Cure AP-4 Research Conference: October 12-14, 2023

Graciously co-hosted by the Rosamund Stone Zander Translational Neuroscience Center and Ebrahimi-Fakhari Laboratory

Registering for the event by September 29th would be greatly appreciated. This will help us to arrange for the right amount of food and other resources. Thank you!

Register Here: https://tinyurl.com/2023CureAP4

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Introduction:

Welcome to the seventh annual AP4-Associated HSP Research Conference! This year's conference includes an ambitious agenda spanning 3 days. Some exciting new developments in the ongoing gene therapy and drug screening projects will be presented, as well as a progress report on the Natural History Study and International Patient Registry. We look forward to productive discussions around next steps for each of these efforts.

The purpose of this meeting is to:

- Recap what has been learned about AP-4 HSP
- Discuss progress in the ongoing research projects
- Discuss human phase 1 trials and gene therapy commercialization

On behalf of the families affected by AP-4-HSP, we truly appreciate your willingness to participate in this conference. We are blessed that so many impressive people are involved in the effort to understand and develop treatments for these devastating disorders!

Meeting Location: Karp Building 1st Floor Boardroom
Karp Research Building
1 Blackfan Circle
Boston, MA 02115

For those unable to attend in person, Zoom info for the meetings can be found at the end of this packet.

Parking: Parking is available at the Longwood Galleria building or at Boston Children's Hospital - corner of Longwood Avenue and Blackfan Circle (Boston Children's Hospital patient garage).

Hotel: If you are planning to stay over night, we suggest:

The Inn at Longwood Medical
342 Longwood Ave
Boston, MA 02115
(617) 731-4700

BCH Contact: Amy Tam or Nicole Battaglia
Department of Neurology
Telephone: 617-355-2698
Email: hsp.research@childrens.harvard.edu

Agenda:

I. ***Clinic Day October 12, 2023:*** *Please contact the HSP Research Study Team to schedule an appointment with Dr. Ebrahimi-Fakhari or Dr. Quiroz for a Natural History Assessment:*

Amy Tam or Nicole Battaglia
Department of Neurology
Telephone: 617-355-2698
Email: hsp.research@childrens.harvard.edu

II. ***Conference Day October 13, 2023 AM:*** *Pre-meeting workshop with scientists and clinicians (Karp Building Boardroom)*

9:00am – 9:45am:
1. Discussion of the clinical outcome measures and clinical trial design
2. Discussion of biomarkers / surrogate markers / exploratory endpoints

Break: 15 minutes

10:00am – 10:45am:
3. Discussion of immunosuppression
4. Discussion of dose

Break: 15 minutes

11:00am – 11:45am:

5. Discussion of efficient patient recruitment & retention
6. Discussion of how to account for probands crossing from matched-controls to treatment arm

11:45am – 12:00pm:

7. Summary and Closing Remarks

III. ***Conference Day October 13, 2023, PM:*** *Conference with families, supporters, scientists, and clinicians (Karp Building Boardroom).*

12:00pm – 1:00pm Lunch (Karp Conference Room)

Lunch is being generously provided by The Rosamund Stone Zander TNC!

1:00 – 1:10pm:

1. Welcome from Cure AP-4: Kasey Edwards (10min)

1:10 – 2:00pm:

2. Quick Update on AP-4 Biology and Drug Screen: A. Davies (Manchester, +5h) / A. Saffari (Boston / Heidelberg, +6h) (20min)
3. Quick Update on the Natural History Study: A. Tam & D. Ebrahimi-Fakhari (Boston) (20min)
4. Q&A: 10 min

Break: 15 minutes

2:15pm – 3:35pm:

4. Gene Therapy: SPG50 Elpida Therapeutics (30min)
5. Gene Therapy: SPG52 M. Chillon (Barcelona, +6h) (20min)
6. Gene Therapy: SPG47 M. Azzouz (Sheffield, +5h) (20min)
7. Q&A: 10 min

Break: 15 minutes

3:50pm – 4:20pm:

8. Unravel Bio Team (20min)
9. Q&A: 10 min

Break: 10 minutes

4:20pm – 4:50pm: Summary & Open Discussion

a. How can we improve recruitment and retention of participants in the natural history study?

b. How can we recruit patients worldwide efficiently?
c. How can we ensure de-central data collection? Regional study visit days? Use of conferences?
d. How can we efficiently recruit to the matched-control arms of the gene therapy trials?
e. How can we promote fundraising?

