Emma, age 10
COLORADO, USA

ISSUE 5 · JANUARY 2023

THE SHINE SYNDROME FOUNDATION

Happy New Year!

LAURA PALMER, PRESIDENT

My son, Nolan, got this diagnosis in 2018. When our online community started, we had three families. I remember thinking how amazing it was to be connected to these two other families who understood, even if we were thousands of miles away from each other. Now, our community has grown to close to 100 families! Community and connectivity are key goals within our foundation. If you have not had the opportunity to meet another SHINE family, you want to! Knowing you are not alone is a HUGE win in this rare disease world. Please help us get a true natural history study of this disorder by participating in the patient registry efforts. Every single patient is important in this quest for treatment for our loved ones. Thank you for being on this ride with us!

NORD Platinum Status

The SHINE Syndrome Foundation is now recognized as a platinum-level patient advocacy organization from the National Organization for Rare Disorders (NORD). NORD is the leading independent patient advocacy organization representing all individuals and families affected by rare diseases in the United States.
Platinum-level organizations demonstrate the highest level of integrity and transparency for patient advocacy involved in medical research, drug development, medical education, registries, or any work involving a Medical Advisory Board.

This issue:

Zacharias, age 7
SWEDEN

SHINE 2023 Foundation Board Members

We are pleased to introduce the 2023 SHINE Foundation board and positions, which are the same positions we held in 2022. Please reach out to any of us with questions, concerns, community engagement ideas, or ANYTHING SHINE/DLG4 related. You can reach us all at the same time by emailing board@shinesyndrome.org. You're also welcome to call Laura at 513-289-7720 with any questions.

- Laura Palmer, President, Cincinnati, OH, lpalmer@shinesyndrome.org
- Marie-France Gervais or "Mara" for short, Vice President, Ottawa, ON, Canada, mfgervais@shinesyndrome.org
- Brian Lareau, Secretary, Wheaton, IL, blareau@shinesyndrome.org
- Nate Palmer, Treasurer, Cincinnati, OH, npalmer@shinesyndrome.org
- Courtney Roche, Patient and Family Engagement, Huntington, NY croche@shinesyndrome.org
- Brooke Amos, Albertville, AL, Comunity Relations and Partnerships, bamos@shinesyndrome.org
- Justin Neduchal, Fundraising, Walton, KY, jneduchal@shinesyndrome.org

Rare Disease Day Shirts & Stickers - February 28

Colleen Lareau, SHINE mom, designed two new SHINE shirt for Rare Disease Day. These can be purchased in our Bonfire store. To guarantee arrival before Rare Disease Day, order by January 30. We also have a small collection of three different SHINE stickers we have available to mail to patient families. If you're interested in a sticker set, send Laura Palmer a FB message or email your mailing address to lpalmer@shinesyndrome.org and we will send them out!

BONFIRE

SHINE Star, Melissa

Melissa is 10 years old and lives in Brazil, in Rondonópolis, Mato Grosso. She is a pleasant child and full of smiles and jokes. But at the same time, her mood can change suddenly, due to Oppositional Defiance Disorder. She likes to attend therapies, go out with her school friends, go to church, play on the tablet and play with her little sister. Her favorite foods are hamburgers, pizza, and barbecue made by her dad. Melissa has an intellectual disability, epilepsy during sleep, and needs support with her daily activities. Finding this group was a light in the darkness for our family here so far away in Brazil (so far, Melissa is the only one diagnosed in our country). We felt welcomed and now we are hopeful that the studies will progress and our children will have a better quality of life.

"Finding this group was a light in the darkness for our family here so far away in Brazil."

DÉBORA - MELISSA'S MOM

Melissa, age 10
BRAZIL

Research Updates

CHEO, UNIVERSITY OF COPENHAGEN AND THE DANISH EPILEPSY CENTRE, CINCINNATI CHILDREN'S, BOSTON CHILDREN'S

CHEO: Drug Repurposing

CHEO, a children's hospital in Ottawa, Ontario, is currently testing the list of drugs from the University of Alabama that could up-regulate PSD-95. They are starting with the drugs our MAB considers to be the most promising using two DLG4 patient iPSC lines and derived neurons. They hope to have the first round of testing finished near the end of March and we hope to update the DLG4 patient population with their data at this time. This could lead to an off-label drug for our children. If you're interested in the list of drugs being tested, have a treating doctor reach out to Aleksandra at UAB: afoksin@uab.edu.

