

SEEING HOPE | Newsletter

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January 2019 | Issue 5

From the Founder

Every January, we spend some time looking back at what's been accomplished, and a lot of time looking forward to what we want to get done. The list of achievements for 2018 is long and impressive, but the to-do list for 2019 is longer and even more challenging.



Sofia Priebe & Laura Manfre

This year we passed our five-year mark. In the life of a nonprofit, the next five years are a critical time. We have moved from a small, local NPO that was born at my kitchen table because of an illness my daughter was diagnosed with. We faced a personal and medical challenge, and we quickly learned that everyone who receives a diagnosis of Leber congenital amaurosis feels much the same as we did.

We created Sofia Sees Hope with the thought that we could fund research to treat our daughter's gene. Since then, we have grown to understand that the world of LCA and all inherited retinal diseases needs to multitask: yes, research and treatments are critical to patients and caregivers, but so are education and advocacy. In such a small world, creating and maintaining a community is of equal importance.

In 2018, we launched our #KnowYourGene campaign to stress the importance of genetic testing on the heels of donating \$80,000 in 2016-17 to provide access to genetic testing and counseling to LCA

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Living with LCA: 'It Does No Good To Have Pity'

By Rosanne Smyle

Mikayla Larson, a 30-year-old mother living with a rare form of Leber congenital amaurosis, wants to reassure children living with the same disease that they're going to be OK.



Mikayla and Andrew Larson

"I feel that there are a lot of parents out there that are terrified for their kids to live this life," she says from her southeastern Texas home. "And while it's not ideal, it doesn't mean that they aren't capable of living a fulfilled life and love it like they should."

Larson's form of LCA, known as LCA6 caused by a mutation of the RPGRIP1 gene, is rare even within the realm of rare disease, accounting for about 5 percent of the total LCA patient population.

Photoreceptors lacking RPGRIP1 are unable to maintain the retina's light-sensing outer segments, resulting in patients losing retinal functions at an early age but retaining photoreceptors in the central retina well into adulthood, according to the National Institutes of Health.

Larson says children born with LCA need to know that others have gone through life with the same inherited retinal disease and survived the bullying, mistreatment or embarrassment.

"I think I'd tell any parent that getting their child into therapy is a necessity," she says. "Most of us need help navigating these very important emotional things in life. Like when you get made fun of, or when your sibling or friends get their driver's license and you can't. Just coping with what this will mean for their life and how to navigate it."

More than anything, she wants to take the element of pity out of dealing with the disease.

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From the Founder

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patients. We held a webinar attended by folks from around the globe on why genetic testing matters. We monitored what states were doing with regard to patient access to LUXTURNA™, which treats LCA2 (RPE65), and we advocated for keeping access as open as possible.

We held our first-ever LCA Family Conference, which was open to all inherited retinal disease families, and people attended from across the country and Mexico. It was rewarding to provide attendees access to the top medical, government, advocacy and scientific experts in the field. It was even better to see families and kids making connections and forming friendships.

In the words of our board member Shanda Easley, whose 14-year-old daughter, Helena, is undergoing genetic testing to determine the cause of her vision loss: "Sofia Sees Hope has helped my family tremendously. SSH helped my family network resources for genetic testing, provided information and knowledge on genetic testing, increased my understanding of IRDs, and the resources that are available. I have connected with other family members as well, that are impacted by IRDs, thanks to SSH."

In 2019, we plan to connect more, advocate more, educate more, fundraise more. We also plan to provide more access to genetic testing and to fund more research. Five years ago we had a sense of hope as we launched our organization; today we are brimming with it. We look forward to continuing the journey with you.



Laura

In January 2014, Laura Manfre co-founded Sofia Sees Hope with her husband, Chuck Priebe, and their friend, Elisse Rosen. The nonprofit funds research to treat blindness caused by LCA and other rare IRDs and provides outreach, support, and advocacy for the patient community.

