SOFIA SEES HOPE

Supporting the LCA and rare retinal disease community.
We see a cure for blindness.

SEEING HOPE | Newsletter

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September 2018 | Issue 4

From the Founder

Wow. It has been a busy five years, with a whole lot of new activity packed into just 2018! Since January alone we have:

Sofia Priebe & Laura Manfre

- hosted our first webinar
- launched the Family Connections program
- debuted our Ambassadors at the VISIONS conference in San Diego
- advocated with lawmakers for sound research and rare disease policy
- continued to fund cutting-edge research and a free genetic testing and counseling program for patients
- scheduled our first LCA Family Conference for October

When we first started the organization, we focused on funding research to treat blindness caused by Leber congenital amaurosis (LCA). After three years of funding, I'm thrilled that one of those projects is now entering a clinical trial phase led by ProQR, to develop a potentially life-changing therapy for people living with LCA10 (CEP290).

But successful research is only one part—what I've learned over the last five years is that so many dots need to be connected before treatments for LCA or any rare eye disease can even begin. One of those critical dots is identifying the exact genetic mutation causing blindness, and getting that genetic diagnosis still isn't easy.

Continued on page 3

Sofia Sees Hope to Host First LCA Family Conference

The conference, October 5–6 in Mystic, CT, will bring together families, researchers, and experts for a day of learning and connecting.

By Elissa Bass

Sofia Sees Hope will host a day of learning and connecting with our LCA (Leber congenital amaurosis) community in October.

The LCA Family Conference takes place the same weekend as the nonprofit's fifth annual Dinner in the Dark, a gala fundraiser that combines a gourmet meal and wines with blindfolds to create a sensory experience for guests.

The conference is October 5–6 at the Mystic Marriott Hotel and Spa in Groton, CT. It opens on Friday night, October 5, with a welcome dinner for families.

On Saturday, the conference will bring together advocates, industry experts, and families. Among the topics to be explored are the LCA landscape at this moment in time; ongoing research; understanding how therapies are developed; the patient/caregiver role in rare disease advocacy; and facilitated discussion among parents and caregivers about living with LCA.

"There are exciting advances being made in the fields of gene therapy and genetic treatments," said Laura Manfre, co-founder and president of Sofia Sees Hope. "With this being our fifth year in existence, we feel like we are at a point where we are able to take this next step and offer our community an

Continued on page 3

Tell Us Your Story

'Do Not Limit Yourself'

Angélica Bretón Morán with her family in Mexico after a performance.

By Angélica Bretón Morán

My name is Angélica Bretón Morán, I am from Mexico, I am 22 years old, and I have Leber congenital amaurosis (LCA). Two years ago I learned that the gene that affects me is RPGRIP1.

I've been reading many sites on the Internet, and I have realized that there are many comments from parents concerned about the development of their children, however there are almost no comments from parents with older children or people with LCA who talk about their development.

My intention is to tell you a little about my story to bring you peace.

When I was 2 months old, my mom realized that I did not follow people or toys with my eyes, and that when they did not speak, I cried as if I was alone. My mother is licensed in special education and specialized in hearing and language, so she realized that something was not completely normal.

The doctor told my parents that my eyes had to mature, but the months passed and nothing changed. My mom was certain that I was blind.

Finally, the doctors diagnosed that I was blind and there was a rain of bad diagnoses, syndromes that would terribly affect me, or that I would die a premature death, or that I would be like furniture, without the ability to do anything. Of course all this broke my parents' hearts.

It was a painful road for my parents until a doctor told them, "I would say to you that it is LCA." I was 2 years old. My dad searched for information about this new diagnosis on the Internet, and what he found was not nice things. In one of the Internet searches, my parents found a writing by a 22-year-old Italian woman who was a musician; this for them was something hopeful.

My mom stimulated my touch with toys with different textures, placing hands in containers with different seeds. She enrolled me in ballet classes where I would meet more girls and teachers. I was very little and I liked the music and the stage. Then I went to kindergarten. It was not easy to find a school where they would admit me, but my parents never agreed that I was in a school for people with disabilities.

