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Knight ADRC Alzheimer's Disease Research Center | WASHINGTON UNIVERSITY ST. LOUIS

Washington University in St. Louis SCHOOL OF MEDICINE

Knight ADRC Core Data and Tissue Available for Sharing

Clinical Core

The Clinical Dementia Rating (CDR) https://knightadrc.wustl.edu/professionalsclinicians/cdr-dementia-staging-instrument/ originated at Washington University. Since 1979 the Clinical Core has assessed participants with an informant-based semi-structured interview assessing six cognitive domains in order to render the CDR. Two cohorts have had longitudinal clinical assessment: 1.) participants, ages 65 and older and 2.) starting in 2003, participants, ages 45-74. **See the Clinical Core Codebook for specific variables available** https://knightadrc.wustl.edu/wp-content/uploads/2021/07/Clinical-Core-Codebook-UDS3.pdf

The following items are available from this interview:

- Global Clinical Dementia Rating (CDR)
- CDR sum of boxes (CDR-SB)
- Diagnostic Impression
- Hollingshead Index of Social Position
- Structural and Social Determinants Influencing Aging and Dementia battery (SS-DIAD) (since 2021)
- Health History
- Medication List (text-based)
- Blood Pressure, Pulse, Height and Weight, abdominal girth, vision testing
- Neurological examination
- Geriatric Depression Scale (GDS)
- Short Blessed Test (SBT)
- Mini Mental State Exam (MMSE) (since 1996)
- Blessed Dementia Scale Cognitive (BDS)
- Montreal Cognitive Assessment (MoCA) (since 2015)
- Boston Diagnostic Aphasia Examination Rating Scale Profile of Speech Characteristics
- Neuropsychiatric Inventory Questionnaire (NPI-Q)

Cognitive Assessment Unit

The Cognitive Assessment component of the Clinical Core provides longitudinal neuropsychological evaluation of a broad range of memory, executive function, and visuospatial skills. For a list of the current content of the psychometric battery, visit the Psychometric Codebook https://knightadrc.wustl.edu/wp-content/uploads/2021/07/Psychometric-Codebook-7-22-19.pdf

The Table of Contents in the Codebook is hyperlinked. When a hyperlink is clicked, you are taken to the page with the information you requested. If there are other scores and tests present on that page, you may need to scroll down to find exactly what you requested. It is, however, on the page that appears. You can save a copy of the codebook to your computer from the Codebook window by click on the "Save a Copy" button in the toolbar. This copy will also contain the hyperlinked Table of Contents. The Psychometric Codebook also includes information about tests used in the past but no longer administered.

Biostatistics Core and Data Freeze

Two times per year there is a Knight ADRC-wide data freeze with cutoff dates on April 30th and October 31st. Each Core is given one month from the cutoff dates to prepare and QC their data to be included as a module in the dataset. This ensures the most current and accurate data is available for researchers. The Biostatistics Core Leader announces the availability of data, and all modules are shared based on data request approval through the Knight ADRC.

External Investigators – Non-WU Investigators

External Investigators, defined as those outside of the WU community, will require data request approval through the Administration Core of the Knight ADRC. The initial approved data request made by an external investigator is good for five (5) years and will receive the previously completed Data Freeze data specific to the inclusion/exclusion criteria listed on the project and will not be charged a data request fee. The external investigator will also receive one update (if data request has not expired*) of the database free of charge. After the first two data requests by external investigators for the same project, additional requests will be charged by averaging the time it takes to fulfill all requests based on the External Investigator table below.

Biomarker Core

Human somatic and stem cell models have emerged as a powerful system for modeling the complexities of pathological gene expression, particularly in the early phase of disease, in the context of a non-neoplastic human genome. Human stem cells can be differentiated into individual cell types affected in disease, such as neurons, astrocytes, microglia, and oligodendrocytes, as well as 3D “mini-brain” organoids. We have established a biorepository of stem cell models of AD and AD related dementias. The collection includes human fibroblasts and induced pluripotent stem cell (iPSC) lines from individuals carrying mutations/variants associated with AD (APP, PSEN1, PSEN2, APOE, TREM2, RAB10, PLD3, ABCA7), FTD (GRN, MAPT, C9ORF72, TREM2) and PD (MAPT) and who have comprehensive clinical histories. Additionally, we have genome engineered iPSC lines available as controls as well as those that carrying CRISPRi machinery for genetic screens and Ngn2 for transcription factor-driven neuronal differentiation.

For more details, please visit: https://karchlab.wustl.edu/

Protocols for culturing and differentiating the stem cell lines can be found at: https://karchlab.wustl.edu/resources/

Fluid Biomarker Core

The Fluid Biomarker Core has studied Alzheimer disease from multiple angles for more than 20 years. Currently, the lab focuses on fluid biomarkers of disease with a particular interest in identifying individuals with preclinical and early-stage AD. Our laboratory uses Enzyme Linked Immunosorbent Assays (ELISAs), bead-based immunoassays, single-molecule counting systems, and automated immunoassays to study protein biomarkers in cerebrospinal fluid and plasma.

