

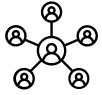
# SP-CERN

Spastic Paraplegia Centers of  
Excellence Research Network

RDCRC IAB Meeting #7

May 4<sup>th</sup>, 2026

# Agenda



- Updates from sites and recruitment numbers (IAB members)



- Research Project 1 (Ebrahimi-Fakhari)
- Research Project 3 (Burns)
- Research Project 2 (Zuchner)
- *Recruitment Liaison* (Kressin)



- Career Enhancement Core (Shy)
- Pilot Project Core (Blackstone and Davis)



- Video Grand Rounds (Christie)
- Update from PAG (PAG representatives)
- *International Collaboration* (Schule)
- *Monthly Report from DMCC* (DMCC)

# Publications & meetings from the consortium



# Updates from sites

SP-CERN Site	Approved under Pilot IRB Protocol	Approved under RDCRC IRB Protocol	Enrolled patients
Boston Children's (BCH)	Approved	Pending	91
Mass General Hospital (MGH)	Approved	Pending	0
Cincinnati Children's (CCH)	Approved	Pending	5
U Michigan (UMI)	Approved	Pending	0
U Iowa (UOI)	Approved	Pending	16
St Jude Children's (SJC)	Approved	Pending	0
Scottish Rite (SRC)	Approved	Pending	0
Texas Children's (TCH)	Approved	Pending	0
U Washington (UWA)	Approved	Pending	2
Seattle Children's (SCH)	Approved	Pending	5

# Updates from sites

From East to West:

- Boston Children's Hospital Darius and team
- Massachusetts General Hospital Chris and Craig
- University of Miami Stephan
- Cincinnati Children's Hospital Don
- University of Michigan John
- St. Jude Children's Research Hospital Richard and Josh
- University of Iowa Mike
- Texas Children's Hospital Dan
- Scottish Rite for Children Dallas Michelle
- University of Washington Marie
- Seattle Children's Hospital Pam

Pending affiliate sites:

- Northwestern University (cleared to be added) Senda Arjoud-Driss
- Children's Hospital of Philadelphia (cleared to be added) Alonso Zea-Vera

# Research Project 1

## Updates:

- Update central IRB to include projects 2 and 3 (Darius and Josh)
  - NIH review completed -> Under review at BCH IRB
  - A second IRB amendment will update the consent forms for all sites
- Re-built REDCap database with DMCC standards (Josh & Judd Jacobs)
  - Completed – will share with sites shortly, training module being built
  - Updated naming convention (especially important for Project 2) (Josh)
- Sub-contracts sent to sites – UOI and SCH already completed (Katie)

## To dos:

1. Give us feedback on the list of individuals interested in coming to your site
2. CCH and UWA please reach out about samples that need to be shipped this quarter (Jan-Mar 2026)
3. Make sure you have access to Zoom and Box:  
<https://members.rarediseasesnetwork.org/home/toolgarden/all?20260427095245>
4. Next monthly coordinator meeting – **May 21<sup>st</sup>**
  - Please remind your coordinators to attend



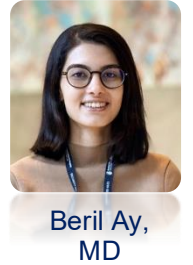
# Project 1: Patient Groups

Group A: Patients with molecularly confirmed HSP forms listed in Aim 1: SPG3A, SPG4, SPG5A	CROM, PROM and biospecimen
Group B: Patients with molecularly confirmed HSP forms listed in Aim 2: SPG47, SPG49, SPG50, SPG51, SPG52, SPG56, SPG83, GPT2 deficiency	CROM + GMFM88, PROM and biospecimen
Group C: Patients with other forms of molecularly confirmed HSP	CROM and PROM and biospecimen
Group D: Patients with clinical diagnosis of HSP and pending clinical genetic testing	CROM and PROM, but no biospecimen
Group E: Patients with clinical diagnosis of HSP and negative clinical genetic testing (that is HSP multigene panel or WES/WGS)	CROM, biospecimen and enrollment in <b>Project 2</b>

