

# FROM PATIENT VOICES TO SCIENTIFIC PROGRESS

## A Message from Our Leadership

### *Report from the President and Executive Director*

For the Spastic Paraplegia Foundation, 2025 was a year of remarkable generosity, growing scientific opportunity, and renewed urgency. It was also a year in which the voices of people living with Hereditary Spastic Paraplegia and Primary Lateral Sclerosis helped guide our mission more directly than ever before.

For more than two decades, SPF has worked to fund medical research, educate and connect families, and support a worldwide community affected by HSP and PLS. These diseases may be rare, but the challenges they create are deeply personal and life-changing. Every loss of mobility, unanswered medical question, delayed diagnosis, and barrier to participating in research reminds us why our work cannot wait.

During 2025, SPF continued investing in research conducted by universities, medical centers, and scientific institutions seeking to understand the causes of HSP and PLS and identify meaningful pathways toward treatments. We also strengthened our support for natural-history research, biomarker development, clinical-trial readiness, patient data collection, and collaborative research networks.

One of the year's most important accomplishments was the 2025 SPF HSP/PLS Patient History Survey. Over 800 patients and caregivers shared their experiences with diagnosis, symptoms, progression, mobility, medical care, financial burden, employment, emotional health, treatment priorities, and participation in research. Their responses provide far more than statistics. Together, they document the unmet needs of our community and help SPF communicate those needs to researchers, clinicians, regulators, industry partners, and other decision-makers.

The year also reinforced an important lesson: promising science alone is not enough. Research must be supported by reliable patient data, meaningful outcome measures, validated biomarkers, shared research standards, strong clinical networks, and a clearer understanding of what matters most to patients. SPF's responsibility is,

therefore, evolving beyond funding individual research projects. We must also help connect those projects into a coordinated roadmap that can move discoveries from the laboratory toward clinical studies and, ultimately, treatments.

None of this work would be possible without the dedication of our donors, volunteers, Board members, medical and scientific advisors, researchers, clinicians, ambassadors, support-group leaders, and families. SPF remains a deeply volunteer-driven organization. Countless hours are contributed each month to patient support, research coordination, fundraising, communications, conferences, financial administration, educational programming, and community outreach.

We are especially grateful to every person and family who supported SPF through a donation, memorial or tribute gift, fundraising event, planned gift, sponsorship, volunteer commitment, survey response, or personal story. Every contribution—whether financial, scientific, organizational, or personal—helps move our mission forward.

We ended 2025 with tremendous momentum and an even clearer responsibility: to transform hope into a coordinated plan of action. Our mission remains constant, but our strategy must continue to mature as science and regulatory expectations advance.

Together, we are building more than a collection of promising research projects. We are building the scientific, clinical, regulatory, and patient-centered foundation required to accelerate meaningful therapies and treatments for HSP and PLS.

With gratitude and determination,

*Greg Pruitt*  
President

*Norma Pruitt*  
Executive Director

Spastic Paraplegia  
Foundation, Inc.



# STEWARDING EVERY DOLLAR TOWARD HOPE

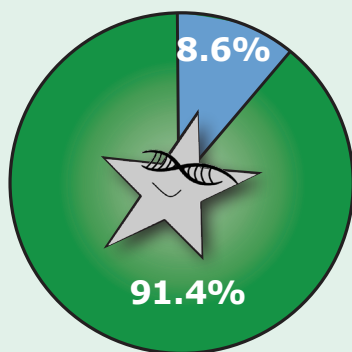
## 2025 Financial Overview

The extraordinary generosity of the SPF community allowed the Foundation to raise \$1,590,580 during 2025, bringing SPF remarkably close to its ambitious \$1.6 million fundraising goal.

This accomplishment represents far more than a financial milestone. It reflects the confidence of patients, families, donors, volunteers, sponsors, and community partners who believe scientific progress is possible—and who trust SPF to use their contributions responsibly in pursuit of treatments and cures for HSP and PLS.

### Financial Activities

### Where your dollars go



**91.4% Mission**

**8.6% Management and Administration**

### REVENUE

|                                        | 2025             | 2024             |
|----------------------------------------|------------------|------------------|
| Donations .....                        | 1,590,580        | 1,597,571        |
| Donated Services .....                 | -                | 43,400           |
| Program Fees & Products .....          | 32,940           | 37,315           |
| Interest and Investment Income .....   | 132,244          | 99,959           |
| Other income .....                     | -                | 5,684            |
| <b>Total Support and Revenue .....</b> | <b>1,755,765</b> | <b>1,783,929</b> |

### DIRECT EXPENSES

|                                                                   |           |         |
|-------------------------------------------------------------------|-----------|---------|
| Management and General .....                                      | 86,864    | 81,604  |
| <i>(including non-cash Donated Professional Services Expense)</i> |           |         |
| Fundraising .....                                                 | 64,285    | 37,811  |
| Program Expense - Education .....                                 | 146,405   | 213,750 |
| <i>(excluding grants)</i>                                         |           |         |
| Program Expense - Grants Awarded .....                            | 1,121,008 | 602,174 |

**Mission..... 91.4%..... 93.3%**

**Mgmt./Admin./Fundraising ..... 8.6%..... 6.7%**

**Total Non-Grant Expenses ..... 297,554..... 333,165**

**TOTAL ASSETS..... 3,551,338,..... 3,089,987**

**TOTAL LIABILITIES\* ..... 1,334,188..... 1,210,040**

**NET ASSETS (as of December 31)..... 2,217,150..... 1,879,947**

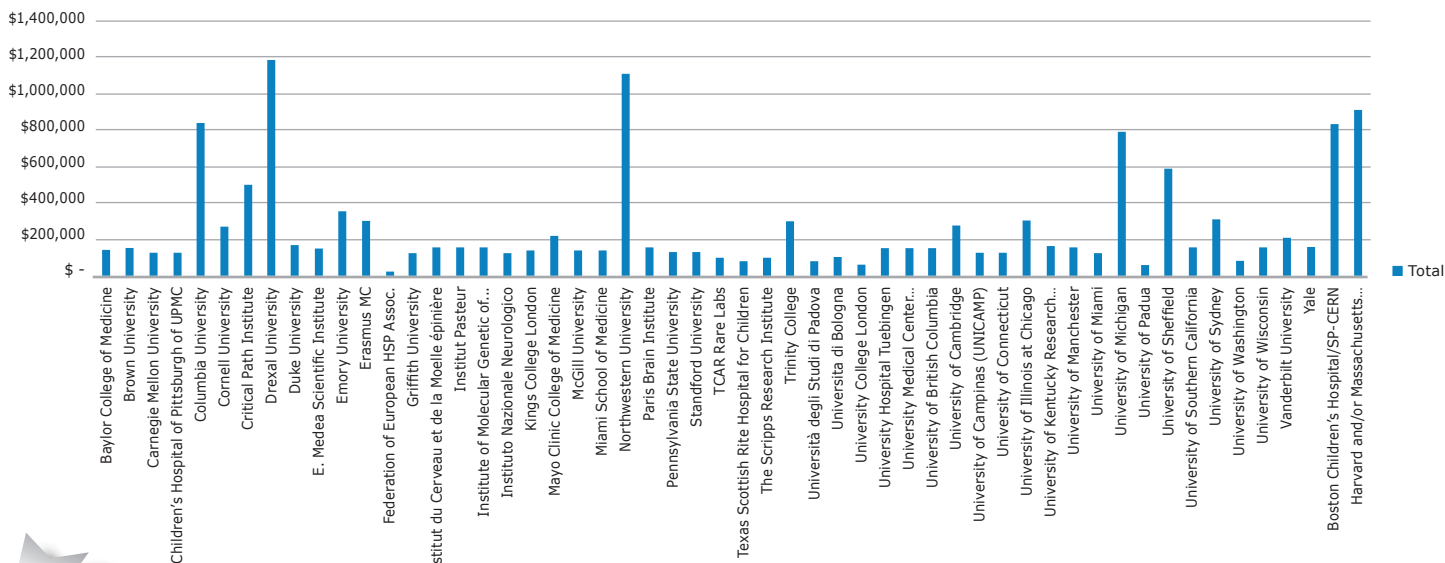
**\*GRANTS PLEDGED ..... 1,329,111..... 1,194,086**  
*(Included in Total Liabilities)*

**Grants Pledged as % of Assets ..... 37.4%..... 38.6%**

**NOTE:** SPF publishes annual audited financial statements and the IRS form 990 on our website as the information is finalized. To ensure complete transparency, the presentation above reflects categorization consistent with the audited financial statements. This information was provided by SPF Treasurer, Lorri Steiner.

