158 Cases, 6,703 Controls

**Replicate in 17,000 IGAP samples**

**genotyping complete  
analysis in progress**

### Rare Variant GWAS

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

Impute to 1,000 Genomes – MAF to 0.5% to 2%

Validate by Sanger sequencing

**Replicate in 19,000 subjects from IGAP**

**genotyping in progress**

### Transethnic analysis

Caucasian

African American

Asian

Caribbean Hispanic

**analysis in progress**

## ADGC Major Projects – new

### Very Rare Variant GWAS

Previous analysis – Impute to 1,000 Genomes

MAF to 0.5% to 2.0%

Impute using ~30,000 genome reference panel

MAF to 0.1% or lower (?) to 1.5%

Goals: Identify AD rare variants

Replicate findings from the ADSP

**Imputation in  
progress**

Whole exome sequencing – 3,200 African

American subjects

**ADC subjects**

**507 cases**

**668 controls**

**Fall 2015 –  
Spring 2016**

# ADGC Major Projects – new

Add cohorts to the ADGC sample

HANDLS

HEALTH ABC

MESA

REGARDS

SOF

NHS

MrOS

SOL

WHS

SWAN

WHIM

Kaiser Permanete

**2015-2020**

**Goals:** Increase sample size  
Increase minority samples  
Add deep-phenotype data

# Alzheimer's Disease Sequencing Project (ADSP)

Whole exome sequencing:

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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: 585 subjects 150 subjects  
111 multiplex families 48 families

All sequencing completed  
QC completed (WGS and WES)  
VCF files (genotypes) available

Replication  
planning

# Alzheimer's Disease Sequencing Project (ADSP)

## Analysis:

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### Family-based study:

WGS data

linkage analysis (*in press*)

genes in linked regions

single variant analysis

gene-based analysis

pathway/gene cluster analysis

### Case-control:

WES data

single variant analysis

gene-based analysis

pathway/gene cluster analysis

Structural variants – insertions, deletions, copy number variation, inversions, rearrangements. 1bp to very large

# Data Access – all subjects

SNP array data – all subjects/studies

Published data sets: NIAGADS

Most recent data: SAG process

3 page application to ADGC

74 approved SAGs

2 under review

ADSP Sequence data

dbGaP – all data, de-identified

available now

Li-San Wang will describe how to obtain subject level information a little later.

# Alzheimer's Disease Genetics Consortium

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## Familial AD

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NIA/NIH, Alzheimer's  
Association