



SPASTIC PARAPLEGIA FOUNDATION, INC
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SPF Research Grant Program RFP Guidelines

Section #1: Who Is Spastic Paraplegia Foundation, Inc.?

Spastic Paraplegia Foundation, Inc. (SPF) was established in 2002 as a nonprofit health organization dedicated to improving the lives of individuals and families affected by **Hereditary Spastic Paraplegia (HSP)** and **Primary Lateral Sclerosis (PLS)**. Through the generosity of patients, families, caregivers, donors, and supporters, SPF invests in scientific research, education, advocacy, and collaboration with one ultimate goal: a future in which every person living with HSP or PLS is accurately diagnosed, effectively treated, and ultimately cured.

As scientific understanding of these diseases continues to advance, SPF is evolving from a traditional grant-making organization into a strategic partner in therapeutic development. In collaboration with researchers, clinicians, regulators, industry, and the global patient community, SPF seeks to accelerate the discovery, translation, and delivery of meaningful therapies by investing in research that advances a coordinated strategy toward treatments, therapies, therapeutics, and cures.

Specific goals of SPF include:

- **Supporting research that applies a pathway-focused approach** to the identification and prioritization of druggable targets in HSP and PLS.
- **Accelerate research** that advances the understanding of HSP and PLS and leads to effective treatments, therapeutics, and cures.
- **Support the development of translational research infrastructure**, including biomarkers, clinical outcome assessments, digital health technologies, and other tools that improve clinical trial readiness.
- **Educate and empower** patients, families, healthcare professionals, and researchers through conferences, educational resources, and community engagement.
- **Foster collaboration** among patients, researchers, clinicians, industry partners, regulators, and advocacy organizations to accelerate scientific discovery and therapeutic development.
- **Provide support and hope** for individuals and families affected by HSP and PLS while advancing the shared goal of improving quality of life and ultimately eliminating these diseases.

Section #2: Research Grants

Since its founding, SPF has invested in innovative research that advances scientific understanding and improves the lives of individuals living with HSP and PLS. Historically, SPF grants have provided critical support for innovative ideas, pilot studies, proof-of-concept investigations, early translational research, and established research programs that demonstrate the potential to significantly advance the field.

SPF recognizes that meaningful progress toward therapies requires investments across multiple stages of scientific discovery and therapeutic development. Accordingly, SPF may support projects ranging from exploratory studies that establish new concepts to more mature investigations that are positioned to accelerate translational research, clinical trial readiness, or therapeutic development.

Funding decisions are based on the scientific merit, innovation, feasibility, strategic importance, and anticipated impact of each proposal, together with available SPF resources. SPF's Board of Directors will consider independent scientific reviews and recommendations from qualified scientific, clinical, translational, regulatory, and other subject-matter experts, as appropriate, in determining the number of awards and funding levels that best advance SPF's overall research portfolio. Consequently, award amounts may vary depending upon the scope, quality, maturity, and potential impact of the proposed research.

SPF also encourages applicants to view SPF funding as one component of a broader research strategy. Priority will be given to proposals that demonstrate how SPF support will complement existing resources, achieve meaningful scientific milestones, and position the project for future funding from governmental agencies, industry, philanthropic organizations, or other external sources.

Today, SPF is evolving from a traditional grant-making organization into a strategic research partner that intentionally manages its investments as a coordinated portfolio designed to accelerate treatments, therapeutics, and ultimately cures for individuals living with HSP and PLS. SPF's research strategy and additional funding priorities are described in the following section.

SPF reserves the flexibility to fully fund, partially fund, or decline any proposal, and may work collaboratively with applicants to modify project scope, budget, timeline, or milestones when doing so enhances scientific value, strengthens SPF's research portfolio, or increases the likelihood of achieving meaningful therapeutic impact.

All proposals, exhibits, progress reports, and any other attachments, thereto shall be provided to SPF in the English language. It is highly encouraged that new applicants review the previously funded research at: https://sp-foundation.org/research/research-grants_issued_between_2003-2020.html.