IV. Reception and dinner for conference attendees hosted by Cure AP-4

5:00pm – 6:00pm: Cocktail reception
6:00pm – 9:00pm: Dinner
The Inn at Longwood Medical
The Fenway Room
342 Longwood Ave
Boston, MA 02115

V. Cure AP-4 Family Meet and Greet October 14, 2023 hosted by Cure AP-4

Please come and meet other families affected by AP-4-HSP. This will be a casual event, with child entertainment, to meet and network with other families, talk with any attending researchers, and for the kids to connect in person. Lunch will be provided.

Hours and location for Family Day are tentative at this time!

10:00am – 1:00pm:
The Inn at Longwood Medical
The Fenway Room
342 Longwood Ave
Boston, MA 02115

Point of Contact:
Kasey Edwards: 781-405-8961
kasey@cureap4.org

Cure AP-4 Leadership:

Kira Dies, ScM, CGC: *Executive Director at Rosamund Stone Zander Translational Neuroscience Center, Boston Children's Hospital*. Kira is a licensed genetic counselor at BCH. She has a deep understanding of the underlying genetics of neurodegenerative diseases like HSP. She has experience managing multi-site clinical trials for neurogenetic conditions

including tuberous sclerosis complex, Rett syndrome, and PTEN hamartoma syndrome.

Kevin Duffy: *Head Golf Professional, Commonwealth National Golf Club*. Kevin is Molly and Owen Duffy's father. He has been working in the golf industry for more than 15 years and is currently responsible for leading the golf operation at Commonwealth on both an operational and strategic level. His areas of expertise include marketing, relationship management, customer service, team building and coaching.

Chris Edwards: *Entrepreneur*. Chris is Robbie Edwards' father. He has founded a series of startup companies during his career. He has extensive experience in building/managing teams with diverse skills sets, and with navigating complex governmental regulations and problem solving.

Kasey Edwards: *Community Relations Coordinator, Cure AP-4.* Kasey utilizes meaningful research-centered communications and patient-community engagement to drive therapeutic and resource discovery to enhance the quality of life for AP-4-HSP patients and patient families.

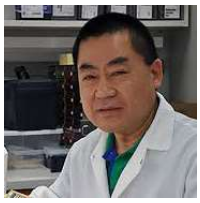
Erika M. Gill: *Vice President / Head of Neuroscience Global Product and Launch Strategy, Takeda Pharmaceuticals.* Erika has over 20 years' experience in health care and biotech, leading several cross-functional areas including program management, patient services and education, marketing and health care administration across multiple disease areas.

Cure AP-4 Medical and Scientific Advisors:

Dr. Mimoun Azzouz: *Chair of Translational Neuroscience, ERC Advanced Investigator, Director of Research and Innovation, University of Sheffield*. Dr. Azzouz has a long-standing interest in developing gene therapy approaches for neurodegenerative diseases. His team utilizes viral-based gene transfer systems both for research and gene therapy applications.

Dr. Craig Blackstone: *Director, Movement Disorders Division, Department of Neurology, Massachusetts General Hospital and Harvard Medical School*. Dr. Blackstone's laboratory investigates the cellular and molecular mechanisms underlying hereditary movement disorders. Craig is one of the most prominent HSP researchers in the world.