Upcoming Events

Foundation Fighting Blindness Vision Seminar Series

February 9 • Houston, TX

www.blindness.org/vision-seminar-series

The Vision Seminar Series provides a supportive learning environment for people living with macular degeneration, retinitis pigmentosa, and other inherited retinal degenerative diseases. Each half-day seminar offers a forum to hear from doctors and scientists about the latest retinal disease research, and new treatments, therapies, and clinical trials.

National Organization for Rare Disorders

Rare Disease Day

February 28 • Worldwide

www.rarediseaseday.org

Globally, millions of patients and families on Rare Disease Day share their stories and promote awareness of the challenges, hopes, and needs of those living with rare disease. The 2019 global theme is: Bridging Health and Social Care. NORD's goal and focus is on bringing national public awareness of rare diseases. To sign up for events and check for announcements, please see rarediseaseday.us.

Connecticut Rare Action Network Rare Disease Day

March 1 (subject to change; check updates online)

Hartford, CT

www.rareaction.org/resources-for-advocates/state-action-center/connecticut/

Hosted by the National Organization for Rare Disorders and NORD's Connecticut Rare Action Network, Connecticut joins the celebration of Rare Disease Day at Hartford's Legislative Office Building. The gathering features doctors, researchers, advocates, patients, caregivers, industry representatives, and legislators focusing on bridging health and social care in the realm of rare diseases.

Global Genes RARE on the Road Rare Disease

Leadership Tour

March 30 • Boston, MA

May 4 • Birmingham, AL

www.globalgenes.org/rotr2019

The EveryLife Foundation and Global Genes partner for RARE on the Road, a Rare Disease Leadership Tour bringing critical education and insights to rare disease patients, caregivers, and other advocates. EveryLife and Global Genes are uniting to build and activate the rare disease community at the local level.

Foundation Fighting Blindness VisionWalk

Nationwide / ongoing

[www.fightblindness.org/site/SPageNavigator/](http://www.fightblindness.org/site/SPageNavigator/VisionWalk_Homepage)

[VisionWalk_Homepage](http://www.fightblindness.org/site/SPageNavigator/VisionWalk_Homepage)

VisionWalk has raised more than \$49 million to fund sight-saving research since its 2006 inception. Join the tens of thousands of people who have taken important steps toward a cure by taking part in a 5K VisionWalk. Find a walk near you and register today.

Do you have an event you want to share?

Let us know! Email Rosanne@sofiaseeshope.org with the information and a link.

Living with LCA: Self-advocacy is critical

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“It does no good to have pity, or on the other side, to put people on a pedestal for doing things everyone can do,” she says. “It’s demeaning and degrading as a human to get praise for doing something everyone else can do, just because we can’t see well.”

She has some light perception and equates her field of vision to the length of a drinking straw. With lenses, her visual acuity is 20/200 and 20/400.

Larson had vision loss early and began learning Braille at age 4. She was diagnosed at age 12, although incorrectly, with Retinitis Pigmentosa (RP). She worked with specialists to improve her independence but being around other kids never was easy.

“You need extra help. You don’t want to stick out,” she recalls. “I made myself want to fly under the radar.”

By middle school, she didn’t want to deal with Braille or learn more about skills and concepts that foster independence.

“It was something that I just despised. I don’t want to be identified that way. I don’t want to be that kind of person.”

Larson did, however, go to Arizona State School for the Deaf and Blind for her last two years of high school, graduating in 2007. She pursued job training through the state’s Vocational Rehabilitation (VR) services, but the program lacked funding and was not accepting new clients.

While on the program’s waiting list in 2008, she met Andrew, who is now her husband, and in 2009 became pregnant with her first child.

They married in 2011, when their first-born, Conner, was 1. The day after the wedding, she was pregnant with her little girl, Aubrie.

She is the mother of four children, “three here and one in heaven.” Their son Liam died from Sudden Infant Death Syndrome on April 3, 2015. He was 4 months old.

