HOPE in FOCUS
Seeing a cure for blindness
Supporting the LCA and rare retinal disease community

SEEING HOPE | Newsletter

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June 2023 | Issue 18

From the Founder:

Laura Manfre

By the time you're reading this, we'll soon be on our way to Indianapolis for our LCA Family Conference. We hope we'll see you there!

Our third LCA Family Conference brings together people living with LCA, family members, advocates, doctors, researchers, and representatives of the biotech industry.

This biennial conference truly is a can't-miss event for people living with LCA because it captures the heart of our mission here at Hope in Focus: Bringing people in the LCA and rare inherited retinal disease (IRD) community together to meet, share stories, talk with researchers, make friends, and foster extraordinary connections leading to life-changing experiences.

People from across the country and from Canada, Mexico, and Turkey will gather from June 23–24 at the Omni Severin Hotel, an historic landmark hotel in downtown Indianapolis.

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Music Brings Together Family Living with LCA6 *RPGRIP1*

By Rosanne Smyle

Atlas with his cane

Jessi Crawford fancied the clarinet in her middle school band, while classmate Ted Beaman favored the trombone and guitar. Never did they dream their love of music would manifest a half lifetime later with the birth of their youngest son.

Music is everything to 2-year-old Atlas — he loves to sing, he loves to dance, and he loves all kinds of music.

Before the toddler developed his interest in music, his parents noticed something about his eye movements.

"Out of nowhere," at 6 weeks old, his mom said, he developed horizontal and vertical nystagmus, characterized by side-to-side and up-and-down rapid, repetitive, uncontrolled eye movements.

Atlas received his first pair of glasses at 3 months from Kellogg Eye Center in Ann Arbor, Michigan, about an hour's drive from the family's home in Toledo, Ohio.

A month later, doctors suspected Atlas had Leber congenital amaurosis (LCA), a rare genetic eye disorder in which the rods and the cones of the retina — the light-gathering cells — do not function properly.

Geneticists confirmed his genetic diagnosis as LCA6 caused by a mutation in his *RPGRIP1* gene. LCA6 can be particularly devastating because of its rapid onset and progression.

"This took us completely by surprise," Jessi said. "What do you *mean*, we *both* have this dysfunctional gene? What are you talking about?"

She was more than floored, especially because her older

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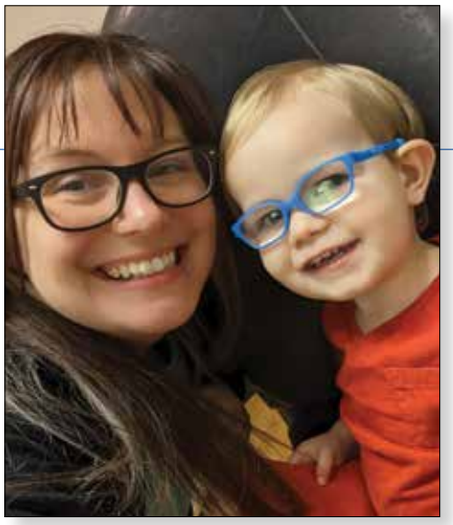
Music Brings Together Family Living with LCA6 *RPGRIP1*



Atlas and mom

Continued from page 1

son, 11-year-old Brayden-Lee, has a rare, life-threatening form of autism and epilepsy. Brayden-Lee and Atlas also have a 7-year-old brother named Ronan.

Jessi found comfort and encouragement from the geneticist and the genetic counselor, but it took time to process the idea that her son's vision would deteriorate.

"You have all these stigmas around losing your vision being the worst thing on the planet, but I realized he could still have a happy life. He's not dying, he's just going to lose his vision — that perspective helped a lot."

She'd already enlisted state and local resources to help Brayden-Lee, so she began searching for any available support and assistance for Atlas.

"I found him an O&M (Orientation and Mobility) specialist, a developmental specialist, and a vision specialist, so he wouldn't fall behind in anything — movement, sensory output, anything.

"I was still really kind of sad and overwhelmed, and, of course, worried, because I never experienced anything like this before. My oldest son had occupational therapy, speech therapy, hospital visits galore, but I never dealt with anyone who couldn't see."

