



Autism Speaks Understanding ASD - Genetics to Behavior - Dataset Analysis 2019 Request for Applications

Deadlines

Letter of Intent due on or before: March 6, 2019, 8:00 pm (U.S. Eastern Time)

Letter of Intent decisions: Mid-March

Application due on or before: April 10, 2019, 8:00 pm (ET)

Other Important Dates (subject to change)

Peer review panels: Late spring 2019

Notification: Summer 2019

Earliest Grant start date: early fall 2019

Autism Speaks is dedicated to promoting solutions, across the spectrum and throughout the life span, for the needs of individuals with autism and their families. We do this through advocacy and support; increasing understanding and acceptance of autism spectrum disorder; and advancing research into causes and better interventions for autism spectrum disorder (ASD) and related conditions. We empower people with autism and their families with resources, online tools and information covering the life span.

We are seeking novel grant applications to increase our basic understanding of autism – from genetics to behavior – by analyzing important datasets generated by Autism Speaks through its many programs and partnerships (see below). Applications that co-analyze both Autism Speaks and non-Autism Speaks datasets in combination are encouraged. However, these grants are not for collecting new data but are to give researchers support to investigate new hypotheses or relationships using these datasets. These autism-specific datasets include the Autism Genetics Research Exchange (AGRE) and MSSNG genetics resource (pronounced “Missing” to represent information we are missing to understand autism.

AGRE (research.agre.org) is a dataset housing phenotypic data and biomaterials from AGRE-participating families, most of whom have two or more children on the autism spectrum. This resource not only houses rich phenotypic data, it is a biorepository of blood and/or cells from affected individuals and family members. All families had blood collected from at least one parent and siblings affected with ASD. Data is from 1,736 families with 3348 affected individuals with ASD, including some 1,271 multiplex families. Additionally, the dataset includes clinical and biomaterial data available on over 500 twin families with zygoty testing. Most families had fragile X testing by a CLIA-accredited lab. Reliable, UMACC Certified ADI and ADOS raters collected phenotypic data. They completed ADIs for every family and collected additional phenotypic data that frequently included ADOS, Vineland, Raven’s, PPV, Stanford-Binet assessments and other demographic information. More than 1,700 whole genome sequences from AGRE biosamples are included in the MSSNG dataset.

MSSNG (<https://research.mss.ng/>) is a groundbreaking collaboration between Autism Speaks, Google, Verily, DNASTack and Hospital for Sick Children/University of Toronto to create one of the world's largest whole genome database on autism spectrum disorder with insightful phenotypic information about individuals with ASD and their family members. A new version of MSSNG (DB6) will be rolled out in early 2019, to coincide with the launching of this new grant program to use high-quality whole genome sequencing of blood DNA (minimum 30x high-quality coverage) of approximately 10,000 individuals from families from AGRE repository and other important, well-phenotyped cohorts. (See above.) The MSSNG database, built using the Google Cloud Platform and Google Genomics, intends to make its data as useful and widely accessible to researchers as possible, including supporting access to local compute and storage resources, and providing genomic exploration tools for standard and custom analyses. Within the database there are 1,500+ simplex families and greater than 650 multiplex families, amounting to 7,321 WGS, in which 3,446 are from people on the autism spectrum. In early 2019, approximately 2,700 additional WGS will be added to the database to expand this free resource. MSSNG's philosophy is to promote and enable "open science" research to lead to a better understanding of autism.

The goal of this Request for Applications (RFA) is to advance our understanding of the molecular underpinnings of ASD and how these changes relate to behavioral outcomes and might be assessed as autism subtypes. A successful application will require the use of at least one of these two resources as the primary source of data to be analyzed to support the hypothesis proposed. Other non-Autism Speaks datasets can be co-analyzed to allow larger dataset to be studied in aggregate. We invite a wide variety of proposals to use these Autism Speaks datasets to advance our understanding of ASD risk by exploring novel hypotheses, new genetic-phenotypic relationships and new science to support clinical assessments or treatments.

