

The Alzheimer's Disease Sequencing Project (ADSP)

Memorandum of Understanding for the ADSP Follow-Up Study (FUS)



1.4.2022

Introduction

In response to the National Alzheimer's Project Act (NAPA) [Public Law 111-375 NAPA 2012](#) [2013](#), and [NAPA 2016](#), NIA instituted a new genetics initiative (the Alzheimer's Disease Sequencing Project [ADSP]) to understand the genetic architecture of Alzheimer's Disease and Related Disorders (AD/ADRD). This project involves a large number of study participants from ethnically diverse populations and will capture and analyze common and rare genetic variation. The ADSP Discovery and Discovery Extension Phases have identified genomic variations associated with AD/ADRD and these findings and new discoveries are being pursued by the ADSP Follow-Up Study (FUS) for which this MOU is instituted.

Definition of the ADSP

The overarching goals of the Alzheimer's Disease Sequencing Project (ADSP) are to:

- Identify new genes and genetic variations that contribute to increased risk for or protection against AD/ADRD
- Provide insight as to why these genes and variations impact AD/ADRD
- Identify potential avenues or approaches to transform genetic results into meaningful therapeutic targets for further development.

The ADSP requires a large number of study participants to capture all of the relevant genetic variation. Using existing samples from numerous studies, the NIA has developed infrastructure including genotyping, sequencing, computational and functional analysis, and data processing and storage centers to produce high quality data and results, which will be made available to the scientific community through NIH-approved data repositories. Analyses of these data are expected to identify new genetic risk and protective variations. Both fundamental scientific discovery and leading-edge analytic approaches will be needed to achieve the research goals. The ADSP will conduct and facilitate analyses of these data to extend previous discoveries that may ultimately result in new directions for AD/ADRD therapeutics.

The samples for the ADSP are obtained from well-characterized, ethnically diverse cohorts and datasets of individuals characterized for AD/ADRD diagnoses with biospecimens (DNA and/or other biomarkers and tissues). Investigators in the ADSP will obtain the resulting data from NIAGADS (the NIA Genetics of Alzheimer's Disease Data Storage Site, <https://www.niagads.org/>) including:

- Quality control checked, cleaned, and harmonized sequence and phenotype data, using a set of routine checks on sample information, phenotype, GWAS, and sequencing data. These processes are performed to ensure the data are of high quality and are ready for downstream analyses.
- Information on the study designs of the included datasets (e.g. case-control, family-based, longitudinal, and prospective cohorts).
- Descriptions of the study datasets including demographics.

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- Accompanying phenotypic information, minimally including age at disease onset, self-reported race/ethnicity, gender, diagnostic status, pathology, relevant biomarkers, and cognitive measures. The ADSP will determine what additional information, if any, is needed by its members to facilitate the project.

Guiding Principles for the ADSP

The following principles of collaboration serve as a guide to the ADSP's interactions and are based on a shared consensus about the best way to fulfill the mission of the ADSP:

Trust: The ADSP is based on a sense of mutual trust and respect among the participating members; trust cannot be imposed but is generated by transparency and fairness in all dealings. Participation in the ADSP is contingent upon each member and each group affirming this fundamental tenet and working with each other in a fair, respectful, and transparent manner.

Open communication: It is extremely important that all decisions and activities be conducted in an open and transparent way. Each principal investigator of the individual groups that comprise the ADSP is responsible for communicating to members of his/her own group the tenets of the ADSP.

Timeliness: The ADSP members will endeavor to develop reasonable timelines for defining their activities including sample identification and transfer of biospecimens and phenotype data, genotyping array data, sequencing, quality control, data management, analytic plans, and drafting and publishing manuscripts.

Respecting priority: The ADSP members will treat existing data contributed to the ADSP with care and adhere to NIH guidelines related to data release and embargoes. Such data contributions can be used only with the consent of the submitters.

Mutual benefit: The ADSP takes seriously the goal of providing mutual benefit for all those involved in the ADSP, not just those directly responsible for a particular discovery.

Supporting early-stage faculty/students: The ADSP puts a high premium on the advancing the careers of trainees and early stage faculty. The ADSP encourages the next generation of scientists working in AD/ADRD and genomics to build on the results of this collaboration.

Based on the above principles, the following are also endorsed:

- All efforts will be considered collaborative and will involve all interested parties in discussions and decisions. This includes design and selection of samples and related phenotype data, pipelines and procedures for sequence and other data processing and analysis, analysis plans and implementation, data management, data interpretation, and manuscript preparation and submission.
- ADSP members will devise scientifically sound plans and initiate the agreed upon studies within the most expeditious timeline possible.