My parents never treated me differently, when I told my mom that when I grew up I wanted to be a pianist and opera singer, she told me that I could reach where I wanted. I liked to hear Charlotte Church and I admired Andrea Bocelli, because he was an example for me.

When I behaved differently from other children, my parents told me that this was not a good behavior. They explained to me how I should behave, without showing myself. When I waved my hands my mother held them and told me not to do it, she did it kindly but firmly and little by little I stopped doing it.

My parents educated me with a lot of love, but above all with discipline, an orderly and coherent discipline. I had to keep my toys like all children, learn to eat correctly like everyone else, not put my hands in food and just touch it with a finger that my mom called "guide finger," this as a support because I cannot see the food.

When I was a girl I could see better than now. Now I see lights and shadows but I cannot distinguish differences between colors as I used to.

My disability has never been a secret, but neither has it been something for which I have to be different from others. It is true that you have to adapt some things, this is logical; however you have to look for how to achieve your objectives.

Going back to my life story, I have always studied in regular school; all my life music has been present. I graduated from music training at the Autonomous University of Nuevo Leon (UANL). I am currently studying a degree in music with an emphasis in piano at the same university and I have been studying professional singing for five years with a private teacher to become an opera singer.

All this I tell you so that you know how important it is not to limit yourself. If you limit yourself as parents, you will limit us as children. I can tell you that when you treat a person differently from the others, that person will behave differently regardless of whether they have a disability.

You have to be aware of the limitations, but you also have to find a way around the obstacles, or pass through them, or use them as a catapult, or see them as a feature that makes us unique and special as people.

I hope my words help many families, since that is my intention. I invite more adults with LCA to tell their stories and how they have faced life! I think we would give a much more encouraging approach when new parents enter the Internet looking for information about the diagnosis of their children. I am greatly moved to see their anguish and I feel that it is my duty to be the 22-year-old girl who brings a hopeful message to those who enter the Internet looking for information about LCA.

From the Founder

Continued from page 1

The dots don't stop connecting with testing. That's why we spend a lot of energy and resources on education and advocacy, making sure the health care and government systems in place are looking out for our constituents, and that our families are informed and feel empowered. From our website to this newsletter—our team continues working hard to make connections that will support and even accelerate treatments for our rare disease.

I hope that this newsletter connects some dots for you—I know it does for me. Finally, someone has explained why some LCA mutations have both names and numbers, and I have a much deeper understanding of the importance of those natural history studies that we need more patients to participate in! Also in this issue, Jack McCormick shares his insights on transitioning out of college (congratulations, Jack!), and did you know that for more than nine years, Judith Millman has hosted a standing LCA support call?

As we approach our five-year anniversary, there is tremendous activity at Sofia Sees Hope and we have enormous hope that more treatments for blindness will move forward with your continued support.

Finally, I look forward to seeing all of you in October at the LCA Family Conference, or Dinner in the Dark, or both!

Laura

In January 2014, Laura Manfre co-founded Sofia Sees Hope with her husband 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.

Sofia Sees Hope to Host First LCA Family Conference

Continued from page 1

opportunity to connect and learn with this family conference."

Through the generosity of Mystic Aquarium, the conference includes a special program for kids ages 6 and up at the Aquarium! Just a 10-minute ride from the conference, transportation, lunch and activities at the Aquarium are included in the fee so moms and dads can focus on the conference sessions. (Families with children 5 and younger are asked to contact info@sofiaseeshope.org to discuss childcare options as needed.)

Registration for LCA individuals and families will be available on a first come, first served basis.

For more information, or to register, visit

sofiasees.org/event/lca-family-conference-2018

SOFIA SEES HOPE

WE SEE A CURE FOR BLINDNESS.

DINNER IN THE DARK

An evening to benefit Sofia Sees Hope

Saturday, October 6, 2018

Mystic Marriott Hotel & Spa • Groton, CT

Visit www.sofiaseeshope.org for more info, tickets and sponsorships

LCA Alphabet Soup: Naming Versus Numbering

By Rosanne Smyle

Genetic mutations within the disease of Leber congenital amaurosis commonly are referred to by their gene name, such as GUCY2D, RPE65 and CEP290. But sometimes, as LCA patients and families have discovered, they are referenced as LCA1, LCA2 and LCA10, respectively.

