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

SEEING HOPE | Newsletter

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March 2022 | Issue 13

Big Journey for Little Girl with LCA3 (SPATA7)

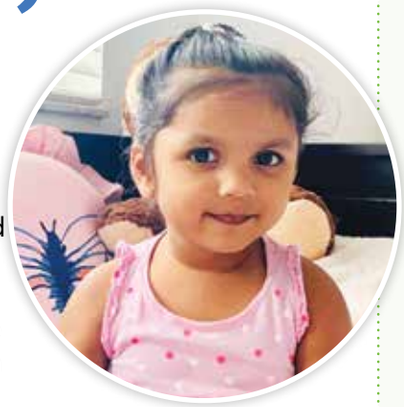
By Rosanne Smyle

Parvi Gaddam has endured a lot for a little girl genetically diagnosed at 6 months old with a form of Leber congenital amaurosis called LCA3 (SPATA7).

Like most parents discovering their child has a rare inherited disease, the diagnosis of their now 3-year-old took Harini and Suresh Gaddam by surprise because no one in their families experienced vision loss or blindness. LCA, usually inherited as an autosomal recessive genetic condition, means a child inherits two copies of the mutated gene, one from each parent.

The couple, who are software engineers living in Tampa, Fla., hoped Parvi's mutated gene would be RPE65 associated with LCA2, because vision in some patients with that mutation improves through the federally approved LUXTURNA® gene therapy.

She underwent rounds of scans and tests, and at 6 months, Parvi and her family traveled to Pennsylvania's University of Pittsburgh Medical Center Children's Hospital, where doctors diagnosed her with a mutation in her SPATA7 gene associated with LCA3, one of the more than 27 known forms of LCA. Rare among rare diseases, LCA3 accounts for less than 2 percent of all LCA cases. Early-stage research using mice models has shown promising results with gene therapy treatment.



Parvi Gaddam

Parvi does have some light perception. Her vision teacher comes to her home because of the COVID-19 pandemic, and helps her by reading storybooks, singing songs, and touching and seeing objects. Parvi also enjoys the company of her older brother, 8-year-old Thanmay, who returned to class in school.

"She's very smart, does her routine, enjoys reading the books, songs, walking, and playing with her brother," Suresh said.

Her parents follow studies on the gene and reached out to Hope in Focus and the

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From the Founder:

Laura Manfre

Here we are in March and it's still very fair to say Happy New Year, as it's turning out to be quite a spectacular time for research advancements into treatments and cures for Leber congenital amaurosis and other rare inherited retinal diseases.

We've got a whole lot of goodness to unpack in this newest edition of *Seeing Hope* on the heels of rebranding our organization from Sofia Sees Hope to Hope in Focus.

In-house, we're happy to welcome to our small, but mighty, team, Courtney Coates, our new Director of Outreach and Development. Courtney's role as the first point of contact for those reaching out to Hope In Focus is to provide a consistent support system for the community and to expand the reach of our organization. She's also focused on helping expand our organization's capacity through grants and donor relationships to increase our global advocacy efforts and contributions to research into rare inherited retinal disease.

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From the Founder:

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In our nation's capital, members of Congress have before them federal legislation — supported by us here at Hope in Focus — describing an innovative financing model to help accelerate the drug development process and bridge the deep chasm between preclinical research and early-stage clinical trials.

The legislation and the advancing biotech studies into treatments for rare retinal diseases could not come sooner with the COVID pandemic having stalled many projects in the last two years as researchers raced to develop vaccinations against the virus and its variants.

We're also excited to share news about a biotechnology company in late-stage preclinical trials into LCA6 (RPGRIP1), and how a Texas family with a toddler living with the disease is among those helping with financial goals to bring studies to clinical trials faster.

You'll meet a little girl, whose Florida family also is working to raise money to advance early-stage research into LCA3 (SPATA7), one of the rarer forms of the rare disease, accounting for fewer than 2 percent of all LCA cases.

We'll also fill you in on two encouraging studies about optogenetics, treatments that give light sensitivity to cells that normally don't respond to light or cells that have lost their light-sensing ability.

Also, we'll hear words of reassurance from our columnist writing about belonging — accepting differences and looking for similarities to create a more connected world.

And, our fun and fabulous Dinner in the Dark fundraiser — with its special menu, paired wines, and lots of dancing — returns live and in person on October 22 at the Mystic Marriott in Groton, Conn. We are so psyched to say Save the Date!