Section #3: SPF's Research Strategy: Building a Pathway to Therapies

SPF recognizes that meaningful advances toward therapies require more than outstanding science—they require a coordinated strategy that connects biological discovery to clinical translation, regulatory readiness, and ultimately patient benefit.

SPF's research strategy is designed not only to advance scientific discovery, but to shorten the time required to translate discoveries into meaningful therapies for individuals and families living with HSP and PLS.

Although significant progress has been made in understanding HSP and PLS, important gaps remain in our knowledge of the biological mechanisms that drive disease onset, progression, and selective neuronal vulnerability. At the same time, it has become increasingly clear that progress toward clinical trials and effective therapies depends not only on understanding disease biology, but also on identifying, validating, and translating therapeutic targets into interventions that can be evaluated in patients.

Both the SPF Global Scientific & Regulatory Forum and ongoing collaboration among researchers, clinicians, regulators, industry, and patient organizations, share a vision for the future: accelerating therapies requires moving beyond individual genes and disease subtypes to gain a deeper understanding of the shared biological pathways that underlie HSP, PLS, and related neurodegenerative disorders. This pathway-based approach has the potential to identify biological processes that may be amenable to therapeutic intervention and strategies that benefit broader patient populations while strengthening opportunities for collaboration and translational research. Areas of particular interest include, but are not limited to, pathways related to axonal

degeneration, lysosomal dysfunction, cellular metabolism and trafficking, and selective neuronal vulnerability, as well as mechanisms that may be shared across multiple HSP genotypes, PLS, and/or related neurodegenerative disorders such as ALS.

Accordingly, SPF is evolving from funding individual research projects to building a coordinated research portfolio designed to accelerate therapies for individuals living with HSP and PLS. SPF seeks to invest in projects that not only advance scientific discovery, but also strengthens the therapeutic development ecosystem. Competitive proposals should clearly describe how the proposed work contributes to one or more of the following objectives:

- Advance understanding of disease biology and shared molecular or cellular pathways.
- Identify, prioritize, or validate therapeutic targets with potential for clinical intervention.
- Develop or validate biomarkers, clinical outcome assessments, or digital health technologies that improve disease measurement and clinical trial readiness.
- Support drug repurposing, therapeutic development, or other near-term clinical opportunities.
- Enable translational research that bridges laboratory discoveries to patient benefit.
- Strengthen regulatory readiness through the development of tools, datasets, methodologies, or evidence that facilitate future therapeutic development.
- Promote collaboration, data sharing, and scientific infrastructure that accelerates progress across the HSP and PLS research communities.

SPF particularly encourages proposals that investigate biological pathways shared across multiple HSP genotypes, PLS, and related neurodegenerative disorders when such work has the potential to identify broadly applicable therapeutic strategies. Innovative approaches utilizing multi-omics technologies, advanced human cellular models, artificial intelligence, computational biology, biomarker discovery, digital health technologies, and integration of existing datasets are encouraged when they strengthen the pathway toward therapeutic development.

Ultimately, SPF seeks projects that not only expand scientific knowledge and advance understanding of disease mechanisms, but also demonstrates clear promise for target identification, target validation, biomarker development, clinical outcome assessments, digital health technologies, drug repurposing, translational research, or clinical trial readiness. By supporting work that connects disease biology to actionable therapeutic strategies, SPF aims to strengthen the pipeline of potential interventions and accelerate progress toward effective treatments for individuals and families living with HSP and PLS.

Section #4: Separate PLS and HSP Grants

SPF is committed to advancing research for both HSP and PLS. These disorders each have unique scientific challenges, research opportunities, and unmet clinical needs. SPF's goal is to maintain a balanced investment strategy that supports meaningful progress across both disease communities. Accordingly, HSP and PLS proposals will generally be evaluated and ranked independently, rather than competing directly against one another for available funding.

Final funding decisions will consider scientific merit, innovation, feasibility, strategic alignment with SPF's research priorities, available funding, and each proposal's potential to advance a pathway toward treatments, therapeutics, and ultimately cures. The number and quality of proposals submitted in each portfolio may influence the final allocation of research funding in any given funding cycle.