Grant proposals using AGRE and/or MSSNG datasets can include, but are not exclusive to developing methods to: identify ASD subtypes, advance our understanding of how genetics can improve diagnostic certainty, enable earlier diagnosis and/or deepen understanding of genetic pathways in ways that could lead to identifying targets for improved treatments and health outcomes.

Finally, an important goal this program is to bring **early career investigators** to autism genetics and have them explore MSSNG resources. Additionally, we encourage investigators from other fields to apply.

Applicants should contact Autism Speaks regarding sample availability or any questions regarding the available resources that influence their proposal.

Awards

We anticipate funding up to four grants for 1 year at \$100,000, inclusive of 10% indirects. Six-month progress reports and a final report will be required to receive full disbursement of funds. Funds are intended to be used primarily for salaries and resources to complete the project. Any funding for heavy storage and computing costs must be discussed in the proposal.

Eligibility

Applicants at U.S. and non-U.S. non-profit and for-profit institutions are eligible for this program. These entities include, but are not limited to, colleges, universities, hospitals, governmental

entities and for-profit research & development entities (e.g. biotechnology and pharmaceutical companies).

Projects involving for-profit entities require a letter from an authorized company representative declaring that the applicant's work can and will be published, and that publication will not be delayed (or without proper justification) because of proprietary issues.

Early Career Investigator: Preference will be given to early career investigators, who are defined as a postdoctoral fellow or an assistant professor with three or fewer years at this rank. Under special circumstances, senior investigators can apply if they will be providing funds to co-support the salary of an early career investigator. Additionally, investigators from other fields are encouraged to apply to advance novel hypotheses.

General Information

All applications must be submitted through the web-based Autism Speaks Science Grants System, <https://science.grants.autismspeaks.org>.

Please Note:

1. Applicants must be an early career scientist, unless a justification is made for an exception as described in eligibility above. Go to <https://science.grants.autismspeaks.org> and register with **your institutional email address** (or log in if you have a profile). Complete your profile information. *Note: Enter the institution where the fellowship will take place, even if you are not located there at the time of LOI submission.*
2. It is advisable to review the LOI page and then the Application page in the grant system well in advance of the submission date.
3. All uploaded documents should be 11-point Arial font with 1-inch margins all around (single spacing is acceptable) with the exception of NIH biosketches. Please do not have headers or footers in submitted documents. *Applications exceeding the specified document limits will not be reviewed.*
4. Preferred file type is PDF and must not be encrypted. Movie files are not acceptable.
5. Applications received after the deadline will not be accepted unless permission has been previously granted by the Autism Speaks Grants Office and then only due to rare and unavoidable circumstance. There are no exceptions to this rule. All decisions of Autism Speaks on late submissions will be final. It is the applicant's responsibility to plan around holidays or any special circumstances at their institution.
6. It is the applicant's responsibility to contact their Office of Sponsored Projects (or the equivalent) to identify the Responsible Official (RO) for this application. The Responsible Official will review and submit the final portion of the application. His or her submission is approval of the application on behalf of the institution. LOI forms should be completed and submitted by the applicant. Full applications can only be submitted by the RO.
7. There are no geographic restrictions on these applications. International applicants are encouraged.

Completing the Letter of Intent (LOI)

Log in and click "Applications" at the top of the profile page or "Go to Applications" at the bottom of the page. Choose "Start a new LOI or application" then "**Dataset Analysis 2019**" The LOI

includes two web pages – the Basic Information Page and the LOI Form. The requirements for each page are as follows:

1. Basic Information Page includes:
 - a. **Title:** Enter less than 100 characters, spaces included.
 - b. **Scientific Abstract:** (up to 1,500 characters, spaces included) Describe the project goal(s) and/or hypothesis, specific aims, research methods, expected results and significance/relevance to the goals of this RFA.
 - c. **Key Personnel:** (tip: start by entering the last name). Enter all individuals participating in the research project. Final changes to this field can be made during completion of the application.
 - d. **Responsible Official:** Choose the Responsible Official from the PI's institution and include his/her institutional email.
 - e. **Keywords:** Carefully select all relevant keywords associated with the research project. We will use this information to select expert reviewers knowledgeable about your field of study.
 - f. **Note: All information will be available for review and editing at the application stage.**