LCA6 *RPGRIP1* preclinical research underway

Atlas turned 2 in May, and he's quite advanced, talking in 4-, 5-, 6-word sentences.

"He knows his shapes and he's working on colors, which is hard because he sometimes blends colors."

Atlas has no vision from the midline of his eye, down. He has vision above, for now, and cannot see close up.

Jessi and Ted's little boy underwent eye muscle surgery in February to release his eyes from crossing, which has helped his vision.

Jessi connected with Odylia Therapeutics, a biotech working on late-stage preclinical studies for a potential treatment for the *RPGRIP1* mutation, and, hoping to help advance research, she authorized the company's use of images taken of her son's eyes during the surgery.

Atlanta-based Odylia is developing an investigational gene therapy to treat vision loss caused by LCA6 and is working with vector technology developed by Co-Founder Luk Vandenberghe, PhD. The research builds on data generated at Massachusetts Eye and Ear in the labs of Vandenberghe and Eric Pierce, MD, PhD, a physician and surgeon at Mass Eye.

The company is preparing its IND submission, or Investigational New Drug application to the U.S. Food and Drug Administration (FDA). An IND is a request from a study sponsor to obtain FDA permission to start human clinical trials.

Odylia hopes to begin those trials in 2025 and is seeking partnerships or philanthropic funding for the estimated $3.5 million development costs.

Jessi said she'd like to enroll Atlas in a clinical trial, just not the first one because she fears possible, yet undiscovered, side effects from the experimental treatment.

Mickey Mouse, Rock 'n' Roll, Country, Celtic, and more

Atlas loves music, singing and watching TV.

"He loves watching Mickey Mouse-anything. He stood at the mirror, pointed at his shirt in the mirror and said, "Mickey Mouse, blue shirt, mamma."

Atlas making music

A happy child who loves raisins and pizza, he reaches for things and gets his spoon or fork to his mouth, while getting food on the utensils is another thing.

Jessi said Atlas has a tough time with the letter ‘f’ and says shork when he means fork.

“He tells me every day, fork and bowl, fork and bowl, or ‘shork a bow, mamma, shork a bow.’” Jessi said just thinking about it makes her laugh.

The couple, both 32, characterize themselves as “both huge, huge, musical people,” beginning back in the school band, when they started dating in their teens and later went their separate ways, only to start dating again four years ago.

“So, the fact that Atlas likes music so much is better for us. He loves Disney music, also rock, country music, and Celtic, and Native American.

“So, when I say we’re well rounded, we’re well rounded.”

Atlas playing

Atlas with his brothers

From the Founder:

Continued from page 1

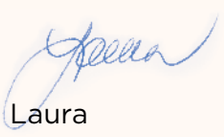
Since 2018, Hope in Focus has presented two successful LCA Family Conferences, and I’m very much looking forward to meeting new families, researchers, clinicians, and all of those who join us because of their connection to LCA.

To help offset costs for those living with LCA who want to attend, we’ve created a special donation allocation at hopeinfocus.org. Just click the green “Donate” button at the top of the page, and, from the drop-down options, select “LCA Family Conference Support.” It’s not too late to help, and we thank you!

As I write, we also are busy planning Hope in Focus’ second “A Rare Opportunity” event, showcasing Anthony Ferraro, a professional athlete, musician, and content creator living with LCA. He is featured in *A Shot in the Dark*, a documentary about his high school journey as a wrestler with vision loss. We’re so looking forward to meeting Anthony and bringing awareness to what it’s like to be a visually impaired athlete and to live with LCA. If you’re unable to join us, please look on our website for the story following the event.

Plus, in this edition of *Seeing Hope*, you’ll read about a musical family with a little boy living with LCA6 (*RPGRIP1*), catch up on our columnist’s athletic goals, and learn about optogenetics, a technique allowing researchers to control nerve-cell communication, potentially to improve vision.

With hope and gratitude,



Laura

Connecticut Residents Living with Rare Disease Voice Concerns to State Lawmakers

L–R, Alissa De Jong, parent and caregiver of a child with a blood disorder; Megan Freeman, who lives with a rare chromosomal disorder; and her friend and advocate Elizabeth Nagle

By Rosanne Smyle

One woman called doctor after doctor, only to hear they would not treat her and her two rare pediatric conditions because she turned 18 and no longer qualified for help.