It's a new day and, indeed, a New Year. Cheers!

All the best,

Big Journey for Little Girl with LCA3 (SPATA7)

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Foundation for Fighting Blindness for help in their journey.

Parvi with her brother Thanmay

Harini and Suresh began raising funds for SPATA7 research through GoFundMe and through the Foundation, with a goal of $5 million.

The family is searching for more people living with the SPATA7 mutation to gather patients and bring research forward to clinical trials in humans, with the hope that a treatment or cure will come to fruition.

"We will not give up," her father said. "And we will continue fighting for my little angel and the SPATA7/LCA3 patient group to bring this treatment to humans."

DINNER IN THE DARK

Saturday, October 22, 2022
Mystic Marriott Hotel & Spa • Groton, CT

Optogenetics: Hope for Vision Restoration for Advanced Retinal Diseases

By Ben Shaberman
Senior Director, Scientific Outreach & Community Engagement

FOUNDATION FIGHTING BLINDNESS

Early, encouraging results from two human studies — trials launched by Bionic Sight and GenSight — are putting optogenetic therapies in the spotlight for patients with advanced vision loss (i.e., only light perception) from retinal conditions, such as retinitis pigmentosa (RP), Leber congenital amaurosis (LCA), and age-related macular degeneration (AMD).

In simple terms, optogenetic treatments bestow light sensitivity to cells that normally don't respond to light or cells that have lost their light-sensing ability. And they're gene-agnostic, designed to work independent of the mutated gene causing the patient's retinal disease.

In the Bionic Sight clinical trial, investigators reported that the first four RP patients dosed can now see light and motion. Two of the patients can detect the direction of motion; that is, they can determine if objects are moving to the right or left. One patient said that one of the first new things he saw was Hanukkah candles on the eighth day of the holiday when they were all lit. Also, two patients who practice martial arts saw the robes of their opponents against the dark blue mat.

GenSight reported results for a 58-year-old man who entered the trial with only light perception due to advanced RP (Usher syndrome type 2A). After receiving the optogenetic therapy, the patient was able to locate and reach for objects on a table while wearing the image-capturing eyewear. Results from the GenSight trial were reported in the journal *Nature Medicine*. The Foundation Fighting Blindness funded lab research that led to initiation of the GenSight study.

The emerging therapies from Bionic Sight and GenSight are designed to enable retinal ganglion cells to respond to light, so they can work like a back-up system for photoreceptors, the cells that normally make vision possible. Ganglion cells often survive after photoreceptors are lost to advanced retinal disease.

In both treatments, copies of an algae-derived gene that express a light-sensing protein are delivered to the ganglion cells. Both approaches use viral gene delivery systems and include eyewear to enhance the visual information sent to the retinas.

Nanoscope Therapeutics recently launched a clinical trial in the United States for its optogenetic therapy, which involves viral delivery of a light-sensitive protein (a multi-characteristic opsin) to bipolar cells in the retina. The company will enroll 27 people with advanced RP in its trial.

An emerging protein-based optogenetic approach being developed by Vedere Bio and funded by the Foundation's Retinal Degeneration (RD) Fund was recently acquired by Novartis. After the acquisition, Vedere Bio II was launched to develop another optogenetic therapy.

Two groups are working on optogenetic therapies designed to resurrect dormant cone photoreceptors in people with advanced retinal disease. One of the groups, SparingVision, is funded through the RD Fund. The other group is led by Hendrik Scholl, MD, Institute of Molecular and Clinical Ophthalmology Basel, and funded by the Foundation's Translational Research Acceleration Program (TRAP).

While there is much promising research activity for optogenetic therapies, the approach is still at an early stage of clinical development; the research community is learning much from optogenetics about the potential for meaningful, natural vision restoration.

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

Mother of Toddler Living with LCA6 (RPGRIP1) Collaborates with Biotech Odylia to Help Advance Gene Therapy Research

Dylan on her slide

By Rosanne Smyle

After crazy months of looking for answers to questions about her infant's vision, Melissa Matias learned her baby girl, Dylan, had a form of Leber congenital amaurosis known as LCA6, caused by mutations in her RPGRIP1 gene, a protein needed for healthy photoreceptors.