“My kids are very independent,” she says of Conner, 8, 6-year-old Aubrie and 5-year-old Carter. “They get up on their own with an alarm and get themselves dressed, and then Andrew and I make breakfast and make sure they have brushed teeth and are ready for school.”



Mikayla Larson

Not being able to drive is a big deal, especially in rural Texas, but cooking is easier with the advent of Air Fryers and Instant Pots.



Mikayla and Andrew Larson, with Conner (L), Aubrie, holding painting of little brother Liam who passed away from SIDS, and Carter.

Tripping over toys and three cats—Max, Teddy and Chester—is part of life. She shops with family and reads with reading glasses and her phone’s camera, zooming in for small print.

“I would say I’m pretty self-reliant and just do what I need without any real thought.” She does suffer from anxiety.

“Once we lost Liam, the anxiety kind of crossed over into other parts of my life.” She is seeking help and open to resources.

Her biggest advocate, Andrew, contacted Spark Therapeutics, the developer of a new gene therapy called LUXTURN[™] for LCA2 (RPE65) because he thought she might have that form of LCA. The company suggested she receive genetic testing.

When Larson visited an ophthalmologist for a genetic testing referral, she was met with disbelief. The

doctor said she couldn’t have LCA. “It’s too rare. That’s not possible,” he told her.

She finally got the doctor’s signature for testing, and, in January 2017 at age 28, was genetically diagnosed with LCA6.

Larson says she then was in touch with Eric Pierce, MD and Ph.D., who is conducting lab-based research on RPGRIP1 at Massachusetts Eye and Ear. Dr. Pierce’s gene research involves evaluating the latest treatment version in a mouse model, with the plan to generate a gene-therapy vector for toxicology studies, ultimately leading to clinical trials.

While hopeful for a treatment, Larson prides herself on helping others and moving forward.

“We are still smart and capable. We have different challenges but that doesn’t mean we aren’t able.”

On the Hunt for Elusive IRD Genes and Mutations

By Ben Shaberman
Senior Director of Communications
Foundation Fighting Blindness



Since the identification in 1989 of Rhodopsin (RHO), the gene associated with an inherited retinal disease (IRD) which, when mutated, is a frequent

cause of retinitis pigmentosa, genetic researchers have identified approximately 270 genes linked to IRDs. More than two dozen of those are associated with Leber congenital amaurosis (LCA). In most cases, defects in a single gene can cause a retinal disease and vision loss.

The cumulative breakthroughs in IRD gene discovery over the past three decades are indeed impressive. It means that today, about 80 percent of LCA patients will have their mutated gene identified when getting tested. However, it also means that the gene mutations for about one-third of all IRD patients are still not identified.

To address the gap in genetically diagnosing patients, the Foundation is funding a five-year, \$2.5 million project to find elusive IRD genes and mutations, including those that may be associated with LCA.

“Patients benefit greatly from the identification of their disease-causing gene mutations. It confirms their diagnosis, identifies risk for other family members, and is often helpful for qualifying for clinical trials,” says Stephen Rose, Ph.D., the Foundation’s chief scientific officer. “The results from the elusive genes project will ultimately help us get more people diagnosed and on a better path for managing their condition. It will also help researchers develop treatments that can help more people.”

Stephen Daiger, Ph.D., a genetic researcher at the University of Texas, Houston, is working on the elusive genes project. “A strategic goal of

the Foundation has been to find the underlying cause of disease in at least 95 percent of patients with inherited retinal diseases,” he says. “We’re almost there. We’re finally in the end stage of understanding the causes of inherited retinal diseases, in my opinion.”

The elusive genes research effort will also include Radha Ayyagari, Ph.D., the project lead at the University of California, San Diego, and Kinga Bujakowska, Ph.D., a retinal geneticist working with Eric Pierce, MD, Ph.D., at Massachusetts Eye and Ear.

