REQUEST FOR APPLICATIONS

Next Generation Research Grant in ASXL-Related Neurodevelopmental Diseases

FUNDED IN COLLABORATION WITH

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Next Generation Research Grant in ASXL-Related Neurodevelopmental Disorders

Funded by the American Brain Foundation and the ASXL Rare Research Endowment (ARRE) Foundation

Important Dates

RFA Opens	May 7, 2026
Applications Due	July 30, 2026 by 5:00 PM CT
Award Announcement	October 1, 2026 (anticipated)
Award and Funding Start	January 5, 2027 (anticipated)

Program Description

Neurodevelopmental disorders affect 10–15% of children in the United States and globally. Forty percent of pediatric neurodevelopmental disorders are monogenic in nature, meaning that changes in a single gene are responsible for impairments in cognition, behavior, communication, motor skills, and multiple organ systems—significantly impacting overall quality of life. Monogenic disorders offer the opportunity to study complex neurodevelopmental disease mechanisms through careful analysis of individual gene functions that underlie these conditions.

Bohring-Opitz, Shashi-Pena, and Bainbridge-Ropers Syndromes are neurodevelopmental disorders caused by mutations in the ASXL1, ASXL2, and ASXL3 genes, respectively. ASXL proteins are members of the Polycomb Repressive De-ubiquitinase (PR-DUB) complex, which serves as a key epigenetic regulator of histone ubiquitination and methylation events with far-reaching effects on downstream gene networks involved in neurodevelopment and other organ systems. Disease-causing variants in the ASXL genes are primarily heterozygous nonsense and frameshift mutations that produce severe effects across diverse organ systems, with gastrointestinal, cardiac, and neurological defects among the most prevalent and life-threatening. Deeper understanding of ASXL gene function and disease mechanisms will contribute critical knowledge toward improving brain health and the function of related organ systems throughout development.

The Next Generation Research Grant in ASXL-Related Neurodevelopmental Diseases is an Early Career Award designed to support high-risk, high-reward translational research on the ASXL genes with strong potential for clinical impact.

Funding Available

The ABF and ARRE Foundation intend to award one Early Career Award of up to USD $120,000 total over two years ($60,000 per year). This grant does not support indirect costs; all funds are expected to go directly toward the proposed project. Final budgets will be subject to review of the proposed work.

The Selection Committee reserves the right to award a lesser amount if the full funding request is deemed unjustified, and to fund additional applications should funds allow. Applicants are encouraged to leverage additional sources of funding and resources to complement, but not overlap with, the work funded through this grant.

Eligibility

Applications may be submitted by basic, translational, or clinical investigators from U.S. and international public and private non-profit entities, including universities, colleges, hospitals, and laboratories, as well as biotechnology, pharmaceutical, or other for-profit companies.

The principal investigator must hold an MD, PhD, or equivalent terminal clinical degree and be within the first five years of their first full-time faculty (or equivalent independent researcher) position at the time of application submission.

Applicants may submit only one application for this RFA. There is no limit on the number of applications submitted from a single institution.

The American Brain Foundation is committed to supporting research that incorporates a broad range of perspectives and includes study populations that reflect the full spectrum of individual affected by ASXL-related neurodevelopmental diseases. The ABF provides equal opportunities to all applicants without regard to race, religion, color, age, sex, pregnancy, national origin, sexual orientation, gender identity, genetic disposition, neurodiversity, disability, veteran status, or any other protected category under applicable law.

Research Priorities

The ABF and ARRE Foundation seek an innovative proposal that addresses a core question of ASXL disease mechanism: Does the pathogenicity of distinct ASXL variants occurring across the three genes result in gain-of-function or loss-of-function, and is the disease mechanism variant-specific?

Pathogenic variants in these genes occur almost exclusively in the final two exons of the three ASXL genes. This clustering raises the possibility that resulting mRNA transcripts may escape nonsense-mediated decay and produce truncated protein products. Some studies suggest that truncated ASXL proteins have increased stability and may act as gain-of-function variants; however, others may be pathogenic through haploinsufficiency via nonsense-mediated decay. Understanding the downstream cellular impact of these variants has significant implications for potential gene therapy or ASO-based treatment approaches.