2. Letter of Intent Form includes:
 - a. **Dataset Choice:** Choose one or both.
 - i. AGRE
 - ii. MSSNG
 - b. **Yes/No** – Will the project also co-analyze one of the above sets with a non-Autism Speaks dataset?
 - c. **Letter of Intent Narrative:** Not to exceed 3 pages and must include:
 - i. A concise description of the proposed project including brief background/study justification, specific aims, key methods, expected results and broader impact on understanding how genetics contribute to the cause or risk of autism; holds the potential to improve diagnostic certainty and identify autism behaviors and/or subgroups; and/or identify molecular pathways to move closer to precision medicine in ASD. Please specify why the Autism Speaks dataset has been chosen for analysis and if other, non-Autism Speaks datasets will be co-analyzed and why.
 - ii. Include no more than 10 references, included in the 3 pages.
 - iii. The LOI should be specific enough to be screened for scientific merit, fidelity to the purpose of this RFA and relevance to Autism Speaks' priorities.
 - d. **Principal Investigator Biosketch:** NIH format not to exceed 5 pages.

IMPORTANT NOTE: LOIs will be subject to in-depth review including PI eligibility. After all LOIs are reviewed, Autism Speaks will send an email indicating approval or disapproval. Please do not contact the grants staff regarding LOI acceptability. Applicants with approved LOIs will be permitted to submit a full application. All decisions are final, and no comments will be available.

Note: All awarded grantees will be required to submit to the [Autism Speaks Genetics application](#) system to get access to these datasets for analysis before funds will be released. Applicants are highly encouraged to apply early to evaluate data available and to complete the required letters and signatures to receive approval to access AGRE and/or MSSNG data.

Please note that the Grants and Genetics systems share the same database of profiles therefore one login will work for both. Please do not create two separate profiles.

Completing your Application

If you are notified that your LOI has been approved, you can begin your application. Log in and select your application.

1. **ORCID profiles – Autism Speaks policy requires all applicants to obtain ORCID profiles and link them to the Autism Speaks Grant System profile.** [Link to Help document](#). See **General Instructions for details**.

2. **Basic Information Page:** Review and edit your entries from the LOI.

All remaining items will be found on the Application Form Page.

3. **Dataset Choice:** repeat the LOI selections.
 - a. AGRE
 - b. MSSNG
4. **Yes/No – Will the project also co-analyze one of the above sets with a non-Autism Speaks dataset?**
5. **Research Plan:** (6-page maximum) the research plan should address the evaluation criteria in section IX below.
 - a. **Background and rationale** for the study. Briefly describe the primary motivations and prior research; no need to reference basic information about ASD.
 - b. **Research strategy**, including specific aims, preliminary data, methods and procedures, statistical power, data matching/merging approaches, and statistical analyses to address specific aims. Potential pitfalls and proposed solutions should also be listed, especially with co-analyzing Autism Speaks and non-Autism Speaks dataset(s).
 - c. **Innovation.** Describe how the project is novel, ground-breaking and has the potential to move the field in new directions.
 - d. **Impact, scalability and sustainability** in potential to improve the lives of persons with ASD.
 - e. **Investigators' qualifications.** Briefly describe and provide biosketches(See "12" below.)
 - f. **Environment.** Briefly describe, with greater detail included in "10," described below.
6. **Figures:** If needed, include a maximum of 2 pages of relevant images, figures and graphics. Images uploaded here will not be counted toward the 6-page limit.
7. **Bibliography:** Include complete literature citations including titles and all authors. References will not be counted toward the 6-page limit.
8. **Budget table:** Complete the online budget table (in USD, no decimals). The budget may include:
 - a. Personnel costs
 - i. Principal investigator and/or co-investigator salaries and benefits
 - ii. Technical research assistant salary and benefits
 - iii. Consultants
 - b. Research supplies, services and related expenses