## Building a Global Infrastructure Across the Research Ecosystem

### Grants by Institution



## *Fueling Discovery Through Generosity Fundraising and Development Priorities*

Every research grant, patient program, educational resource, scientific meeting, and collaborative initiative supported by SPF begins with generosity.

During 2025, donors responded with extraordinary commitment. Families organized grassroots events, individuals made gifts in honor or memory of loved ones, businesses provided sponsorships, and longtime supporters continued standing beside the Foundation. These contributions brought SPF close to its \$1.6 million annual fundraising goal and strengthened our ability to plan for future research opportunities.

SPF's fundraising model is deeply personal. Many donors are themselves living with HSP or PLS, caring for someone affected, or honoring a family member whose life was changed by one of these diseases. Their gifts carry both hope and expectation: hope that scientific progress is possible and an expectation that SPF will steward every contribution responsibly.

### *Building Relationships, Not Simply Raising Funds*

Fundraising is not limited to asking for donations. It also includes thanking supporters, reporting the impact of their gifts, maintaining accurate donor records, listening to families, reconnecting with past supporters, developing sponsorship opportunities, and helping people find meaningful ways to participate in the mission.

During the year, SPF continued strengthening both direct fundraising activities and the infrastructure that supports long-term development. This work included:

- ★ Donor stewardship and acknowledgment
- ★ Sponsorship development
- ★ Memorial and tribute giving
- ★ Community-led fundraising events
- ★ Annual and year-end campaigns
- ★ Planned and legacy giving
- ★ Database improvement and record standardization
- ★ Financial reporting and donation reconciliation.
- ★ Improved campaign and donor communications
- ★ Development of reusable fundraising and marketing materials

Community events remain an important part of SPF's fundraising story. They bring people together, introduce new supporters to the mission, honor those affected by HSP and PLS, and turn personal determination into collective action.

**WE DID IT  
TOGETHER!**



## *Responsible Financial Stewardship*

SPF's financial priorities remain grounded in three responsibilities:

Investing in credible research directed toward treatments and cures for HSP and PLS.

Supporting patient education, engagement, conferences, advocacy, and community programs.

Maintaining the financial and organizational infrastructure required to manage donor resources responsibly and transparently.

SPF predominantly funds research proposals received from universities, medical schools, hospitals, and other qualified scientific institutions. These investments support disease-mechanism studies, translational research, natural-history studies, biomarker development, outcome measures, clinical-trial readiness, rehabilitation approaches, and other work that may help move HSP and PLS closer to meaningful treatments.

In addition to research grants, Foundation resources support the Annual HSP/PLS Patient and Family Conference, SPF TALKS, educational resources, scientific meetings, patient outreach, research participation, advocacy, fundraising programs, and the administrative systems necessary to operate responsibly.

SPF remains a deeply volunteer-driven organization. Most of the Foundation's work is performed by Board members, volunteers, patients, caregivers, ambassadors, and community leaders who contribute many hours each month. Limited professional assistance is used for specialized responsibilities such as accounting, financial reporting, development and fundraising, conference operations, and essential organizational support.

SPF remains committed to making its financial information available to the public. Independently prepared financial statements, annual reports, IRS Form 990 filings, and other governance information are available on SPF's website.

Every dollar entrusted to SPF carries the hopes of people and families living with progressive diseases. The Foundation's responsibility is not merely to spend those dollars carefully, but to place them where they can create the greatest possible opportunity for scientific progress and meaningful patient benefit.



## Preparing for Sustainable Growth

As SPF's scientific opportunities expand, fundraising must grow with them. The Foundation's future development strategy will focus on building a broader and more sustainable base of support while preserving the personal relationships that have always defined SPF.

Priorities include cultivating individual donors, strengthening stewardship, expanding corporate and institutional partnerships, pursuing appropriate grants and sponsorships, developing planned-giving opportunities, supporting community fundraisers, and improving the systems used to measure and communicate donor impact.

This work is not the responsibility of one person. Sustainable fundraising requires shared participation among leadership, the Board, staff, volunteers, patients, families, researchers, and community partners. Every person may contribute differently—through giving, introducing a potential partner, sharing SPF's story, hosting an event, thanking a donor, volunteering a skill, or helping another family understand why research support matters.

SPF is profoundly grateful to everyone who invested in the mission during 2025. Your generosity is helping build the bridge from scientific discovery to meaningful treatments.

## A Growing Record of Research Investment

The historical research perspective presented during the 2026 Annual Conference demonstrates how steadily SPF's scientific impact has grown. During its first decade, the Foundation awarded approximately \$3 million in research grants. By 2022, that investment had surpassed \$7.5 million. Through the 2025 research cycle, SPF had awarded 103 research grants totaling \$13,705,317 since its founding in 2002.

These numbers tell an important story. What began as a small, volunteer-driven organization created by patients and families has become one of the most consistent nonprofit funders of research devoted specifically to HSP and PLS.

*SPF's research grants have helped scientists:*

- ★ Generate preliminary evidence needed to pursue larger NIH and institutional awards.
- ★ Establish disease models and investigate genetic and cellular mechanisms.
- ★ Study upper motor-neuron vulnerability and degeneration.
- ★ Explore therapeutic targets, drug repurposing, gene-based strategies, and neuroprotective approaches.
- ★ Build natural-history studies, biomarkers, biospecimen collections, and outcome measures.
- ★ Prepare the HSP and PLS fields for future clinical trials.

The value of these grants therefore extends beyond the amount initially awarded. SPF funding frequently serves as the seed that allows a researcher to test a new idea, produce essential preliminary data, attract collaborators, publish findings, and compete for substantially larger public or private investments.

## The 2025 Research Funding Cycle

The 2025 grant cycle revealed both extraordinary scientific momentum and the continuing gap between available research opportunities and the resources needed to support them.

SPF received **36 research proposals requesting approximately \$4.87 million**. Following scientific and organizational review, SPF approved an initial allocation of approximately **\$764,000 to support six projects** addressing PLS natural history, extracellular-vesicle research, noninvasive spinal-cord neuromodulation, SP-CERN infrastructure, SPG4 drug discovery, and combination therapy for SPG4.

The difference between the nearly \$4.9 million requested and the \$764,000 initially available for awards is one of the year's most significant revelations. It shows that the scientific community is increasingly prepared to investigate HSP and PLS, but many potentially valuable projects remain unfunded—not because they lack merit, but because available resources cannot yet meet the opportunity.

This gap gives SPF both a challenge and a mandate: to grow fundraising capacity while becoming increasingly strategic about which investments can produce the greatest scientific leverage and patient impact. ★

### Building the Scientific Foundation:

*103 Research Investments since 2003*

More than \$13.7 million invested across 103 research awards, helping build the scientific knowledge, global collaborations, and infrastructure that now support therapeutic development.

#### Awards by Year and Amount

| Year               | Count per year | Sum of Grant Amount |
|--------------------|----------------|---------------------|
| 2003               | 2              | \$80,000            |
| 2004               | 2              | \$180,000           |
| 2005               | 5              | \$512,930           |
| 2006               | 4              | \$422,070           |
| 2007               | 3              | \$333,561           |
| 2008               | 4              | \$403,935           |
| 2009               | 2              | \$240,000           |
| 2010               | 4              | \$432,952           |
| 2011               | 5              | \$600,000           |
| 2012               | 3              | \$360,000           |
| 2013               | 1              | \$200,000           |
| 2014               | 5              | \$600,000           |
| 2015               | 6              | \$815,955           |
| 2016               | 5              | \$601,450           |
| 2017               | 6              | \$900,000           |
| 2018               | 4              | \$583,998           |
| 2019               | 6              | \$900,000           |
| 2020               | 6              | \$771,000           |
| 2021               | 8              | \$1,061,209         |
| 2022               | 7              | \$1,414,438         |
| 2023               | 6              | \$1,078,000         |
| 2024               | 6              | \$764,000           |
| 2025               | 3              | \$449,819           |
| <b>Grand Total</b> | <b>103</b>     | <b>\$13,705,317</b> |

# OUR RESEARCHERS: PROGRESS WITH PURPOSE

For this Annual Report, each SPF-funded researcher was asked to reflect on three questions that matter most to patients and families: 1. What problem is your research trying to solve? 2. How does this research move the field one step closer to therapies? 3. What have you accomplished so far, and what are the next major milestones? Their answers demonstrate something important: progress does not come from a single discovery, laboratory, gene, or research project. It comes from connecting discoveries—understanding disease mechanisms, identifying shared biological pathways, developing biomarkers and outcome measures, building natural-history data, testing potential interventions, and preparing promising science to move toward clinical studies. Each project represents an important piece of that larger journey.