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- All ADSP members will have equal access to releases of the ADSP data through NIAGADS, or under certain exceptional circumstances, from another NIH approved database. Access to data is subject to informed consent limitations and NIH policy. No analyses other than the quality control checks (described above) will begin until all partners have access to the data.
- The data and results of the ADSP studies will not be communicated to study participants, relatives of participants, personal physicians, or insurance companies. Individual constituent cohorts may make their own policies on return of data to study participants outside of the auspices of the ADSP after consultation with NIA.
- All submitters of samples and related data to the ADSP will receive any ADSP generated data specific to their own datasets. They may use these ADSP generated data for their own analyses. ADSP data may be used for analyses not related to AD/ADRD, subject to any informed consent limitations and NIH policies. Members must notify the ADSP of the use of the ADSP generated data in a publication and assure appropriate ADSP authorship or acknowledgement according to current ADSP policies.
- All submitters of samples and/or related data to the ADSP may analyze any data they themselves have collected and submitted to the ADSP. In the interest of good faith and trust, the ADSP requests sharing the news of activities that may be relevant to the ADSP.
- The ADSP data is considered a community resource and will be shared in accordance with existing NIH and Institute-specific protocols. Access to the ADSP data will be made as soon as possible according to current ADSP guidelines, with the goal of making the data available as quickly as possible. Release of the DNA sequence data will be in accord with NIH NOT-AG-16-033, which stipulates that ADSP DNA sequence data are not subject to embargo.

Membership in the ADSP

To accomplish its primary goal, the ADSP requires many different sources of participant data and biospecimens, data analyses, data interpretation, and infrastructure for genomic data generation and data management. This requires a wide variety of expertise, which may evolve over time. The list of members of the Executive Committee (see below) as conceived under the first (2012) ADSP MOU is represented by the PIs of each participating group, is provided in Appendix A (current version available on the ADSP website). Under the umbrella of the ADSP, support for these activities is provided competitively through a number of funding opportunity announcements (FOAs). FOAs relevant to the ADSP are listed in Appendix B (current version available on the ADSP website). New members may join the ADSP by funding through relevant FOAs or upon agreement of the ADSP Executive Committee.

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Each ADSP group is free to add new investigators to its own group for participation in the ADSP with concurrence from NIA. The PI of each of the ADSP groups is responsible for communicating the terms of participation in the ADSP to each new investigator.

Organization of the ADSP

Executive Committee: The governing body of the ADSP will be its Executive Committee (EC). EC members will represent the interests and scientific expertise of the ADSP under the guiding principles of this MOU. The EC will be responsible for making ADSP policy decisions and resolving any conflicts that arise in the conduct of this project. The EC is composed of 13 members who are PIs with significant NIA funding relevant to the ADSP. NIA representatives will attend as *ex officio* members, but with the ability to break ties if votes are necessary. Decisions are made by majority vote, with a quorum of eight required for a vote. EC Membership should represent the diversity of ADSP funded activities; ethnic and gender diversity is also encouraged. Individual EC members are reviewed every three years on a rolling basis (5, 4, 4). Should a member resign, a new member will be appointed by majority vote of the remaining EC members. The EC is expected to meet monthly. Appendix C (current version available on the ADSP website) lists the current membership of the EC.

External Advisory Committee (EAC): To assure progress and provide expert advice, the ADSP has an external advisory committee, which will meet with the ADSP at least once annually. The constitution of the EAC is recommended by the EC with final approval by NIA staff. The current EAC membership is provided in Appendix D (current version available on the ADSP website).

Additional Committees and Workgroups: As a dynamic project, the ADSP requires flexibility in its organization. Standing or ad hoc committees may be created by the EC as needed to address specific policy or process issues. Project-specific workgroups will be formed as needed to accomplish the goals of the ADSP. Workgroups may be created, expanded, contracted, or sunsetted, as needed. Creation and sunsetting of workgroups requires EC approval. Each workgroup will have at least two co-chairs chosen based on interest, expertise, and performance, with an attempt to balance workload across ADSP members. Membership and attendance in the workgroups is open to all ADSP members based on interest and expertise. Workgroups are expected to meet at least monthly, but can meet more often as necessary. The current list of committees, workgroups, and co-chairs is provided in Appendix E (current version available on the ADSP website).

Policies and Procedures: The complex nature of the ADSP requires periodic development or modification of specific policies and procedures relating to issues such as publications, authorship, data access, analysis plans, data sharing, etc. These are developed or modified as needed and approved by the EC. Approved policies and procedures are available on the ADSP website (<https://www.niagads.org/adsp/>).