- **Tissue**
  - Fasted CSF (500 uL aliquots)
  - Fasted plasma (300 or 500 uL aliquots)

- **Data**
  - CSF concentrations of Ab42, Ab40, total tau, and p-tau181 measured with the Lumipulse assay (Fujirebio)
  - CSF concentrations of neurofilament light measured with the Uman assay

For more details, please visit: https://fluidbiomarkercorelab.wustl.edu/

Genetics Core

The goal of the Genetics and High Throughput -Omics Core at the Knight ADRC is to obtain, bank and QC biospecimens (DNA, RNA and plasma) for the Knight ADRC participants. The Core shares these biospecimens with qualified investigators who want to generate genetic or other -omic data for these samples.

The Core also stores and harmonizes all GWAS, WES, WGS, epigenomic, transcriptomic, proteomic, metabolomic and lipidomic data generated for the Knight ADRC participants, to share with the scientific community and to guarantee the integrity and compatibility of the data.

Samples

- Longitudinal
  - DNA
  - Blood RNA
  - CSF cell pellet
  - PBMCs
  - Non-fasted plasma

- Cross-sectional
  - Brain RNA, DNA, protein extract

Data

- Genetics
  - GWAS
  - APOE, PRS, mutation status

- Proteomics (Somalogic 7K)
  - CSF, plasma, brain

- Metabolomics (Metabolon HD4)
  - CSF, plasma, brain

- RNA-seq
  - Parietal brain samples

Data sharing hub: https://neurogenomics.wustl.edu/open-science/resource-sharing-hub/

For more details, please visit:
https://cruchagalab.wustl.edu/
https://sites.wustl.edu/hararilab/
https://www.niagads.org/knight-adrc-collection

Imaging Core

The Knight ADRC Research Imaging (KARI Imaging) Core fulfills the role of imaging acquisition and processing for the Knight ADRC and its 2 affiliated PPGs, HASD (P01 AG03991) and ACS (P01 AG026276), using identical methods.

Data is available for access in several permutations

- Derived variables in spreadsheets (SAS or Excel)
- Source (DICOM) and derived data via web download from the Central Neuroimaging Data Archive (CNDA) cnda.wustl.edu
- Open Access Series of Imaging Studies (OASIS) www.oasis-brains.org
  - The OASIS datasets hosted by central.xnat.org provide the community with open access to a significant database of neuroimaging and processed imaging data across a broad demographic, cognitive, and genetic spectrum an easily accessible platform for use in neuroimaging, clinical, and cognitive research on normal aging and cognitive decline.

Raw data currently available

- PET: PIB, Florbetapir (AV-45), Flortaucipir (AV-1451)
- A subset (~300) have FDG PET
- MRI: T1-weighted, T2*, FLAIR, DTI, ASL

Derived data currently available

- MRI
  - T1-weighted MRIs (1.5T and 3T) are processed using Freesurfer to derive regional volume and cortical thickness estimates
  - An AD signature of atrophy is also calculated (Dincer et al., 2020)
  - Lesion volumes are estimated on FLAIR scans using the Lesion Segmentation Toolbox
- PET
  - Regional estimates of standardized uptake value ratios (SUVRs) using regions of interest derived from Freesurfer
  - Regional mean cortical binding potentials (MCBPs) when full dynamic data are available for amyloid tracers
  - With and without partial volume correction
  - Summary measures of amyloid (Su et al., 2013 PLOS ONE) and tau (Mishra et al., 2017)
  - Global Centiloid value calculated for amyloid data (Su et al. 2019)

For more details, please visit: https://www.mir.wustl.edu/research/research-centers/neuroimaging-labs-research-center-nil-rc/labs/benzinger-lab/

Neuropathology Core

The Knight ADRC Neuropathology Core is supported by the Translational Human Neurodegenerative Disease Research (THuNDR) Laboratory (formerly the Betty Martz Laboratory for Neurodegenerative Research), directed by Richard J. Perrin, MD, PhD.

Data available

Knight ADRC Neuropathology data are collected and maintained in the format of the Neuropathology Data Form of the National Alzheimer's Coordinating Center (NACC) established by the National Institute on Aging/NIH (U01 AG016976). As this form has been updated periodically by NACC, the data available for a given case may depend upon when the case was assessed.

For more information see: https://files.alz.washington.edu/documentation/rdd-np.pdf

Beginning with the NACC NP v10 form (released in 2014), the neuropathology data relevant to Alzheimer disease (AD) are derived from application of the National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of AD (1). Data relevant to other neurodegenerative diseases (e.g., synucleinopathies, non-AD tauopathies, TDP-43 proteinopathies, hippocampal sclerosis, vasculopathies, infarctions) and non-neurodegenerative diseases (e.g., neoplasms, infections, inflammatory conditions) are derived from the application of other appropriate contemporary neuropathologic guidelines.

> **Reference**: Montine TJ, et al. National Institute on Aging - Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease: a practical approach. *Acta Neuropathol*. 2012; 123: 1-11.

Tissue Available

- Formalin-fixed paraffin-embedded (FFPE) tissue sections (4-8 μm in thickness)
- Fresh-frozen brain tissue (stored at -80°C)
- Formalin-fixed wet tissue (limited availability)

> **Note:** Investigators requesting samples from brain areas that are relatively small and/or commonly requested in the field of AD research (e.g., hippocampus, dorsolateral prefrontal cortex) should provide a strong justification for why those areas are required for their project. Requestors should also be aware that each restriction imposed by sample inclusion/exclusion criteria (e.g., postmortem interval, age at death, *APOE* genotype, co-existing neuropathologies) may negatively affect sample availability. Cost recovery will be required for large requests; cost estimates will be provided after a request is submitted and a tissue request number has been assigned.