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USHER SYNDROME COALITION

CONNECTING THE GLOBAL USHER COMMUNITY

GROUNDED IN SCIENCE: May 2024

A balance of research news and well-being for the Usher syndrome community

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We are only 10 weeks away from our next conference! Who else is getting excited? We certainly are! Be sure to follow us on social media to see more conference-related content leading up to the event.

USH Connections Conference | July 19-20, Rochester, NY + Online

Hosted in partnership with the National Technical Institute for the Deaf

Register here.

Have you joined the Usher Syndrome Coalition Discord Community Server? It's a safe place for the community to connect with each other. Join here: https://discord.gg/czwHGaDu7W

RESEARCH SPOTLIGHT

AAVantgarde announces its innovative clinical study design for its lead program in Usher 1B

AAvantgarde is a clinical-stage, Italian-based international biotechnology company with two Adeno-Associated Viral (AAV) vector platforms for large gene delivery. AAV vector platforms use viruses that can be engineered to deliver DNA to target cells (Naso 2017). Typically, AAV vectors are limited because they can accommodate only small genes. AAVantgarde utilizes an AAV dual hybrid program to accommodate the larger-sized *MYO7A* gene.

At the 9th Annual Retinal Cell and Gene Therapy Innovation Summit held in Seattle on May 3rd, AAVantgarde shared a presentation titled, "Design of a Phase

1/2 clinical trial using a dual vector strategy for the treatment of MYO7A-related Usher syndrome (USH1B)."

This first-in-human clinical study will be called "LUCE-1." Prof. Francesca Simonelli is the trial's Principal Investigator.

"I am delighted to be presenting the pre-clinical and clinical activities that paved the way to the design of this first-in-human Phase 1/2 clinical study at the Summit. Through this innovative design, we aim to revolutionize our approach to understanding and treating Usher 1B patients. We are poised to generate robust evidence that will not only advance scientific knowledge, but also directly impact patient care," said Prof. Francesca Simonelli, Head of Ophthalmology at the University of Campania Luigi Vanvitelli (Naples).

This study aims to provide supporting evidence for the effectiveness and safety of AAVB-081, designed to treat RP caused by *MYO7A*-related Usher syndrome (USH1B) following previous animal studies that demonstrated improved retinal phenotypes.

Check out our Current USH Research page specific to USH subtype as well as gene-independent therapeutic approaches.

View Current USH Research

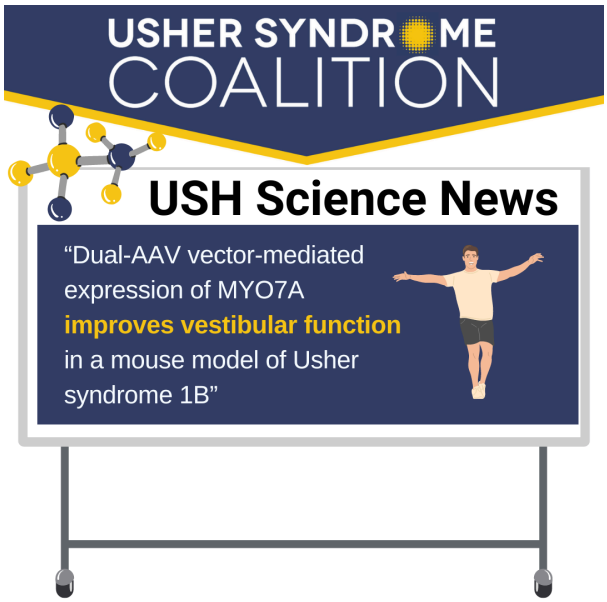
IN CASE YOU MISSED IT: SCIENCE NEWS FEATURE

Dual-AAV vector-mediated expression of MYO7A improves vestibular function in a mouse model of Usher syndrome 1B

August 21, 2023: Usher syndrome type 1B (USH1B) is the most common form of USH Type 1 and is caused by a mutation in the MYO7A gene. USH1B patients are born with profound hearing loss, vestibular dysfunction (balance disorder), and progressive vision loss due to retinitis pigmentosa that begins within the first 10 years of life.

Recent advancements in gene therapy can address a genetic mutation by replacing the defective gene with a healthy copy. Viral vectors such as adeno-associated viruses (AAVs) are commonly used for gene delivery due to their safety (only inducing a mild immune response) and ability to infect a broad range of cells. However, AAVs can only carry (or package) up to 4.4Kb of DNA, and the MYO7A gene is ~6.7Kb. To work around this limitation, researchers at the National Institutes of Health (NIH) and the University of Florida split the healthy copy of MYO7A into two halves and inserted each half into separate AAV vectors

for dual gene delivery of each half. When these two separate AAV vectors infect the same cell, the two halves join together to form a complete, healthy copy of the MYO7A gene with full functionality. Injection with dual-AAV delivery of MYO7A into a mouse model of USH1B restored MYO7A gene expression in both the cochlear and vestibular hair cells, leading to improved vestibular function.