- c. Essential equipment. A vendor estimate is required for any single item of equipment costing more than \$5,000 US.
 - d. Travel to professional meetings
 - e. Publication and data analysis costs
 - f. Indirect costs: An amount not to exceed 10% of direct costs may be included for the sponsoring institution's indirect (overhead) costs. The total grant cannot exceed \$100,000 USD.
 - g. Collaborations, if applicable.
9. **Budget justification:** (4 pages max) The budget justification should provide an explanation for all lines in the budget. Any funding for heavy storage and computing costs must be discussed in the proposal
10. **Human participants:** Because MSSNG uses de-identified human data, applicants must obtain a review from either an ethics board or an Institutional Review Board (IR) indicating their approval of the project or that no ethics approval is needed. This memo will need to be uploaded.
11. **Resources and research environment:** (1 page max) Describe the resources and environment that will support the successful completion of the project. If the project will use existing samples and/or collecting samples, specify how and when they will be used and shared with the autism community following the end of the project.
12. **Letters of collaboration:** If needed in support of the research project, combine multiple letters into one file for upload.
13. **Biographical sketches:** For the principal investigator, named co-investigators and collaborators – in NIH format (5 pages max each). Indicate education, personal statement, positions and honors, contribution to science with relevant citations, selected list of published work, and ongoing and completed research support with emphasis on projects relevant to the proposed investigation. Combine multiple biosketches of co-investigators and collaborators into one file for upload.
14. **Current and pending grant support:** Indicate funding source, total award amount, award duration (inclusive dates) and project title for all investigators and significant collaborators. Financial and substantive overlap will be examined after review.
15. **Supporting files:** Reference other documents relevant to the application in the research plan and upload to "Additional Materials." Combine multiple documents into one file for upload.
16. **Peer-reviewed research publications:** A maximum of two (including manuscripts accepted for publication) will be accepted, but NOT manuscripts not yet accepted for review, review articles, book chapters, popular press articles or meeting abstracts. Publication files MUST NOT be locked or protected in any way.

NOTE: *Supporting files, publications and updates (see VIII) are provided as a courtesy to the reviewers who are not obligated to refer to them in evaluating an application.*

Endorsing and Submitting the Application

Applications must be submitted electronically using the [Autism Speaks Science Grants System](#). Applications that are late, incomplete, exceed the document limitations or do not adhere to the required format will not be reviewed. Applications that are faxed or emailed will not be reviewed.

When an LOI is approved, the Responsible Official named in the LOI will be copied on the notification email. When the application is ready, it is the responsibility of the applicant to contact their Responsible Official, who must complete the submission. The Responsible Official's submission of the application signifies endorsement on behalf of the institution.

Autism Speaks reserves the right to return without review any application that in its judgment is not in compliance with its rules and procedures for application preparation and submission, is not responsive to its research goals or exceeds its funding limits or available resources. It is the responsibility of the applicant to ensure that the application is complete and conforms to the guidelines.

Review Process and Evaluation Criteria

Autism Speaks is committed to efficient, fair and expert review and funding of meritorious applications that are relevant to the mission of Autism Speaks. Review of scientific merit is provided by a group of highly accomplished researchers from the Autism Speaks Medical and Science Advisory Board with additional expertise, as needed, from other researchers in the specific research areas of the applications.

Applications will be evaluated using the following criteria:

Rationale

Will this research advance our understanding of the molecular underpinnings of ASD or lead to improved behavioral outcomes? Does the application directly address the RFA priority areas as described above? Is there a solid scientific rationale for the choice of the dataset or datasets, and how will it match the hypothesis? Will this application support an early career investigator or a new investigator entering the autism field? Are there possible problems and possible alternative approaches?