In addition, David Gamm, MD, Ph.D., at the University of Wisconsin-Madison, will use induced pluripotent stem cells (stem cells derived from patients’ skin or blood) to create IRD models for studying expression in newly identified genes to determine if a defect is causing the disease.

The study will include more than 140 families and 400 individuals.

“The results from the elusive genes project will ultimately help us get more people diagnosed and on a better path for managing their condition. It will also help researchers develop treatments that can help more people.”

**—Stephen Rose, Ph.D.,
FFB chief scientific officer**

Investigators will be looking for ultra-rare IRD genes yet to be discovered, as well as hard-to-find defects in known genes.

“To find the very rare genes, we need to conduct studies in large numbers of patients,” says Dr. Ayyagari. “Once we find a possible IRD gene, we need to study it in a cell or animal model to determine if it is truly critical to retinal health and function.”

A DEEP DIVE INTO ELUSIVE GENE MUTATIONS

Genes (DNA) are like recipes that cells use to make proteins. Proteins are essential to the health, survival, and function of our cells. The recipes are delivered to protein-making machinery in the cell through messages (RNA). If there is a mistake in the DNA or the RNA, then the cell will make the wrong or too little protein, and bad things happen to the cell.

Most disease-causing mutations occur in regions known as exons. Exons are like instructions in a recipe: “Add 1 tablespoon of yeast.” In simple terms, a mutation in an exon might be a misspelling like: “Add 1 tablespoon of yeast.” While no mutation is easy to locate, “misspellings” in exons are the most obvious place to find them—that’s where researchers look first.

However, sometimes entire instructions in DNA are either missing or duplicated. These mistakes are difficult to identify.

Difficult-to-find mutations can also occur in introns, regions between the instructions (i.e., between the exons). On some occasions, there is too much space, or not enough, between the instructions. These intronic mutations can lead to mistakes in creation of the messages (RNA).

Think of it as if the assistant in a bakery copied down the recipe incorrectly from a book, because there were two instructions on the same line. The master baker, in receiving the incorrect message from the assistant, makes a bread that doesn’t rise.

Keep in mind that a person’s entire collection of DNA, their genome, is comprised of about six billion letters. That alone often makes finding new disease-causing mutations a very challenging endeavor.

Visit [FightBlindness.org](https://www.fightblindness.org) to stay abreast of the latest research advances for LCA and other IRDs.

Should You Tell Others About Your Vision Loss?

To disclose or not to disclose, for many with IRDs that is the question.

For me, it was a question I struggled with for a long time. I didn't want to be judged based on my vision loss, but on the other hand, I didn't want people to think I was weird for bumping into something or looking extra closely at my phone. The issue was pretty much resolved when I got my guide dog. Walking around with a 70-pound dog in a harness makes my vision loss apparent. I can't exactly hide him.

So I was more or less forced to start disclosing my vision loss. But there are more benefits to disclosing than not, and I hope to convince you of this.

ASSISTANCE

This is perhaps the most obvious benefit to disclosing. There are challenges associated with having vision loss. Many times it doesn't take much to eliminate these barriers. People are naturally helpful and I've found that when I disclose, people want to do what they can to assist me.

CONFIDENCE

When I chose not to disclose my vision loss, it was something I felt vulnerable about—I didn't want everyone to know. When I was forced to disclose, I accepted that part of myself and in turn became more accepting of who I am. You can't be yourself if you hide a part of you from the rest of the world, no matter how small that piece is. Today I know who I am and I am proud to share that with the world. Be proud of who you are. The things you hide become much bigger when you choose to hide them.

DISCOUNTS

Who doesn't like to save some money? Disclosing your vision loss can result in some serious savings! Discounted cable and cell phone bills; 2-for-1 travel and movie tickets; and free seat upgrades at concerts and sporting events, to name a few. Mention your vision loss to the places where you do business and you might be surprised what they can do to help you save money.

I hope that next time you face the question you will make the decision to disclose. It won't go the way you want it to every time but repeating the decision to disclose over time certainly has its benefits.