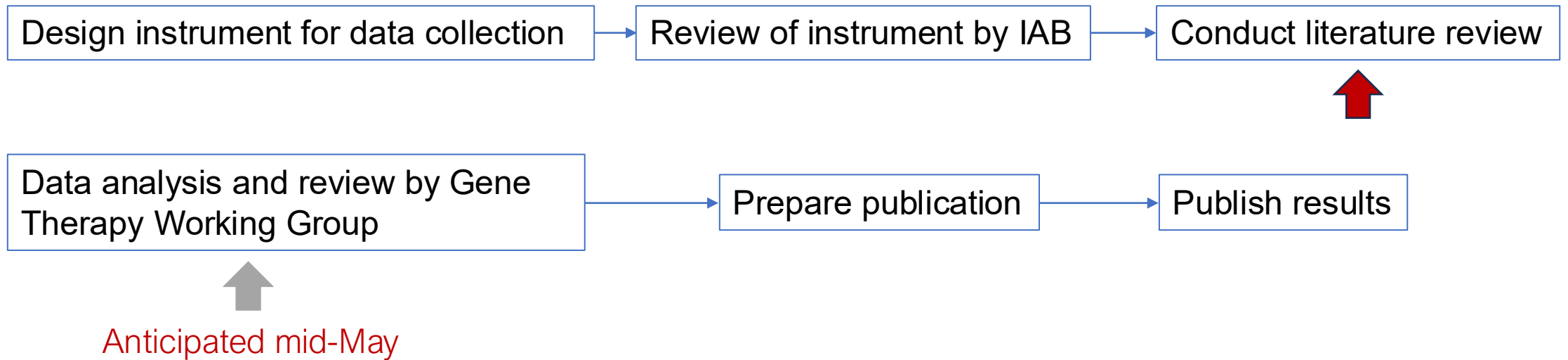
We suggest making site-specific recruitment lists at this point.

Site can continue to enroll probands under the SP-CERN Pilot Project IRB-approved protocol for Groups A, B, and C. Updated consent forms will be provided with the next IRB amendment.

# Research Project 1



## Gene therapy readiness map for all HSPs:



# Research Project 3



## Digital surrogates for disease progression in hereditary spastic paraplegia

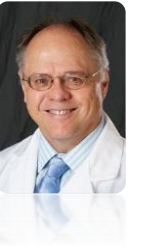
- Aim 1:
  - Characterize the range of daily activity of children and adults with Hereditary Spastic Paraplegia (HSP) using wearable activity monitors
    - ✓ On-Demand Actigraph Management by St. Jude
    - ✓ ActiGraph GT3x received
- Aim 2:
  - Evaluate gait and movement disorders in young children with HSP in anticipation of early phase trials to detect the earliest signals of therapeutic effect
    - ✓ Delivery of the first BioSensics LegSys and BalanSens systems for St. Jude has been delayed due to a vendor-initiated algorithm upgrade, expected to be received by mid May.



# Research Project 2



# Career Enhancement Core (CEC)



- NIH approved the career enhancement fellowships.



Beril Ay, MD

Identification of genetic modifiers of age at onset in SPG4



Habibah Agianda, MD

Identification of blood-based biomarkers for HSP using unbiased proteomics and lipidomics

Habibah and Beril to present their updates at the annual investigator meeting in September 2026

# Pilot Project Core (PPC)



- NIH approved the pilot award.



