September 2021

Another ADCFB Update!

As of October 1, 2021, NCRAD has added collection instructions and kit components for **optional** CSF visits to the ADCFB study. Samples collected with this standardized collection protocol ensure researchers have access to high quality specimens across all participating centers. If your center is interested in collecting and sending CSF through the ADCFB study, the new kit options have been added to the kit request website here. If you have any questions about these new instructions, or your center would like to join the ADCFB study, please reach out to Kaci Lacy at lacy@iu.edu.

Jeff Dage Joins NCRAD

Jeff Dage, Ph.D. has joined Indiana University School of Medicine as a Senior Research Professor of Neurology and Primary Member of the Stark Neurosciences Research Institute. He is a NCRAD co-investigator and assists in establishing the NCRAD biomarker laboratory and implementing biofluid biomarkers across studies.

The goal of this new biomarker laboratory is to build a central laboratory to process blood-based biomarker samples in a standardized manner, and to deliver reliable and consistent research biomarker results to researchers working in Alzheimer's disease and related dementias. The laboratory is expected to open in 2022, and key plasma assays include: P-tau 181, NfL, $A\beta_{1-40}$ and $A\beta_{1-42}$.

If you'd like to receive updates on this new biomarker laboratory, please sign up for our Researcher and Professional Staff Mailing List or email alzstudy@iu.edu.

Globally Unique Identifiers (GUIDs)

Some ADRCs are generating and sending NCRAD samples with Globally Unique Identifiers (GUIDs). GUIDs are generated by the Biomedical Research Informatics Computing System (BRICS) platform's centralized NIA/NINDS portal. The same GUID will be assigned to subjects that participate in both NIA and NINDS studies, allowing for data to be associated with a particular subject without exposing any protected health information (PHI). This reduces redundant analyses and maximizes the amount of information that can be gathered. We encourage all ADRCs to begin generating and sending GUIDs to NCRAD.

NCRAD GWAS Plan

We are currently pulling and shipping samples from UDS subjects that do not meet ADGC criteria for GWAS. This shipment will include samples from nearly 1,400 UDS subjects! Just like the samples genotyped by the ADGC, these samples will be sent to the Center for Applied Genomics (CAG) at the Children's Hospital of Philadelphia (CHOP). We will continue to send samples for GWAS from UDS subjects not meeting ADGC criteria annually to ensure GWAS data is available for all UDS subjects. GWAS data will be returned to the contributing ADRC.

NCRAD APOE Data at NACC

As a reminder, NCRAD now performs *APOE* genotyping internally, periodically sending these data to NACC. To obtain the most recent APOE data, visit the NACC website here, select your center and choose the option to download *APOE* data from NCRAD. As always, please compare these data with any internal *APOE* genotype data you may have generated. Please notify Kaci Lacy (lacy@iu.edu) if you have any questions or find any discrepancies.

Key for *APOE* results on NACC site

1=e3/e3	4=e4/e4	9=missing/unknown/
2=e3/e4	5=e2/e4	not assessed
3=e2/e3	6=e2/e2	

Sending ADRC Samples for DNA to NCRAD

NCRAD continues to accept samples from all subjects with an MDS or UDS at NACC. NACC has updated the lists of samples for submission to NCRAD as of June 2021. The lists of subjects eligible to send to NCRAD have now been separated into "active" participants and "inactive" participants. Please see the lists on the NACC website here. While receiving samples through ADCFB is preferred, NCRAD also accepts fresh or frozen whole blood, frozen buffy coats, transferred DNA and brain tissue samples. Our goal is to have a DNA sample banked and available from all MDS and UDS subjects.

Requesting ADRC Samples from NCRAD

If you are interested in requesting samples from NCRAD, you can learn more information about samples currently available for distribution here. You may access the catalog of ADRC samples which includes DNA, PBMCs, plasma, serum, and RNA.

