

The Alzheimer's Disease Sequencing Project

Memorandum of Understanding

12/10/12

Introduction

On February 7, 2012, a new Presidential Initiative was announced to fight Alzheimer's Disease (AD). As part of this effort, the National Human Genome Research Institute (NHGRI) was asked by the Director of the National Institutes of Health (NIH) to use \$25M already committed to its Large-Scale Sequencing Centers (LSSC) for genomic studies in AD. The NIH director asked the National Institute on Aging (NIA) and the NHGRI to work together to develop and execute a large scale sequencing project to analyze the genomes of a large number of well characterized individuals in order to identify a broad range of AD risk and protective gene variants, with the ultimate goal of facilitating the identification of new pathways for therapeutic approaches and prevention. The analysis will also provide insight as to why individuals with known risk factor genes escape from developing AD. The project developed jointly by NIA and NHGRI is called the Alzheimer's Disease Sequencing Project (ADSP).

Definition of the Alzheimer's Disease Sequencing Project

The overarching goals of the ADSP are to: (1) identify new genomic variants contributing to increased risk of developing AD, (2) identify new genomic variants contributing to protection against developing AD, and (3) provide insight as to why individuals with known risk factor variants escape from developing AD. Such a study of human genomic variation and its relationship to health and disease requires examination of a large number of study participants and needs to capture information about common and rare variants (both single nucleotide and copy number). Using existing samples from NIH funded and other studies, the NHGRI LSSC will produce the DNA sequence data and generate variant calls, that will be made available to the scientific community through NIH-approved data repositories. Statistical analysis of the sequence data is anticipated to identify new genetic risk and protective factors. Both fundamental scientific discovery and leading edge analytic approaches will be needed to achieve the research goals. The ADSP will conduct and facilitate analysis of sequence data to extend previous discoveries that may ultimately result in new directions for AD therapeutics.

The specific aims of the ADSP are to: (1) identify protective genomic variants in older adults at risk for AD, (2) identify new risk variants among AD cases, and (3) examine these factors in multi-ethnic populations as applicable in order to identify new pathways for disease prevention.

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The samples for the ADSP will be selected from well-characterized, cohorts of individuals characterized for AD diagnosis as well as having known AD genetic risk factors. Investigators in the ADSP will obtain from the NIH approved data repositories: (1) quality control checked and 'cleaned' sequence data. "Quality control checked and cleaned" means a set of routine checks will have been performed for sample information, phenotype, and GWAS data to ensure the sequence data are of high quality and are ready for downstream genetic analysis and that likely sources of false-positives have been ruled out, and that samples that are outliers which may skew project-level analyses have been identified; (2) information on the composition of the study cohorts (e.g. case-control, family based, and epidemiology cohorts); (3) descriptions of the study cohorts included in the study; and (4) accompanying phenotypic information such as age at disease onset, self-reported race/ethnicity, gender, diagnostic status, and cognitive measures. The ADSP will determine what additional information, if any, is needed by its members to facilitate the project.

General Principles for the Alzheimer's Disease Sequencing Project (ADSP)

In acknowledgement of the expertise of all the partners in the ADSP, all efforts will be considered collaborative and will involve all interested parties in discussions and decisions. This will include design and selection of samples (including families), pipelines and procedures for sequence analysis, analysis plans and implementation, data management, data interpretation, and manuscript preparation and submission.

It is agreed that ADSP members will devise a scientifically sound plan and initiate the agreed upon study within the most expeditious time line possible. It is agreed that "phenotype data" includes measurements collected on ADSP study participants that are necessary to execute this study plan. In general, this includes an AD diagnosis in addition to measurements thought to be directly related to the diagnosis, treatment, and outcomes of AD at the time of the analysis in addition to reasonable covariates and confounders. It is further agreed that the primary sequencing data includes, but is not exclusively Binary Alignment/Map (BAM); variant call frequencies (.vcf's files including SNV, insertion / deletion [indel], and structural calls) and first pass analysis results including common variant and burden test association analysis for protective and risk raising allele, insertion / deletion (indel), and structural variant calling. Data will be made rapidly available to the investigators in the study and to the public in a timely fashion using existing funds.