Critical Path Institute (C-Path) brings the scientific and regulatory expertise needed to translate research in HSP and PLS

to solutions that advance therapeutic development. Applying a regulatory lens to research paves the way for successful clinical trials and derisks drug development for researchers and industry. What makes the SPF-C-Path partnership unique is that it combines SPF's deep understanding of the lived experience and priorities of individuals and families with C-Path's expertise in data standards, clinical outcomes, translational research, biomarkers, and regulatory science. Together, we are creating a neutral, collaborative environment where key stakeholders can align around shared goals, improve the impact of research, and accelerate progress toward new therapies. This model ensures that patient priorities remain central while also creating a more coordinated research ecosystem and accelerating the path from discovery to treatments.

During the past year, SPF and C-Path collaborated to convene a Global Regulatory and Scientific Forum, which brought together scientific and medical experts, drug development and regulatory expertise, and the patient community to align on key research priorities in HSP and PLS. The outputs of this meeting will directly inform an updated scientific investment strategy for SPF. C-Path has also identified available clinical research datasets and is working on compiling the data into a central repository (RDCA-DAP). Separately, C-Path's Translational Therapeutics Accelerator provided \$150,000 to support translational research, providing scientific and regulatory guidance to researchers developing a novel small molecule treatment for HSP. Over the next year, C-Path will support SPF in finalizing a new Scientific Strategy that drives strategic and measurable progress toward treatments for HSP and PLS.



Hereditary Spastic Paraplegia (HSP) linked to SPG4 can occur when a genetic mutation leads to a lack of a crucial protein called SPASTIN. In our specific project, the patient's mutation causes a process known as Nonsense-Mediated Decay (NMD), which effectively destroys the mutated genetic instructions before the body can use them. Because of this decay, the patient only produces half the normal amount of SPASTIN from their one remaining healthy gene—a condition scientists call haploinsufficiency. This shortage of SPASTIN protein is what drives the pathology and symptoms of the disease. Our research aims to solve this problem by finding a way to safely boost the output of the healthy gene. We are actively searching for a small molecule drug capable of "upregulating," or increasing the activity of, the patient's remaining functional SPG4 allele. By compensating for the missing SPASTIN protein, we hope to address the root cause of this specific form of HSP. Ultimately, correcting this underlying protein deficiency could help alleviate the symptoms that patients navigate daily.

This research accelerates the path to therapeutic solutions in two critical ways. First, our screening process specifically utilizes a library of over 3,000 FDA-approved small molecule drugs. Because these compounds have already been evaluated and approved for human use, they possess established safety profiles. If we successfully identify a therapeutic candidate that effectively boosts SPASTIN production, the timeline to transition that drug into clinical translation for HSP patients is drastically shortened compared to developing a completely novel drug. Second, this work contributes to a broader, scalable strategy for tackling similar genetic conditions. By combining our current findings in SPG4 with our ongoing work in SPG11, we are actively striving to develop a comprehensive platform approach. This platform could ultimately be applied to address various Lysosomal disorders being studied within the SP community. By establishing a reliable pipeline for patient-derived cell engineering and automated drug screening, we are creating a reproducible roadmap that moves the entire field closer to targeted, effective therapies.

We have achieved several critical milestones in preparing our patient-derived cell models. First, we successfully collected patient blood samples and reprogrammed them into Induced Pluripotent Stem Cells (iPSCs). Next, we used CRISPR/Cas9 technology to successfully insert a highly sensitive HiBiT tag into the remaining healthy SPG4 allele, allowing us to accurately measure endogenous SPASTIN levels without disrupting normal cell function. Currently, these engineered cells are being differentiated into

*Continued on next page*

Neural Stem Cells (NSCs) and cryopreserved in a bank to ensure a uniform source for our upcoming assays. Over the next month, we will transfer the banked NSCs to our screening partner. In the next 3 to 4 months, we will run the drug repurposing screen, treating the cells with 3,000+ FDA-approved compounds for a 72-hour soak. We will utilize the Opera Phenix Plus, an AI-controlled confocal microscope, for automated readout and data analysis of SPASTIN expression. In 4 to 6 months, we will advance a shortlist of successful "hits" for further testing on patient cell lines. This will involve dose-response testing and toxicity profiling in mature, patient-derived neurons.

The Spastic Paraplegia Foundation's (SPF) support has been instrumental in advancing our therapeutic pipeline and expanding our research capabilities. Primarily, SPF's backing has provided us with invaluable collaborative partners within the broader SP community. This collaborative network is essential for sharing insights, accessing specialized resources, and ensuring our research remains closely aligned with patient needs. Furthermore, this support has directly enabled the highly technical work required for our SPG4 small molecule screen. From the initial cellular reprogramming and complex CRISPR mutagenesis to the impending automated high-throughput screening, SPF's foundation has made these crucial scientific

milestones a reality. Beyond our immediate focus on SPG4, the foundation's support also holds the significant potential to further our ongoing findings and treatments regarding SPG11. Ultimately, this partnership has provided the necessary foundation for further research and science within SPG4 and related conditions, bringing us much closer to viable treatments.

# YOU CAN Make a Difference

## WAYS TO SUPPORT SPF

There are many ways to support the SPF mission. Find the one that's right for you.

### GIVE

One-Time Gifts • Partners in Hope  
Tribute Gifts

Make a gift today or provide ongoing support through monthly or quarterly giving.

### PLAN

Estate Gifts • Stock & Securities  
Matching Gifts

Extend your impact through planned giving, appreciated assets or your employer's matching gift program.

### ENGAGE

Fundraise • Sponsor • Advocate

Create your own fundraiser, introduce SPF to a potential corporate partner, or help raise awareness in your community.

### PARTICIPATE

Volunteer • Ambassador • Committees

Your time, talents and connections can be every bit as valuable as a financial contribution.

*Together,*  
we move closer to a future without HSP and PLS.

The Spastic Paraplegia Foundation is your foundation. We need the support of everyone to fund research toward treatments and ultimately a cure for HSP and PLS.

From Giving Tuesday and year-end giving to personal fundraisers and special events, there is always a way to get involved.

*Every gift. Every action. Every voice.*  
Moves our mission forward.

#### YOUR SUPPORT. YOUR WAY. OUR MISSION.

Education • Support • Research

Thank you for being part of the SPF community. *Together, we bring hope to life.*

The Spastic Paraplegia Foundation is your foundation. We need the support of everyone here, virtually, and in your communities to fund research toward treatments and ultimately a cure for HSP and PLS.

Learn more and explore all the ways you can make a difference.

[sp-foundation.org](https://sp-foundation.org)

Scan to give or get involved!

6

2025 Annual Report – Spastic Paraplegia Foundation



### What problem is your research trying to solve?

Our proposal aims to develop and implement a novel combinatory therapy approach for Hereditary Spastic Paraplegia Type 4 (HSP-SPG4) by targeting both neurodegenerative and regenerative pathways. Using established mouse and organoid

models, we aim to isolate the mechanism through which we can halt the harmful degeneration process while reinforcing the much-needed regeneration pathway to help improve quality of life. In addition, we also aim to learn from spinal cord injury treatment regiments, such as the well-studied activity-based rehabilitation (ABR), and utilize that on our mice models to determine potential combinatorial beneficial effects and inform treatment approaches for SPG4. Our work will help establish a novel treatment regimen with combinatorial drugs as well as establish the potential of ABR in SPG4 in both individual as well as combinatorial roles.

### How does this research move the field one step closer to therapies?

This integrated strategy is expected to yield mechanistic insight into disease modification and provide a strong foundation for the future clinical repurposing of Vorinostat for HSP-SPG4 and potentially other types of HSPs. In addition, the ABR approach will be critically analyzed as a combinatorial supplement to treatment regiments identified in the future. If successful, this project could lay the groundwork for first-in-class, disease-modifying interventions in SPG4 and open new avenues for treating other Corticospinal Motor Neuron (CSMN) (aka upper motor neuron) relevant disorders. This study will help in identifying pharmacodynamic biomarkers, defining therapeutic windows, and demonstrating corticospinal tract (CST) specific structural and functional rescue. Importantly, this is not simply a two-year research project; instead,

it is a strategic continuation of a long-term vision to elucidate the cellular and molecular mechanisms of CST degeneration in HSP-SPG4 and to translate those insights into safe, mechanism-based treatments.