Alzheimer's Disease Variant Portal (ADVP): The Newest Curated Population-specific Alzheimer's Disease Genetics Resource

Alzheimer's disease (AD) genetics has seen significant progress by implementing genome-wide association studies (GWASs). However, differences in GWAS design and focus—association with disease risk (i.e., case-control status) versus related phenotypes (e.g., cognitive decline, family history) and inclusion of different populations—limit the AD community's ability to leverage the richness of these findings.

Dr. Yuk Yee Leung (co-investigator of NIAGADS) and colleagues created the Alzheimer's Disease Variant Portal (AVDP), an easy-to-use resource that houses the newest curated, harmonized, and searchable collection of genetic association study results (Kuksa et al.).

The uniqueness and necessity of having a curated and harmonized interactive platform that provides unified access and visualization of a uniquely extensive up-to-date collection of GWAS data for AD.

As of August 2021, the ADVP includes data from 125 curated AD GWAS publications and contains 6,990 associations across more than 900 loci, 1,800 variants, 80 cohorts, and eight populations.

In describing the usefulness of the ADVP, Dr. Leung describes this resource as "great for people who want introductory knowledge or in-depth understanding of AD genetics findings."

To learn more about ADVP, click here.

ADVP is freely accessible at http://advp.niagads.org.

New Datasets available at https://www.niagads.org/datasets

NG00105 - MiGA – Microglia Genomic Atlas

NG00108 - Profiling microglia expression profiles in AD using single-nuclei RNA-seq

NG00109 - Genetic architecture of subcortical brain structures in 38,851 individuals summary statistics - Satizabal et al. 2019

NG00110 - Exome-wide age-of-onset analysis reveals exonic variants in ERN1 and SPPL2C associated with Alzheimer's disease

NG00111 - Genome-wide association identifies the first risk loci for psychosis in Alzheimer disease

NG00112 - A novel age-informed approach for genetic association analysis in Alzheimer's disease summary statistics- Guen et al. 2021

80	90,899	12
DATASETS	SAMPLES	DATA TYPES

NIAGADS presents at AAIC 2021

Heather Issen presented the 2021 update for The National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS).

As of January 2021, NIAGADS houses 74 datasets comprised of >90,000 samples including GWAS, sequencing, gene expression, annotations, deep phenotypes, and summary statistics. Qualified investigators can retrieve ADSP sequencing data with ease and flexibility through the NIAGADS DSS. As of February 2021, the ADSP and other contributing studies have completed whole exome sequencing (WES) of 20,504 samples and whole-genome sequencing (WGS) of 16,896 samples. Raw WES and WGS files, quality controlled VCF files, and phenotype data files are available via qualified access. The next round of sequencing currently underway will generate around 18,000 additional genomes to be released at the end of 2021.

NIA Genetics of Alzheimer's Disease Data Storage Site (NIAGADS): 2021 Update

NIAGADS

Heather Issen[12], Amanda Kuzma[12], Otto Valladares[12], Emily Greenfest-Allen[24], Conor Klamann[12], Prabhakaran Gangadharan[12], Zivadin Katanic[12], Andrew Wilk[12], Yi Zhao[12], Liming Qu[12], Michelle K Moon[12], Alexis Lerro[12], Joseph Manuel[12], Peter Keskinen[12], Carlos Thomas[12], Shin-Yi Chou[6], Wan-Ping Lee[12], Yuk Yee Leung[123], Adam Naj[15], Christian J. Stoeckert Jr. [124], Gerard D. Schellenberg[13], Li-San Wang[123]

1 Penn Neurodegeneration Genomics Center, Department of Pathology and Laboratory Medicine, 2 Institute for Biomedical Informatics, 3 Institute on Aging, 4 Department of Genetics, 5 Department of Epidemiology, University of Pennsylvania Perelman School of Medicine, 6 Department of Economics, Lehigh University

NIAGADS Data Sharing Service

Introduction

The National Institute on Aging (NIA) established the NIA Genetics of Alzheimer's Disease Data Storage Site (NIAGADS) as a national genetics data repository that facilitates access of genetic data to qualified investigators for the study of the genetics of early onset Alzheimer's Disease (EOAD), late-onset Alzheimer's disease (LOAD), and Alzheimer's Disease Related Dementias (ADRD).