Denmark: University of Copenhagen and the Danish Epilepsy Centre

We now have clinical and genetic information from 49 previously unpublished individuals, and updated clinical data from 17 of those published in the 2021 paper. This brings the total number of known DLG4 patients to 102. The LOVD DLG4 database is in progress
We have made constructs for all the 16 missense variants we have knowledge of. Together, with constructs that will represent the truncating loss of function variants, these will be used to transduce mouse neurons and carry out functional studies to understand what is going on including electro-physiological measurements. The epilepsy group is submitting its research for publication on seizures in DLG4 in the near future. We will share their publication once available.

Cincinnati Children's Hospital

Cincinnati Children's is currently working with one DLG4 mouse model. It is a frameshift variant of a child who is severely impacted by DLG4. Currently, the mice are in the process of "building a colony" and development. Their plans include doing functional studies of the mice in Cincinnati (focusing on sleep and epilepsy, the S and E of SHINE) as well as sharing mice with other U.S. and international researchers.

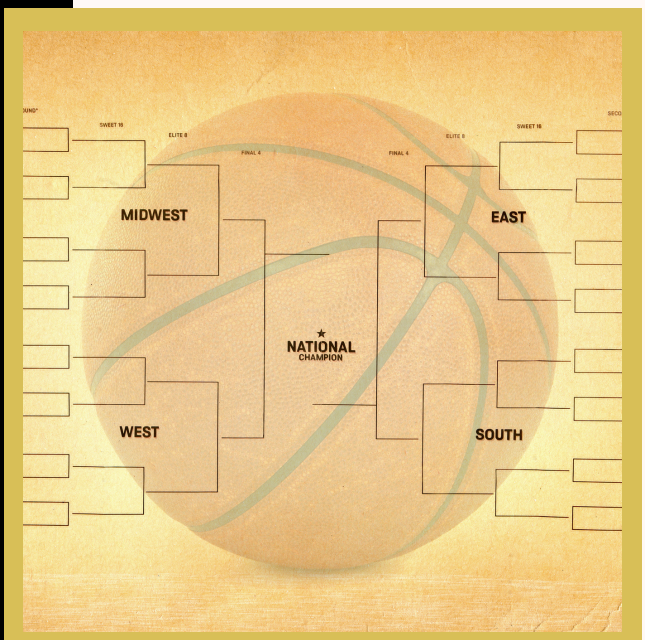
ASO with HOPE for Harvey

HOPE for Harvey continues its work toward an ASO (Antisense oligonucleotides) with Dr. Tim Yu and Everlum Bio. The Yu Lab has a potential target in mind for the ASO, and we hope to have a viable neuronal line soon to test this ASO. In theory, this ASO could potentially work for the entire DLG4 population, but more work has to be done first to determine that. In addition, we had a great meeting with Jackson Labs in mid-January about other DLG4 mice to be made, and have an upcoming meeting with the University of Alabama at Birmingham about other potential mouse models as well including missense. We are excited to continue collaborating and sharing our efforts with the SHINE Foundation as the research moves forward!

FUNDRAISING EFFORTS

FLYING PIG MARATHON

SHINE President, Laura Palmer, is going to push her son, Nolan, in the full Flying Pig Marathon in Cincinnati on May 7, 2023, as a fundraiser. All funds generated from this event will first be used to hire DLG4 researcher, Amanda Levy to continue her research in 2024. There are many ways to support this effort. You can donate directly, become a corporate sponsor, or purchase tickets (U.S. only) for the "Piggest Raffle Ever." Everything about this marathon is pig-themed, perhaps because many people say they'll run a marathon "when pigs fly!"



MARCH MADNESS BRACKET

We will have our first-ever March Madness SHINE Syndrome Foundation Fundraising bracket. If you are an international family, March Madness is an NCAA college basketball bracket where 64 teams compete for the college championship, bracket-style. Points are earned in the tournament by correctly predicting game winners. Entries to participate will be $20.

More information and specific details will be posted closer to the start of the tournament. Anyone is welcome to participate; please share with family and friends!