What this means for Usher syndrome: Vestibular dysfunction puts USH1B patients at greater risk of falling and injury. Gene therapy treatment using this dual-AAV approach to repair the mutated MYO7A gene shows promise in helping USH1B patients lead safer lives.

READ ARTICLE

For more science news, check out our Science News page, organized by treatment approach and type of Usher syndrome.

DISCLAIMER: The Usher Syndrome Coalition does not provide medical advice nor promote treatment methods. USH Science News is intended to help summarize more complex literature for the community to use at their own discretion.

ON WELL-BEING
Acknowledging stress associated with self-advocacy: A parent and mental health provider perspective

by Rya Freeland, MSW

My child has been praised for their self-advocacy skills ever since they were a toddler. We as parents, have been advised that their ability to self-advocate will greatly impact their success in mainstream environments. I greatly believe in the strength of self-advocacy, which is defined as "the ability to assertively state wants, needs and rights, determine and pursue needed supports."[1] The ability to understand one's individual needs and confidently convey them is reflective of personal insight, agency and empowerment. I can also imagine it can feel overwhelming, stressful, and perhaps a bit isolating. While discussing the subject with my 8-year-old, they reported "I can do it, but sometimes it gets tiring. I wish

people would just understand sometimes." As a parent, I have proudly witnessed my child's seemingly advanced ability to share their perspective and experience. I have also wondered what it is like to have that expected of you.

Usher syndrome is classified as a rare disease. A 2023 study of the awareness of Usher syndrome among allied health professionals showed limited education in training around Usher syndrome and the needs of the patients who have it. This results in missed opportunities for diagnosis, treatment and referrals[2]. This was our family's experience. Late diagnosis, navigating multiple healthcare systems with little to no knowledge of Usher syndrome, missed symptoms and improper treatment. The strain of advocacy for the individual and families can feel discouraging.

Basas, 2015 defines the concept of "advocacy fatigue" as the increased strain on emotional, physical, material, social, and wellness resources that comes from continued exposure to system inequalities."[3] Although, not characterized as a mental health disorder, advocacy fatigue, like the concept of burnout, can present with stress-induced symptoms. Some include emotional exhaustion, feelings of hopelessness, lack of motivation and feelings of defeat as well as somatic symptoms.[4]

As a mental health provider, I understand that multiple feelings can be true at the same time. In this case, it is possible to both value and uphold the ability to self-advocate while sometimes needing a break. Understanding your limits and signs of stress are ways in which you can learn to set boundaries and incorporate stress reduction skills before you become overwhelmed. Exploring the physical, emotional and cognitive impacts can help you determine what basic needs you need to nurture – like breathwork, sleep, movement, nutrition, and incorporating grounding and mindfulness techniques[5]. Asking for support through community-based advocacy groups, peer advocacy programs, or organizations such as the Usher Syndrome Coalition, is a great way to increase connection and address feelings of isolation. Additionally, increasing awareness through policy change and research advocacy will help with systematic understanding and inclusion to ultimately lessen the burden on the individual.

I believe that community plays a pivotal part in coping and that we were not meant to do it all on our own. Individually you can manage symptoms by focusing on what it is you can control. Collectively, you can access validation, shared experiences, functional support and strength in numbers.

References:

1. Martin, J. E., Marshall, L. H. (1995). ChoiceMaker: A Comprehensive Self-Determination Transition Program. *Intervention in School and Clinic*, *30*(3), 147–156.
2. Ayton LN, Galvin KL, Johansen L, O'Hare F, Shepard ER. Awareness of Usher Syndrome and the Need for Multidisciplinary Care: A Cross-Occupational Survey of Allied Health Clinicians. J Multidiscip Healthc. 2023 Jul 13;16:1927-1936.
3. Carrie Griffin Basas, Advocacy Fatigue: Self-care, Protest, and Educational Equity, 2015 32-2 *Windsor Yearbook on Access to Justice* 37, 2015
4. Sekułowicz M, Kwiatkowski P, Manor-Binyamini I, Boroń-Krupińska K, Cieślik B. The Effect of Personality, Disability, and Family Functioning on Burnout among Mothers of Children with Autism: A Path Analysis. Int J Environ Res Public Health. 2022 Jan 21;19(3):1187.
5. Metcalf, B (May, 25 2022) Three Ways Traumatic Stress Presents and How to Handle it. *National Alliance For The Mentally Ill, U.S.*

We share the research and peer-reviewed literature that offers insight into well-being: the science behind staying grounded. Fill out this poll to request a topic.

Check out our Mental Health Resources webpage

DISCLAIMER: The information and resources on this website are provided for educational and informational purposes only and do not provide medical or treatment advice.

USH Life Hack of the Day

Send your USH life hacks to info@usher-syndrome.org

A team of researchers at Massachusetts Eye and Ear developed an app called All_Aboard, which is designed to complement GPS navigation by using auditory cues to guide the user to their destination. The app uses the phone's camera to detect street signs in order to improve micro-navigation for people who are blind or visually impaired.