RELEASE NOTES- Knight ADRC GWAS

Data Release Date: December 13, 2022, **Dataset Version:** ng00127.v1

Release Information:
The first release (November 13, 2022) includes GWAS and phenotypic data.

A longitudinal study of Alzheimer Disease and other dementing illnesses – KnightADRC GWAS:
The search for novel risk factors for Alzheimer disease relies on access to accurate and deeply phenotyped datasets. The Knight-ADRC (Knight ADRC-MAP) collects plasma, CSF, fibroblast, neuroimaging clinical and cognition data longitudinally and autopsied brain samples.

We are using multi-tissue (brain, CSF and plasma) multi-omic data (genetics, epigenomics, transcriptomics, proteomics and metabolomics) to identify novel risk and protective variants, create new prediction models and identify drug targets. Knight-ADRC participants have to be at least 45 years old and have no memory problems or mild dementia at the time of enrollment. There is no age at onset criteria for this cohort. Cases had to have a CDR >=0.5 whereas controls had to have a CDR=0 at last assessment. AD definition is based on a combination of both clinical and pathological information if available. Pathologic diagnosis will overrule clinical diagnosis.

Participants are Non-Hispanic white from North America (82.47%) and African American (13.3%). Autopsy information was provided if available, but it is not a requirement for enrollment. Samples have been obtained from over 5,510 participants, including 2,426 AD cases, 148 FTD, 88 DLB and 2,156 cognitive normal healthy individuals. In addition, there is autopsy material from over 1,182 participants, 600 with fresh tissue with multiple regions per sample. We have banked more than 8,000 DNA samples form 5,220 unique participants and 1,973 blood RNA from 1,172 unique participants. Plasma was collected from over 3,798 participants, and 1,650 have longitudinal plasma. We have logged over 8,000 plasma draws during the course of this study. CSF samples was obtained from 1,231 unique participants, and amyloid and tau imaging was obtained from 1,058 unique participants in a longitudinal manner. In addition, we have collected more than 164 PBMCs and 51 CSF cell pellets from this participant cohort. Fibroblasts were obtained from 207 participants including 16 TREM2 carriers, 27 with different APOE genotypes, 11 African American and 20 with extreme polygenic risk scores. IPSC are available for 22 of these fibroblasts.

Deep molecular profiling has been generated in this study, through the NeuroGenomics and Informatics Center at Washington University (https://neurogenomics.wustl.edu/). GWAS is available for 4,799 participants, and next generation sequence data (NGS) for 2,466 participants, 1,050 whole exome sequencing (WES) and 1,322 whole genome sequence (WGS) data. For 453 brain samples genetics (WGS), methylation (Illumina 880K), transcriptomics (bulk RNA-seq), proteomics (Somalogic 7K), metabolomics and lipidomics (Metabolon HD4) has been generated. CSF samples have proteomics (Somalogic 7K) and metabolomics (Metabolon HD4). A total of 3,000 cross-sectional

plasma samples have proteomics (Somalogic 7K), metabolomics (Metabolon HD4), RNA-seq and methylation data.
Additional information about Knight ADRC datasets available through NIAGADS can be found on the Knight ADRC Collection page: https://www.niagads.org/knight-adrc-collection

Cohort: Washington University in St. Louis - Knight ADRC
The data being submitted is from participants from the Knight-ADRC MAP study. Genotyping for 4495 participants were generated through 10 different genotyping arrays (Infinium CoreExome-24, Infinium Neuro Consortium Array, Infinium Global Screening Array-24, Infinium OmniExpress-24, Illumina Human660W-Quad, Human610-Quad, Illumina Omni1-Quad, Affy UK Biobank Axiom, Infinium OmniExpressExome-8, and Illumina Human1M-Duo).

In particular, 1955 AD cases (57% Females, 56% APOE4+, average age 74), 839 ADRD participants (51% females, 34% APOE4+, average age 63), and 1699 cognitively healthy participants (60% Females, 31% APOE4+, average age 74) individuals are being submitted. Approximately 85% of the samples are self-defined as “White”, and 10% are self-defined as “African-American”.

File Manifest: https://st1.niagads.org/portal/download-public/NG00127.v1/fm

Subject Consents:
Subjects in this dataset belong to the following consent levels as indicated by the submitting study IRBs:

Consent Level*	# Subjects
DS-ADRD-IRB-PUB	4379
DS-ADRD-IRB-PUB-NPU	2
HMB-IRB-PUB	119
Total	4500

*Consent level definitions can be found on the Data Use Limitations page.

Dataset Accession Numbers Available in ng00127:

Type	Description	Accession
Dataset	A longitudinal study of Alzheimer Disease and other dementing illnesses – KnightADRC GWAS	NG00127
Study	Charles F. and Joanne Knight Alzheimer’s Disease Research Center	sa000008
Sampleset	KnightADRC GWAS	snd10036
Fileset	KnightADRC GWAS	fsa000033

Related Publications:

Yang, 2021, Genomic atlas of the proteome from brain, CSF and plasma prioritizes proteins implicated in neurological disorders. PMID: 34239129 DOI: 10.1038/s41593-021-00886-6;

Ali, 2021, Leveraging large multi-center cohorts of Alzheimer Disease endophenotypes to understand the role of Klotho heterozygosity on disease risk; accepted for publication in PLoS One;

Olive, 2020, Examination of the Effect of Rare Variants in TREM2, ABI3, and PLCG2 in LOAD Through Multiple Phenotypes. PMID: 32894242 DOI: 10.3233/JAD-200019;