GENERAL FUNDRAISING

There are several ways to donate to the SHINE Syndrome Foundation. We are about halfway to a second-year salary for Amanda Levy. We are also currently exploring other opportunities to support, including treatment options, such as ASO, AAV, and PROTAC. If any families would like to host a fundraiser, reach out to us. General donations can be made via:

Website: www.shinesyndrome/takeaction
Venmo: @shinesyndrome
Mail: 4906 White Blossom Blvd. Mason, OH 45040.

DONATE NOW

Upcoming Events:

Caregiver virtual chat:
February 16th at 9:00 PM EST
& February 23rd at 3:00 PM EST

Rare Disease Day,
February 28, 2023

Midwest Meetup
May 6, 2023

Participating in the SHINE Community

First, welcome to our new families! Getting a rare genetic diagnosis can be overwhelming and isolating, especially with our wide geographic spread.

When you first join our SHINE family support FB group, you'll be greeted personally by SHINE board member, Courtney Roche, who is a great patient advocate and will connect you with information and resources.

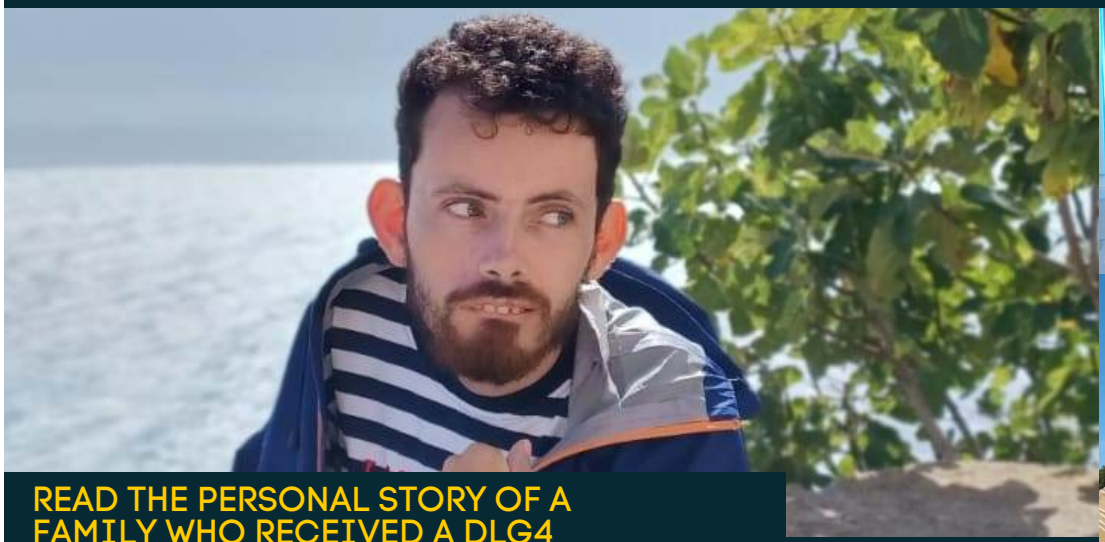
The How-to-SHINE guide is another excellent resource when starting this journey. Feel free to share this with friends, family, and medical providers. The most recent version of this document will always be located on our website, www.shinesyndrome.org.

We want every SHINE family to feel heard and be represented in our research efforts, so please participate in as many registry efforts as you can. Even though our children all have a DLG4 gene variant, the presentation varies widely from child to child.

The best way to participate in the research at this time is to participate in the registry process. More information about registries can be found in the chart below and on our website. We recommend starting with Simons Searchlight, then CoRDS, and finally Ciitizen. Currently, Simons has the most DLG4 patient data with 36 patients. The latest quarterly report from Simons can be found here.

FEATURES	SIMONS SEARCHLIGHT	CORDS	CIITIZEN
Who can participate?	Open to US and international	Open to US and international	US only
Available languages	English, Dutch, French, Spanish	English only	Medical records must be in English
Purpose	Compare many neurodevelopmental disorders	A close look at DLG4 only	Stores patient medical records in one place
Includes VUS data	No	Yes	Yes
Collects biospecimen samples	*US only	No	No
Estimated Time Commitment	2-4 hours	1 hour	5-10 minutes
Incentives	Amazon Gift Cards for each survey	$100 International Visa gift card to first 20 particpants	No incentives

MY NAME IS FLORIAN



READ THE PERSONAL STORY OF A FAMILY WHO RECEIVED A DLG4 DIAGNOSIS IN ADULTHOOD

I am 30 years old and I live in France on the shores of Lake Geneva with my parents in our family home. I am the oldest of 3 children, my brother Thomas is 28 and my sister Sixtine is 22.