Georg Borner, PhD: *Max Planck Institute of Biochemistry Group Leader.* Dr. Borner is investigating the molecular details of AP-4 deficiency syndrome. His lab recently uncovered a direct link between AP-4 mediated transport and the spatial control of autophagy, via sorting of the core autophagy machinery protein ATG9A, providing a potential mechanism for AP-4 pathology.



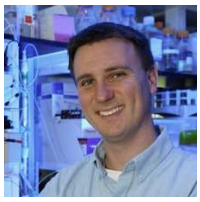
Xin Chen, MD, PhD: *Assistant Professor, UT Southwestern Medical Center.* Dr. Chen has been successfully generating favorable efficacy and safety data using AAV9 gene therapy to treat both AGU and CLN7 knockout mouse models in Dr. Steven Gray's laboratory. Both of these projects are now at the stage of IND enabling. He is now leading the work as a Co-PI on gene therapies for SPG50 and multiple other neurological disorders under the direction of Dr. Gray.

Dr. Basil Darras: *Associate Neurologist-in-Chief, Chief-Division of Clinical Neurology, Director- Neuromuscular Center, Boston Children's Hospital*. Dr. Darras' research is focused on the molecular genetics, diagnostics and therapeutics of pediatric neuromuscular diseases.

Alexandra Davies, PhD: *Postdoc with Georg Borner, Max Planck Institute of Biochemistry, Germany*. The focus of Alex's postdoc research involves studying AP-4 function in neurons.

Darius Ebrahimi-Fakhari, MD, PhD: *Child Neurologist at Boston Children's Hospital / Harvard Medical School.* Dr. Ebrahimi-Fakhari has a long-standing interest in childhood-onset neurometabolic-, neurodegenerative-, and movement disorders. His group is leading several research projects on AP-4-HSP including "Development of iPSC-Derived Neurons from Patients with AP-4-associated Hereditary Spastic Paraplegia to Support an Unbiased Phenotypic Screening for Novel Therapeutic Targets" and "An International Registry and Natural History Study For AP-4-associated Hereditary Spastic Paraplegia".

Dr. John Fink: *Professor, Department of Neurology, Director, Neurogenetic Disorders Program, University of Michigan*. In addition to being one of the world's foremost investigators of upper motor neuron disorders, Dr. Fink also maintains the largest clinic in the U.S. for persons with HSP or PLS.



Dr. Steven Gray: *Associate Professor at UT Southwestern Medical Center*. Dr. Gray's core research focus is to develop adeno-associated virus (AAV) gene transfer vector systems, for clinically-relevant global gene transfer to the central and peripheral nervous system.

Neil Hackett, PhD: *Independent Consultant.* Neil Hackett has extensive experience in pre-clinical and translational gene therapy programs. He advises on many areas including study design and regulatory filings. His background includes professorial appointments at Vanderbilt University and Weill-Cornell Medical College resulting in over 100 academic publications.

Mustafa Sahin, MD, PhD: *Director, Rosamund Stone Zander Translational Neuroscience Center, Professor in Neurology, Harvard Medical School*. Dr. Sahin's lab investigates the normal cellular functions of signaling pathways implicated in childhood neurological diseases. His research is focused on proteins affected in Tuberous Sclerosis and related neurodevelopmental disorders.

Zoom Meeting:

Join from your computer or mobile device:
https://bostonchildrens.zoom.us/j/94237636849?pwd=TjNkV1kzVElZcmZxVUtOZHBscDZLUT09&from=addon
Meeting ID: 942 3763 6849
Password: AP4HSP

Or dial in from your telephone:
Internally: x28882
Externally: 646-558-8656 (Primary)
301-715-8592 (If you are unable to dial into the primary)
312-626-6799 (Alternate)

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EWS link: https://zoom.us/wc/94237636849/join

Meeting ID: 942 3763 6849


Cure SPG47
Cure SPG50
Cure SPG51
Cure SPG52
Cure AP-4