Why the difference? It's confusing.

LCA1 through LCA18 exist in a continually updated online catalog of human genes and genetic disorders called Online Mendelian Inheritance in Man. Mendelian inheritance is based on the ideas of Gregor Johann Mendel, a 19th-century Moravian monk known as the father of modern genetics.

One source of confusion for LCA families is that there are 27 genes that can cause LCA, but only LCA1 through LCA18 are cataloged. For most genes, OMIM includes only selected mutations based on criteria such as the first mutation discovered, high-population frequency, distinctive phenotype and more. LCA families with genes not included in that list are left to wonder why they've been left out.

OMIM focuses on the molecular relationship between genetic variation and phenotypic expression and is considered a phenotypic companion to the Human Genome Project, which funds the database. The HGP international research effort from 1990 to 2003 culminated in a blueprint for building a person by completing an entire sequence of the human genome.

OMIM is a continuation of Dr. Victor A. McKusick's Mendelian Inheritance in Man published through 1998. Created in 1985 through a collaboration between the National Library of Medicine and the William H. Welch Medical Library at Johns Hopkins University School of Medicine, OMIM went online in 1987.

For example, OMIM refers to GUCY2D as LCA1, #204000 (phenotype MIM number), located at 17p13.1 with a gene/locus MIM number of 600179.

TRANSLATED:

"A number sign (#) is used with this entry because of evidence that Leber congenital amaurosis-1 (LCA1) is caused by a homozygous mutation in the gene encoding retinal guanylate cyclase (GUCY2D: 600179) on chromosome 17p13."

There's more, but that can be left to physicians, genetics' professionals, researchers and students studying advanced science and medicine.

"For a patient with LCA or their family, what's important is not the LCA## symbol, but, rather, a) the underlying affected gene; b) whether inheritance is dominant or recessive (dominant is rare); and c) the specific mutation or mutations," according to Stephen P. Daiger, PhD Professor in Environmental and Genetic Sciences at the University of Texas Health Science Center and director of the Laboratory for Molecular Diagnosis of Inherited Eye Diseases.

"This is the information which decides, for example, whether someone is eligible for a clinical trial focused on a specific gene, e.g., LUXTURNA™ for RPE65," he said. "It is very important to know and remember this information."

Natural History Studies: Finding the Windows of Opportunity to Save Vision

By Ben Shaberman,
Director, Science Communications
Foundation Fighting Blindness

Though Leber congenital amaurosis (LCA) affects fewer than 4,000 people in the United States, the disease took front and center stage at the 2018 meeting of the Association for Research in Vision and Ophthalmology (ARVO). One of the largest eye research events in the world, it attracts more than 11,000 scientists, physicians and industry professionals annually, this year in Honolulu, Hawaii.

Of course, LUXTURNA™, as the first gene therapy approved for the eye, garnered much attention at ARVO. The groundbreaking, vision-restoring treatment developed by Spark Therapeutics is for people with mutations in RPE65, which cause certain forms of LCA and retinitis pigmentosa.

However, two of the most prestigious and well-attended lectures at ARVO—delivered by the University of Pennsylvania's Sam Jacobson, MD, PhD, and Artur Cideciyan, PhD—highlighted LCA caused by mutations in GUCY2D and CEP290 genes. The investigators, co-recipients of ARVO's coveted Proctor Medals, discussed how people with LCA that is caused by these gene mutations may also be good candidates for gene therapies.

Their patient studies of these two forms of LCA revealed that, despite significant vision loss early in life, some of the photoreceptors for those affected—namely cones, which provide the ability to read, recognize faces and perceive colors—survive for several years. Rescuing and reviving these photoreceptors, despite significant vision loss later in life, may lead to restored vision.

The lectures of Drs. Jacobson and Cideciyan underscored the need to understand the natural history of retinal diseases—how conditions like LCA progress in patients over time—so researchers know if and when a gene therapy or other treatment has a good chance of saving or restoring vision.