It is agreed that all partners in the ADSP will have immediate access to sequence data through an NIH approved data base and that no analysis other than initial quality control checks and variant calling will begin until all partners have access to the data. It is further agreed that the partners in the ADSP will receive the sequence data specific to their own sample sets.

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It is agreed that the data and results of these studies will not be communicated to study participants, relatives of participants, personal physicians, or insurance companies. Since these data will not be released to participants or the participant's family, the data will not be available for genetic counseling. If genetic counseling is requested by a participant, the participant will be referred to a genetic counselor who may then request new blood samples to be used for genetic testing that will be done in a Clinical Laboratory Improvement Amendments (<http://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index.html?redirect=/clia/> CLIA) approved laboratory. Individual constituent cohorts may make their own policies on return of data to study participants outside of the auspices of the ADSP; these cohorts may elect to return results that they have separately re-validated in a CLIA approved laboratory.

Principles of Collaboration

The following principles of collaboration serve as a guide to the ADSP's interactions. This document is a work in progress and it is expected that it will be modified in the months and years to come as the ADSP and the science that it serves evolves and matures. The collaboration is based on certain values and a shared consensus about the best way to identify genomic variants relevant to AD susceptibility. These are outlined below:

Trust. Any collaborative agreement is fundamentally based on a sense of mutual trust and respect among the participating groups; trust cannot be imposed but is generated by transparency and fairness in all dealings. Without this initial trust and respect, no collaboration is possible. Members may disagree with each other but that should not erode the fundamental sense of trust and respect. 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 among members. For this collaboration to succeed it is extremely important that all decisions and activities be conducted in an open and transparent way. This is best accomplished through clear, frequent, and open communication among all the participating groups, by in-person meetings, phone, and/or by email. Each principal investigator of the individual groups that comprise the ADSP is responsible for communicating to members of his/her own group of investigators.

Timeliness of activities/research. There is a commitment to adhere to reasonable timelines for defining the study design, identifying appropriate samples to be sequenced, sample transfer, sequencing, allele calling, data transfers, developing analytic plans, carrying-out first pass analyses, sending summary statistics to the common server, and publishing manuscripts.

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Use of individual group's own data in research studies outside ADSP. There is general agreement that individual groups may analyze any data they themselves have collected and submitted to the common ADSP data set. No review of the analytic plan or molecular work by the group at-large is necessary. However, sharing the news of such ongoing and planned activities relevant to the ADSP is expected to prevent surprises. Further, individual groups may relate any of the sequencing data to phenotypic data not thought to be directly related to the etiology of Alzheimer's disease at the time of the analysis.

Commitment to respect priority. In the course of the ADSP, it is expected that groups will share data that they or their parent cohort studies have generated on their own, either prior to the establishment of the ADSP or independently from it. In order to encourage such sharing, all participants agree to treat those data with care, particularly in the case of pre-release data, and adhere to NIH guidelines related to data release and embargoes. For example, other individual groups within the ADSP should not use those data in a publication until they are released into a public database or published by the original group that generated those data. However, it is expected that some of these data will be critical to aspects of the ADSP as a whole. These data can be included in publications of the entire ADSP with the consent and participation of the individual group that produced the data.

All parties to the collaboration benefit. The first and foremost benefit of the ADSP collaboration will be finding genomic variants that confer or protect from susceptibility to AD, leading to a better understanding of the causes of AD and potential for development of treatments. Participating investigators may also benefit through increased or stabilized funding, further learning opportunities, the potential for career advancement, and learning more about the most appropriate strategies to uncover the genetic mechanisms of complex disease. There is a clear recognition that for this collaboration to flourish, any decisions that are made must attempt to provide mutual benefit for all those involved in the ADSP, not just those directly responsible for a particular discovery. Admittedly it will be difficult to ensure that the benefit is equally distributed, or that it is equal in kind among all participants; nevertheless there must be an assurance of serious attention to the goal of mutual benefit.