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Progress Reports: In addition to grant-specific progress reports, NIA program staff expect regular written progress reports on the activities of the ADSP. In addition, regular scientific reports are to be provided to the Director of the NIH through a process determined by NIA program staff.

Endorsement of this Memorandum of Understanding:

The Executive Committee of the ADSP (as of July 2021) has reviewed and approved this MOU, as indicated below:

Eric Boerwinkle, Baylor College of Medicine
Clifton Dalgard, Uniformed Services University of the Health Sciences (USUHS)
Anita DeStefano, Boston University (CHARGE)
Lindsay Farrer, Boston University (CADRE)
Alison Goate, Mt. Sinai School of Medicine
Jonathan Haines, Case Western Reserve University
Richard Mayeux, Columbia University
Peggy Pericak-Vance, University of Miami
Jerry Schellenberg, University of Pennsylvania
Sudha Seshadri, University of Texas Health San Antonio
Li-San Wang, University of Pennsylvania
Ellen Wijsman, University of Washington

Appendix A: Current (July 2021) ADSP Projects

ADSP Discovery and Discovery + Extension Phase Sequencing and Analysis Grants

[PAR-12-183](#) **National Institute on Aging Analysis of Alzheimer's Disease Genome Sequencing Project Data [U19]**

Consortium for Alzheimer's Sequence Analysis (CASA), U01 AG047133; Gerard D. Schellenberg
Project Period: June 15, 2014 – May 31, 2018

CHARGE: Identifying Risk & Protective SNV for AD in ADSP Case-control Sample, U01 AG049505;
Sudha Seshadri
Project Period: June 15, 2014 – May 31, 2018

Sequence-based Discovery of AD Risk & Protective Alleles, U01 AG049506; Eric A. Boerwinkle
and William J. Salerno
Project Period: June 15, 2014 – May 31, 2018

Sequence-based Discovery of AD Risk & Protective Alleles, U01 AG049507; Ellen M. Wijsman

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Project Period: June 15, 2014 – May 31, 2018

ADSP Replication and Extension

[RFA-AG-16-002 Alzheimer's Disease Sequencing Project \(ADSP\) Replication Phase Analysis Studies \(U01\)](#)

Replication and Extension of ADSP Discoveries in African-Americans, U01 AG052410; Margaret A. Pericak-Vance, Gary W. Beecham, Goldie S. Byrd, and Richard P. Mayeux
Project Period: June 15, 2016 – May 31, 2022

Identification and characterization of AD risk networks using multi-dimensional omics data, U01 AG052411; Alison M. Goate, Carlos Cruchaga, and Bin Zhang
Project Period: July 15, 2016 – May 31, 2021

ADSP Follow-up in Multi-Ethnic Cohorts via Endophenotypes, Omics & Model Systems, U01 AG052409; Sudha Seshadri and Myriam Fornage
Project Period: September 1, 2016 – May 31, 2021

[PAR-15-356 Major Opportunities for Research in Epidemiology of Alzheimer's Disease and Cognitive Resilience \(R01\)](#)

Harmonized Diagnostic Assessment of Dementia (DAD) for Longitudinal Aging Study of India (LASI)-Genomic study, 5 U01 AG064948-03; Jinkook Lee and Sharon L. Kardya
Project Period: September 15, 2019 – August 31, 2024

ADSP FOLLOW-UP STUDY: SEQUENCING AND ANALYSIS

[PAR-16-406 Limited Competition: Additional Sequencing for the Alzheimer's Disease Sequencing Project \(U01\)](#)

Whole Genome Sequencing in Ethnically Diverse Cohorts for the ADSP Follow-Up Study (FUS), U01 AG057659; Margaret A. Pericak-Vance, Richard P. Mayeux, Badri N. Vardarajan
Project Period: September 30, 2017 – August 31, 2022

Additional Sequencing Cohorts for the Alzheimer's Disease Sequencing Project, U01 AG062943; Margaret A. Pericak-Vance and Richard P. Mayeux
Project Period: September 1, 2019 – August 31, 2022

[PAR-17-214 Limited Competition: Analysis of Data from NIA's Alzheimer's Disease Sequencing Project Follow-Up Study \(U01\)](#)

The Familial Alzheimer Sequencing (FASe) Project, U01 AG058922; Carlos Cruchaga and Alison Goate
Project Period: August 1, 2018 - July 31, 2023

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Genomic approach to identification of microglial networks involved in Alzheimer disease risk, U01 AG058635; Alison M. Goate

Project Period: August 1, 2018 – July 31, 2023

Therapeutic target discovery in ADSP data via comprehensive whole-genome analysis incorporating ethnic diversity and systems approaches, U01 AG058589; Anita L. DeStefano, Eric A. Boerwinkle, Phil L. De Jager, Myriam Fornage, Sudha Seshadri, and Ellen M. Wijsman