John B. Sanderson, MD

Transcutaneous Spinal Cord  
Stimulation in  
Hereditary Spastic  
Paraplegias

John to present the project at the June 1<sup>st</sup> IAB Meeting and updates at the annual investigator meeting in September 2026

# Video Grand Rounds



SP-CERN Virtual Grand Rounds: 2025-2026  
Fridays; 12:00 PM EST - 1:00 PM EST

Next: May 8<sup>th</sup>

Upper Limb Impairments and Functional Profiles in Hereditary Spastic Paraplegia  
**Angela Shierk, PhD, OTR, Scottish Rite for Children**

“A rose by any other name would smell as sweet:” Complex hereditary spastic paraplegia or something else?  
**Christopher R. Cashman, MD, PhD, MGB**

Date	Speaker	Topic
11/14/25	Guest speakers: Michael Pacold, M.D., Ph.D. & Claire Miller M.D., Ph.D. NYU Langone	Treating HPDL encephalopathy (SPG83) with CoQ10 headgroup intermediates
12/12/25	Julian Alecu, M.D., Ph.D. Boston Children's Hospital	Genotype-Structure-Phenotype Correlations Define Divergent Natural Histories in Early-Onset SPG4
1/9/26	Scottish Rite for Children (Michelle Christie, M.D.) & Massachusetts General Hospital (Chris Cashman, M.D.)	Case Presentations
2/13/26	University of Iowa - Carver College of Medicine (Mike Shy, M.D. & Cincinnati Children's Hospital (Don Gilbert, M.D.)	Case Presentations
3/13/26	St Jude Children's Research Hospital (Joshua Burns, Ph.D. & Richard Finkel, M.D.)	FDA Draft Guidance: Plausible Mechanism Framework to Develop Individualized Therapies
4/10/26	Katerina Bernardi, M.D. Boston Children's Hospital	Spectrum of movement and motor disorders in KIF1A-associated neurological disorder
5/8/26	Guest Speaker: Eric Morrow, M.D., Ph.D. Brown University	A Targeted Therapy for GPT2 Deficiency
6/12/26	Texas Children's Hospital (Daniel Calame, M.D., Ph.D.) & Massachusetts General Hospital (Chris Cashman, M.D & Reza Sadjadi, M.D.)	Case Presentations

# Update from PAGs



# Update on international collaboration

**“Global Convergence of Trial Readiness Networks for HSPs.”**

**Preliminary Program – May 7th, 2026 – Morning Reference time zone: Porto Alegre / Brasília (UTC-3)**

**•08:15–08:20 (5 min)** *Welcome and Introduction*

**Speaker:** Jonas A. M. Saute, iAXON-HSP

**•08:20–08:35 (15 min)** *Trial Readiness Networks for HSPs: TreatHSP, iAXON-HSP, and SP-CERN*

**Speaker:** Darius Ebrahimi-Fakhari, SP-CERN

**•08:35–08:50 (15 min)** *Major Gaps in Trial Readiness for HSPs*

**Speaker:** Jonas A. M. Saute, iAXON-HSP

**•08:50–09:05 (15 min)** *Framework for Trial Readiness in HSPs and Meeting Dynamics*

**Speaker:** Rebecca Schüle, Treat-HSP

**•09:05–10:05 (60 min)** *Trial Readiness: Clinical Outcome Assessments (COAs) and Digital Health Technologies (DHTs)*

**Chair:** Rebecca Schüle, Treat-HSP

**•\*\*10:05–10:20 (15 min) - \*\*Break**

**•10:20–11:10 (50 min)** *Biomarkers: Imaging and Wet Biomarkers*

**Chair:** Marcondes França Jr., iAXON-HSP

**•11:10–12:00 (50 min)** *Genetic Diagnosis and Genomic Technologies: Harmonized Databases and Analytical Pipelines*

**Chair:** Stephan Züchner, SP-CERN

**•\*\*12:00–14:00 (120 min) - \*\*\*Break \***

**•14:00–14:20 (20 min)** *Summary of Working Group Discussions (5 minutes per topic)*

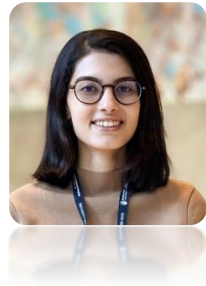
**Speakers:** Jonas A. M. Saute & Rebecca Schüle