Impact and Relevance

Will this research be proposing a new hypothesis or scientific relationship? Will the proposed research and expected results contribute new knowledge or methods to improve our understanding of the lives of people with autism spectrum disorder? To what extent do the aims and hypotheses have the potential to move the field forward? Will this proposal include other non-Autism Speaks datasets, and how will that influence the outcome and impact the field?

Innovation

Does the application develop innovative and creative approaches to analyze dataset(s) or combine datasets? Does the project propose to develop or employ novel concepts, approaches or methodologies, tools, or technologies for this area? Does the application challenge an existing associations or paradigms? Will the project application propose ideas or methods that have not been previously used in autism research or have not been applied in the way that is proposed?

Research Strategy

Is the project proposed well designed? Is there preliminary data to establish feasibility and support the likelihood of further success? Are the key components of the sample, methods and data-analytic approaches well described and reasonable? Do the proposed design, sampling and analytical methods align with the study hypotheses? Does the application present milestones and a proposed project timeline that are well-reasoned, realistic and appropriate to the strategy? Are potential problem areas acknowledged, alternative tactics considered and benchmarks for success presented? Will the required methods and analyses be available and

implemented appropriately and are they feasible for this research team relative to the scope of the proposed project? Is the timeline reasonable?

Investigators' Qualifications

Do the investigators have the appropriate training and expertise to conduct the proposed research? Have they demonstrated productivity that is satisfactory relative to their career stage in terms of peer-reviewed publications and other benchmarks relevant to the proposed research? Have the necessary collaborations been established and documented with letters of agreement?

Environment

Do the performance sites where the work will be done contribute to the probability of success? Is the scientific environment conducive to the work proposed, in terms of institutional support, physical resources and clinical and intellectual resources? Will the proposed studies benefit from unique features of the scientific environment, subject populations or collaborative arrangements? Has access to necessary research equipment, data bases and/or facilities been appropriately documented with letters of agreement? Does the application document access to the appropriate clinical/laboratory resources needed to conduct the proposed study?

Public Access/Dissemination/Attribution:

Acknowledgement: Grant recipients must acknowledge Autism Speaks (including grant #) on all publications and presentations based, in whole or in part, on data derived from the funded research. In addition, you should cite Autism Speaks support in any publicity or communication (internal or external) about the funded project. This includes press releases, interviews and oral or poster preview of data.

Public Access: Autism Speaks has adopted a public access policy for all Autism Speaks funded research. Grantees are required to retain copyright on their manuscript submissions and ensure deposit in PubMed Central so they are made publicly available no later than 12 months after initial publication. This requirement applies to all grants awarded after December 3, 2008, whether Autism Speaks funds the research in whole or in part. [Public Access Policy Guide](#)

Autism Speaks reserves the right to make information about funded grants publicly available. Funded research projects may be subject to data and resource-sharing requirements.

Miscellaneous

All awarded grantees will be required to submit to the [Autism Speaks Genetics application](#) system to get access to these datasets for analysis before funds will be released. Applicants are highly encouraged to apply early to evaluate data available and to complete the required letters and signatures to receive approval to access AGRE and/or MSSNG data. *Please note that the Grants and Genetics systems share the same database of profiles therefore one login will work for both. Please do not create two separate profiles.*

Human Subjects Certifications must be documented with a copy of an official letter of approval (or equivalent for non-US applicants) that identifies the Principal Investigator, project title and date of approval, and is signed by the Review Committee Chair or equivalent responsible institutional/government official. Prior certification for another project cannot be substituted, but can be officially amended to include the proposed project (identified by project title and Autism Speaks grant ID# for the project).

IMPORTANT: IRB (or equivalent ethical) certification is NOT required to submit an application; however, IRB (or equivalent ethical) certification must be submitted as soon as possible following official notification of an award. Autism Speaks will NOT issue any payment of a grant until this certification is received.

The first payment will be contingent upon receipt of the countersigned grant agreement letter and certification of ethics approval, if applicable. Subsequent payments are dependent on reports submitted to the online [Autism Speaks Science Grants System](#).

Contacts:

Grants Administration/Online Application/Budget Questions:

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