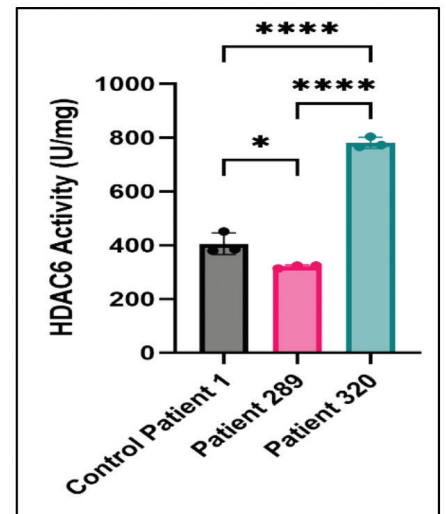
### What have you accomplished so far and what are the next major milestones?

During the current funding period, we have successfully

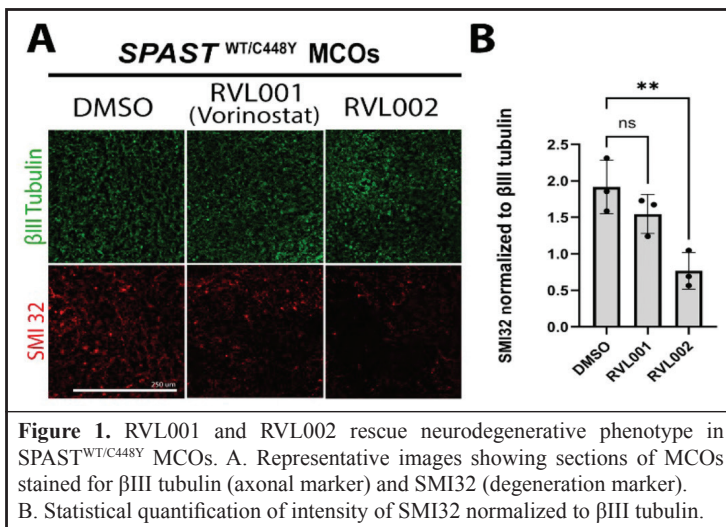
established and are actively expanding the SPAST<sup>WT/C448Y</sup> and SPAST<sup>WT/KO</sup> mice colonies and are preparing to use parent/breeding pair to generate the double heterozygous (dHet) population. From which we will focus on further expanding that colony to get the required number of mice for the experiment. In the meantime, we have performed preliminary dosage and neurodegenerative phenotyping on motor cortical organoids (MCOs) carrying SPAST<sup>WT/C448Y</sup> (a specific SPG4 mutation). We found that when these organoids were treated with Vorinostat at 5μM (drug concentration) and RVL002 (undisclosed compound developed by Unravel Inc.) at 1μM (drug concentration), for 7 days, we noticed a reduction in SMI32 (an early axon degeneration marker) marked neurodegeneration (Figure 1). Interestingly, although both RVL001 and RVL002 show reduction in SMI32 intensity, RVL002 showed significantly higher potency in rescuing the neurodegenerative phenotype seen in the SPAST<sup>WT/C448Y</sup> MCOs.

As mentioned in the progress summary, we have decided to include a new set of organoid models for the proposed study. We have had the opportunity to receive fibroblasts from people carrying the prominent pediatric mutation SPAST<sup>WT/R499H</sup>. These serve as better models since they carry the pathogenic mutation in addition to the person's genomic background, making it a more robust pre-clinical human model for SPG4. We have now established human induced pluripotent stem cell (hiPSC) lines from these fibroblasts. In addition, we established that the new SPAST<sup>WT/R499H</sup> MCOs show the same histone deacetylase 6 (HDAC6) hyperactivation seen with the SPAST<sup>WT/C448Y</sup> MCOs at 3-month time point (figure 2).

Ongoing studies include experiments involving dose response curve, toxicity analysis of RVL001 and RVL002 and time point analysis to determine the best time frame for treatment regimen utilizing both the SPAST<sup>WT/C448Y</sup> MCOs as well as the SPAST<sup>WT/R499H</sup> MCOs. We also expect to start



**Figure 2.** Patient derived MCOs – 289 and 320 – carrying the SPAST<sup>WT/R499H</sup> mutation, show HDAC6 hyperactivation similar to SPAST<sup>WT/C448Y</sup> MCOs.



**Figure 1.** RVL001 and RVL002 rescue neurodegenerative phenotype in SPAST<sup>WT/C448Y</sup> MCOs. A. Representative images showing sections of MCOs stained for βIII tubulin (axonal marker) and SMI32 (degeneration marker). B. Statistical quantification of intensity of SMI32 normalized to βIII tubulin.

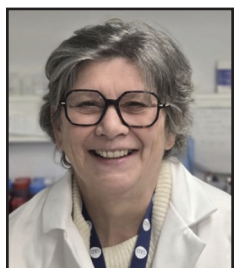
establishing gait defects/ catwalk training experiments with the dHet mice and start the treatment regimen on them as well.

Support from the Spastic Paraplegia Foundation has been and continues to be pivotal in advancing our research mission. Dr. Qiang received a previous SPF funding in 2020, which directly enabled the publication of three original research articles and two review papers focused on HSP-SPG4. Building on this foundation, our latest findings on HDAC6 inhibition in HSP-SPG4 have been published through peer review at Cell Reports (PMID: 41739645). He received the current SPF funding at the end of 2025. SPF's investment has allowed his team to establish innovative human and mouse disease models and generate compelling proof-of-concept data that now underpin multiple NIH R21 and R01 submissions focused on combinatorial therapeutic strategies. With continued support from SPF, his team aim to bridge basic discovery and clinical application, moving closer to meaningful disease modification and improved outcomes for individuals living with HSP-SPG4.



### **Florence Rage, PhD | Institute of Molecular Genetics of Montpellier**

#### ***Decoding Neuronal Network Dysfunction and Extracellular Vesicle Signatures in Primary Lateral Sclerosis***



Primary Lateral Sclerosis (PLS) is a rare, progressive disease that damages the nerve cells in the brain responsible for sending movement signals to the body. Over time, this leads to increasing stiffness and loss of muscle control, profoundly affecting a person's independence. Despite its serious impact, PLS remains poorly understood, there

is currently no treatment that can slow or stop its progression, and scientists still don't fully know what goes wrong at the cellular level to cause the disease.

**What problem is your research trying to solve?** Our research aims to close this gap by growing living models of the affected nerve cells directly from PLS patients' own cells in the laboratory. This allows us to observe, for the first time, how these cells communicate, misfire, and break down insights that simply cannot be gathered from patients directly. We are especially focused on tiny cellular "messengers" called extracellular vesicles, which may carry signals between cells and contribute to disease spread, a mechanism never before studied in PLS. By understanding these fundamental processes, we hope to uncover why PLS develops and identify meaningful starting points for future treatments, bringing real hope to patients and families currently facing this disease with no therapeutic options.

This project strengthens several key steps on the path toward effective PLS therapies. First, by creating patient-derived nerve cell models and measuring their electrical activity, we are generating the first detailed picture of how PLS neurons actually dysfunction (filling a major gap), since this has never been characterized before. This foundational biology is essential before any targeted treatment can be designed.

Second, we are conducting the first-ever investigation of extracellular vesicles in PLS. In related diseases like ALS, these cellular messengers have been shown to spread harmful proteins and genetic material between cells, and they've become promising targets for both biomarkers and new therapies. If similar patterns exist in PLS, this could open an entirely new avenue for treatment development and for tracking disease progression through simple biological samples representing an important step toward better clinical trial design.

Third, our combined use of patient stem cells, engineered "organ-on-chip" devices, and gene activity profiling gives us a versatile platform that can later be used to test how nerve cells respond to potential drugs, directly supporting future drug screening and repurposing efforts. Altogether, this work builds the essential biological knowledge and technical tools needed before therapies can realistically be developed and tested in PLS patients.

#### **How does this research move the field one step closer to therapies?**

To date, we have successfully established co-cultures combining two types of nerve cells relevant to PLS (cortical neurons and motor neurons) grown together on specialized microfluidic devices that mimic how these cells connect in the body. Using advanced imaging techniques, we have already recorded and mapped patterns of activity and communication between these cells, confirming that our system faithfully captures key features of a functioning nerve circuit. We have also built a 16-chip recording platform capable of monitoring electrical activity across many samples simultaneously, and initial testing with related motor neuron disease cells has already revealed detectable abnormalities.

#### **What have you accomplished so far and what are the next major milestones?**

Over the next 12–24 months, our major milestones include: growing and characterizing nerve cells directly from PLS patients; comparing gene expression between PLS and healthy cells to spot early warning signs of disease; recording the electrical activity patterns specific to PLS nerve cells for the first time; and isolating and analyzing extracellular vesicles from these cells to determine whether they carry harmful signals, as seen in ALS. Together, these milestones will provide the field's first comprehensive, multi-layered picture of PLS at the cellular level, a critical foundation for identifying future treatment targets and biomarkers.