Preferred proposals will address the impact of a spectrum of disease-relevant pathogenic ASXL variants on ASXL mRNA and protein levels and will measure the downstream impact on PR-DUB complex activity. Projects that develop, characterize, and utilize an in vitro model system for determining disease-related ASXL variant mechanisms, and devise methods to measure downstream effects with clear potential for translatability to drug screens, are strongly encouraged.

Evaluation and Selection

Applications will be reviewed by a selection committee of experts appointed by the American Brain Foundation and the ARRE Foundation. Proposals will be evaluated according to the following criteria:

- Alignment with the research priorities of this RFA
- Scientific rationale, innovation, and methodological rigor, including a well-developed and testable hypothesis and a detailed statistical plan
- Potential clinical impact and translational value
- Investigator expertise and lab team composition
- Feasibility of proposed aims, including identification of potential pitfalls and alternative approaches
- Approach to data sharing
- Potential impact across multiple disease areas or populations
- Quality and nature of mentorship, including demonstrated commitment to the applicant's training and career development

Application Instructions

All application materials must be submitted via ProposalCentral by 5:00 PM CT on July 30, 2026. Incomplete or late submissions will not be reviewed. Please do not submit materials beyond those listed below; additional materials will not be considered.

Note that funding is contingent upon receipt of all necessary institutional, ethical, and regulatory approvals (including IRB approval where applicable) prior to the award start date.

Required Materials

1. **Lay Summary**

   In 250 words or fewer, describe how the proposed project, if successful, will contribute to improved treatments and/or clinical care for people with ASXL-related disorders. This summary should be written for a non-specialist audience—imagine explaining your project to a patient's family member who has no scientific training. It may be used publicly and should not contain any confidential information.

What makes a strong lay summary:

- Write in plain language. Avoid scientific jargon, acronyms, and technical terms.
- Lead with the problem, not the methods. Start with why this research matters to patients and families, then explain what you hope to learn or accomplish.
- Be specific about impact. Don't just say the research will "advance understanding"—explain what a successful outcome would mean for diagnosis, treatment, or quality of life.
- Avoid describing your methodology in detail. The lay summary is not a mini abstract; reviewers and donors want to understand the "why," not the "how."
- Write it last. The lay summary is often stronger when written after the research plan is complete.

2. **Research Plan**

   A PDF of up to five single-spaced pages. References do not count toward the page limit. The research plan should include:

   a. A brief statement of aims summarizing the project's hypothesis, objectives, and specific aims
   b. Background and preliminary data
   c. Contemplated approaches to methodology, including potential pitfalls and alternative approaches
   d. A data sharing plan
   e. Bibliography (does not count toward page limit; DOI, PMID, or PDF link encouraged where available)

3. **Budget and Budget Justification**

   A brief budget outlining how grant funds will be spent, along with a short justification. Please note that this grant does not support indirect costs; all funds must be used directly for the proposed project. If other sources of funding support related work, please indicate whether there is any overlap with the proposed project and explain how funds from each source will be allocated.

4. **NIH Biosketch**

   A PDF of the applicant's current NIH Biosketch. Access the template here: https://grants.nih.gov/grants-process/write-application/forms-directory/biographical-sketch-common-form

5. **Letter of Support**

   The applicant's academic advisor, mentor, or lab head will receive a link via email to submit a letter of support of 1,000 words or fewer. The letter should address:

   a. How the proposed research fits into the letter writer's research program
   b. The letter writer's expertise in the proposed area of research and their anticipated time commitment to supervising and training the applicant
   c. Prior experience supervising and mentoring early-career researchers
   d. The applicant's potential for a future research career and contributions to ASXL-related neurodevelopmental diseases

   The applicant will also be asked to upload their letter writer's NIH Biosketch.

6. **Institutional Sign-Off**

   The applicant's department chair or equivalent institutional official will receive a link via email to confirm that the applicant has institutional support and adequate protected research time to carry out the proposed work. No letter is required.

Questions?

For questions about this RFA or the application process, please contact the American Brain Foundation at grants@americanbrainfoundation.org.