Junior faculty/students. The ADSP puts a high premium on the training of students and junior faculty. Every opportunity must be given to students and junior faculty to refine their research skills and methodologies, to have an opportunity to be first author on publications, and to take the lead in certain components of the research collaboration. In this way, the next generation of scientists working in AD and genomics will be able to build on the results of this initial collaboration and so continue to make progress.

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Membership in the ADSP

At the time of acceptance of this document as indicated by the full array of signatories the ADSP is comprised of five groups: two large, independent genetics consortia: the NIA-funded Alzheimer's Disease Genetics Consortium (ADGC) and the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) and three NHGRI-funded Large Scale Sequencing Centers (LSSC): the Human Genome Sequencing Center at the Baylor College of Medicine, the Broad Institute Genome Center, and the Washington University Genome Institute. Each of the five groups will have pre-publication access to ADSP data, and can participate in the design of experiments and analysis to achieve the goals of the collaboration.

New members: Each ADSP group is free to add new investigators to its own group, for participation in the ADSP. In some cases, groups of investigators may be added. The PI of each of the ADSP groups is responsible for communicating the terms of participation in the ADSP to each new investigator. New members may also join when they receive an award under <http://grants.nih.gov/grants/guide/pa-files/PAR-12-183.html>, "National Institute on Aging Analysis of Alzheimer's Disease Genome Sequencing Project Data" [U19] or other ADSP-related funding opportunity announcements, or upon agreement of the ADSP Steering Committee (see ADSP Governance below for a definition of the Steering Committee).

ADSP Governance

Steering Committee: An ADSP Steering Committee (SC) will be formed. SC members will represent the interests and scientific expertise of their own group. The SC will be responsible for making ADSP decisions and resolving conflicts in all areas, including organization, priorities, collaborative projects, working group selection, authorship, new membership, and data sharing. The SC is initially comprised of a balance of three AD geneticists, three LSSC representatives, and NIH staff:

- Dr. Gerard Schellenberg, Principal Investigator (PI) of The Alzheimer's Disease Genetics Consortium
- Dr. Richard Mayeux, who is thoroughly familiar with family based sample sets, genetic epidemiology, and ADGC samples from diversity populations
- Dr. Sudha Seshadri, PI of the NeuroCHARGE
- Dr. Richard Gibbs, PI the Human Genome Sequencing Center at the Baylor College of Medicine

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- Dr. Eric Lander, PI of the Broad Institute Genome Center
- Dr. Richard Wilson, PI of the Washington University Genome Institute
- One staff member from NHGRI
- One staff member from NIA

Decisions on modification of ADSP policy will be affirmed by the SC. Decisions on issues affecting the ADSP as a whole will be voted upon by the SC. Any decisions requiring a vote will be documented in the SC meeting minutes. A quorum, the number of SC members required to hold a vote, will be greater than one-half of members of the SC.

The SC will have two votes: one cast by a majority of the NIA-associated members and one cast by a majority of the NHGRI-associated members. Decisions will require unanimity of these two votes. In unusual situations that require additional consultation with NIH, the NHGRI and NIA Institute Directors will be invited to assist in decision making. Scientific project plans, and substantive changes to any of those plans involving the LSSC will require final approval by NHGRI, according to its standard procedures, in consultation with NIA. Scientific project plans involving the two AD genetics consortia will require final approval with NIA in consultation with NHGRI.

In some instances study cohorts included in the ADSP data sets are associated with parent studies or have genetic or phenotypic data not specified in this MOU deposited in data bases not associated with the sequencing project. In cases where these data are to be requested, requestors do not need approval for the request from the ADSP SC and requestors will follow the relevant approval process established by the NIH institute funding the study. In cases where data sets such as those involving a nested study within a study cohort directly related to the AD phenotype are to be requested, application for data from the parent cohort related to the AD phenotype will be made through the approved dbGaP / NIA Genetics of Alzheimer's Disease Data Storage site (NIAGADS) data user application process.