Section #5: Publicity, Scientific Stewardship, and Confidentiality

SPF recognizes that research proposals often contain confidential scientific information. Accordingly, all grant applications, supporting materials, reviewer comments, and proposal deliberations will be treated as confidential and will be shared only with members of SPF's Scientific Advisory Board (SAB), SPF's Research Grant Committee, and SPF Officers and Board of Directors, or others as necessary to facilitate the review and evaluation process.

If a proposal is selected for funding, SPF may publicly announce the award, including the project title, principal investigator, and affiliated institution through SPF's website, Annual Report, newsletters, conference materials, press releases, social media, and other appropriate communications. Applicants are therefore requested to include both a scientific title and a second title written in language understandable to patients, families, donors, and the general public.

As a patient advocacy organization, SPF believes that communicating the impact of research is an essential part of scientific stewardship. Investigators receiving SPF funding become valued partners in helping educate and inspire the community whose generosity makes this research possible.

Accordingly, grant recipients should expect to work collaboratively with SPF throughout the award period by:

- ☐ providing periodic lay-language summaries describing research progress and its potential impact;
- ☐ participating in educational activities such as the SPF Annual Conference, webinars, SPF TALKS, or similar scientific and patient-focused programs;
- ☐ assisting with Annual Report updates and other SPF communications that demonstrate the impact of donor-supported research; and
- ☐ sharing publications, presentations, and other accomplishments arising from SPF-supported work.

SPF recognizes that every research project contributes to a larger therapeutic development pathway. Communicating both scientific progress and future opportunities helps patients, families, donors, researchers, industry, regulators, and other stakeholders better understand how individual projects collectively advance the development of treatments, therapeutics, and ultimately cures for HSP and PLS.

Section #6: Open Science, Collaboration, and Scientific Stewardship

SPF believes that accelerating therapies requires more than outstanding individual research—it requires collaboration across institutions, disciplines, patient organizations, industry, regulators, and the broader scientific community. SPF is committed to fostering an open, collaborative research environment in which scientific discoveries, tools, knowledge, and resources are leveraged to maximize their impact for individuals living with HSP and PLS.

Accordingly, SPF strongly encourages grant recipients to embrace principles of scientific collaboration, responsible data sharing, and research transparency whenever appropriate and consistent with applicable laws, institutional policies, ethical standards, and intellectual property protections. Proposals that demonstrate meaningful collaboration, integration with existing research efforts, or opportunities to build shared scientific resources will be viewed favorably during the review process.

As part of this commitment, grant recipients are expected to work collaboratively with other investigators and institutions by sharing research findings, methodologies, tools, datasets, biospecimens, and other resources

whenever doing so is reasonably expected to accelerate the development of treatments, therapeutics, and cures for HSP and PLS. SPF believes that bringing together diverse expertise, complementary technologies, and multidisciplinary perspectives will improve research efficiency, reduce unnecessary duplication, strengthen scientific rigor, and accelerate therapeutic development.

SPF recognizes that scientific progress depends upon learning from both successful and unsuccessful investigations. Accordingly, investigators are encouraged to communicate scientifically meaningful positive, negative, neutral, or inconclusive findings whenever such information may reasonably benefit the broader HSP and PLS research community.

To support these objectives, the following provisions are incorporated into the SPF Research Grant Agreement that will be signed by all grant recipients:

If a proposal is selected for funding, the applicant agrees that SPF shall have the right to utilize, summarize, publish, and share research reports, lay summaries, and other non-confidential information arising from the funded project for non-commercial scientific, educational, regulatory, patient advocacy, fundraising, and collaborative purposes consistent with SPF's mission to accelerate treatments, therapeutics, and cures for HSP and PLS.

SPF's rights to utilize and disseminate research reports and related information include supporting collaborations with academic institutions, nonprofit organizations, patient advocacy organizations, regulatory agencies, and other scientific partners, provided such use remains non-commercial and consistent with the purposes of advancing research and therapeutic development.

Nothing in the Research Grant Agreement shall be construed as transferring ownership of intellectual property or copyright to SPF. All right, title, and interest in inventions, discoveries, know-how, patents, patent applications, copyrights, software, databases, data, and other protectable intellectual property arising from the funded research shall remain with the recipient institution in accordance with its institutional policies and applicable law, except as otherwise expressly provided in the Research Grant Agreement.