Collaborations with:

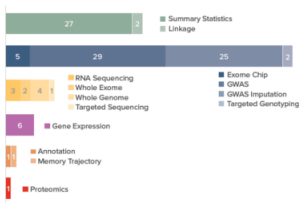
- Alzheimer's Disease Genetics Consortium (ADGC)
- Cohorts for Heart and Aging Research in Genetic Epidemiology (CHARGE)
- Alzheimer's Disease Sequencing Project (ADSP)
- Genome Center for Alzheimer's Disease (GCAD)

NIAGADS Data Repository

Data Availability

76	which include >90,000	and 12
DATASETS	SAMPLES	DATA TYPES

Data Type Statistics



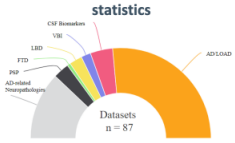
How to Apply

https://www.niagads.org/data/request/data-request-instructions

Alzheimer's Genomics Database (GenomicsDB)

GenomicsDB is an open platform for exploring and real-time mining of genetic evidence and genomic annotations for Alzheimer's disease and related neuropathologies from the NIAGADS repository.

Figure 1: GenomicsDB dataset statistics

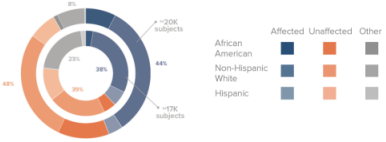


NIAGADS Data Sharing Service (DSS)

Currently Available Data

The NIAGADS Data Sharing Service (DSS) currently hosts 16,906 whole genomes and 20,503 whole exomes that were sequenced by the Alzheimer's Disease Sequencing Project (ADSP) and other Related Dementia studies. Available data types include BWA-MEM aligned CRAMs against GRCh38 and GATK called individual-level gVCFs generated by GCAD, ADSP quality-controlled project level VCFs, and corresponding phenotypes and pedigree structures.

Figure 2: NIAGADS DSS currently available data statistics



Data Growth

We anticipate releasing an additional 18K whole genomes in 2022. After this release, there will be a total of 60k sequenced samples (20k WES and 40k WGS).

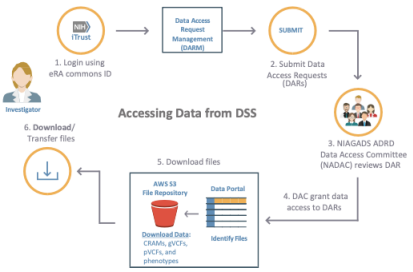
Alzheimer's Disease Sequencing Project

The ADSP was announced by NIH in February 2012 to sequence genomes/exomes of thousands of subjects to discover new AD genetic variants. To date, approximately 34,000 subjects have been sequenced. Additional information about the ADSP is available through their website https://www.niagads.org/adsp. https://www.niagads.org/adsp/content/acknowledgement-statement

Data Access Request Management System (DARM)

Investigators can log into the DARM using their eRA commons ID to submit a Data Access Request (DAR). Once an investigator submits a request, it will be reviewed by the NIAGADS ADRD Data Access Committee (NADAC) and Data Use Committee (DUC) to ensure that the data use limitations are appropriate and to review the secondary data return plan.

Figure 3: Accessing Data from DSS



Data Portal

Once a DAR has been approved, the Investigator can log into the Portal with their eRA Commons ID to download the files they have access to.

All users will need an Amazon Web Services account, and all files need to be downloaded from Amazon directly. gVCFs and CRAMs are available via a "Requestor Pays" option, and phenotype and genotype files can be downloaded for free.

How to Apply

dss.niagads.org/application-instructions

Contact:
Heather Issen
heather.issen@pennmedicine.upenn.edu

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