



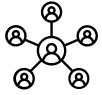
SP-CERN

Spastic Paraplegia Centers of
Excellence Research Network

RDCRC IAB Meeting #6

April 6th 2026

Agenda



- Updates from sites and recruitment numbers (IAB members)



- Research Project 1 (Ay for 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



SPG4 Symposium

SP-CERN:

- Stephan Züchner
- Josh Burns
- Beril Ay
- Habibah Agianda
- Michael Shy
- Craig Blackstone
- Josh Rong
- Darius Ebrahimi-Fakhari

Key takeaway:

1. Collaborative work on gene therapy for SPAST (Umass (Esteves, Gray), Drexel (Liang, Baas), U Wisconsin (Lettman), BCH (Ebrahimi-Fakhari))
2. Big unmet need: blood-based biomarkers -> links to SP-CERN CEC Fellow Project

3. Drug-purposing for HDAC-inhibitors -> need additional proof of concept

4. Involving FDA to explore paths for gene based therapies without proof-of-concept in vivo

Suggestion: For collaborative work on gene therapy: Invite teams to present quarterly at SP-CERN IAB meeting (30min time slot)

Publications & meetings from the consortium

RESEARCH ARTICLE

The Movement Disorder Spectrum of *ATP1A3*-Related Disorders: Cross-Sectional Analysis and Video Archive of 88 Patients

Katerina Bernardi, MD,^{1†} Anna Zhou, MD,^{2†} Kathryn Yang, MBChB, FRCPC,¹ Joshua Rong, BSc,¹ Vicente Quiroz, MD,¹ Julian E. Alecu, MD, PhD,¹ Habibah A. P. Aglanda, MD,¹ Henri J. D. Schmidt cand. med.,¹ Army Tam, BSc,¹ Siofra Carty, BSc,¹ Natalia Espasandin-Hueter, MD,³ Alfons Macaya, MD, PhD,³ Maria Stamelou, MD,⁴ Tamara Pringsheim, MD,⁵ Margaret Means, MD,⁶ Arpita Lakhotia, MBBS,⁶ Joanna Blackburn, MD,⁷ Alonso Zea Vera, MD,⁸ Leonie Fellicia Becker, MD,^{9,10} Norbert Brüggemann, MD,¹¹ Alexander Münchau, MD,¹⁰ Yury Seliverstov, MD, PhD,¹² Lindsey Vogt, MD, MSc,¹³ Carolina Gorodetsky, MD, MSc,¹³ Jesse M. Levine, MD, PhD,^{14,15,16} Alyssa D. Runco, MD,^{14,15,16} Daniel G. Calame, MD, PhD,^{14,15,16} Lifang Dai, MD,^{2†*} Changhong Ding, MD,^{2†*} and Darius Ebrahimi-Fakhari, MD, PhD^{1*}

Bernardi, Katerina et al. “The Movement Disorder Spectrum of *ATP1A3*-Related Disorders: Cross-Sectional Analysis and Video Archive of 88 Patients.” *Movement disorders* : official journal of the Movement Disorder Society, 10.1002/mds.70227. 18 Mar. 2026, doi:10.1002/mds.70227



12-year-old male with spastic paraparesis and no extrapyramidal features. On exam, patient ambulates with posterior walker for longer distances

Updates from sites

SP-CERN Site	Approved under Pilot IRB Protocol	Approved under RDCRC IRB Protocol	Enrolled patients
Boston Children's (BCH)	Approved	Pending	83
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	9
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	1
Seattle Children's (SCH)	Approved	Pending	4

Updates from sites

From East to West:

- Boston Children's Hospital
- Massachusetts General Hospital
- University of Miami
- Cincinnati Children's Hospital
- University of Michigan
- St. Jude Children's Research Hospital
- University of Iowa
- Texas Children's Hospital
- Scottish Rite for Children Dallas
- University of Washington
- Seattle Children's Hospital

Beril for Darius and team
Chris and Craig
Stephan
Don
John
Richard and Josh
Mike
Dan
Michelle
Marie
Pam

Pending affiliate sites:

- Northwestern University (final signature on reliance agreement pending, submitted for NIH review)
- Children's Hospital of Philadelphia -> submitted for NIH review

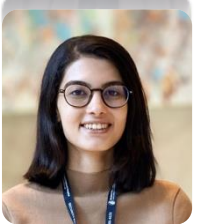
Research Project 1

Updates:

- Update central IRB to include projects 2 and 3 (Darius)
 - Submitted to NIH for review
 - Need additional information for project 3
- Re-building REDCap database with DMCC standards (Josh)
 - Now in validation phase with DMCC
- Contracts need to be updated (Katie)

To dos:

1. Give us feedback on the list of individuals interested in coming to your site
2. Have your coordinators reach out about samples that need to be shipped this quarter (Jan-Mar 2026)
3. For pediatric sites: Please confirm PT availability for the GMFM88 assessment (**missing: Baylor, Seattle Children's, Scottish Rite**); St. Jude will be central site for training
4. Next monthly coordinator meeting – **April 16th**
 - Please remind your coordinators to attend