Another fights for life-saving medicine to treat her rare disease that causes dangerous swelling.

While another faces $60,000 in annual medical bills for her two teenagers with a rare metabolic disorder requiring a special diet to stave off life-threatening symptoms.

“The medicine is there but you can’t get to it,” Candice Flewharty told the group gathered in Hartford, Connecticut, for Rare Disease Day. “Each phone call I make is a battle for my childs’ lives.”

People living with rare diseases told their stories to Connecticut legislators during Rare Disease Day on March 23, about a month after a New England snowstorm canceled the event usually celebrated the last day of February.

Through the state’s newly minted Rare Disease Advisory Council, known as the RDAC, legislators of Connecticut’s General Assembly now have a collaborative and organized way to improve the lives of residents living with rare diseases. The council’s first report of findings and recommendations is due in November.

Council needed to help the rare disease community

The RDAC will give patients, families, caregivers, health-care providers, advocates, researchers, and other stakeholders the opportunity to make formal recommendations to state agencies and the legislature about policy development and health-care legislation to improve the lives of people living with rare disease and their caregivers, according to Lesley Bennett, Volunteer Ambassador for the Connecticut Rare Action Network of the National Organization for Rare Disorders (NORD).

Governor Ned Lamont signed legislation establishing the council after rare disease advocates worked for years to get it going.

“We did it,” Lesley said. “It took eight years, but we did it.”

RDAC members will include Insurance, Public Health, and Social Services commissioners, or their designees, and 10 members appointed by the Governor and the Public Health Committee leadership. Six new members were introduced at the Rare Disease Day event; four have yet to be announced. For details on the new members, please see: hopeinfocus.org/connecticut-rare-disease-advisory-council-begins-to-take-shape.

Kristen Angell, NORD’s Associate Director of Patient Advocacy, said the gathering is important for our population living with rare diseases.

“It gives them an opportunity to speak face to face with our General Assembly and let them know the daily struggles and challenges they face, and it provides the legislators an opportunity to assist in making a possible impact.”

“Everybody is here to help each other out.”

Connecticut Public Health Committee Co-Chair Senator Saud Anwar, MD, said the time is here to find solutions to take care of and invest in the health of the rare disease population, adding that the council must go forward with this mindset:

“Every illness is treatable. Every disease has an answer and a solution.”

The state senator spoke about the realities of national and international collaborations resulting in developing regenerative medicine.

(L), Candice Flewharty, mother of two children with a rare metabolic disorder, with CT State Sen. Catherine Osten, who advocates for people living with rare diseases

James Rawlings, newly appointed RDAC Patient Representative

Laura Manfre of Hope in Focus with Kristen Angell (L) and Jennifer Huron (R) of the National Organization for Rare Disorders

"We will put our hearts together to make sure we come out of the room with solutions. Everybody is here to help each other out."

Connecticut Public Health Committee Co-Chair Representative Cristin McCarthy Vahey told the group, "I look forward to working with you and being supportive in making things happen for all of you."

Annissa Reed, NORD's Associate Director of State Policy, said she hopes the collaborative effort makes the dream of finding more rare disease solutions and access to medicine a reality. Forty years ago, fewer than 40 treatments existed for rare diseases, and now that number is 600.

Connecticut-based Hope in Focus advocated throughout the years with the Rare Action Network to help create the council, with Co-Founder and President Laura Manfre attending the Rare Disease Day event.

To see this year's Hope in Focus statement in support of raising awareness of rare disease, including Leber congenital amaurosis (LCA) and other rare inherited retinal diseases (IRDs), please go to: hopeinfocus.org/hope-in-focus-rare-disease-day-statement-to-connecticuts-legislature.

Having a voice at the state level

Connecticut joins 23 states in establishing a council specifically to address the complexities of living with a rare disease, caring for someone with a rare disease, gaining access to treatment, and getting better insurance coverage. To find out whether your state has an RDAC or is developing one, please go to: rarediseases.org/rare-disease-advisory-councils/map.

A rare disease in the United States is characterized as any disease, disorder, illness, or condition affecting fewer than 200,000 people. With more than 7,000 known rare diseases, upwards of 90 percent have no FDA-approved treatment. About one in 10 people — more than 30 million Americans — live with a rare disease.