Benefits of natural history studies

Natural history studies of patients not only help answer the question of when to treat, but where in the retina to deliver the treatment (i.e., where the surviving photoreceptors remain). They also gauge the best outcome measures for evaluating vision changes in patients in clinical trials for an emerging treatment.

Will an eye chart suffice for capturing vision improvements or will researchers need something more innovative and sophisticated like the multi-luminance mobility test (MLMT) developed by Spark for its LUXTURNA clinical trial? (Spark's MLMT measured functional vision, or a person's ability to perform, on his or her own, visually dependent activities of daily living. The reasoning was that measuring functional vision, rather than visual function, may have been a more appropriate way to evaluate changes in vision loss in patients with inherited retinal diseases or IRDs.)

While natural history studies may not seem compelling because no treatment is being evaluated, they can be essential to designing successful clinical trials and enrolling the best patients for them. A company or research team could have a magical treatment, but if they don't design a good trial and recruit the appropriate patients, the treatment may not demonstrate efficacy and get approval by the Food and Drug Administration.

"Natural history studies of patients not only help answer the question of when to treat, but where in the retina to deliver the treatment (i.e., where the surviving photoreceptors remain), and the best outcome measures for evaluating vision changes in patients in clinical trials for an emerging treatment."

The cost of natural history studies varies, depending on the number of patients enrolled, the duration of the study, the number of required patient visits, and the types of tests performed at each visit.

In some cases, a study may be retrospective—a review of patients' records. Also, the study could require only a single visit—this would be considered a "patient characterization" study, because little, if any, history is captured.

A prime example of a large-scale natural history for retinal conditions is ProgStar launched by the Foundation Fighting Blindness (FFB) for people with Stargardt disease, an inherited form of macular degeneration. ProgStar was held at nine clinical sites and enrolled more than 300 people who were evaluated for two years. (Some also were evaluated retrospectively.) The study will ultimately cost more than $6 million.

The ProgStar study is complete, though analyses of the data continue. FFB is making the study results available to researchers and companies to inform clinical trial designs and boost interest in therapy development.

Participating in a natural history study

Will there be a formal natural history study for every form of LCA? Probably not. The need for such studies will vary depending on how each form of LCA affects the retina and vision. Also, some clinics may be able to garner sufficient natural history information through existing patient records or by collaborating and/or sharing disease data with other clinics.

If you or a loved one is interested in participating in a natural history study, register in FFB's free and secure patient registry, www.MyRetinaTracker.org. Many researchers launching studies will be recruiting participants through My Retina Tracker®. Natural history studies may also be posted at www.ClinicalTrials.gov.

Editas, a biotech developing gene-editing (CRISPR/Cas9) technology for LCA10 (caused by a mutation in CEP290), is currently recruiting participants for its natural history study through My Retina Tracker.

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

College Connection
by Jack McCormick

What I Wish I Knew

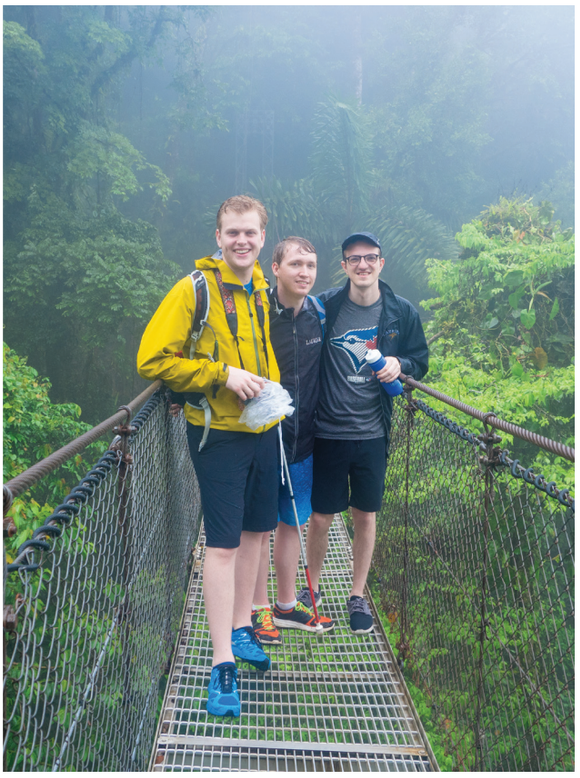
On August 3, I wrote the last exam of my bachelor's degree. I thought this would be as good a time to reflect on what I have learned navigating college with vision loss, and what I wish I knew. While this newsletter is designed for individuals who have inherited retinal diseases (IRDs), I think this is an article that can apply to anyone experiencing college.