"I put my big-girl pants on and said, 'This is the card she and I have been handed.'" The Georgetown, Texas, mom said.

When Dylan received her confirmed genetic diagnosis in May 2020 at age 5 months, her mother did not assume someone else had the time or resources to search for a treatment or cure for her daughter's form of blindness. Melissa organized people, advocates, and information. She created the RPGRIP1.com website and began collaborating with the nonprofit biotech Odylia Therapeutics on a $4 million fundraising effort to advance therapy for the RPGRIP1 LCA6 program.

The Atlanta-based biotechnology company is in late-stage preclinical trials, with the goal to be in clinical trials in about two years. Melissa is hoping Dylan — a gregarious trampoline-jumping gymnast — will benefit from this developing gene therapy.

"This therapy, if it's in reach, let's get going," Melissa said. "Let's get the word out and open the door to gene therapy, not just for RPGRIP1, but for other genetic visual impairments and rare diseases."

LCA6 (RPGRIP1) Gene Therapy — Following LUXTURNA'S® Path

Currently, LUXTURNA® is the only gene therapy on the market. Developed by Spark Therapeutics and federally approved in 2017, the drug treats a form of LCA known as LCA2 (RPE65), and it is the only gene therapy approved in the U.S. for any inherited disease.

Odylia hopes to follow in LUXTURNA's® path with its research.

Delivered by injection under the retina in each eye, LUXTURNA® has helped improve vision in patients for the last four years. The company says its goal is to bring proven therapeutics to patients, regardless of the number of people with the disease or the opportunity for a company to make money.

Between 400 and 600 people are affected with LCA6 in the U.S., with about 20,000 globally. LCA6 is one of the more than 27 forms of the disease.

The FDA recently granted both orphan drug and rare pediatric disease designations for Odylia's lead gene therapy. The company said the designations are granted for the "treatment of RPGRIP1 mutation-associated retinal dystrophies," which most commonly includes LCA6 but is also associated with diagnoses of cone-rod dystrophy 13 (CORD13) and forms of early-onset retinitis pigmentosa (RP).

Struggle to Find Confirmed RPGRIP1 Diagnosis

Melissa's persistence pushed her through incredibly trying times, having six back-to-back miscarriages during 2016 and 2017 after having her two sons. Two years later, she and her husband, James, got the news she was pregnant with Dylan.

"She was so meant to be," Melissa said. "It was unreal when it came time to deliver. Everyone in that room was crying.

"They had all seen on my chart that I had 10 pregnancies. They were all just like…" she said trailing off. "It was such an emotional time."

Dylan with mom (Melissa) and dad (James)

Dylan playing

Dylan with brothers, Colton & Brayden

Two months later, though, Melissa and James realized something didn't seem right with Dylan's vision; her eyes jerked from side to side from a condition known as nystagmus. It was February 2020 with the tentacles of COVID spreading, creating an overworked, overwhelmed medical world focused on patients infected with this strange new virus.

Finding an initial diagnosis for Dylan proved extremely difficult, especially when one doctor said nothing was wrong, probably just delayed maturation of vision, and another mentioned LCA but brushed it off. So, Melissa did what we all do now when we don't get answers: She Googled the disease.

"The more I learned about LCA, I knew in my heart right away what we were looking at. But I'd also think, it's so rare, what are the chances?"

She learned the next step to move forward with treatment or care for 2-month-old Dylan depended on a confirmed genetic diagnosis determined through genetic testing.

No genetic testing, not now, she was told. Not until COVID is over. Melissa wasn't waiting for the end of the pandemic, now in its third year. She knew she needed a doctor's order but hadn't yet connected with a retinal specialist; she sought the help of Dylan's pediatrician, a doctor she characterized as amazing, who ordered the test.

Waiting for the results, Dylan's parents scheduled a May 28 appointment with a Houston retinal specialist; the confirmed diagnosis of LCA6 (RPGRIP1) came through May 27, paving the way to find resources in orientation, mobility, and education for Dylan.

Living with LCA6 (RPGRIP1) / Like Mother, Like Daughter: Stubborn and Persistent

Dylan is now 2 years old. Her parents believe she has tunnel vision and does best seeing objects 10 or 15 feet away. She's better now at keeping her glasses on, rather than ripping them off all the time like she used to.

On Dylan's first day of Orientation and Mobility training, she picked up a cane and used it just the right way, a milestone the instructor said he had never seen in a child her age.