Most rare diseases are genetic or have a genetic component, more than half of those affected by rare diseases are children, and all pediatric cancers are rare.

Keep telling your rare disease stories

Amy LaChance, the mother and caregiver of a child with SynGAP1, a genetic mutation affecting 1,200 people worldwide, said people need access to genetic testing to support research and trials for a treatment to fix this genetic typo.

She said it makes a difference when people with rare diseases tell lawmakers their stories about needing access to tests and medicine, adding, "The squeaky wheel really does get the grease."

Amy's advice echoed the encouragement we at Hope in Focus give to our LCA and IRD community — tell your stories to feel less isolated in your journey of living with a rare inherited retinal disease and to help advance research into treatments to improve vision or to halt vision loss.

For the full version of this story, please go to: ***hopeinfocus.org/connecticut-residents-living-with-rare-diseases-voice-concerns-to-state-lawmakers***

Bionic Sight Reports Meaningful Vision Improvements for RP Study Participants Receiving Emerging Optogenetic Therapy

Ben Shaberman
Vice President,
Science Communications
Foundation Fighting Blindness

All 12 individuals with advanced retinitis pigmentosa (RP) dosed thus far in a Phase 1/2 dose-escalation clinical trial for Bionic Sight's emerging optogenetic treatment have demonstrated significant vision improvements. Those receiving the highest dose of the therapy had the most vision restored. The trial, which began in March 2020, is ongoing at Ophthalmic Consultants of Long Island.

The Bionic Sight optogenetic treatment is designed to restore vision regardless of the mutation causing RP and may be beneficial to people with Leber congenital amaurosis (LCA) and other retinal conditions.

The four top responders in the trial gained the ability to recognize shapes and objects. In one set of vision tests, patients were asked to identify images of shapes, such as hearts, diamonds, clubs, and spades. In another, they were asked to identify eight kinds of fruits and vegetables. The success rate for recognizing the objects ranged from 80 to 100 percent for the four top responding patients. Prior to treatment, their success rate was much lower, equivalent to just guessing (25 percent correct when given four choices, and 12.5 percent with eight choices).

"The tests are all videotaped, and one can see that these patients were clearly frustrated when performing the tests at baseline, prior to treatment. They often said aloud they couldn't see the objects, much less recognize them," said Bill Seiple, PhD, an investigator on the Bionic Sight trial and the scientific director at the Lighthouse Guild.

"For the four top responders, that frustration was replaced with exuberant outbursts of 'banana!' or 'I see the carrot!' It was joyous to watch."

One patient said he saw the technician testing him, including the shape of their body and the movement of arms and hands, and he exclaimed that the person appeared like a superhero, "waving their arms, going off to fight the good fight."

The four top responders also showed improvement in visual acuity as measured using the ETDRS chart (standard eye chart). Two individuals went from not being able to see anything on an eye chart to correctly reading the second line.

"A particularly exciting and important aspect of the study is that the perceptual tests were corroborated by non-invasive brain recordings similar to EEGs," said Sheila Nirenberg, PhD, founder of Bionic Sight. "Patients who showed strong improvement on the perceptual tests also showed a clear increase in neural activity in the visual cortex. Thus, two independent measures demonstrated efficacy."

Bionic Sight's approach involves two components: A one-time optogenetic treatment enabling expression of a light-sensitive protein in retinal ganglion cells that survive after photoreceptors are lost to an advanced retinal disease like RP; and a device worn like a pair of glasses, capturing the scene a person is looking at and generating vision-enabling code, which is sent to the light-sensitive ganglion cells, and then on to the brain.

Unlike other emerging optogenetic approaches, which may use glasses or goggles to enhance the shape and intensity of the image, the Bionic Sight device produces neural impulses, similar to those produced by normal ganglion cells in the healthy retina. Dr. Nirenberg believes that using the retina's normal code can lead to better vision.

Study investigators are evaluating vision restoration for participants receiving the optogenetic treatment with and without the code-delivering goggles. They believe the goggles will be most helpful to those individuals at the most advanced stage of disease and have little retinal circuitry remaining.