Jack McCormick and his guide dog, Jake.

You may notice a new name on this regular column by Jack McCormick. That's because Jack graduated last spring from Canada's Wilfrid Laurier University in Waterloo, Ontario. Jack was diagnosed in high school with LCA2. He is a Sofia Sees Hope ambassador, helping people living with LCA and IRDs. You can read his blog at jackdamccormick.wordpress.com

The Important Role of the Patient Voice

By Rosanne Smyle

It's all about you.

The journey from identifying a rare disease to conducting studies to getting approval for a treatment is long, but it always starts with the patient, and the information patients share among the medical, biotechnological and advocacy communities, as well as within the patient community.

At a fall gathering of families living with Leber congenital amaurosis (LCA) and inherited retinal diseases (IRDs), Lisa Bernier found help and support for her visually impaired daughter for the first time in seven years. Bernier and her 25-year-old daughter, Aimee, attended the first-ever Sofia Sees Hope LCA Family Conference. They traveled to the conference at the insistence of Aimee's optometrist.

"Advocacy ends after school ends," Bernier says.

Aimee has Bardet-Biedl Syndrome (BBS), a complex disorder affecting many parts of the body, including the retina. She and others with BBS have retinal degeneration similar to retinitis pigmentosa (RP). Aimee attended the private Perkins School for the Blind, graduating in 2011. After graduation, it became difficult for them to find support.

"Simply connecting with other people is probably the most important thing you can do ... and having the clarity of your diagnosis allows you to do that most effectively."

**—Jamie Ring,
Head of Patient Advocacy
at Spark Therapeutics**

"We're basically on our own, to advocate for ourselves," Bernier says. Her 30-year-old son also has BBS. His vision loss is five years advanced.

(Editor's note: Laws vary from state to state, but typically, public education is required



Lisa Bernier and her 25-year-old daughter, Aimee.

to provide services to students in need until age 21, even after high school graduation. Children with learning disabilities who receive services under the Individuals with Disabilities Education Act (IDEA) or the Rehabilitation Act of 1973 (RA) in public elementary and secondary school may continue to have legal rights under federal laws in college programs and in employment. When students graduate from high school or reach age 21, their rights under the IDEA come to an end. As resources can vary greatly from state to state, finding support and resources for a child may fall on the family post-graduation.)

During the early years, Bernier searched for any information on BBS and RP through reading the New England Journal of Medicine, which described those with BBS as having low cognitive skills and dying from kidney failure. Even when Aimee was born, the doctors didn't understand BBS. Bernier and her husband were grateful to be introduced to the doctors and genetic staff at Shriners Hospitals for Children in Springfield, Massachusetts, where they helped with the health care needs of Aimee and her brother until they were 18.

Bernier said she was thrilled to be at the Conference, in a roomful of retinal experts, patient advocates, and families. During

multiple sessions at the day-long gathering, attendees heard updates on research, learned about the roles played by organizations developing treatments and gained insight into how an active patient community can support and accelerate treatment.

Spark Therapeutics, Applied Genetic Technologies Corporation (AGTC), National Organization for Rare Disorders (NORD), Foundation Fighting Blindness (FFB) and Sofia Sees Hope are among the many partners working to collaborate with and learn from the patient community and propel research momentum.

More than 50 people from across the country and Mexico attended the conference, including the session titled “The Role of the Patient Voice in Developing Treatments for Rare Disease.” Sofia Sees Hope Executive Director Annette Tonti moderated a three-member panel comprised of:

Jamie Ring, Head of Patient Advocacy at Spark Therapeutics, which developed the gene therapy called LUXTURNA™ that helps restore vision to people with RPE65 genetic mutations;

Jill Dolgin, PharmD, Head of Patient Advocacy at AGTC,

a clinical stage biotechnology company focusing on rare IRDs and developing therapies that replace “broken” genes with normal, functional genes;

Kristen Angell, Associate Director of Advocacy at NORD, a voice for the 30 million Americans with rare diseases and the official U.S. sponsor of Rare Disease Day, which takes place annually on the last day of February.

