STEP UP 4 AHC

FOUR PROJECTS FOR ALTERNATING HEMIPLEGIA OF CHILDHOOD

AHC Foundation Newsletter

December 2018

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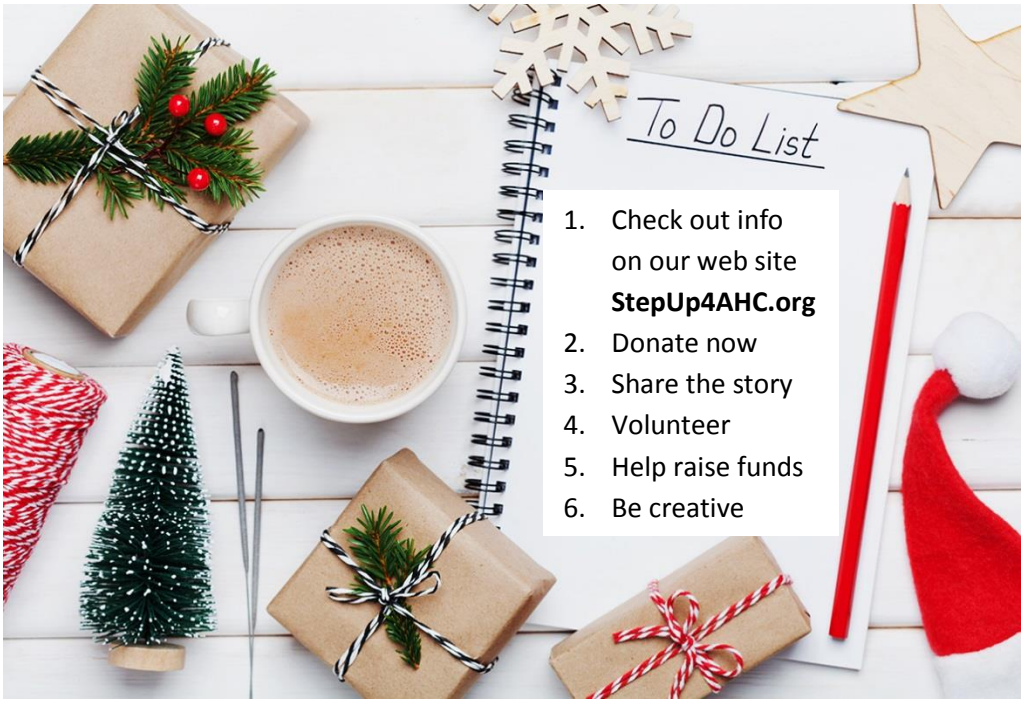
HANG YOUR STOCKINGS BY THE FIREPLACE AND HELP A GENE THERAPY GET STARTED

The **biggest year end fundraising campaign** ever undertaken by AHCF is underway! As we prepare to make the largest investment ever made in AHC research in 2019 you'll be amazed at what is now within reach for our AHC community.

The campaign is called "Step Up 4 AHC" because it will build off current research and initiate new research on gene therapy.

The cost to take the next steps needed to make this a reality is significant. While we are off to a great start, we need your help.

There are a few simple steps you can take to help fill everyone's stocking with a gene therapy gift to End AHC.



To comment on the newsletter contact: Vicky Platt at vicky@ahckids.org

AHCF Serving the International AHC community since 1993

It is time to join the movement.

●

Be part of the team making the AAV Project a reality.

●

Contact Lynn Egan for more info on how you can help.

lynn@ahckids.org

The Time for a Treatment for AHC is Finally Here.

Ring in the New Year and a New Treatment with AHCF.

Gene therapy is part of the treatment plan and we're calling it THE AAV PROJECT!

- **Gene Therapy Works -** Put simply, gene therapy works by changing the genetic information of a population of cells in a way that alleviates or combats the cause or symptoms of a disease.
- **Risk is Reduced -** Put simply, gene therapy uses viral vectors to reduce the risk of adverse effects, and each vector is rigorously tested in cells and animals before considered for human use.
- **It is Working for Other Rare Diseases -** Put simply, gene therapy is the focus of current research for SMA where they are also working on issues similar to AHC, like protecting motor neurons.
- **Researchers Think This will Work for AHC -** Gene therapy for AHC presents some challenges, but a team of the top scientists in this field are already assembled to begin addressing these challenges.
- **Collaboration is in Place –** AHCF, CureAHC and Hope for Annabel foundations are currently working together to make this project a reality for the AHC community.