*Visit **FightBlindness.org** to stay informed about the latest research advances for LCA and other IRDs.*

Trying Not to Use Visual Impairment as an Excuse to Avoid Life's Challenges

As a kid I always loved sports. I was never very good at them though. Barely being able to see the ball so many sports use had something to do with it.

This was the case until I discovered wrestling as a teenager. Wrestling is one of the most inclusive sports.

It has official rules on how to accommodate people with many different disabilities, including visual impairments. Rules that made it so I didn't need to be able to see my opponent. Rules that gave me an opportunity to compete on an even playing field for the first time in my life.

I wrestled for six years and got pretty good at it, if I do say so myself — even placing at a few provincial tournaments.

I stopped wrestling when I began university — feeling like I wouldn't have enough time for five two-hour practices per week and still be able to do as well as I wanted to in school.

For several years after stopping wrestling, I rarely exercised, telling myself that I didn't have the motivation to be fit when I wasn't working toward a goal like winning wrestling matches.

I occasionally felt the desire to get back into shape, but I used my visual impairment as an excuse. I told myself that gyms were large, overwhelming, and hard to navigate when you can't see well, and I told myself that most recreational activities weren't accessible — remembering one of the last times I rode my bike and ran into a parked car.

Thankfully, over time I've stopped letting my visual impairment be an excuse, remembering — as with wrestling's inclusive rules and most things in life — there is always a way.

I started with downhill skiing where I had a sighted guide ski behind me and tell me which way to turn. Later I tried tandem cycling, sailing, and returned to the gym.

Jack and his guide dog, Baloo

My most recent and favorite is long-distance running. In fact, I like it so much that I just came back from a 12-mile run with my guide and friend in preparation for a half-marathon we are running together.

As I've gotten more active, I've become healthier, I'm much happier, I feel more energetic, and I require less sleep.

The moral of the story is much like many of the articles I've written for this column: Learn from my mistakes. Don't use your visual impairment as an excuse.

You will live a much happier and fulfilling life if you find creative solutions to challenges and ask yourself "how can I do it?" instead of looking for reasons why you can't.

Jack McCormick graduated in 2018 from Canada's Wilfrid Laurier University in Waterloo, Ontario. He was diagnosed in high school with LCA2 (RPE65). Jack is a Hope in Focus ambassador, helping people living with LCA and IRDs. You can read his blog at ***jackdamccormick.wordpress.com***

Events

DO YOU HAVE AN EVENT YOU WANT TO SHARE? LET US KNOW!
Email rosanne@hopeinfocus.org with the information and a link.

Let's Chat About...
hopeinfocus.org/for-families/lets-chat-about

A new "**L**et's **C**hat **A**bout..." webinar episode is coming soon. We've developed the series with those living with LCA and IRDs in mind, but it is open to anyone interested in what's happening in our communities. Please check our website for upcoming sessions.

Medicine Congress 2023
June 28–30, 2023 • London, UK
medicine.pulsusconference.com

The 6th International Conference on Medicine and Surgery brings together global experts to discuss the latest developments and best practices in the medicine and surgery field.

Global Genes
2023 RARE Advocacy Summit
Sept. 19–20, 2023 • San Diego, CA
globalgenes.org/event/rare-advocacy-summit

Global Genes convenes one of the world's largest gatherings of rare disease patients, caregivers, advocates, health-care professionals, researchers, partners, and allies at the summit.

Hope in Focus
Dinner in the Dark
October 14, 2023 • Groton, CT
hopeinfocus.org

Dinner in the Dark, our primary fundraiser for the year, helps fund research to cure blindness caused by LCA, provides support for genetic testing, and drives awareness, education, and connections for LCA and IRD families. Get ready for a stellar menu, fine wines, and a lively sensory adventure.

Foundation Fighting Blindness
VISIONS Conference
June 21–22, 2024 • Chicago, IL
www.fightingblindness.org/events/visions-2024-503

The Foundation's national conference features sessions on research advancements, practical adapting and thriving, and opportunities to connect with the blind and low-vision community. A dynamic actionable program and agenda have been developed in collaboration with the Orphan Disease Center of the University of Pennsylvania.

HOPE in FOCUS
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To learn more about Hope in Focus, visit www.hopeinfocus.org.

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