



**ROSAMUND  
STONE  
ZANDER**

**TRANSLATIONAL  
NEUROSCIENCE  
CENTER**



**Cure AP-4**

## **Cure AP-4 Research Conference: 10/28/2022**

*Graciously hosted by the Rosamund Stone Zander Translational Neuroscience Center*

*Registering for the event in advance would be greatly appreciated. This will help us to arrange for the right amount of food and other resources. Thank you!*

**Please register by October 14th, 2022:**

**[https://docs.google.com/forms/d/1VjPKgKy\\_8VVU7mS7Ayqp2O2aG1sZIOTEqvqd5IPCFA0/prefill](https://docs.google.com/forms/d/1VjPKgKy_8VVU7mS7Ayqp2O2aG1sZIOTEqvqd5IPCFA0/prefill)**

**Meeting Time:** Friday October 28<sup>th</sup>, 10 am - 4 pm Eastern Standard Time

**Meeting Location:** The Inn at Longwood Medical  
The Fenway Room  
342 Longwood Ave  
Boston, MA 02115

We will be meeting in the Fenway Room. Lunch will be provided!

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

**Contact phone:** Carrie Johnson, Executive Assistant for Dr. Mustafa Sahin  
(617) 919-6258

**Zoom Meeting:**

Join from your computer or mobile device:

<https://bostonchildrens.zoom.us/j/94263417934?pwd=cXNhallia0hGeEFVMmNI>

[REUycldGQT09](#)

Password: 911241

Or dial in from your telephone:

Internally: x28882

Externally: 646-558-8656 (Primary)  
408-638-0968 (If you are unable to dial into the primary)

Australia:

+61 2 8015 6011, +61 3 7018 2005, +61 7 3185 3730, +61 8 6119 3900,  
or +61 8 7150 1149

Belgium:

+32 1579 5132, +32 2 290 9360, +32 2 585 5574, +32 2 588 4188, +32 2  
788 0172, or +32 2 788 0173

Brazil:

+55 11 4632 2236, +55 11 4632 2237, +55 11 4680 6788, +55 11 4700  
9668, or +55 21 3958 7888

Canada:

+1 204 272 7920, +1 438 809 7799, +1 587 328 1099, +1 647 374 4685,k  
+1 647 558 0588, +1 778 907 2071, or +1 780 666 0144

Germany:

+49 69 3807 9883, +49 69 3807 9884, +49 69 5050 0951, +49 69 5050  
0952, +49 695 050 2596, or +49 69 7104 9922

Italy:

+39 020 066 7245, +39 021 241 28 823, or +39 069 480 6488

Netherlands:

+31 20 241 0288, +31 20 794 0854, +31 20 794 6519, +31 20 794 6520,  
+31 20 794 7345, or +31 707 006 526

Portugal:

+351 211 202 618, +351 308 804 188, or +351 308 810 988

Russia:

+7 495 283 9788, +7 499 951 6379, +7 499 951 6380, or +7 812 426  
8988

Spain:

+34 84 368 5025, +34 91 787 0058, or +34 917 873 431

Turkey:

+90 212 391 0651, +90 212 391 0652, +90 850 272 0651, or +90 850 272  
0652

United Kingdom:

+44 131 460 1196, +44 203 481 5237, +44 203 481 5240, +44 203 901 7895, +44 208 080 6591, +44 208 080 6592, or +44 330 088 5830

Or iPhone one-tap:

+16465588656,,94263417934# or +14086380968,,94263417934#

EWS link: <https://zoom.us/jc/94263417934/join>

Meeting ID: 942 6341 7934

### **Introduction:**

Welcome to the sixth annual AP4-Associated HSP Research Conference! 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 some productive discussion this year about 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 plans for 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 effort. We are blessed that so many impressive people are involved in the effort to understand and treat these devastating disorders!

### **Cure AP-4 Board of Directors:**



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, Riverton Country 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 Riverton CC on both an operational and strategic level. His areas of expertise include marketing, relationship management, customer service, team building and coaching.



Chris Edwards: *Chief Executive Officer, Blackfin Ventures Inc. and Coastal Infusions, LLC.* 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.