Project Period: September 30, 2018 – August 31, 2023

The Alzheimer Disease Sequence Analysis Collaborative, U01 AG058654; Jonathan L. Haines, William S. Bush, Lindsay A. Farrer, Eden R. Martin, and Margaret A. Pericak-Vance

Project Period: September 30, 2018 – August 31, 2023

Gene Discovery in Multi-ethnic Late-Onset Alzheimer's Disease Families, U01 AG066752-02; Badri N. Vardarajan and Suzanne M. Leal

Project Period: June 15, 2020 – May 31, 2025

KBASE2: Korean Brain Aging Study, Longitudinal Endophenotypes and Systems Biology, U01 AG072177; Andrew J. Saykin, Dong Young Lee, and Kwangsik Timothy Nho

Project Period: April 1, 2021 – March 31, 2026

[PAR-18-890](#) **Limited Competition: Additional Sequencing for the Alzheimer's Disease Sequencing Project: Opportunity for Revision Requests for Active Cooperative Agreements (U01)**

Quality Control Activities for the ADSP Follow-Up Studies, U01 AG057659-03S1, Margaret A. Pericak-Vance, Richard P. Mayeux, and Badri Vardarajan

Project Period: September 30, 2017 – August 31, 2022

Inclusion of sub-group of ASPREE samples into the ADSP, U01 AG066767-02S1, Jeffery Vance, Michael Cuccaro, and Brian Kunkle

Project Period: September 30, 2021- June 30, 2025

[PAR-19-234](#) **Limited Competition: Additional Sequencing for the Alzheimer's Disease Sequencing Project (U01)-competitive supplements to existing awards**

Additional Sequencing for the Alzheimer's Disease Sequencing Project (ADSP), U01 AG066767; Jeffery M. Vance, Michael L. Cuccaro, and Brian W. Kunkle

Project Period: July 1, 2020 – June 30, 2025

[PAR-14-070](#) **Limited Competition: Renewal of, and Revisions to, the Alzheimer's Disease Genetics Consortium (U01)**

Alzheimer's Disease Genetics Consortium, U01 AG032984; Gerard David Schellenberg

Project Period, April 1, 2009 – March 31, 2025

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ADSP FOLLOW-UP STUDY 2.0 DIVERSITY INITIATIVE: SEQUENCING AND ANALYSIS

[PAR-21-212](#) **Limited Competition: Alzheimer's Disease Sequencing Project Follow-Up Study 2.0 (ADSP FUS 2.0): The Diverse Population Initiative (U01 Clinical Trial Not Allowed)**

Diversity: TBD

Place holder award TBD

FUS 2.0 Diversity Initiative Recruitment and Retention of Diversity Cohorts

Asian

Asian Cohort for Alzheimers Disease (ACAD), R56 AG069130; Li-San Wang, Helena C. Chui, and Van My Ta Gyungah Park
Project Period: September 30, 2020 – May 31, 2022

African American and Hispanic

Place holder award TBD

[PAR-19-070](#) **Research on Current Topics in Alzheimer's Disease and Its Related Dementias (R01 Clinical Trial Optional)**

Asian

Genetic Studies of Alzheimer Disease in Koreans, U01 AG062602; Lindsay Farrer
Project Period: September 15, 2019 – August 31, 2024

ADSP INFRASTRUCTURE

[PAR-16-047](#) **National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (U24)**

The NIA Genetics of Alzheimer's Disease Data Storage Site, U24 AG041689; Li-San Wang
Project Period: April 1, 2012 – March 31, 2022

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[RFA-AG-16-001](#) **NIA Coordinating Center for Genetics and Genomics of Alzheimer's Disease (U54)**

Genome Center for Alzheimer's Disease (GCAD), U54 AG052427; Gerard Schellenberg and Li-San Wang
Project Period: April 15, 2016 – March 31, 2026

[RFA-AG-22-001](#) **National Institute on Aging (NIA) Late Onset of Alzheimer's Disease (LOAD) Family-Based Study (FBS) (U24)**

Place holder award TBD

The National Institute on Aging (NIA) Late Onset of Alzheimer's Disease (LOAD) Family-Based Study (FBS), U24 AG056270; Richard P. Mayeux, Tatiana M. Foroud, and Alison M. Goate
Project Period: August 1, 2017 – May 31, 2022

PHENOTYPE HARMONIZATION

[PAR-20-099](#) **Harmonization of Alzheimer's Disease and Related Dementias (AD/ADRD) Genetic, Epidemiologic, and Clinical Data to Enhance Therapeutic Target Discovery (U24 Clinical Trial Not Allowed)**