Working Groups. The ADSP will form project specific working groups as needed including a publication work group, on a task-driven basis. Each working group will have at least two co-chairs selected from different groups. The selection of co-chairs will be based on interest, expertise, and performance, with an attempt to balance workload across ADSP members. A key objective of the selection of co-chairs will be appropriate representation from the two AD consortia and the three LSSCs. The chairs and composition of the work group members will be selected by the SC.

Communication. The ADSP will have regular bi-monthly calls to discuss progress and to plan new initiatives. Each working group will also have regularly scheduled phone meetings, and

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report the results to the ADSP SC on the bi-monthly calls. The ADSP will also have a least one face-to-face meeting a year. There may be additional face-to-face meetings of the ADSP SC, as needed, as determined by NHGRI and NIA.

Definition of ADSP data

The term “ADSP data” is defined as information actually generated by joint project activities of the ADSP and includes all data needed to perform likely or actual ADSP analyses.

NHGRI and NIA recognize that there are datasets that will be used in the course of the ADSP by members of the ADSP that have been generated outside the ADSP. Although the following examples do not cover all possible cases, they provide a framework:

- All data that are essential to carrying out the scientific plan must be shared within the ADSP. These could include but are not exclusive to, for example: data critical to choosing samples; metadata or phenotype data that accompany the samples that are actually going to be sequenced; phenotype and sequence data related to samples used in the sequencing project; and specific data needed to support analyses described in consortium papers.
- These data will be considered “ADSP project data” if they are directly relevant to project analyses that will be published as part of the ADSP. Ancillary data associated with samples that are not chosen for any further work by the ADSP are not ADSP data. However, there may be other policies that govern these data.

Sharing of ADSP Data

Sharing data with the research community and within the ADSP

i. *Sharing data as a community resource.* A fundamental purpose of this study is to make the data and the resulting analyses widely available to the research community to accelerate the development of therapeutic approaches, diagnostic methods, and prevention of AD. Towards that end, ADSP data will be shared in accordance with existing NIH and Institute-specific protocols and policy, including requirements for consent and IRB approval. The ADSP agrees to optimize accessibility and usefulness of the information generated by the study in a timely manner and to provide both raw and processed data to the research community through an NIH approved data storage site. Data derived from analysis of either raw or

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processed data from the study will be deposited into dbGaP (<http://www.ncbi.nlm.nih.gov/gap>) and/or the NIA Genetics of Alzheimer's Disease Data Storage Site (NIAGADS; <http://alois.med.upenn.edu/niagads/>) or another NIH approved data storage site for access by the research community. All sequence and phenotype data shall be placed in the public domain via a qualified access database and shared freely by methods and within time periods to be specified by the NIH policy. In general this will be immediately upon completion of analysis of variant calling. In particular, sequence data generated by the LSSC under NHGRI funding must be released rapidly to the repository at NCBI, and other repositories designated by the NHGRI or NIA. The ADSP will make readily available processed data and summary statistics from published analyses to the entire research community.

The Bermuda Principles (<http://www.gene.ucl.ac.uk/hugo/bermuda.htm>) in 1996 and the Ft. Lauderdale Large Scale Biological Sequencing Projects accord in 2003 (<http://www.genome.gov/Pages/Research/WellcomeReport0303.pdf>) were developed by the scientists engaged in the International Human Genome Sequencing Consortium and their funding agencies. These documents observe that pre-publication data release might conflict with a fundamental scientific incentive: publishing the first analysis of one's own data. It is not possible to guarantee this incentive without applying restrictions that would undermine the rationale for rapid, unrestricted release of data from community resources. Nonetheless, it is essential that excellent scientists continue to be attracted to these projects. To encourage this, the scientific community should understand that pre-publication data release needs active community-wide support if it is to continue to receive widespread support from the producers. The ability of the producers to analyze and publish their own data should be respected by the research community and the contributions and interests of the data producers should be recognized and respected by the users of the data. As an extension of the Bermuda Principles and the Ft. Lauderdale Accord, the following obtains with regard to ADSP data:

ADSP sequence and phenotypic data would be made available rapidly after generation; all partners in the ADSP will have immediate access to sequence data through an NIH approved data base. In keeping with the Bermuda Principles, the Ft. Lauderdale accord, and the ADSP MOU, ADSP phenotype and sequence data will be made available to the research community at large immediately after quality control checks and variant calls are completed. Data can be accessed by application either through dbGaP: <http://www.ncbi.nlm.nih.gov/gap> or the NIA Genetics of Alzheimer's Disease Data Storage Site <http://www.niagads.org/>.

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In the spirit of the clear benefit that ensues from converting such data sets into community resources as rapidly as possible, it is expected that users of the ADSP data will withhold publication until the producers of the data have published their findings. ADSP participants will publish their data in an expeditious fashion at least one major paper reporting the results of the ADSP to be jointly submitted by all of the members.

ii. *Sharing of data within the ADSP.* All participating investigators agree to provide previously or newly acquired data that are necessary to the production and analysis of the sequence data for the ADSP before the sequencing project begins and as needed throughout the course of the project. Individual-level data must have appropriate IRB approval and consent. These primary data include but are not exclusive to the following: [1]. Variable specification for samples included in the studies: Consortium (ADGC or CHARGE), study identification number, study name, number of affected subjects in the study, number of unaffected subjects in the study platform for the associated GWAS data. [2]. Variable specification: study identification number, family identification number, subject identification number, father ID where applicable, mother ID where applicable, gender, status for prevalent AD, status for incident AD, age at onset for cases; age at last exam for controls, age at baseline, APOE genotype, whether autopsy data are available and used for case/control selection, Braak stage from autopsy; PET imaging data availability, self-reported primary race, self-reported ethnicity, risk score as defined by the sample selection working group and computed by ADGC/CHARGE for sample selection, whether the sample is from a family-based study, whether the pedigree of the family is available and posted, whether the subject is consented for broad data sharing, amount of DNA available for sequencing and validation, and individual level GWAS data.

Use of individual consortium's own data in research studies outside ADSP. Membership in ADSP does not preclude members from using their own samples and their own data for their own publication and analyses. However, data developed by and results produced by the ADSP will be published under the authorship of the ADSP. Sharing the news of such ongoing activities is encouraged to prevent surprises or the erosion of the collective effort.

Conflicts of interest. All scientists involved in collaborations that involve similar studies to those undertaken by the ADSP will declare possible conflicts of interest by signing and dating this document and adding a statement of conflict of interest, including financial conflicts of interest.

Access to ADSP data. Investigators in academic and clinical communities will have immediate access to the ADSP genomic and associated data, for performing their own analyses. Investigators wanting additional data not included in the primary data set may apply to the dbGap or National Institute on Aging Genetics of Alzheimer's Disease Data Storage Site (NIAGADS <https://www.niagads.org/>) for those additional data. Data on the genetics of AD as

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well as related data relevant to the AD phenotype that are distributed for analysis to qualified scientific investigators conducting research on the genetic bases of AD are stored at NIAGADS. The researcher will indicate what data they are requesting and this request will be reviewed by the NIAGADS Data Use Committee (DAC) using a process paralleling the dbGaP DAC approval procedure. Applicants must have appropriate IRB approval. Investigators making a data request will receive genomic and associated data on the condition that they provide back to the database any data and summary statistics that they derive from the ADSP data. All members of the ADSP will have access to data in NIAGADS.

