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:

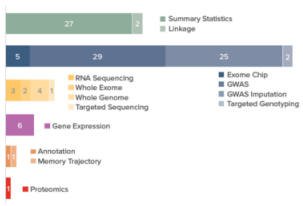
- Alzheimer's Disease Genetics Consortium (ADGC)
- Cohorts for Heart and Aging Research in Genetic Epidemiology (CHARGE)
- Alzheimer's Disease Sequencing Project (ADSP)
- Genome Center for Alzheimer's Disease (GCAD)

NIAGADS Data Repository

Data Availability

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

Data Type Statistics



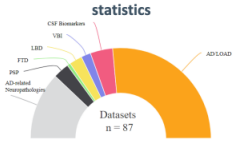
How to Apply

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

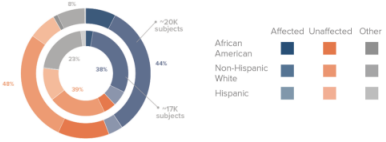


NIAGADS Data Sharing Service (DSS)

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).

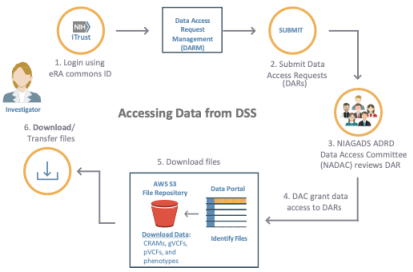
Alzheimer's Disease Sequencing Project

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

NIAGADS is supported by NIA U24-AG041689