Alzheimer's Disease Sequencing Project Phenotype Harmonization Consortium, U24 AG074855; Timothy J. Hohman, Michael L. Cuccaro, and Arthur W. Toga
Project Period: September 1, 2021 – August 31, 2026

ADSP FUNCTIONAL GENOMICS

[RFA-AG-21-006](#) **Alzheimer's Disease Sequencing Project Functional Genomics Consortium (U01)**

Alzheimer Variants: Propagation of Shared Functional Changes Across Cellular Networks, U01 AG072572; Philip L. De Jager and Peter St. George-Hyslop
Project Period: July 15, 2021 – June 30, 2026

Circular RNAs and Their Interactions With RNA-Binding Proteins to Modulate AD-Related Neuropathology, 1 U01 AG072577; Xiaoling Zhang and Benjamin L. Wolozin
Project Period: July 1, 2021 – June 30, 2026

Epidemiological Integration of Genetic Variants and Metabolomics Profiles in Washington Heights Columbia Aging Project, RF1 AG066107; Richard P. Mayeux, Gary W. Miller, and Badri Vardarajan
Project Period: September 30, 2020 – August 31, 2024

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Functional Genomic Dissection of Alzheimer's Disease in Humans and Drosophila Models, U01 AG072439; Joshua M. Shulman, Hugo J. Bellen, Juan Botas, and Aleksandar Milosavljevic
Project Period: July 1, 2021 – June 30, 2026
Functional Genomic Studies in Diverse Populations to Characterize Risk Loci for Alzheimer Disease, U01 AG072579; Jeffery M. Vance, Derek Michael Dykxhoorn, and Juan Isaac Young
Project Period: July 15, 2021 – June 30, 2026

Genetic Epidemiology and Multi-Omics Analyses in Familial and Sporadic Alzheimer's Disease among Secular Caribbean Hispanics and Religious Order, R01 AG067501; Richard P. Mayeux, Gary W. Miller, Tosto Giuseppe, and Badri Vardarajan
Project Period: June 1, 2020 – March 31, 2025

Genetic Modifiers of Cerebrospinal Fluid TREM2 in Alzheimer's Disease, RF1 AG058501; Carlos Cruchaga and Laura Piccio
Project Period: July 15, 2018 – March 31, 2023

Identifying Protective Variants in Local Ancestry of African Americans for ApoE4, RF1 AG059018; Jeffery Vance
Project Period: July 1, 2018 – March 31, 2023

Investigating the Functional Impact of AD Risk Genes on Neuro-Vascular Interactions, U01 AG072464; Sally Temple, Oscar Harari, Martin Kampmann, Celeste M. Karch, Kevin M. Pumiglia, and Kristen L. Zuloaga
Project Period: July 1, 2021 – June 30, 2026

Mendelian Randomization for Unbias Biomarker Discovery for AD and Other Complex Traits, R01 AG057777; Oscar Harari
Project Period: September 15, 2018 – May 31, 2023

Multi-Omic Functional Assessment of Novel AD Variants Using High-Throughput and Single-Cell Technologies, U01 AG072573; Thomas J. Montine, Anshul Kundaje, and Stephen B. Montgomery
Project Period: July 1, 2021 – June 30, 2026

ADSP MACHINE LEARNING

[PAR-19-269](#) Cognitive Systems Analysis of Alzheimer's Disease Genetic and Phenotypic Data (U01)

Learning the Regulatory Code of Alzheimer's Disease Genomes, 5 U01 AG068880-02; Towfique Raj and David A. Knowles
Project Period: September 1, 2020 – August 31, 2025

Ultrascale Machine Learning to Empower Discovery in Alzheimer's Disease Biobanks, 5 U01 AG068057; Paul M. Thompson, Christos Davatzikos, Heng Huang, Andrew J. Saykin, and Li Shen
Project Period: September 15, 2020 – August 31, 2025

Alzheimer's MultiOme Data Repurposing: Artificial Intelligence, Network Medicine, and Therapeutics Discovery, U01 AG073323; Feixiong Chen, Lynn M. Bekris, and James B. Leverenz
Project Period: July 1, 2021 – June 30, 2026

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Assessing Alzheimer Disease Risk and Heterogeneity Using Multimodal Machine Learning Approaches, U01 AG068221-01A1; Honguang Lin and Anita L. Destefano
Project Period: July 1, 2021 – June 30, 2026

Cognitive Computing of Alzheimer's Disease Genes and Risk, U01 AG068214; Olivier Lichtarge
Project Period: July 1, 2021 – June 30, 2026