In August 2022, I discovered that I am rare when the results of genetic research were read. At the very beginning of my story, there was a mutation in the gene DLG4. Today, it's referred to as SHINE Syndrome. It's the answer to a question my parents have been wondering about for 30 years. And it doesn't change anything for me, at least for now. Nor for them. I've discovered that there are children, teenagers, and adults like me all around the world as well as parents who live with this new aspect to their lives.

A community of people who want to communicate and share. I see myself in all these beautiful faces and beautiful smiles that characterize us. Our gazes speak for us, our eyes express our honesty. My mom will tell you my story, our story, because I don't know how to read or write

When I was 3, my pediatrician noticed delays in my skill acquisition which confirmed my parent's suspicions about my psychomotor development. It was the start of a medical and institutional path for me, full of appointments, consultations, and care. The discovery of absence seizures, fine and gross motor skill issues, disturbed sleep, difficulties with walking and standing, and language issues.

We made many changes in treatment until we found the one that worked for years. During my adolescence, doctors diagnosed issues with my spine: scoliosis, kyphosis, and lordosis. For 4 years, for 20 hours out of every day, I wore a brace to limit their damage. I grew tall and thin: a real supermodel. I spent my days in medical educational institutes and my evenings and weekends with my family.

My parents always ensured that I could participate in both family and social life within my abilities. I became sociable, chatty, and even a bit clingy and always tried to get attention from those around me. Here are some of the things I would have said to you only a few years ago:

- I like walks in the mountains, the forest, or around the lake
- I like running, cross-country skiing, and sledding
- I like music, shows, and concerts
- I like horseback riding, going in the water, and adaptive skiing in a chair with my Dad
- I love my dogs and my cats
- I like celebrating, dancing, singing, being surrounded by people
- I like laughing, asking questions, and eating yummy food
- I like being with my family
- I like going to the institute Monday to Friday and being with my friends there
- I like going on vacation
- I love life, I love laughing, I love talking

I was that boy. My institutional life changed a little when I transitioned to the adult side. I wanted to keep my childlike soul, making jokes and being clingy. Sadly, they didn't like that very much... I had to grow up and I wasn't ready yet. And it's disruptive when you're clowning around. I became frustrated and anxious.

In 2017, I fell and broke my left femur. This was the start of a difficult period and we discovered I had severe osteoporosis. My parents were told "your son has the bones of a 90-year-old grandma", in other words very weak. Once again, changes in treatments, hospitalizations, new health concerns, behavior changes, weight loss, sleep disturbances, lack of motivation to go to the institute, loss of speech, loss of smile...

I'm still me, the same Florian, but where did my former life go?

> "I SEE MYSELF IN ALL THESE BEAUTIFUL FACES AND BEAUTIFUL SMILES THAT CHARACTERIZE US."

Today, I am not institutionalized, my health doesn't allow me to go back and see my friends. I live at home with my parents 24/7. And since they both work, professionals from associations providing in-home support come to care for me. I still have medical appointments with various specialists who follow me. Micropakine is back in my life to control my epilepsy.

Other treatments help provide comfort and improve my sleep. I don't walk as confidently, I need to be accompanied for everything. I still have the same, even deeper, gaze, but I haven't regained my smile or my speech. I stay silent, I keep my secrets. I still love the same people, I still enjoy the same things...I still love life, but now silently so.

Dear parents of all our rare, precious youngsters. I am Florian's mom, my own, our, "handsome guy". My name is Liliana Voisin. Through this tale, I wish to share my son's and our family's story with you. We are a very close-knit family, even if Thomas and Sixtine don't live at home anymore. They are very close to each other and share a lot of sibling love. We've always tried to do our best for Florian and still do.

Science is advancing much faster these days to provide answers and adapted solutions. DLG4 includes multiple variants on the same gene, but they can manifest differently from one person to the next. Listen to yourself and listen to your children. They know how to tell us or let us know what they need. We know them better than anyone else. We're their first doctors and nurses.

Our vigilance can alert us to and prevent risks and help doctors treat them.
Trust yourself and trust in science which I hope will soon bring us answers and solutions.