"Indoors, she's just amazing," Melissa said. "She loves picture flashcards, playing in her toy kitchen, always wants someone to read her books, and she loves her new mini trampoline she got for Christmas. And music — she loves to sing and dance."

She's also very vocal and visual.

"Her vocabulary is comparable to a child much older than 2," Dylan's mom said. "We know she is very visual, something we feel blessed with, since LCA can present with a wide range of visual capabilities. We've actually had to teach her to bend down and feel for objects she drops, because her instinct is always to look for something first."

She's also persistent.

"She has a very strong desire for mastery, having to do things over and over again. She likes a challenge.

"I have no doubt this girl is going to change the world. No matter what happens if gene therapy comes about for her or not. She's going to be on skis this winter. I'm not going to give her an excuse not to do something or at least to not try.

"She can and will do anything she wants, just in her own ways. Stubborn and persistent, exactly what she needs."

Innovative Federal Legislation — BioBonds — Would Help Finance Early-Stage Clinical Trials

By Rosanne Smyle

A proposed Congressional Act designed to help researchers launch clinical trials for emerging treatments gives hope for getting more treatments across the finish line for people living with a broad range of medical conditions, including rare retinal diseases, such as Leber congenital amaurosis (LCA).

The BioBonds legislation establishes loans up to $25 million to a researcher or company as an innovative way to finance early-stage clinical trials. The program would provide $10 billion annually for three years.

Researchers would be required to repay the low-interest, government-backed loans.

Hope in Focus, along with Foundation Fighting Blindness (FFB) and more than two dozen other entities, have signed on in support of the legislation.

"Funding for research for all diseases, including rare conditions such as LCA and other rare inherited retinal diseases (IRDs), is always a challenge and was made even more so when COVID hit and so much of biomedicine research was held up," according to Laura Manfre, President and Co-Founder of Hope in Focus (formerly known as Sofia Sees Hope).

"While we are ever grateful to our funders and grantors, we are excited that the loans provided through this legislation have the capacity to increase momentum and accelerate the development of treatments and cures for blindness and an array of other diseases."

Officially known as The Long-Term Opportunities for Advancing New Studies (LOANS) Biomedical Research Act — H.R. 3437 — the proposed legislation creates a unique way of mobilizing capital of long-term investors to give loans to companies developing treatments and cures for a wide range of disease and disability.

U.S. Representatives Bobby L. Rush (D-IL) and Brian Fitzpatrick (R-PA) introduced the LOANS for Biomedical Research Act to help bridge the financial "valley of death" that separates promising research from clinical trials necessary to delivering federally approved treatments and cures.

Congressional Proposal Needs Wide Range of Support

Hope in Focus and FFB, along with other organizations, sent a letter to the representatives in support of this initiative to leverage billions of dollars in private-sector investment to advance early-stage clinical biomedical research.

FFB plays a key role as a partner in outreach and awareness. Foundation Board Director Karen Petrou and her late husband, Basil, were visionaries for the legislation.

FFB CEO Ben Yerxa, PhD., applauded the introduction of the Act.

As head of the world's leading organization committed to find treatments and cures for blinding retinal diseases, Yerxa said, "As the remarkable speed of the COVID-19 vaccines development and approval processes have demonstrated, financial capacity — not scientific knowledge — is our biggest hurdle to advancing medical research and delivering the life-saving treatments and cures millions of Americans so desperately await."

Doctors diagnosed Karen Petrou in her teens with retinitis pigmentosa (RP) and she went blind in her 40s.

A *New York Times* article describes Petrou's challenges over four years in developing a new funding model for curing blindness. The piece by Ephrat Livni can be found at: **nytimes.com/2021/07/12/business/dealbook/biobonds-karen-petrou.html**

An in-depth paper written by Petrou describing the funding model — Generating Billions in Private-Sector Investment Speeding Treatment and Cure — can be found at: **biobonds.org**

For more about BioBonds, including signing on as a supporter, viewing the sponsor list, reading the legislation, and getting assistance in contacting your U.S. House Representative, go to: **biobonds.org**

Belonging — Jack McCormick column

Accepting Differences and Looking for Similarities

Jack and his guide dog, Baloo

I've often felt like I don't belong.