Genetics of Deep-Learning-Derived Neuroimaging Endophenotypes for Alzheimer's Disease, U01 AG070112; Degui Zhi, Myriam Fornage, and Shuiwang Ji
Project Period: July 1, 2021 – June 30, 2026

Artificial Intelligence Strategies for Alzheimers Disease Research; R01 AG066833; Jason Moore, Marylyn Ritchie, and Li Shen
Project Period: September 30, 2021 – August 31, 2026

Causal and integrative deep learning for Alzheimers disease genetics; U01 AG073079; Wei Pan
Project Period: September 15, 2021 – August 21, 2026

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Appendix B: List of NIA FOAs for the ADSP

National Institute on Aging Analysis of Alzheimer's Disease Genome Sequencing Project Data [U19]

<https://grants.nih.gov/grants/guide/pa-files/PAR-12-183.html>

ADSP study design ADSP Study Design

<https://www.nia.nih.gov/research/dn/alzheimers-disease-sequencing-project-adsp-description-discovery-phase-and-follow-study>

Alzheimer's Disease Sequencing Project (ADSP) Replication Phase Analysis Studies (U01)

<https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-16-002.html>

Limited Competition: Additional Sequencing for the Alzheimer's Disease Sequencing Project (U01)

<https://grants.nih.gov/grants/guide/pa-files/PAR-16-406.html>

Notice of Information: The Alzheimer's Disease Sequencing Project Policy (ADSP) on the Publication of Study-Related Data

<https://grants.nih.gov/grants/guide/notice-files/NOT-AG-16-033.html>

Limited Competition: Additional Sequencing for the Alzheimer's Disease Sequencing Project (U01 Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/pa-files/PAR-19-234.html>

Limited Competition: Analysis of Data from NIA's Alzheimer's Disease Sequencing Project Follow-Up Study (U01)

<https://grants.nih.gov/grants/guide/pa-files/PAR-17-214.html>

Limited Competition: Additional Sequencing for the Alzheimer's Disease Sequencing Project: Opportunity for Revision Requests for Active Cooperative Agreements (U01 Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/pa-files/par-18-890.html>

Limited Competition: Additional Sequencing for the Alzheimer's Disease Sequencing Project (U01 Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/pa-files/PAR-19-234.html>

Notice to Extend the Expiration Date for PAR-17-214 "Limited Competition: Analysis of Data from NIA's Alzheimer's Disease Sequencing Project Follow-Up Study (U01)"

<https://grants.nih.gov/grants/guide/notice-files/NOT-AG-20-021.html>

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ADSP FUS 2.0: Diversity Initiative

Limited Competition: Alzheimer's Disease Sequencing Project Follow-Up Study 2.0 (ADSP FUS 2.0): The Diverse Population Initiative (U01 Clinical Trial Not Allowed PAR-21-212)
<http://grants.nih.gov/grants/guide/pa-files/PAR-21-212.html>

Transposable Elements

Elucidating the Roles of Transposable Elements in AD/ADRD and Aging (R01 Clinical Trial Not Allowed)
<https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-22-021.html>

ADGC

Limited Competition: Renewal of, and Revisions to, the Alzheimer's Disease Genetics Consortium (U01)
<https://grants.nih.gov/grants/guide/pa-files/PAR-14-070.html>

Renewed as <https://grants.nih.gov/grants/guide/pa-files/par-18-889.html>

Limited Competition: Renewal of, and Revisions to, the Alzheimer's Disease Genetics Consortium (U01 Clinical Trial Not Allowed)
<https://grants.nih.gov/grants/guide/pa-files/par-18-889.html>

NIAGADS

National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (U24)
<https://grants.nih.gov/grants/guide/pa-files/PAR-16-047.html>

National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (U24 Clinical Trial Not Allowed)
<https://grants.nih.gov/grants/guide/pa-files/PAR-20-110.html>

GCAD

NIA Coordinating Center for Genetics and Genomics of Alzheimer's Disease (U54)
<https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-16-001.html>

Limited Competition: NIA Genome Center for Alzheimer's Disease (GCAD) (U54 Clinical Trial Not Allowed) PAR-19-288
<https://grants.nih.gov/grants/guide/pa-files/PAR-19-288.html>

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NIA LOAD FBS

The National Institute on Aging (NIA) Late Onset of Alzheimer's Disease (LOAD) Family Based Study (FBS) (U24)

<https://grants.nih.gov/grants/guide/pa-files/PAR-16-205.html>

RFA AG-21-017 National Institute on Aging (NIA) Late Onset of Alzheimer's Disease (LOAD) Family-Based Study (FBS) (U24 Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-22-001.html>