SPF's investment allows us to take on a disease that has historically been overlooked in research due to

# Noninvasive Spinal Cord Neuromodulation

## to Enhance Motor Function in Hereditary Spastic Paraplegia

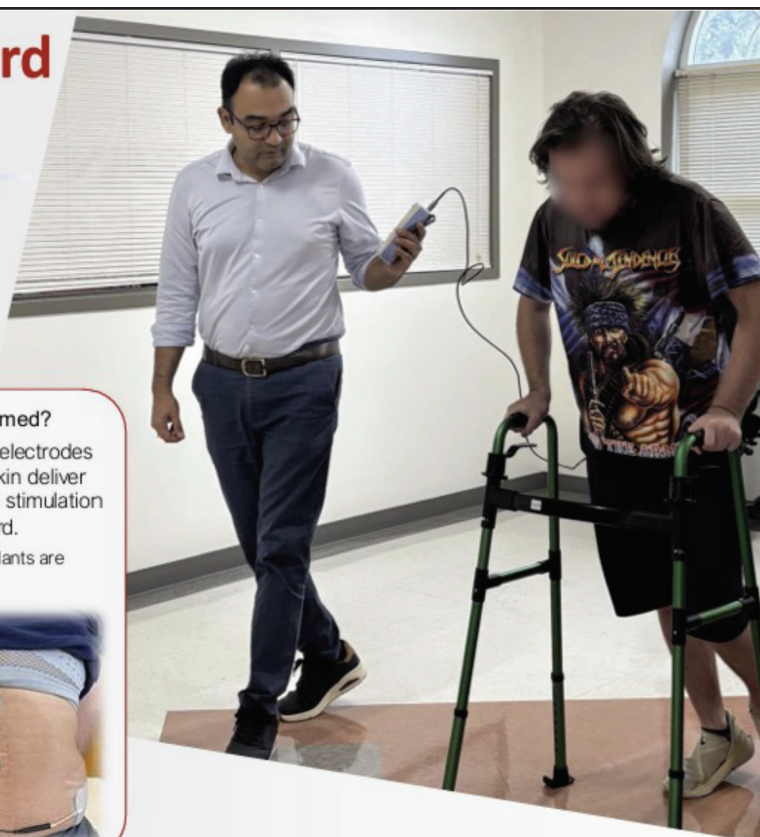
Dr. Rahul Sachdeva and colleagues at the University of Kentucky are conducting a clinical trial to determine whether transcutaneous spinal cord stimulation (tSCS)\*, a noninvasive form of spinal cord neuromodulation, can improve walking, reduce stiffness, and enhance mobility in people with Hereditary Spastic Paraplegia.

Participants receive 8 weeks of tSCS treatment, with walking, balance, stiffness, and other functional outcomes assessed throughout the study.

### How is it performed?

Small adhesive electrodes placed on the skin deliver gentle electrical stimulation to the spinal cord.

No surgery or implants are required.



SCS for HSP is investigational and is not FDA-approved for this indication.

University of  
Kentucky

College of Medicine  
Department of Physical Medicine and Rehabilitation

its rarity and the difficulty of studying it. Because PLS patients and samples are scarce, most tools and models used to study related conditions like ALS simply haven't been applied to PLS until now. This funding directly enables us to acquire and grow patient-derived cell lines, access specialized genetic sequencing platforms, and use advanced microfluidic and recording technologies that would otherwise be out of reach for a project focused on such a rare disease.

Importantly, SPF's support also strengthens our ongoing collaboration between neuroscience and bioengineering expertise, allowing us to combine cutting-edge cell modeling with custom-built lab-on-chip devices specifically suited to studying PLS. This interdisciplinary approach would not be possible without dedicated funding aimed at rare motor neuron diseases.

Most significantly, this project represents the first pioneering effort to study extracellular vesicles in PLS, an entirely unexplored area with real potential to uncover new biomarkers and therapeutic targets. Thanks to SPF, we can pursue this original, high-risk but high-reward line of investigation, generating knowledge that will directly benefit the broader motor neuron disease community and bring us closer to real treatment options for PLS patients and their families.

## Rahul Sachdeva, PhD | University of Kentucky *Noninvasive Spinal Cord Neuromodulation to Enhance Motor Function in Individuals with Hereditary Spastic Paraplegia*

### What problem is your research trying to solve?

People living with HSP gradually lose their ability to walk easily because the nerve pathways that control movement become damaged over time. This often leads to muscle stiffness, poor balance, impaired gait, and increasing difficulty with everyday activities. While current treatments can help manage symptoms, there are no therapies that have been shown to improve how these nerve pathways function. Our team is studying whether transcutaneous spinal cord stimulation (tSCS), a safe, noninvasive treatment that delivers gentle electrical stimulation through the skin, can improve walking, reduce stiffness, and make movement easier for people with HSP. We are also trying to understand why some people may respond better than others. By learning who benefits most and how to measure those improvements, we aim to provide foundation for larger studies that could eventually lead to new treatment options for people living with HSP.

### How does this research move the field one step closer to therapies?

Developing new treatments for a rare condition like HSP takes many small but important steps. Before a therapy can become widely available, researchers first need to show that it is safe, feasible to deliver, and has the potential to improve patients' lives. Our study is helping answer those questions. We are measuring changes



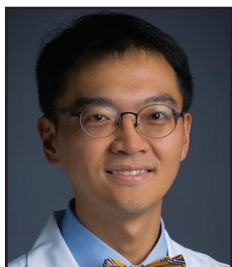
in walking, balance, muscle stiffness, and participants' day-to-day experiences to determine whether tSCS shows enough promise to justify larger clinical studies. We are also identifying which tests best capture meaningful improvements and whether certain people are more likely to benefit than others. The knowledge gained from this study will help researchers design stronger future clinical trials, not only for tSCS, but also for other potential HSP treatments. In this way, our project is helping build the foundation needed to move promising therapies closer to the people who need them.

**What have you accomplished so far and what are the next major milestones?** With funding support from SPF, we have successfully launched the clinical study. We obtained all required regulatory approvals, registered the trial on ClinicalTrials.gov, and began enrolling volunteers. To date, four participants have been enrolled in the study, and two have completed the full 8 week treatment program. We have also shared the study with the HSP community through presentations at the Spastic Paraplegia Foundation Annual Conference, where we received valuable feedback and encouragement from individuals and families living with HSP. Over the next 12 to 24 months, we plan to complete enrollment, analyze the results, and share what we learn through scientific meetings and publications. These milestones will provide the early evidence needed to support larger studies and help determine whether tSCS has the potential to become a treatment for HSP.

SPF's support has turned this project from an idea into an active clinical study. It provided the resources needed to obtain regulatory approvals, launch the trial, begin enrolling participants, and start collecting the data needed to evaluate this new treatment approach. Just as importantly, SPF has helped connect our research team with the HSP community. Through the Foundation, we have been able to share our work directly with individuals and families living with HSP, hear their experiences, and ensure that our research focuses on the questions that matter most to them. As an early-stage investigator, this support has also helped us generate the preliminary data needed to pursue larger research grants. By investing in projects like ours, SPF is helping build the evidence and momentum needed to bring new therapies closer to people living with HSP.



**Ikjae Lee, MD MSc | Columbia University**  
**PLS Natural History Study**



**What problem is your research trying to solve?** Primary Lateral Sclerosis (PLS) is a rare and understudied motor neuron disease. Right now, there is no treatment that can slow or stop its progression. Through the PLS Natural History Study — and its extension, which follows patients for a longer period of time — we're

building a complete picture of the disease: who it affects, how quickly it progresses, which parts of the body are affected, how it impacts daily function and mobility (including use of assistive equipment), and how it affects survival. We're also working to identify reliable ways to measure the disease and detect it in the body (biomarkers), which are essential tools for any future clinical trial.

**How does this research move the field one step closer to therapies?** Before you can test a new treatment in a clinical trial, you need to know what "normal" disease progression looks like, who to study, and how to measure whether a treatment is working. Through the PLS Natural History Study, we're identifying and confirming the best tools for measuring disease progression and figuring out how many patients a future trial would need to reliably detect a treatment effect. We're also working to discover biomarkers — measurable biological signals — that could help diagnose PLS earlier and track how it's progressing. Altogether, this work lays the groundwork needed to launch the first-ever therapeutic trial for PLS.