**•14:20–14:40 (20 min)** *Final Discussion and Consolidated Report*

**Participants:** All

**Chair:** Rebecca Schüle, Treat-HSP

# Call for collaboration



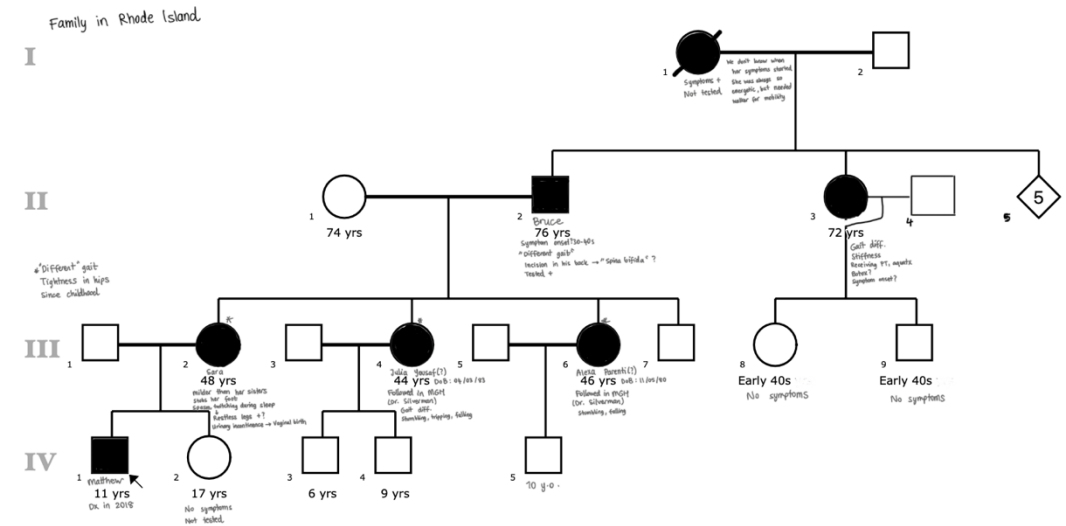
## Beril Ay, MD: Identifying Genetic Modifiers of Age at Onset in SPG4

Aims: We will perform comprehensive short- and long-read genome sequencing in large multigenerational SPG4 families to systematically evaluate the apparent anticipation pattern observed in clinic and identify genetic modifiers that contribute to earlier age at onset in younger generations.

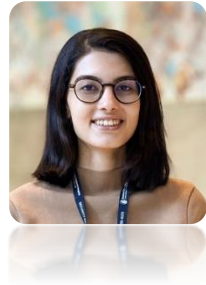
We are looking for:

- Multigenerational family history of SPG4 ( $\geq 2$  affected generations, 3 preferred)
- Clear difference in the age at onset between generations
- Living in the US

Update: 12 families enrolled and 11 sequenced.



# Call for collaboration



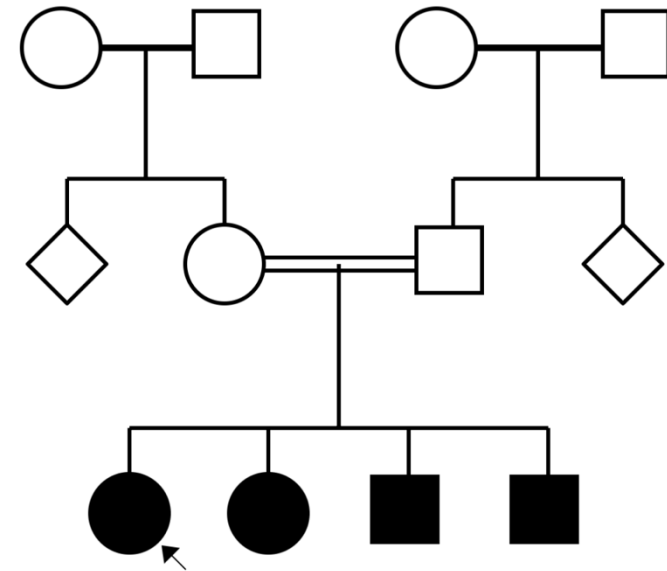
## Beril Ay, MD: **An update on Troyer Syndrome (SPG20)**