MACHINE LEARNING

Cognitive Systems Analysis of Alzheimer's Disease Genetic and Phenotypic Data (U01 Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/pa-files/PAR-19-269.html>

FUNCTIONAL GENOMICS

Alzheimer's Disease Sequencing Project Functional Genomics Consortium (U01)

<https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-21-006.html>

Data Harmonization

Harmonization of Alzheimer's Disease and Related Dementias (AD/ADRD) Genetic, Epidemiologic, and Clinical Data to Enhance Therapeutic Target Discovery (U24 Clinical Trial Not Allowed) <https://grants.nih.gov/grants/guide/pa-files/PAR-20-099.html>

ADRD

Notice of Information: Alignment Among the Disease Definitions Utilized to Govern Genetic and Genomic Data Sharing for Studies Involving Alzheimer's Disease

<https://grants.nih.gov/grants/guide/notice-files/NOT-AG-17-007.html>

NCRAD

Limited Competition: National Centralized Repository for Alzheimer's Disease and Related Dementias (NCRAD) (U24 Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/rfa-files/rfa-ag-21-005.html>

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NACC

National Alzheimer's Coordinating Center (U24 Clinical Trial Not Allowed)

<https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-21-014.html>

Endosome

Notice to Specify High-Priority Research Topics for PAR-18-596

<https://grants.nih.gov/grants/guide/notice-files/NOT-AG-18-001.html>

Alleviating lysosomal lipid defects in ADRD by blocking cholesterol storage; Ta Yuan Chang

Project Period: September 30, 2018 – May 31, 2022

Axonal endo-lysosome transport mechanisms that regulate APP processing; Shawn Ferguson

Project Period: September 30, 2018 – May 31, 2022

Systematic elucidation of endosomal trafficking as a therapeutic opportunity in AD using CRISPR-based functional genomics; Martin Kampmann

Project Period: September 30, 2018 – May 31, 2022

A quantitative framework for understanding endosomal trafficking networks in Alzheimer's Disease; Jeffrey Harper

Project period: September 30, 2019-August 31, 2023

Endosome Dysfunction in Alzheimers Disease; Ralph Nixon

Project Period: September 30, 2018 – May 31, 2022

Dissection of endosomal trafficking mechanisms in Alzheimers Disease; Li-huei Tsai

Project Period: September 30, 2018 – May 31, 2022

Probing the role of SORL1 and endosomal network genetic variation on Alzheimers disease phenotypes in human neurons; Jessica E. Young

Project Period: September 30, 2018 – May 31, 2022

Notice to Specify High-Priority Research Topic for PAR-19-070 and PAR-19-071

Genetic Underpinnings of Endosomal Trafficking as a Pathological Hub in Alzheimer's Disease and Alzheimer's Disease-Related Dementias (AD/ADRD)

<https://grants.nih.gov/grants/guide/notice-files/NOT-AG-18-053.html>

<https://grants.nih.gov/grants/guide/pa-files/par-19-070.html>

<https://grants.nih.gov/grants/guide/pa-files/par-19-071.html>

The Alzheimer's Disease Sequencing Project (ADSP) Memorandum of Understanding for the ADSP Follow-Up Study (FUS)



Role of the endolysosomal pathway in Lewy body dementia - from population genomics to single cells;

Jose Bras

Project Period: July 1, 2021 – June 30, 2022

Genetic Epidemiology and Multi-Omics Analyses in Familial and Sporadic Alzheimers Disease Among Secular Caribbean Hispanics and Religious Order; Richard P. Mayeux, Gary W. Miller, and Badri Vardarajan

Project Period: June 1, 2020 – March 3, 2025

Overlapping Molecular Dysregulation of Endolysosomal Function in Alzheimers Disease and FTLT-TDP; Stephen M. Strittmatter

Project Period: September 15, 2019 – May 31, 2024

The molecular mechanism of PICALM-dependent endosomal trafficking; Marilyn Miller

Project Period: September 15, 2019 – May 31, 2022

Appendix C: Current (July 2021) Members of the Executive Committee

Eric Boerwinkle, Baylor College of Medicine

Clifton Dalgard, Uniformed Services University of the Health Sciences (USUHS)

Anita DeStefano, Boston University (CHARGE)

Lindsay Farrer, Boston University (CADRE)