**What have you accomplished so far and what are the next major milestones?**

**Accomplished:**

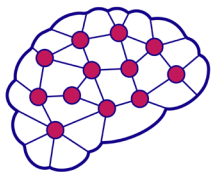
- ★ We developed and validated the PLS Functional Rating Scale (PLSFRS) — the first tool designed specifically to measure disease severity and progression in PLS.
- ★ In a recent paper published in *Annals of Neurology*, we reported how quickly the disease progresses, both overall and in specific patient subgroups, and calculated how many patients would be needed for different clinical trial designs — information trial planners will need.
- ★ We discovered that a blood marker called neurofilament light (NfL) can help predict how quickly a patient's disease will progress, and can even flag when someone's diagnosis is likely to shift from PLS to ALS, a related but faster-progressing disease.

**Next milestones:**

- ★ Extend patient follow-up to 5 years, to understand disease behavior beyond just the first year.
- ★ Study blood metabolites (metabolomics) to find new biomarkers, comparing PLS patients, ALS patients, and healthy volunteers. We will engage machine learning approach to analyze big dataset that will provide us lens to detect more complex patterns and combined signals.

SPF's support was essential to building the PLS Natural History Study in the first place, and continued funding has allowed us to follow patients for longer and analyze blood samples for new biomarker discovery. Just as important as the funding itself has been the sense of shared mission SPF has helped create — bringing together 30 research sites across the country around the urgency of this work. We're deeply grateful for SPF's continued support through grants, education, and advocacy for this research community.





# SP-CERN

Spastic Paraplegia Centers of  
Excellence Research Network

## *SP-CERN: Building the Infrastructure for clinical Trials*

One of SPF's most consequential research priorities is its continuing association with the Spastic Paraplegia Centers of Excellence Research Network—or SP-CERN. SP-CERN is the first coordinated HSP clinical research consortium of its kind in the United States. It brings together physician-scientists, multidisciplinary clinical teams, research institutions, patients, and advocacy organizations to create the infrastructure required for translational research and future clinical trials.

SPF's early support (**\$600,000**) helped establish the groundwork for SP-CERN, while an additional **\$75,000 bridge award in the 2025 grant cycle** helped sustain and expand the network as it transitioned into a federally supported research consortium.

On September 30, 2025, SP-CERN subsequently secured an **\$8.4 million NIH Rare Diseases Clinical Research Network award**. The SP-CERN and SPF are part of the NIH-funded **Rare Diseases Clinical Research Network**, led by the National Center for Advancing Translational Sciences in collaboration with several NIH institutes. Its goals are to create clinical-trial readiness, support therapy development, improve access to high-quality HSP care, and harmonize research nationally and internationally. SP-CERN's stated goals include natural-history studies, biomarkers, outcome measures, shared databases, biobanking, genomic research, digital measures, and adequately powered clinical trials.

*SP-CERN's principal research activities include:*

- ★ A longitudinal natural-history study covering children and adults with HSP.
- ★ A shared clinical database and biobank of patient-derived biospecimens.
- ★ A genomic data repository and advanced genetic-discovery program.
- ★ Biomarker and clinical outcome-measure development.
- ★ Wearable sensors and AI-supported measures of gait and real-world function.
- ★ Pilot studies that can respond to emerging scientific opportunities.
- ★ Training and mentoring for the next generation of HSP clinicians and investigators.
- ★ Coordination among clinical sites, international consortia, advocacy organizations, and potential therapy developers.

This work addresses a central problem in rare-disease research: a potential therapy cannot be tested effectively unless researchers understand how the disease progresses, know which patients may be eligible, have reliable clinical sites, and can measure whether an intervention produces meaningful change.

SP-CERN is creating that foundation. Its integrated natural-history, genomic, biomarker, biospecimen, and digital-measurement programs are intended to prepare HSP for gene-based treatments, small molecules, repurposed drugs, and other disease-modifying approaches. The resources of the network's consortium overview are being combined into a comprehensive clinical-trial-readiness platform.

## *SPF and SP-CERN Collaboration*

SPF's association with SP-CERN demonstrates the multiplying effect that strategic patient-organization funding can achieve: SPF contributions helped prepare a promising collaborative concept to compete successfully for a much larger federal investment.

This is the kind of leverage SPF increasingly seeks—investments that fund important work today while creating the evidence, partnerships, tools, and infrastructure required to attract additional support tomorrow. The collaboration is especially meaningful because the Foundation did not simply join the network after it received federal recognition. SPF helped support the work required to build it.

Early SPF funding helped investigators establish the collaborations, pilot research, patient participation, and organizational foundation needed to pursue a larger national network. SPF's later bridge funding helped protect that momentum during an important period of transition.

*For SPF and the HSP community, this association means:*

- ★ Patient priorities can be represented within the development of research studies.
- ★ Patients and families can receive clearer information about enrollment and research opportunities.
- ★ SPF can help communicate practical barriers that affect participation.
- ★ Researchers can connect with a broader and more informed patient community.
- ★ SPF-funded projects can be considered alongside larger natural-history, biomarker, genomic, and clinical-readiness initiatives.
- ★ Scientific findings and patient experiences can inform each other earlier in the research process.
- ★ The Foundation can help promote collaboration rather than duplication among researchers and organizations.
- ★ The HSP community has a more direct connection to NIH-supported rare-disease research infrastructure.

This relationship also strengthens SPF's ability to identify where donor-funded grants can complement, rather than duplicate, federal investments. SPF can use its flexibility to support pilot projects, emerging opportunities, patient engagement, bridge needs, and scientific gaps that may fall outside larger government awards.

# SP-CERN LOCATIONS

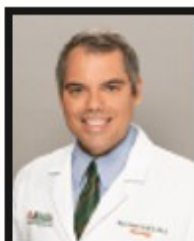
The first round of the SP-CERN includes eleven centers as follows:



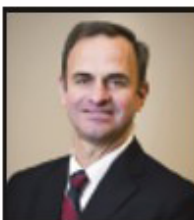
Darius Ebrahimi-Fakhari, MD, PhD  
Boston Children's Hospital  
300 Longwood Ave., Fegan 11  
Boston, MA 02115  
Telephone: 617-355-6388



Stephan Züchner MD, PhD &  
Hussman Institute for Human Genomics  
Biomedical Research Building (BRB)  
Room 616, LC: M-860  
1501 NW 10th Avenue  
Miami, FL 33136  
Telephone: 305 9897835



Mario Saporta MD, PhD  
Hussman Institute for Human Genomics  
Biomedical Research Building (BRB)  
Room 616, LC: M-860  
1501 NW 10th Avenue  
Miami, FL 33136  
Telephone: 305 9897835



Craig Blackstone, MD, PhD  
Mass General Neurology  
55 Fruit St.  
Boston, MA 02114  
Telephone: 866-934-3881



Michael Shy, MD  
University of Iowa Health Care  
2007 RCP  
200 Hawkins Drive  
Iowa City, IA 52242  
Telephone: (319) 356-7199



Matthew Harms, MD  
Columbia University Irving Medical Center  
710 West 168th Street  
New York, NY 10032  
Telephone: 646-426-3876



Michelle Christie, MD  
Scottish Rite For Children  
2222 Welborn St  
Dallas TX 75219  
Telephone: 214-559-7830



Daniel Calame, MD, PhD  
Baylor College of Medicine,  
Texas Children's Hospital  
One Baylor Plaza, Room 604B,  
Houston, TX 77035  
Telephone: 832-492-4843



Marie Davis, MD, PhD  
UW Institute on Human  
Development and Disability  
1959 NE Pacific  
Seattle, WA 98195  
Telephone: 206-598-4030



John Fink, MD  
University Of Michigan Neurology  
1500 E Medical Center Dr Fl 1-C,  
Ann Arbor, MI, 48109  
Telephone: 734-936-9020



Donald Gilbert, MD  
Cincinnati Children's Hospital  
Medical Center  
3333 Burnet Avenue ML 2015  
Cincinnati, OH 45229-3039



Joshua Burns, PhD  
St. Jude Children's Research Hospital  
262 Danny Thomas Place  
Memphis, TN 38105  
Telephone: 901-595-1293

**Rare Diseases Clinical Research Network - National Institutes of Health, SPF and the RDCRN Coalition of Patient Advocacy Groups**

SPF is formally listed as SP-CERN's participating patient advocacy organization associated with the Rare Disease Clinical Research Network (RDCRN), also known as the Coalition of Patient Advocacy Groups (CPAG). This designation reflects SPF's responsibility to serve as a bridge between the people living with rare diseases and the researchers building the studies, tools and trials intended to help them.