Analysis proposals within the ADSP. In order to facilitate communication, the ADSP will establish a mechanism whereby proposals from ADSP investigators for all planned analyses of ADSP phenotypes in relation to the sequence data will be submitted to the ADSP SC before analysis begins. This will include the primary analysis as well as any secondary study analysis defined by the SC as being essential for critical aspects of the project. Critical aspects include but are not limited to analyses that form the major conclusions of the main publication(s) or primary analyses that underpin multiple secondary analyses.

The SC or its delegates will review proposals in a timely fashion by a mutually agreed upon protocol and will provide feedback on the proposal. Analysis, manuscript proposals, and related feedback will be discussed at a subsequent meeting of the SC. The goal of this process is to provide transparency and to provide a mechanism whereby proposals can be discussed by the SC. The intent is not to limit analyses but rather to provide input from the diverse types of expertise available within the ADSP membership.

The SC expects regular written progress reports on the analysis to be provided in a timely fashion to the group as a whole in a format that is acceptable to the ADSP membership as a whole. In the spirit of this MOU, it is agreed that manuscripts will be brought to the ADSP SC early in the process of their development. For analyses and publication of data not related to the AD phenotype, an ADSP SC review is not needed; in these instances review will follow relevant standards established by the NIH institute funding the study.

It is acknowledged that the ADSP is one of several potential AD projects that NHGRI is considering for potential support under the NHGRI Sequencing Networks. These projects will be considered by the NHGRI's normal internal processes for approval of large-scale sequencing projects, which includes discussion by the NHGRI's Sequencing Center Network Steering Committee, and recommendations for approval by both the NHGRI's Scientific Advisors to the Sequencing Program (SAP) and the NHGRI Council. The amount of total support ultimately committed to AD projects will be determined based upon scientific merit and available funds.

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Authorship and Acknowledgements on ADSP Publications

ADSP participants agree to publish at least one major paper reporting results of the Project to be jointly submitted by all of the members in an expeditious fashion. This publication will list the authorship of all participants and will acknowledge the funding of the NIH Institutes participating in the study (see below). As with other large genomic consortia, multiple papers may be published simultaneously with, or as companions to, the main paper, to augment the impact of the work. Consortium members wishing to submit other manuscripts or make meeting presentations using ADSP data prior to the primary publication for those data must clear these with the SC.

For ADSP publications, the main author list at the top of the manuscript will include investigators who have significantly participated in collecting, generating and analyzing the data in the manuscript. The ADSP recognizes that projects are driven by more than one person; thus publications will often have multiple equal co-authors. If the journal can accommodate it, the paper will include a description of the role of each author. The members also will work to promote young investigators and encourage their leadership and placement as first authors. The first and last co-authors should be distributed among groups to maximize credit and exposure for each. The ADSP member consortia and LSSC will also appear in a manner determined by the SC as author groups at the top with individual authors from these consortia appearing in the supplementary material provided that individuals are searchable via Medline, PubMed, etc. The corresponding author and the last coauthor may differ. The SC may need to modify the details of how authorship is represented, within the spirit of the proposal above, because the eventual journal format and other variables related to publication are not known at the time of the signing of this document. Likewise, it is recognized that there may be multiple publications, some with the entire ADSP and others with subgroups as authors that may affect manuscript authorship.

Qualification as an author will follow typical academic criteria. To qualify as an author, an individual will need to contribute to study design, and/or study execution, and/or preparation of results for publication. For some publications, a large number of authors will be appropriate. The composition of the author group will be determined by individual groups. The number of authors will not be a consideration when the author list is compiled. Each group will determine who should be an author for a particular publication with information provided describing the contribution by each nominated author.

In all cases where ADSP data or summary statistics are used in publications or presentations by the ADSP, the authors or presenters will acknowledge the contribution of the ADSP and funding agencies. This will pertain to any and all oral and written presentations, disclosures, publications, and patents resulting from any and all analysis of genetic analysis data and

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associated phenotypic data received from the ADSP. The PI will use the following acknowledgement: "Data and analyses used in this presentation were produced by the Alzheimer's Disease Sequencing Project." The website for the ADSP should be included in the acknowledgement. In addition, credit should be given to the groups and their parent cohort studies, family-based studies, case-control studies, clinic based studies, and all investigators and funding agencies that contribute to the ADSP or that provided the phenotype and/or additional genotype data using mutually agreed language.