YOU PAY FOR CLASSES BUT THE REAL LEARNING IS OUT IN THE WORLD.

Education is expensive. There is a lot to be learned by doing the reading and going to class but if this is all you make time for you are going to miss out. College is a time of self-discovery and growth; a time where you get to find you. The only way to do this is by exposing yourself to lots of new experiences.

YOU ARE GOING TO MESS UP.

Part of self-discovery is making mistakes. Not everything is going to work out perfectly. Everyone regrets doing things, you are going to be no different. But it is better to regret doing something than regret not doing it; at least you can learn from the things you did do.



From left to right; Alex, Jack and Jacob standing in the center of a hanging bridge during their recent trip to Costa Rica. Plenty of tall trees connected by lots of vines and other plants are creating a luscious green rainforest background.

"Everyone regrets doing things, you are going to be no different. But it is better to regret doing something than regret not doing it; at least you can learn from the things you did do."

FIND A SUMMER JOB.

This is especially important for people who have IRDs. There is a lot of stigma associated with the employability of people who have vision loss. The earlier you get out there and prove that you are able, the more opportunities will come your way. I recommend accessing organizations that specifically help people who have disabilities find work. One that has helped me a lot is Lime Connect.

This past year I was a Residence Advisor in my dorm. I left my students with some advice that I would like to end with now:

"University is hard—you will question what you are doing at least once; shed a few tears; and toward the end worry about what is next. But if you work hard, build meaningful connections with the people around you and work toward things that you actually care about, you will have some of the most rewarding moments of your life during your university years."

"And a few last attempts at advice—learn to enjoy the present moment because before you know it you are on to the next; the most valuable thing you can seek is memories with people you care about; and the people who you share those memories with are the most important thing."

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

PATIENT ADVOCACY

Family Support On Line Two

By Rosanne Smyle

In the sometimes-isolating world of rare inherited retinal diseases (IRDs) such as Leber congenital amaurosis (LCA), another option exists to help bring people together—support by telephone.

The Lighthouse Guild of New York City offers a Parent Tele-Support Group in which parents of children with LCA across the country can come together every other week to share problems and solutions about parenting, genetic testing, education, socialization, accessibility and more.

The Lighthouse Guild is a not-for-profit vision and healthcare organization helping people who are blind or visually impaired gain their maximum level of independence.

The Guild offers nine Parent Tele-Support Groups to help connect families living with LCA, Cortical Visual Impairment, Autism and Blindness, Retinopathy of Prematurity and other eye conditions.

For the past nine years, social worker Judith Millman, LCSW, has facilitated the LCA tele-support group that usually convenes every other Wednesday evening, 8:45 p.m. EST. Nationwide, the group reaches people of all ages who may not have access to those having similar experiences.

She estimates about 50 families have been supported through the group over the years. Occasionally, the sessions include a special guest.

Some years ago, Dr. Jean Bennett, part of the

Judith Millman

research team that created the breakthrough genetic treatment for LCA2 (RPE65) called LUXTURNA™, took part in a call, back when her research was still in its clinical trial stages. Spark Therapeutics developed LUXTURNA™, which received approval in December 2017 from the Food and Drug Administration.

Other guests have included the inventor of a cane for toddlers, specialists in orientation mobility, and Betsy Brint, the mother of a child with LCA who is affiliated with the Foundation Fighting Blindness (FFB).

Parents of children—from babies to teen-agers—participate in the sessions. The LCA telephone group is not gene-specific and includes people from across the LCA gene-mutation spectrum that includes an estimated 27 genes.

Even more so, the group is an avenue to inclusion, another resource for people to find comfort and a sense of belonging within the LCA community.