Grant recipients shall retain ownership of the copyrights and other rights associated with scholarly publications, presentations, educational materials, and other copyrightable works arising from the funded research, subject to applicable publisher agreements and institutional policies. SPF may reproduce, distribute, reference, summarize, or otherwise utilize such materials for educational, scientific, patient advocacy, fundraising, and other non-commercial purposes consistent with applicable copyright law, publisher permissions, and the terms of the Research Grant Agreement. SPF views research funding as the beginning of a collaborative partnership rather than the conclusion of a grant award. SPF seeks to foster ongoing dialogue among investigators, patients, clinicians, industry, regulators, and other stakeholders to strengthen the scientific, clinical, and regulatory ecosystem needed to accelerate meaningful therapies for individuals and families living with HSP and PLS.

Section #7 Publications

All manuscripts, publications, papers, posters, and exhibits by a SPF Research Grant recipient, based on work supported by a SPF grant, must carry a credit line to Spastic Paraplegia Foundation, Inc. That credit and prominence must be commensurate with SPF's contribution as compared to other funding sources.

A copy of manuscripts, publications, papers or posters must be submitted to SPF when a paper or poster by a SPF Research Grant recipient is published or presented before a scientific or patient advocate organization based on work supported by a SPF grant award.

Section #8: Research Grant Agreement (RGA) Overview

Proposals receiving grant approval will be required to execute a RGA with SPF. The RGA will summarize the payment and reporting schedule. It will include Exhibits to be completed: when the RGA is countersigned, with interim progress reports and with the final clinical and financial report. Written progress reports are required to receive interim payments. A final clinical report and a financial report detailing the use of the funds are required to receive the final payment.

Section #9: Evaluating Proposals

SPF seeks proposals that combine scientific excellence with a clear translational pathway toward therapeutic impact. Applications will be evaluated not only on scientific merit, innovation, and feasibility, but also on their potential to advance therapeutic development, strengthen clinical trial readiness, foster meaningful collaboration, and complement SPF's broader strategic research portfolio.

Section #10: Application/Proposal Procedure

The scientific proposal shall be limited to six (6) pages, excluding the curriculum vitae (CV)/NIH Biosketch, bibliography, budget justification (if requested), and any required supporting documentation. SPF encourages applicants to use this limited space thoughtfully by clearly articulating the significance of the proposed research, its scientific and translational merit, and how it contributes to SPF's strategic pathway toward therapies for individuals living with HSP and PLS.

1. Project Title:

Provide (1) the formal scientific title; and (2) a second title written for patients, families, donors, and the general public.

2. Disease Focus:

Identify whether the proposal focuses on:

- HSP
- PLS
- Both

If HSP, identify the relevant SPG gene(s), molecular pathway(s), or indicate whether the work addresses multiple genetic forms.

3. Primary Area(s) of Impact:

To assist SPF in managing a balanced research portfolio and evaluating how proposed projects contribute to the therapeutic development pathway, (1) identify the one or two primary areas that best describe the focus of your proposal (check the boxes below or include a brief summary on the "Other" line), and (2) briefly explain (2–3 sentences) why you selected these area(s) and how they represent the primary impact of your proposal.

Discovery Science

- ☐ Disease Mechanisms / Biology
- ☐ Shared Biological Pathways

Therapeutic Discovery

- ☐ Therapeutic Target Identification
- ☐ Therapeutic Target Validation
- ☐ Drug Repurposing or other near-term clinical opportunities
- ☐ Small Molecule Therapeutics
- ☐ Gene Therapy / RNA Therapeutics

Translational Science

- ☐ Biomarkers
- ☐ Clinical Outcome Assessments
- ☐ Digital Health Technologies
- ☐ Clinical Trial Readiness

Research Infrastructure

- ☐ Natural History
- ☐ Patient Registries / Data Integration
- ☐ Development of tools, datasets methodologies or evidence that facilitate therapeutic development
- ☐ Collaboration and data sharing amongst the scientific community
- ☐ Artificial Intelligence / Computational Biology
- ☐ Translational Research Platforms

Other _____

4. Specific Aims:

Summarize the project's major scientific objectives, requested budget, and proposed timeline.