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 Network of Medical and Scientific Advisors:**



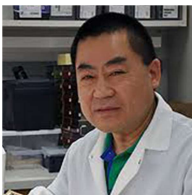
Dr. Mimoun Azzouz: *Chair of Translational Neuroscience, ERC Advanced Investigator, Director of Research and Innovation, University of Sheffield.* Dr. Azzouz has a long-standing interest in developing gene therapy approaches for neurodegenerative diseases. His team utilizes viral-based gene transfer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



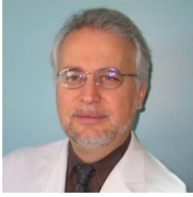
Dr. Craig Blackstone: *Director, Movement Disorders Division, Department of Neurology, Massachusetts General Hospital and Harvard Medical School.* Dr. Blackstone's laboratory investigates the cellular and molecular mechanisms underlying hereditary movement disorders. Craig is one of the most prominent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



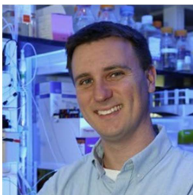
Alexandra Davies, PhD: *Postdoc with Georg Borner, Max Planck Institute of Biochemistry, Germany.* The focus of Alex's postdoc research involves studying AP-4 function in neurons.



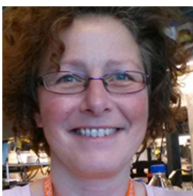
Darius Ebrahimi-Fakhari, MD, PhD: *Child Neurologist at Boston Children's Hospital / Harvard Medical School.* Dr. Ebrahimi-Fakhari has a long-standing interest in childhood-onset neurometabolic-, neurodegenerative-, and movement disorders. His group is leading several research projects on AP-4-HSP including "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.



Dr. Jennifer Hirst: *Principal Research Associate, Robinson lab, Cambridge Institute for Medical Research.* Dr. Hirst is a cell biologist who discovered the AP-4 and AP-5 adaptor complexes and has been studying their function and link with Hereditary Spastic Paraplegia.



Robin Kleiman, PhD: *Senior Director, Translational Cellular Sciences, Biogen.* Dr. Kleiman's team within Research and Early Development is focused on establishing translatable human disease models of CNS disorders to enable testing of novel therapeutic molecules.



**Professor Margaret (Scottie) Robinson:** *Principal Investigator, Cambridge Institute for Medical Research.* Prof Robinson has worked on identifying and characterizing adaptor protein complexes for 30 years.



**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.



**Sarah Sheikh, MD MSc MRCP:** *Senior Vice President, Neuroscience at Takeda Pharmaceuticals.* Before joining Takeda, she held leadership positions of increasing responsibility in clinical development at Celgene and Biogen.

### **Meeting Agenda:**

1. Brief introductions (10:00 - 10:15)
2. Presentations:

#### **Block 1: The science of AP-4-HSP and progress to date**

- a. AP-4 cell biology update, Alex Davies (10:15 – 10:45, including 10 minute Q&A)
- b. AP-4-HSP Natural History Study update, Darius Ebrahimi-Fakhari (10:50 – 11:20, including 10 minute Q&A)

10 minute break (11:20 – 11:30)

- c. Gene therapy for SPG47 update, Mimoun Azzouz (11:30 – 12:00, including 10 minute Q&A)
- d. Gene therapy for SPG50 update, Xin Chen (12:00 – 12:30, including 10 minute Q&A)

30 minute lunch break (12:30 – 1:00)

- e. Gene therapy for SPG52 update, Miguel Chillon (1:00 – 1:30, including 10 minute Q&A)
- f. Update on the phase 1 trial of scAAV9/JeT-GAN for the treatment of Giant Axonal Neuropathy (GAN), Carsten Bönnemann (1:30 – 2:00, including 10 minutes Q&A)

10 minute break (2:00 – 2:10)

- g. AP-4-HSP Drug Screening update, Darius Ebrahimi-Fakhari (2:10 – 2:40, including 10 minute Q&A)

Block 2: Discussion topics

- 10 Discussion topics/Open Discussion (2:40 - 3:00)
  - a. What crucial knowledge gaps need to be addressed next?
  - b. What are the best short and long term approaches to finding a cure for AP-4-HSP?
    - Next steps for the Natural History Study?
    - Next steps for the preclinical development of gene therapy vectors?
    - Next steps for approval by regulatory agencies and clinical trial design?
- 11 Conclusion and review of next steps

**\*\*\* Cocktail reception and dinner to follow at 4pm in the Fenway Room.  
Hosted by Cure AP-4! \*\*\***

**Cure AP-4 Family Meet and Greet: 10/29/2022**

***Hosted by Cure AP-4***

**Meeting location:** The Inn at Longwood Medical  
The Fenway Room  
342 Longwood Ave  
Boston, MA 02115

**Meeting Time:** October 29<sup>th</sup>, 10am to 1pm

**Contact phone:** Kasey Edwards: (781) 405-8961

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

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.

 Cure SPG47 +  Cure SPG50 +  Cure SPG51 +  Cure SPG52

=  Cure AP-4