The value flows in both directions: SPF brings patient experience, community reach, urgency, and accountability to the research network, while SP-CERN and the RDCRN provide scientific coordination, clinical expertise, shared infrastructure, and access to a broader rare-disease research ecosystem. Together, these relationships give SPF a stronger platform from which to help convert individual research investments into a coordinated pathway toward therapies.

This association places SPF alongside other patient organizations representing many different rare diseases and creates opportunities to exchange knowledge about natural-history studies, registries, trial recruitment, informed consent, patient-reported outcomes, research communications, data sharing, and barriers to participation.

For SPF, participation within this structure means that the patient voice is not limited to responding after studies have already been designed. SPF can help bring the experiences and priorities of people living with HSP and PLS into conversations about research planning, education, recruitment, accessibility, and meaningful outcomes.

### *Advancing the Pathway to Therapies Research Priorities*

In 2025, SPF continued supporting a diverse research portfolio while laying the groundwork for a more coordinated, treatment-oriented research strategy.

Historically, SPF has helped researchers investigate the genes, proteins, cellular processes, and motor-neuron vulnerabilities associated with HSP and PLS. This foundational science remains essential. Researchers cannot develop effective therapies without first understanding what causes upper motor neurons and their long axons to become damaged or lose function.

At the same time, the field is entering a period when SPF must ask an additional question of every potential investment: **How could this work contribute to a pathway toward a treatment?**

That question does not mean every project must produce a medicine immediately. It means that research investments should increasingly contribute to one or more connected needs:

- ★ Understanding disease biology and identifying therapeutic targets
- ★ Testing potential medicines, repurposed drugs, gene-based approaches, or rehabilitation interventions
- ★ Developing meaningful biomarkers and clinical outcome assessments
- ★ Improving natural-history data and understanding disease progression
- ★ Preparing clinical research networks and study sites
- ★ Establishing data standards that allow information to be combined and reused
- ★ Identifying measures sensitive enough to show whether a treatment is working
- ★ Expanding collaboration and responsible data sharing
- ★ Ensuring that patient priorities are incorporated throughout research planning

### *Strengthening Natural-History and Biomarker Research*

SPF's support for natural-history research continued to be especially important. Natural-history studies help researchers understand how a disease changes over time, which symptoms progress, how quickly progression occurs, and what measurements may be useful in a clinical trial.

The SPF-supported **Primary Lateral Sclerosis Natural History Study Extension** received Institutional Review Board approval on April 17, 2025. Among 62 participants who completed the original two-year visit, 29 had enrolled in the extension study at the time of reporting. Twenty participants created NeuroPRO accounts, and 12 completed their first online surveys.

The study is gathering longer-term information about function, quality of life, respiratory health, cognition, diagnosis, and disease progression. Baseline neurofilament analysis was completed, follow-up analysis was planned, and metabolomics work was underway. These biomarker studies may help identify biological changes that can be measured alongside clinical symptoms.

Findings from this work were presented during our SPF TALKS program and can be found on the Spastic Paraplegia Foundation YouTube channel and at major neurological and motor-neuron disease meetings, helping elevate PLS-specific data within the larger scientific community.

### *Building Collaborative Research Infrastructure*

SPF's earlier investment in the Spastic Paraplegia Centers of Excellence Research Network helped create the groundwork for a larger, federally supported collaborative network. This progress demonstrates how strategic seed funding from

a patient advocacy organization can help promising ideas grow into national research infrastructure.

Natural-history studies, biospecimen collection, biobanking, genetic characterization, patient registries, clinical outcome measures, and coordinated study sites are not separate from treatment development. They are the infrastructure that allows future clinical trials to be designed and conducted more effectively.

SPF also continued considering how research data collected by different investigators could be aligned, harmonized, and used more broadly. When appropriate standards, agreements, and protections are in place, shared data can help researchers answer questions that may be impossible for a single institution or small study to address alone.

### *Organizing Research Around Shared Biological Pathways*

Although HSP includes many genetic subtypes and PLS does not currently have a single known genetic cause, these conditions can share important biological problems affecting upper motor neurons. SPF is increasingly organizing scientific discussions around biological systems that may connect multiple diagnoses and research programs, including:

- ★ Axonal transport and microtubule stability
- ★ Mitochondrial health and cellular energy
- ★ Autophagy and lysosomal function
- ★ Endoplasmic reticulum stress, protein processing, and membrane trafficking
- ★ Upper motor-neuron protection, survival, and regeneration

This pathway-based approach may help researchers identify opportunities that apply across more than one HSP subtype and may also reveal meaningful connections among HSP, PLS, ALS, and other motor-neuron disorders—while continuing to recognize the important differences among these conditions.

## **Connecting, Educating, and Building Awareness and Advocacy**

### *Communication Priorities*

Communication is one of the most important ways SPF serves its community. Patients and families need reliable information, researchers need opportunities to share progress, donors deserve to understand the impact of their gifts, and the public must be reminded that HSP and PLS deserve greater recognition and investment.

Throughout 2025, SPF used multiple platforms to educate, connect, and engage the community. These included email/eblasts communications, the SPF website, social media, SPF TALKS, YouTube videos, educational resources, support networks, the Annual Conference, and direct responses to patients and families seeking help.

### *Translating Science into Understanding*

Research can be complex, but patients should not be excluded from understanding the work conducted on their behalf. SPF continued helping researchers explain discoveries, study results, biological pathways, natural-history research, clinical-trial readiness, and emerging therapies in language that patients and families can understand.

SPF TALKS and the Annual HSP/PLS Patient and Family Conference played an especially important role in connecting the scientific and patient communities. These programs allowed patients to hear directly from researchers and clinicians while helping investigators better understand the lived experience of HSP and PLS.

Communications also encouraged patients to participate in surveys, registries, research studies, and educational opportunities. This work is essential because research readiness depends not only on scientific tools but also on an informed and engaged community.

## **The Voices That Guide Our Mission**

### *Patient Voices - a HSP/PLS Patient History Survey*

People living with HSP and PLS are not simply the beneficiaries of SPF's work. They are essential partners in shaping it.

During 2025, the SPF HSP/PLS Patient History Survey provided one of the clearest and most comprehensive opportunities for patients and caregivers to describe their lived experiences. Approximately **772 individuals had responded as of August 2025**, representing a significant contribution from the community.

The survey explored the diagnostic journey, genetic testing, disease progression, symptoms, mobility, assistive devices, treatment experiences, access to care, emotional health, employment, financial burden, quality of life, support needs, and willingness to participate in research.

Across the responses, several messages emerged clearly. If you have not yet completed the survey, please use the **QR code included in this Annual Report** to participate. Your voice and experiences help guide SPF's priorities and strengthen our work on behalf of the HSP and PLS community.

To review the comprehensive survey results presented at the 2025 Annual Conference, visit [SP-Foundation.org](https://SP-Foundation.org) to download your copy of the full report.



### *Progression Creates Urgency*

HSP and PLS are progressive diseases. Patients are not simply waiting for a future cure; many are losing mobility, independence, employment opportunities, and the ability to participate fully in family and community life. For some, the damage that occurs while waiting may be difficult or impossible to reverse.

This makes time a critical factor. Research strategies must consider not only whether a therapy might eventually work, but also how promising approaches can be evaluated more efficiently and responsibly.

### *Function Matters*

Patients consistently emphasize practical goals: preserving or regaining walking ability, improving balance, reducing spasticity, preventing falls, maintaining hand and leg function, reducing pain and fatigue, and remaining independent.

These priorities should help guide the development of clinical outcome measures and the design of research studies. A statistically measurable change is meaningful only when it reflects something that matters in a patient's daily life.

### *Participation Must Be More Accessible*

Patients expressed strong interest in research but also identified barriers. Transportation, travel, physical accessibility, limited information about available studies, time commitments, distance from research centers, concerns about effectiveness or side effects, and restrictive eligibility requirements can prevent participation.

Addressing these barriers may require decentralized study options, remote assessments, digital tools, better communication, travel assistance, broader site participation, and earlier patient involvement in protocol design.

### *Patients Need Information and Partnership*

The survey reinforced the need for clearer information about genetics, disease progression, symptom management, research opportunities, clinical trials, and emerging therapies. Patients also want to understand how their information is being used and how participation contributes to the larger research effort.

SPF is committed to protecting participant information and using patient-reported data responsibly. Survey information is intended to help communicate unmet needs, guide research priorities, improve study readiness, and inform discussions with researchers, clinicians, regulatory organizations, government agencies, and potential therapy developers.

Patients should not be invited into the process only after a research study has been designed. Their perspectives should help shape the questions being asked, the outcomes being measured, and the burdens participants are expected to carry.

The message from the community is unmistakable: people living with HSP and PLS are ready to contribute, but they need meaningful opportunities, clear communication, and a coordinated path forward.