Fundraising can be Easy & Fun

amazonsmile You Shop. Amazon Gives.

Fundraising can be Cost Free

Do you still have holiday shopping to do? If you do, you too can help raise money for the AHC Foundation's Year End Campaign.

Simply switch to AmazonSmile and the Amazon Foundation will donate 0.5% of the purchase price of eligible products to the AHCF.

This small switch can **help raise money for AHC all year long** and will cost you nothing extra.

Setting up AHCF as your charity of choice will make sure the funds come to us.
Thank you for helping achieve the mission of Ending AHC!

AHCF Donated over $3 million to fund AHC research prior to the AAV Project

DONATE

To verify the financial strength of our foundation, check out our status with GuideStar or Great NonProfits.

AHC COMMUNITY CONNECTIONS

Dr. Al George Reports from the Symposium: Part 2 (Continuing from November Newsletter)

The 7th Annual ATP1A3 in Disease Symposium took place on October 13-14, 2018 at the Feinberg School of Medicine at Northwestern University in Chicago, Illinois.

Experts on Na+/K+-ATPase and ATP1A3-related diseases from all over the world were attended this scientific meeting with a very impressive program.

The following summary of the meeting was kindly put together by Dr. Alfred L. George so the AHCF could share it with our parents. It is long, but an amazing summation of the wonderful work being done around the world to help End AHC. We sincerely thank Dr. George for his hard work and professionalism in tending to all aspects of this symposium. This is part 2 of the article which was also featured in the November newsletter.

Non-motor Symptoms

This session emphasized neuropsychiatric symptoms associated with ATP1A3-related disorders. Dr. Hendrik Rosewich led the session with a review of psychiatric and cognitive features of ATP1A3 diseases. He reported that impaired cognitive function is common in AHC, but less prominent in RDP and CAPOS. In RDP, cognitive impairment is more severe in patients with motor symptoms. Psychiatric symptoms are less well described in ATP1A3-related diseases, and there is a need to systematically collect these data. Mood disorders occur in approximately 20% of patients. He gave a preliminary report on a pilot study to assess social, cognitive, and practical competencies among patients with ATP1A3 mutations.

Dr. Diane Doummar reported discussed four French patients with novel ATP1A3 mutations that had epileptic encephalopathy without hemiplegic attacks. All subjects shared features of hypotonia, seizures, intellectual disability, and early age at onset of symptoms (less than 6 weeks of age). She suggested that epileptic encephalopathy should be considered part of the clinical spectrum of ATP1A3-related disorders.

The remaining presentations of this session focused on psychiatric symptoms associated with ATP1A3 mutations. Dr. Catherine Brownstein presented a case of congenital schizophrenia associated with a novel ATP1A3 mutation. This was followed by two young investigator presentations (Richard Smith, Christopher Thompson) who described cellular and molecular mechanisms for the dysfunction of ATP1A3 in this case. These findings add to the expanding clinical spectrum of ATP1A3 disorders. The last presentation by Dr. Thomas Holm described his hypothesis that,

Continue to page 4…

The Board of Directors of the AHC Foundation wish everyone in the AHC Community a very Happy & Healthy New Year. May your 2019 be filled with new adventures which bring you joy and happiness.

Gene, Shannon, Sharon, Cate, Lynn, Heather, Bill, Rik, April, Renee, Josh, Mario, Vicky, Carol, and Meredith

AHC COMMUNITY CONNECTIONS

Dr. Al George Reports Continued…

many features observed in the D801Y mutant mouse model of ATP1A3 disease are shared with schizophrenia, and he showed preliminary data in which a novel compound could reverse some of these features.

Clinical Symptoms and Treatment of Dystonia

In this session, we heard an update on a systematic effort to delineate the clinical features of RDP given by Dr. Ihtsham Haq, and a presentation on the use of deep brain stimulation to treat Parkinson disease by Dr. Harrison Walker. Dr. Haq emphasized how the features of RDP have become clearer with review of data from a 10-year follow up study of 50 cases. For example, the onset of symptoms was not 'rapid' in all cases. Other 'typical' features of RDP may not be as uniform among patients as previously thought. He concluded that there should be a lower threshold for performing genetic testing for ATP1A3 mutations in cases that have some, but not all, features of RDP.