### Aims:

- Report a cohort of patients with SPG20 from four different ethnic backgrounds
- Detailed review and phenotyping of the literature to identify possible genotype-phenotype correlations

### We are looking for:

- Previously unpublished patients with confirmed SPG20
- Clinically diagnosed Troyer Syndrome patients without molecular confirmation, who are living in the United States or Canada



# Outlook: Investigator Meeting 2026



## DATE

**September 25 – 26, 2026**

## LOCATION

**Boston Children's Hospital**

Karp Family Research Building • Boston, Massachusetts

## MEETING HIGHLIGHTS

- **Keynote Address** – TBD
- **Year 1 Progress** – Enrollment, biomarkers, genomics
- **Rater Training** – Patient-assisted hands-on sessions
- **Projects & Future Directions** – Trial readiness, genomics, digital endpoints

## REGISTER

**Registration via Google Form**

For inquiries: [spcern@childrens.harvard.edu](mailto:spcern@childrens.harvard.edu)  
<https://sp-cern.rarediseasesnetwork.org>

Please save the date: September 25 (afternoon) & September 26 (all day)

# First Annual SP-CERN Consortium Meeting

September 25–26, 2026 • Boston Children’s Hospital • Karp Boardroom

DRAFT — For IAB Review

## FRIDAY, SEPTEMBER 25 • 1:00 – 6:00 PM

1:00 PM	<b>Welcome &amp; Opening Remarks</b> <i>Ebrahimi-Fakhari</i>
1:10 PM	<b>Keynote Address</b> <i>Speaker TBD</i>
1:50 PM	<b>SP-CERN Year 1 Review &amp; Progress</b> <i>Enrollment, biomarkers, DMCC</i>
2:30 PM	<b>Coffee Break</b>
2:45 PM	<b>CEC Update</b> <i>Shy</i>
3:05 PM	<b>PPC Update</b> <i>Blackstone &amp; Davis</i>
3:25 PM	<b>International Collaboration Updates</b> <i>TreatHSP, iAXON-HSP, Seoul, CAN-</i>
3:45 PM	<b>Challenges &amp; Discussion</b> <i>Facilitated</i>
4:15 PM	<b>IRB &amp; Reliance Agreements</b>
4:35 PM	<b>Project Logistics (P1 / P2 / P3)</b> <i>Ebrahimi-Fakhari, Züchner, Burns</i>
5:15 PM	<b>Future Directions &amp; Open Discussion</b>
5:45 PM	<b>Day 1 Wrap-Up</b>

**EVENING 7:05 PM Red Sox Game at Fenway Park**

## SATURDAY, SEPTEMBER 26 • 8:00 AM – 5:00 PM

### MORNING — RATER TRAINING (Patient-Assisted)

8:00 AM	<b>Welcome, Coffee &amp; Orientation</b>
8:15 AM	<b>Rotation 1</b>
9:20 AM	<b>Rotation 2</b>
10:20 AM	<b>Coffee Break</b>
10:35 AM	<b>Rotation 3</b>
11:40 AM	<b>Rotation 4</b>
12:40 PM	<b>Debrief &amp; Q&amp;A</b>

- 1 Neurological Exam** — SPRS, MAS, MRC
- 2 Motor Function** — GMFM-88, 10MWT, 2MWT, Video
- 3 PROMs & REDCap** — Questionnaires, data entry
- 4 Biospecimens & Devices** — Collection, ActiGraph, BioSensics

### AFTERNOON — OPEN DISCUSSION & NEXT STEPS

1:00 PM	<b>Lunch</b>
2:00 PM	<b>Open Discussion: Year 1 Priorities</b>
2:45 PM	<b>Site-Specific Updates</b>
3:45 PM	<b>Next Steps &amp; Year 2 Planning</b>
4:15 PM	<b>Closing Remarks</b>

**EVENING 6:30 PM Group Dinner (for those staying)**

# Discussion and Questions