Their voices are not an addition to SPF's mission. They are its foundation.

### *From Momentum to Medicine – Looking Ahead*

Looking Ahead SPF research is entering a new chapter—one focused not simply on supporting excellent science, but on connecting excellent science into a pathway toward treatments. Our emerging collaboration with the Critical Path Institute (C-Path) represents an important part of that evolution. Through this relationship, SPF is working to better understand where critical research and data gaps remain; strengthen regulatory readiness;

align biomarkers and outcome measures with drug-development needs; encourage data harmonization; and help establish the infrastructure necessary to support multiple future therapeutic programs. At the same time, SPF is bringing together researchers studying different genetic forms of HSP, PLS, upper motor-neuron biology, and the cellular pathways that may connect them. A discovery made in one form of HSP may reveal a biological mechanism relevant to another. A biomarker developed for one research program may ultimately help evaluate several potential therapies. A better understanding of mitochondrial dysfunction, axonal transport, ER stress, autophagy and lysosomal function, microtubule biology, or upper motor-neuron survival may create opportunities that extend beyond any single SPG number. That is why connecting the research matters.

Rather than viewing each grant as an isolated project, SPF is increasingly building a research portfolio in which each investment should move the larger field forward. A project may identify a therapeutic target, validate a shared disease mechanism, develop a biomarker, establish critical patient data, test a promising intervention, answer a regulatory question, or provide the evidence needed to justify the next study. Not every experiment will produce a treatment. But every well-designed project should help us determine what the next step should be. This represents a meaningful evolution for the Spastic Paraplegia Foundation. We will continue supporting innovative discovery, while placing increasing emphasis on research that can be connected to a larger translational strategy—from understanding what is going wrong in the cell, to identifying what can be targeted, to measuring whether an intervention works, and ultimately to determining whether it can be safely and effectively studied in patients.

## **The Destination Has Not Changed. The Roadmap Is Becoming Clearer**

Our goal is ambitious, urgent, and unmistakable: Move promising discoveries out of the laboratory and toward meaningful therapies for people living with HSP and PLS. Patients and families are already providing what science cannot accomplish alone—their participation, experiences, data, generosity, courage, ideas, and determination. Researchers are contributing discoveries and expertise. Strategic partners are helping build the data, regulatory, and clinical infrastructure necessary to translate those discoveries. SPF's responsibility is to help connect those pieces. From gene to pathway. From pathway to target. From target to therapy. From possibility to patients. There is still much work ahead, but the direction is increasingly clear. We are united by urgency, guided by patient voice, strengthened by collaboration, and committed to ensuring that every research investment helps build toward something larger. We are no longer funding research simply to learn more about HSP and PLS. We are building a research strategy designed to do something about them. That is the next chapter of SPF research. From momentum to medicine—and, ultimately, to treatments that change lives.

# LEGACY & PLANNED GIVING

**Honoring a Lasting Legacy: \$425,000 Planned Gift to Advance HSP/PLS Research\***

A BEACON OF HOPE

## BARBARA “BARBI” ANN SEIPP SEIBERT

*A devoted member of the SPF community  
whose foresight and generosity will  
accelerate the search for treatments and  
improve lives for generations to come.*



MAY 31, 1949 - APRIL 29, 2024  
CROSSLAKE, MN

*\*Received by SPF in 2025*

## LEGACY OF HOPE

### Legacy Giving — Building a Future of Hope

Leaving a gift to the Spastic Paraplegia Foundation (SPF) means joining our Legacy Circle, a community of visionaries who ensure progress in the fight against HSP and PLS continues far into the future. Planned giving is more than a financial contribution; it is a lasting expression of your values and commitment to advancing research, support, and education. SPF has become a trusted resource and strong voice for individuals, families, and children affected by HSP and PLS, and through legacy gifts, that impact will grow for generations to come. Whether through a bequest in your will, a trust, or another charitable planning tool, your gift secures a brighter tomorrow while also helping you achieve your own estate and financial goals. Together, we can ensure that the work of today builds the breakthroughs of tomorrow.

*Through legacy giving, your impact doesn't end — it grows.*



## MEMORIAL GIVING

The Spastic Paraplegia Foundation invites you to honor the life of a loved one through our *Circle of Love Memorial Giving Fund*. This meaningful opportunity allows families to create a personalized tribute page that celebrates the legacy of someone special while advancing our shared mission to fund research for HSP and PLS.

Creating a memorial fundraiser through our Network for Good platform is simple, heartfelt, and impactful. We provide the tools, guidance, and resources to help you share your story and inspire others. Your support—whether in remembrance, gratitude, or hope, helps accelerate medical research and brings us closer to treatments and a cure.

*In lieu of flowers, please consider a donation to the*  
**Spastic Paraplegia Foundation**

Text "DONATE" to 956-666-7954  
 Donate directly at [SP-Foundation.org](https://SP-Foundation.org) or

**Mail a donation to:**

6952 Clayborne Drive,  
 O'Fallon, MO 63368-6202

Note In Memory of: \_\_\_\_\_

*Your donation is fully tax deductible and  
 greatly appreciated to help us find a cure.*



Find this Donation Card on [SP-Foundation.org](https://SP-Foundation.org)

### Memorial Giving



Start by scanning the QR Code with your phone camera. We are here to assist you every step of the way.

*Planned giving keeps hope alive – your legacy fuels  
 research, support, and progress for generations to come.*

(877) 773-4483 | [information@SP-Foundation.org](mailto:information@SP-Foundation.org)



# 2025 SPF OFFICERS



**Greg Pruitt**  
SPF President  
SPF Board Member



**Jim Sheorn**  
Vice President Chair,  
SPF Fundraising  
Former SPF President  
SPF Board Member



**Hank Chiuppi**  
SPF Secretary  
SPF Board Member



**Lorri Steiner**  
SPF Treasurer, CPA



**Frank Davis**  
President Emeritus  
SPF Board Member



**John Cobb**  
Chair, SPF Research  
SPF Board Member



**Becki Cochran**  
SPF Board Member



**Carina Thurgood**  
SPF Board Member



**Sara Kramer**  
SPF Board Member



**Tina Croghan**  
Co-Chair, SPF Advocacy  
SPF Board Member



**Jackie Wellman**  
Co-Chair, SPF  
Education/Ambassador  
SPF Board Member



**Dina Landphair**  
Co-Chair, SPF  
Education/Ambassador  
SPF Board Member



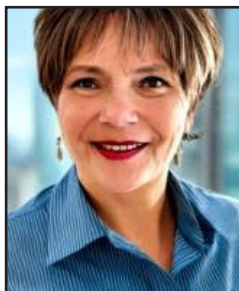
**Norma Pruitt**  
Executive Director



**John K. Fink, M.D.**  
SPF Medical Advisor



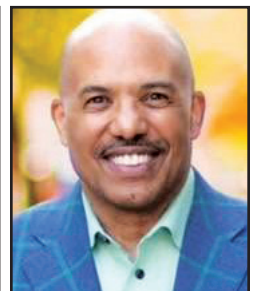
**Adam Futrell, Esq.**  
SPF Legal Counsel



**Linda Arnold**  
Fundraising &  
Relationship  
Development Manager



**Tim Croghan**  
Conference Emcee Chair,  
SPF Marketing



**Leonard Erskine**  
Co-Chair,  
SPF Advocacy



RESEARCH | EDUCATION | SUPPORT

6952 Clayborne Drive  
O'Fallon, MO 63368-6202



## STAY CONNECTED TO THE SPF COMMUNITY

### STAY IN TOUCH



Update your contact information, share your story, reach out anytime

### SPF TALKS



Hear from Leading researchers, medical experts, and clinicians

### PATIENT SURVEY



Real-Life Experiences Shared by Patients Living with HSP & PLS

### OUR WEBSITE



Support, education and research documents  
Learn more about SPF

## TOGETHER WE ARE MAKING A DIFFERENCE



Spastic Paraplegia Foundation is dedicated to improving the lives of individuals and families living with **Hereditary Spastic Paraplegia (HSP)** and **Primary Lateral Sclerosis (PLS)**. SPF continues to: Advance promising research; Provide trusted education; Connect patients and families with valuable resources; Support caregivers and healthcare professionals ; Build a compassionate community where no one walks this journey alone. Whether you participate in an SPF Talk, attend our annual conference, follow us online, or simply keep in touch, **you are an important part of the SPF family.**

**Our Promise: Hope. Education. Research. Community.**

Because together, we are building a brighter future for everyone affected by HSP and PLS.

**FOLLOW AND SHARE ON SOCIAL MEDIA**