Personal experiences of family and/or friends dealing with rare diseases motivated all three women to become advocates for patients. Ring, Dolgin, and Angell are a critical part of a relatively new profession—patient advocacy—to help people find support and learn how to become engaged in



Jill Dolgin, PharmD, Head of Patient Advocacy at AGTC



Kristen Angell, Associate Director of Advocacy at NORD

the process of drug development and research to find treatments for rare diseases.

“People feel their story doesn’t matter,” Ring said. “The thing in rare disease is that YOU ARE the expert,” and patient information is critical to doctors and biotechnology companies alike. “At Spark, we want to make sure that patient voice has a seat at the table.”

“There’s no one-size-fits-all,” Ring said. “Simply connecting with other people is probably the most important thing you can do...and having the clarity of your diagnosis allows you to do that most effectively.”

For IRDs, it is essential to know your gene and it’s a good idea to register with My Retina Tracker, a confidential, online, patient registry managed by the Foundation Fighting Blindness. Patient data tracked through registries and collected by researchers helps scientists and biotechnology companies develop clinical drug trials.

AGTC’s Dolgin told the audience that 7,000 rare diseases exist, but fewer than 15 percent have advocacy groups that can assist patients with resources, advocate for clinical research, and find access to vital therapies.

“As patient advocates in the pharmaceutical industry, we’re representing the patient at the corporate table,” Dolgin said. A priority for the company is to find and educate people with IRDs and encourage them to get genetically tested.

Patients need to be identified, encouraged to enroll in natural history studies, and followed systematically through natural history studies long before beginning the clinical drug trials necessary to seek approval for commercial use from the U.S. Food and Drug Administration. Natural history studies are critical components to clinical research, providing an understanding of the rate of disease progression without treatment to the rate of disease progression after treatment.

SAVE THE DATES

Do you have an event you want to share? Let us know! Email Rosanne@sofiaseeshope.org with the information and a link.

National Organization for Rare Disorders 2019 Living Rare, Living Stronger/ NORD Patient & Family Forum

June 21-23 • Houston, TX
ow.ly/UL3f50jyyCQ

During this inaugural event, the rare community will come together with physicians, medical students, and allied health professionals for a program of learning, sharing, and connection in a fun atmosphere of support and understanding. The gathering also features the Rare Impact Awards.

Global Genes 2019 RARE Patient Advocacy Summit September 18-20 • San Diego, CA globalgenes.org/2019summit/

The RARE Patient Advocacy summit, a can't-miss event of the year for rare disease stakeholders, is the largest gathering of rare disease patients, advocates, and thought leaders worldwide. Join Global Genes, partners, and rare disease community members to become equipped with the tools needed to persevere and thrive. Online registration opens in March.

Sofia Sees Hope 6th Annual Dinner in the Dark October 19 • Groton, CT

sofiasees.org/get-involved/dinner-in-the-dark/

Save the date for the Sofia Sees Hope 6th Annual Dinner in the Dark. Our primary fundraiser, this gala event at the Mystic Marriott is not to be missed. Diners enjoy a multi-course gourmet dinner paired with fine wines, followed by live music and dancing. The evening event is preceded by Sofia Sees Hope's 2nd Annual LCA Family Conference of morning and afternoon sessions with scientists, researchers, and advocates in the inherited rare disease community.

National Organization for Rare Disorders (NORD) Rare Diseases and Orphan Products Breakthrough Summit October 21-22 • Washington, D.C.

Rarediseases.org/summit-overview

National Organization for Rare Disorders' annual Breakthrough Summit brings together more than 800 leaders from the Food and Drug Administration, the National Institutes of Health, industry groups, payers, and research institutions. The summit features networking with today's rare disease innovators, cutting-edge keynote speakers, and six breakout sessions.

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