Cincinnati Children's
Hospital, December 2025



U of Iowa Medical Center,
January 2026

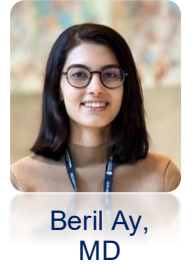
Project 1: Patient Groups

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 Project 2

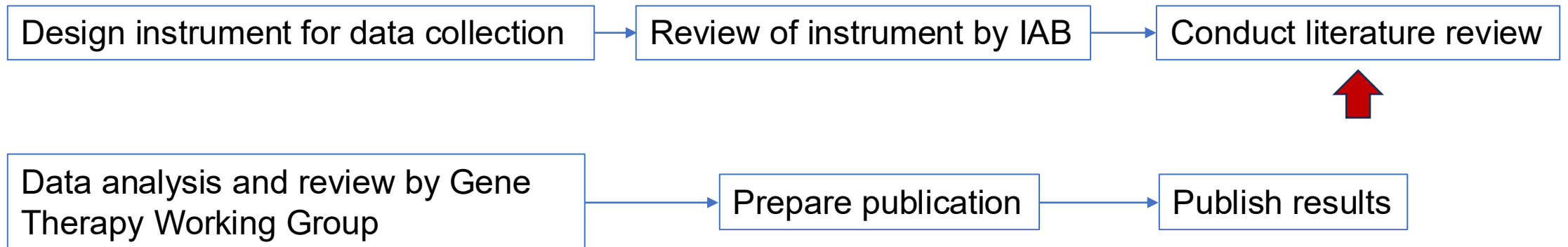
We suggest making site-specific recruitment lists at this point.

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



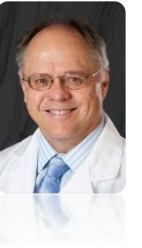
- **Status:** Working on the BCH IRB amendment to incorporate project 3
- Aim 1: Characterize habitual physical activity of children and adults with HSP using wearable activity monitors
- Aim 2: Validation of wearable inertial sensors to measure gait and balance in young children with HSP



Research Project 2



Career Enhancement Core (CEC)



- NIH approved the fellowship applications.

Pilot Project Core (PPC)



John B. Sanderson, MD

Transcutaneous Spinal Cord Stimulation in
Hereditary Spastic Paraplegias

Video Grand Rounds



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

Next: April 10th

Boston Children's Hospital
Katerina Bernardi, M.D.

Spectrum of movement and motor disorders in KIF1A-related neurological disorder (KAND)



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)*

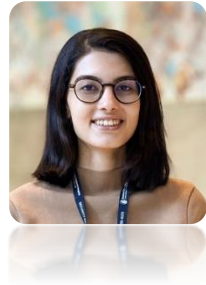
Speakers: Jonas A. M. Saute & Rebecca Schüle

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

Participants: All

Chair: Rebecca Schüle, Treat-HSP

Call for collaboration

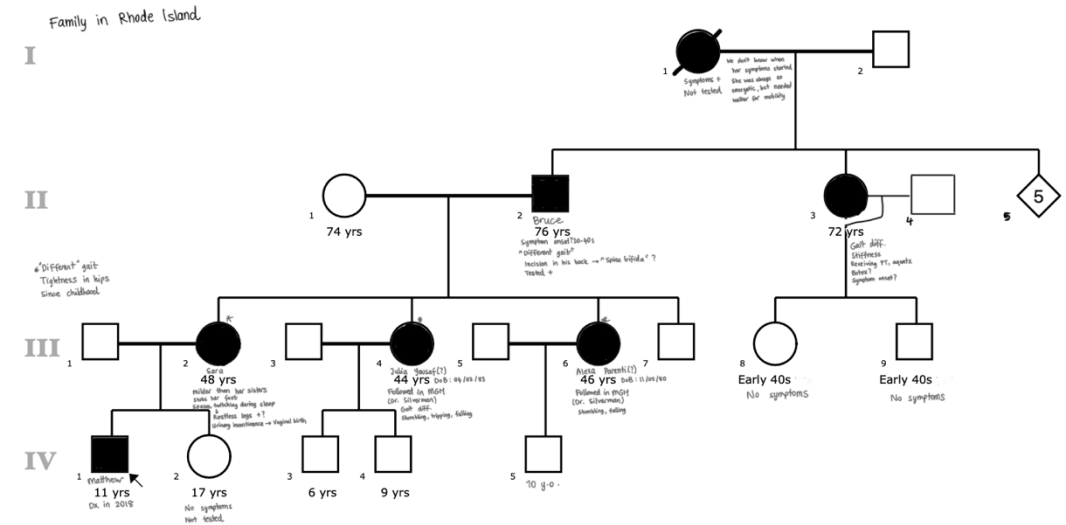


Beril Ay, MD: Identifying Genetic Modifiers of Age at Onset in SPG4

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 (≥ 2 affected generations, 3 preferred)
- Clear difference in the age at onset between generations
- Living in the US



Outlook: Annual meeting of IAB

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

- EAC invited
- Presentation of annual report
- Rater and investigator training for project 1 and 3

Discussion and Questions