Most of the time I am the only visually impaired person in the room. As a child this made me feel different. Being different felt bad. I felt like I needed to hide my vision loss to belong.

Over time I've realized that we are all different and that belonging isn't about being the same.

To find belonging we first must accept ourselves. Having a visual impairment isn't easy but accepting this challenge is the only option. Like most of life's challenges, it makes you stronger.

Once you've accepted yourself, you can get to the good stuff. What do you care about? What do you enjoy doing? What are your values? Who are you really?

I am visually impaired; however, my vision loss is not who I am. It is simply one of my many physical characteristics. I care about helping people and making the world a better place. I enjoy spending time outside with the people I care about. I value compassion, inclusion, and a good laugh, to name a few.

After answering these questions for yourself, you can begin looking for belonging. I said that belonging isn't about being the same, but sharing similar interests and values certainly helps form connections.

I decided to write about belonging this time because I know that I'm not the only one who struggles with it. It is especially challenging for people with visual impairments because our differences are visible. If you feel alone, know that you never are. I promise it gets better.

Let's accept each other's differences, look for our similarities and create a more connected world where we can all find belonging.

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 LCAs and IRDs. You can read his blog at ***jackdamccormick.wordpress.com***

WELCOME, COURTNEY!

Hope in Focus is happy to announce the addition of Courtney Coates to our team as Director of Outreach and Development.

Courtney is an excellent communicator and brings to us her organizational leadership skills and her talents in marketing and business.

Her focus is to reach out to the Leber congenital amaurosis and inherited rare disease community by consistently giving support to those living with LCA and their families. She also concentrates on our development activities, such as grants and donor management, and office management and administration.

In other words, she's going to be a vital force in helping Hope in Focus grow and expand our global advocacy efforts and our contributions toward advancing sight-saving treatments and cures.

"I'm honored to join the team at Hope in Focus and look forward to meeting more of you over the coming year. This is one of the most dedicated groups I've worked with so far and the passion is inspiring."

We wish you the best, Courtney!

Courtney can be reached at 860-266-6062 or Courtney@hopeinfocus.org

Events

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

Hope in Focus Let's Chat About…" webinar: *Opus Genetics*

March 24th, 2022 at 1:00 pm EST
hopeinfocus.org/for-families/lets-chat-about
Join our chat with Ben Yerxa, PhD Co-Founder & President Opus Genetics — a patient-first, science-driven gene therapy company tackling manufacturing obstacles standing in the way of treatments for ultra-rare blinding conditions. Yerxa will speak about the Opus Genetics' business model, pipeline, manufacturing process, and their focus on tried and true methods.

RARE Drug Development Symposium Global Genes

June 9–10, 2022 • Virtual
globalgenes.org/event/rare-disease-drug-development
The RARE Drug Development Symposium, in partnership with the Orphan Disease Center of the University of Pennsylvania, is designed to connect, educate, and inspire rare disease participants, whether they're beginning or advanced.

Visions 2022 Conference Foundation Fighting Blindness

June 17, 2022 • Lake Buena Vista, FL
fightingblindness.org/visions-2022
VISIONS 2022, the national conference of the Foundation Fighting Blindness, is a one-of-a-kind event in which individuals who are visually impaired, and their families, can hear about exciting advancements in blindness research. The program is designed specifically for individuals and families affected by blinding retinal diseases such as age-related macular degeneration, retinitis pigmentosa, Usher syndrome, and related conditions.

Living Rare, Living Stronger Patient and Family Forum®

June 2022 • National Organization for Rare Diseases • livingrare.org
NORD plans once again to bring the rare disease community together for a day of thoughtful learning, networking, and celebration at the Rare Impact Awards. Check the website for updates.

Dinner in the Dark • Hope in Focus

October 22, 2022 • Groton, CT
hopeinfocus.org
Our primary fundraiser of the year, Dinner in the Dark helps fund research to cure blindness caused by LCA, provide support for genetic testing and drive awareness, education, and connections for families living with LCA and IRDs. Be prepared for a unique menu, fine winces, and a lively sensory adventure!

HOPE in FOCUS
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The *Seeing Hope* Newsletter is published quarterly by Hope in Focus, 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 Hope in Focus, visit www.hopeinfocus.org.

***Seeing Hope* Newsletter Team**
- Courtney Coates, Director of Outreach and Development
- Rosanne Smyle, Writer
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