*Parents interested in joining the group can enroll at **lighthouseguild.org**. For more information, including upcoming dates for tele-support sessions, please email Judith at judithmillman@aol.com.*

UPCOMING EVENTS

Global Genes RARE Patient Advocacy Summit

October 3–4 • Irvine, CA
globalgenes.org/2018summit
The RARE Patient Advocacy Summit brings together the largest gathering of rare disease patients, advocates and thought leaders worldwide. Connect and learn from more than 200 rare disease experts leading 100 educational sessions on topics that include living with a life-altering condition, becoming a successful architect of your health, building on advances in drug development, and learning the latest in science and technology that drive innovation.

LCA Family Conference

October 5–6 • Mystic, CT
sofiasees.org/event/lca-family-conference-2018
Join Sofia Sees Hope for a day of learning and connecting with our LCA community. We kick off on Friday night with a welcome dinner reception, and on Saturday we'll hear from experts how treatments go to market, we'll explore ways you can support and accelerate research, and you'll have time to discuss living with LCA with other individuals and families.

Bring the kids! Our generous sponsor, Mystic Aquarium, is preparing a special day for your kids at the Aquarium. Just a 10-minute ride from the conference—transportation, lunch and activities are included in the fee so you can focus on the conference sessions.

Sofia Sees Hope Dinner in the Dark

October 6 • Mystic, CT
sofiasees.org/get-involved/dinner-in-the-dark
Sofia Sees Hope's primary annual fundraiser helps fund research to treat and cure blindness caused by LCA, provide support for genetic testing, and drive awareness, education and connections for LCA and IRD families. This is a lively sensory adventure and a true culinary event offering a unique menu and fine wines.

National Organization for Rare Disorders Rare Diseases and Orphan Products Breakthrough Summit

October 15–16 • Washington, DC
rarediseases.org/summit-overview
More than 700 leaders from FDA, NIH, industry, patient groups, payers and researcher institutions, together with attendees, will address and explore the New Era of Patient-Focused Innovation at the 2018 National Organization for Rare Disorders (NORD) Rare Summit.

World Orphan Drug Congress Europe 2018

Strategy, Advocacy and Partnering for the Orphan Drug Industry
November 6–8 • Barcelona, Spain
terrapinn.com/conference/world-orphan-drug-congress/index.stm
The World Orphan Drug Congress, Europe's meeting place for the rare disease community, offers strategic keynote plenaries, themed tracks and dedicated networking sessions to tailor the event to the needs of your day-to-day role. Topics include cell and gene therapies, genetic testing, orphan drug policy and global patient advocacy.

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

LCA Connections

VISIONS 2018

Sofia Sees Hope representatives attended the Foundation Fighting Blindness VISIONS 2018 conference in San Diego at the end of June. We had a booth in the exhibit hall, staffed by SSH Director of Development Mardy Pryor, Board President Laura Manfre, Board Member Shanda Easley, and SSH Ambassadors Michael and Tami Morehouse and Scott Soady.

We also hosted a bonfire for LCA families, which gave everyone the opportunity to connect and talk in a relaxed atmosphere. Workshop sessions included experts in the field of rare retinal disease, including David Brint, Ben Yerxa, Jim Platzer, and Dr. Emmett Cunningham.

From left, SSH Ambassadors Tami and Mike Morehouse, SSH Director of Development Mardy Pryor, SSH Ambassador Scott Soady, and Annemarie Dillon, senior director of Patient & Medical Community Engagement, proQR.

Other booths included My Retina Tracker, Two Blind Brothers, Foundation Fighting Blindness, Spark Therapeutics, and Guide Dogs of America.

The 500 attendees learned about Optogenetics, Stem Cell Research, Gene Therapies, Prosthetics, and Genetic Technologies.

SOFIA SEES HOPE
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The *Seeing Hope* newsletter is published quarterly by Sofia Sees Hope, a 501(c)3 patient advocacy organization dedicated to generating awareness, raising funds for research, and providing education and outreach to the LCA and rare inherited retinal disease community.

To learn more about Sofia Sees Hope visit our website at www.sofiaseeshope.org.

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