Dr. Walker discussed how deep brain stimulation can result in dramatic improvements in adults with Parkinson disease. There has been limited experience using this therapy in RDP, and the results were not encouraging. He emphasized the need for a more systematic study to determine if deep brain stimulation can help these patients.

Two trainees complemented this session with their presentations on the use of patient-derived induced pluripotent stem cell technology to study ATP1A3 mutations (John Snow), and illustrations of novel ATP1A3 mutations associated with atypical clinical features (Linh Tran).

Epilepsy in ATP1A3 Diseases

This session featured two speakers (Erin Heinzen, Mohamed Mikati) who discussed different aspects of seizure disorders associated with ATP1A3 mutation. Dr. Heinzen focused on genetic epilepsy disorders and use of exome sequencing to discover novel genes. She provided an update on efforts to find other genes associated with AHC-like disorders. Dr. Mikati reviewed his approach to managing epilepsy in the setting of ATP1A3 mutations, and reported on the clinical features of seizures in these patients. Seizures are common among AHC patients (60%) and some exhibit seizures before the onset of motor symptoms of AHC. He concluded by emphasizing the importance of treating seizures, sleep disturbances and neuropsychiatric symptoms associated with ATP1A3 mutations.

Dr. Nina Schor highlighted the importance of studying rare neurological disorders from her perspective as Deputy Director of NINDS. She emphasized that in child neurology clinics, rare diseases collectively are not rare. The NIH deems rare disease research important for many reasons. **Continue to page 5…**

DONATE

Contribute financially to the campaign for Gene Therapy and 3 other projects for AHC. Get creative, if you have a big donation, maybe make a matching challenge for the community!

To volunteer with the AHCF contact Lynn Egan at: lynn@ahckids.org

SHARE AHC INFO

If you know of friends, family teachers, or therapists who would benefit from our newsletter, share this issue with them & ask them to join our mailing list.

Check out our website

www.ahckids.org

AHC COMMUNITY CONNECTIONS

Dr. Al George Reports Continued…

Dr. Simona Balestrini gave a brief update on their study of electrocardiographic (ECG) abnormalities in patients with ATP1A3 mutations. Their study now has 112 participants, mostly with AHC (97). They have largely confirmed their previous published study, but had interesting follow-up data for some patients who required pacemakers because of abnormal heart rhythms.

New Therapeutic Approaches

In the last session of the conference, attendees were energized by talks about future therapeutic opportunities for ATP1A3-related diseases. The session began with a discussion of imaging biomarkers given by Dr. Christopher Whitlow. His ongoing study using MRI to image the brains of RDP patients has provide insights into the brain regions most affected by the disease, along with new correlations between brain structure and clinical features. Biomarkers are important for following the clinical course of the disease, and will help evaluate the success of therapies.

Alan Lewis presented his work investigating the therapeutic benefits of transdermal nicotine to control challenging behaviors in children with autism and other neurodevelopmental disorders. In an exploratory trail of adults with autism, transdermal nicotine improved irritability, suppressed aggressive behaviors, and improved sleep in many, but not all, subjects. This therapy may have value in some older patients with ATP1A3 mutation who exhibit such behaviors.

In the last two talks of the meeting, Dr. Steven Gray and Dr. Barry Ticho presented two distinct approaches for gene therapy of rare genetic neurological disorders. Dr. Gray discussed use of viral gene delivery to the brain through the spinal fluid (intrathecal delivery). He is developing an adeno-associated virus (AAV) to deliver ATP1A3 to mouse brain, with the short term goal of testing the efficiency of delivery. There are many AAV gene therapy trails ongoing for various genetic conditions, and ATP1A3-related diseases may one day benefit from this therapeutic strategy.

Dr. Ticho from Stoke Therapeutics introduced a strategy to boost expression of proteins expressed in the brain. The technology, called TANGO, exploits a natural form of 'poison' exon that can be suppressed to force cells to make more of a targeted protein. Their company is working on a therapy for Dravet syndrome, but has begun exploring ATP1A3 as a potential therapeutic target.

The AHCF is grateful to Dr. George for taking the time to provide this summary to our families and the AHC community.

Do you have questions about AHC?
Are you looking for people who understand life with AHC?
We're here to help.
www.ahckids.org

The AHCF Board of Directors is pleased to announce that Cate Cohen has been elected to serve the foundation for a three year term beginning this month. Please join us in welcoming Cate back to the board.

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