In addition, briefly address the following:

- **Scientific Aim(s):** What are the primary biological or clinical questions your research is designed to answer?
- **Biological Pathway(s):** Identify the molecular, cellular, physiological, or disease pathway(s) being investigated. If applicable, describe whether these pathways are shared across multiple HSP genotypes, PLS, or related neurodegenerative disorders.
- **Therapeutic Relevance:** Describe how achieving these aims will improve understanding of disease mechanisms, identify or validate therapeutic targets, support biomarker or endpoint development, advance drug repurposing, strengthen clinical trial readiness, or otherwise contribute to the therapeutic development pathway.
- **Expected Deliverables:** Describe the key scientific, translational, or technical deliverables anticipated at the completion of the project (for example, target validation, biomarker identification, datasets, animal or cellular models, therapeutic candidates, clinical outcome assessments, digital health technologies, publications, or other resources that will advance the field).

5. Background and Significance:

Describe the scientific rationale and significance of the proposed work.

6. Research Design and Methods:

Describe the experimental approach, methodologies, statistical analyses, and, where appropriate, power or sample-size calculations.

7. Budget and Resources:

Describe available facilities and both specify and justify the requested budget. Detail the desired budget timeframe and steps you will take to minimize the need for extensions. All amounts must be in US dollars. Indirect costs, major equipment purchases, conference travel, and Principal Investigator salary are not allowable expenses.

8. Funding Landscape and Leverage:

Identify all current, pending, or anticipated funding sources that support, or may support, the proposed research. Include funding that has been awarded, is under review, or is planned for submission to other governmental agencies, foundations, nonprofit organizations, industry partners, or other sponsors.

Describe briefly how SPF funding would complement these efforts and whether the proposed work represents:

- a stand-alone project;
- one component of a larger research program;
- pilot or preliminary work intended to support future funding applications (e.g., NIH, DoD, industry, or other foundations); or
- a project submitted concurrently to other funding organizations.

Applicants should clearly identify any overlap between this proposal and applications submitted elsewhere. If funding from another source is awarded for substantially the same scope of work before an SPF funding decision is made, applicants are expected to promptly notify SPF so that SPF may evaluate whether revisions to the proposed scope, budget, or funding allocation are appropriate. SPF encourages investigators to leverage SPF funding to attract additional research support; however, transparency regarding complementary funding sources is essential to ensuring appropriate stewardship of donor contributions and strategic portfolio management.

9. Therapeutic Development Strategy

Describe how your project contributes to SPF's pathway toward therapies. Specifically address:

- where your work fits within the therapeutic development pathway;
- the anticipated next scientific or clinical milestones;
- opportunities for translation, biomarker development, clinical outcome assessments, digital health technologies, drug repurposing, or clinical trial readiness, where applicable;
- the long-term vision for advancing this work toward patient benefit; and
- your strategy for obtaining future funding beyond the SPF award.

10. Collaboration and Strategic Leverage:

Describe existing or planned collaborations and explain how they strengthen the scientific, translational, and clinical impact of the proposed work.

Identify opportunities to leverage complementary expertise, infrastructure, datasets, biospecimens, funding, patient organizations, industry partners, or international initiatives that could accelerate therapeutic development.

If applicable, describe how SPF funding would increase the impact of the project beyond what any single funding organization could accomplish independently.

11. Programmatic Impact:

Provide a concluding summary (approximately one page) describing:

- how your overall research program advances understanding of HSP and/or PLS;
- how this proposal builds upon your previous work;
- how the project aligns with SPF's strategic research priorities; and
- the anticipated impact on patients over both the short and long term.

Investigators are encouraged to discuss development of animal models, cellular models, biomarkers, therapeutic targets, digital health technologies, computational approaches, translational tools, or other resources that strengthen the broader research community.

12. Curriculum Vitae:

Provide NIH Biosketches or Curriculum Vitae for key personnel together with a bibliography.

Email your proposal to Research@SP-Foundation.org. If you have not received acknowledgement within five (5) business days, please re-submit the proposal.