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, Aβ1-40 and Aβ1-42.

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.

Please contact us with any questions or concerns about NCRAD at 800-526-2839, by email at alzstudy@iu.edu or visit our website: www.ncrad.org. Thanks!!
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.niag-ads.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
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 comprising 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.

Data Sharing Service (DSS)

Investigators can log into the DARM using their eRA commons ID or 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 2: NIAGADS currently available data statistics

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 “Request Pay” option, and phenotype and genotype files can be downloaded for free.

Contact: heather.issen@pennmedicine.upenn.edu