Intellectual Property

The ADSP agrees to abide by the principles set forth in the ruling by the Supreme Court of the United States (SCOTUS):

[http://www.scotusblog.com/?s=gene+patent+BRCA: U.S.: No patent on human genes SCOTUS](http://www.scotusblog.com/?s=gene+patent+BRCA:U.S.:No+patent+on+human+genes+SCOTUS) (<http://www.ibtimes.com/articles/320140/20120327/supreme-court-case-overturns-human-genes-patent.htm>).

Disagreements

Occasionally disagreements may arise regarding scientific matters that are within the scope of the ADSP, authorship on publications, or appropriate behavior in the ADSP. These matters should be brought to the attention of NIH staff by the affected party. First, NHGRI and NIA will consult with the affected participants and attempt to mediate these disagreements. If necessary, NIH in consultation with the ADSP SC may decide to enlist Dispute Resolution for assistance in mediation. A Dispute Resolution Panel composed of three members selected by the SC will be convened. Disagreements that cannot be resolved by the Dispute Resolution Panel will be brought to arbitration. An Arbitration Panel composed of three members will be convened: one designee each from the two affected parties and a third designee with expertise in the relevant area who is chosen by the other two. Decisions by the Arbitration Panel will be final.

Funding Agencies

Funds for the sequencing component of the ADSP come from the NHGRI Large-Scale Sequencing program provided to the LSSC. As is the case with all NHGRI sequencing funds, the use of those funds for specific projects is subject to final vetting and approval by NHGRI, which involves discussions with the NHGRI Scientific Advisory Panel to the Sequencing Program, and the National Council on Human Genome Research. In this case, the process will also involve

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consultation with the advisors to the NIA-funded ADGC and the NeuroCHARGE grant. NIA intends to provide funding for informatics infrastructure support (NIAGADS) and for some analysis of the data within the ADSP, although the specifics of support are contingent on competitive review and NIA policy.

The following signatories are in agreement with the tenets set forth by this Memorandum of Understanding:

Large Scale Sequencing Centers:

Richard Gibbs	Baylor
Eric Lander	BROAD
Richard Wilson	Washington University

Alzheimer's Disease Genetics Consortium (ADGC):

Gerard Schellenberg, P.I.	University of Pennsylvania
Lindsay Farrer	Boston University
Jonathan Haines	Vanderbilt University
Richard Mayeux	Columbia University
Margaret Pericak-Vance	Miami University

Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Genome Wide Association Study

Sudha Seshadri	Boston University
Eric Boerwinkle	University of Texas Health Science Center
Reinhold Schmidt	Medical University Graz, Graz
Bruce M. Psaty	University of Washington
Cornelia van Duijn	Erasmus Medical University, Rotterdam, Netherlands
Albert Hofman	Erasmus Medical University, Rotterdam, Netherlands

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BAYLOR LSSC
Richard Gibbs

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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BROAD LSSC
Eric Lander

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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WASHINGTON UNIVERSITY LSSC
Richard Wilson

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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ADGC
Gerard Schellenberg

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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ADGC
Lindsay Farrer

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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ADGC
Jonathan Haines

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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ADGC
Richard Mayeux

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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ADGC
Margaret Pericak-Vance

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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CHARGE

Sudha Seshadri

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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CHARGE

Eric Boerwinkle

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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CHARGE

Reinhold Schmidt

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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CHARGE

Bruce M. Psaty

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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CHARGE

Cornelia van Duijn

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator

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CHARGE
Albert Hofman

Signature of the Principal Investigator

Date

Printed name of the Principal Investigator