Alison Goate, Mt. Sinai School of Medicine

Jonathan Haines, Case Western Reserve University

Richard Mayeux, Columbia University

Peggy Pericak-Vance, University of Miami

Jerry Schellenberg, University of Pennsylvania

Sudha Seshadri, University of Texas Health San Antonio

Li-San Wang, University of Pennsylvania

Ellen Wijsman, University of Washington

Appendix D: Current (July 2021) External Advisory Board Membership

Ewan Birney, European Bioinformatics Institute

Mike Boehnke, University of Michigan

Nancy Cox, Vanderbilt University

Brad Hyman, Massachusetts General Hospital/Harvard University

William Mobley, University of California, San Diego

Steve Rich, University of Virginia

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Appendix E: Committee and Work Group Co-Chairs

Committee / Work Group	Chair / Co-Chairs
Executive Committee	Rotating (see Appendix C)
Analysis Coordination Group	Eric Boerwinkle Jerry Schellenberg
Analysis Working Group	Gary Beecham Elizabeth Blue Gina Peloso Badri Vardarajan
AI/ML Working Group	TBD
CADRE	Jonathan Haines
CHARGE	Anita DeStefano Sudha Seshadri
FUS Sequencing	Brian Kunkle Peggy Pericak-Vance
Functional Genomics Work Group	Carlos Cruchaga Edoardo Marcora Jeff Vance Phil De Jager Myriam Fornage Josh Shulman
GCAD	Fanny Leung
Gene Verification Committee	Jerry Schellenberg
QC Work Group	Anita DeStefano Eden Martin Adam Naj
Phenotype Harmonization Consortium	Mike Cuccaro Tim Hohman

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Protective Variants Work Group	Alan Renton Alison Goate Edoardo Marcora Lindsay Farrer
Structural Variant Work Group	Jerry Schellenberg Kim Worley

Appendix F: Process for Selecting and Managing the ADSP Executive Committee

Background:

As described in the current (10/2021) Memorandum of Understanding (MOU), the ADSP is managed, in part, by an Executive Committee (EC): *“The EC members will represent the interests and scientific expertise of the ADSP under the guiding principles of this MOU. The EC will be responsible for making ADSP policy decisions and resolving any conflicts that arise in the conduct of this project. The EC is comprised of 13 members who are PIs with significant NIA funding relevant to the ADSP. NIA Program Staff will attend as ex officio members but with the ability to break ties if votes are necessary. Decisions are made by majority vote, with a quorum of eight required for a vote. EC Membership should represent the diversity of ADSP funded activities; ethnic and gender diversity is also encouraged. Individual EC members are reviewed every three years on a rolling basis (e.g., reviewing 5, 4, and 4 members over 3 years). Should a member resign, a new member will be appointed by majority vote of the remaining EC members. The EC is expected to meet monthly.”*

Purpose:

The purpose of this document is to define the process for determining the composition of the EC and reviewing its membership on an ongoing basis.

Composition:

The EC is composed of 13 members of the ADSP. Eligibility criteria for membership are:

- Contact or Multi-PI on an ADSP related multi-year cooperative agreement (including but not limited to U01, U19, U24, U54)
- Expertise in an area relevant to the ADSP

It is critical that the EC represent the breadth of activities of the ADSP. To assure this representation, two individuals will be selected with expertise to represent the following six areas:

- Genetic data analysis

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- Functional genomics
- Computational genomics (e.g., Artificial Intelligence/Machine Learning)
- Sample/cohort contributions
- Data infrastructure (e.g., GCAD/NIAGADS)
- Phenotype and harmonization

One additional person will be selected as an “at large” representative.

Each member will serve for a three-year term, with the possibility of re-nomination and selection. To maintain continuity, the selection process will be staggered such that no more than 5 positions will be up for selection in any one year, and no more than one position from each category will be up for selection. Should an individual resign for any reason, that position will be subject to nomination and appointment by majority vote of the remaining members, and the new member will serve the remaining term.

Selection Process:

The annual selection process will begin in January of each year. Individuals meeting the selection criteria can self-nominate for an available position within one of the six categories. In the interest of maintaining breadth, no more than one multi-PI from one grant can be nominated for membership on the EC. If an individual is a multi-PI on more than one ADSP relevant grant, they may be nominated in a different category from any other multi-PIs from their joint grants.

Once nominations are complete, a list of nominees for each position will be generated and sent to all the multi-PIs of all the ADSP relevant grants for voting. Each PI may vote only once, even if they are a multi-PI on multiple grants. A ranked voting approach will be used, with each PI ranking their choices (up to 3) in each category. If an individual receives a majority of first place votes, they will be selected. If no individual receives a majority of votes, the lowest ranking nominee will be eliminated and the votes retabulated to identify the successful candidate.

Succession of Chairs of the Executive Committee:

The Chair of the Executive Committee will serve two successive months. Following the two-month rotation, a new chair will rotate into the position until all 13 members have each served two months. Decision on the order of succession will be determined by the EC as a whole with consultation from NIA.