



SHINE SYNDROME FOUNDATION

news

Noah, 10 New York, USA

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SHINE Updates

We have a lot of exciting things on the horizon. The more we learn about the DLG4 gene, the more we've realized that we need to have multiple therapeutic options for our families.

The SHINE Board has been meeting with various universities, biotech companies, and researchers over the past few months. We've learned a lot about DLG4, PSD-95, and the need to potentially have multiple shots on goal, as we have a huge spread in the actual patient variants.

Though many of our cases seem to be true haploinsufficiency, or LoF, there is some new evidence that some of our patients may actually show a GoF or have too much PSD-95. Dr. Tümer and team are working on studies to determine which variants act differently. One thing I'll say is we couldn't ask for a more dedicated researcher for DLG4.

My son is one of the cases that may be GoF and once this was realized, Dr. Tümer asked to send blood to Denmark for a full analysis, something she has done for many other DLG4 families.

The point of sharing all of this, is that we are going to need multiple treatment options to make sure we are providing treatment options for all families. This takes both time and money, but most options are in the works and/or being explored. We submitted one patient to n-Loem for ASO feasibility and HOPE for Harvey is also working with Dr. Yu's lab on an ASO. We've also signed a contract for an AAV9 gene therapy in Israel.

DLG4 impacts all of our children differently. We all have slightly different experiences, which is why it's so important to participate in the research opportunities, ask questions, and be involved. We are working hard for the community and need everyone's help! With sincere thanks,
Laura Palmer, SHINE President and mom to Nolan (9)



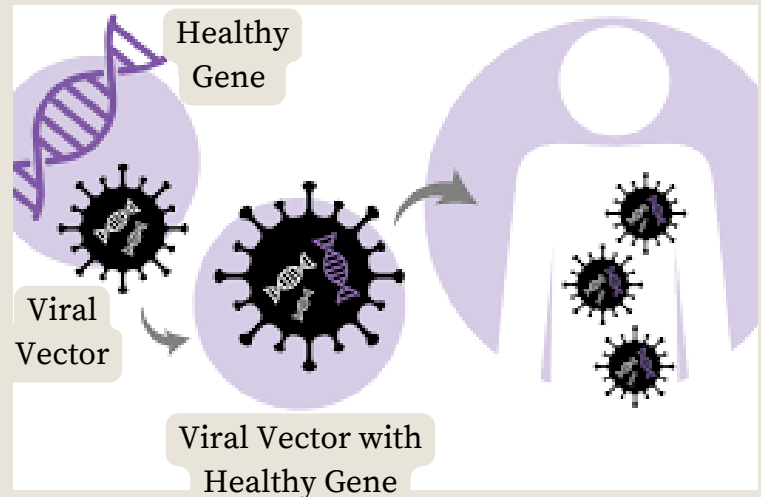
Jace, 6 Kentucky, USA

Hebrew University

AAV9 Project

Timeline 12-18 months

The SHINE Syndrome and HOPE for Harvey Foundations are collaborating on a very exciting research opportunity in Israel. The lead investigator, Rami Aqeilan at Hebrew University, will be developing an AAV9 gene therapy to upregulate PSD-95 in DLG4 patients. Essentially, an AAV is a virus that is engineered to deliver DNA to target cells. In the case of SHINE Syndrome, the ultimate aim is to compensate for the mutation in the DLG4 gene and restore PSD-95 production to normal levels.



AAV9 Visual

Project UPDATES



Choosing

VARIANTS

The iPSC variants that are included in this research include two lines (one each frameshift and nonsense) that were developed at CHEO and a missense line currently in the biorepository at COMBINEDBrain. The animal models used will be from Cincinnati Children's, JAX lab, and UAB. Collectively, these variants cover all the symptoms we see in DLG4, including seizures, ESES, ID, ASD, and hypotonia.

TIMELINE

The timeline for this work is 12-18 months. We have signed a contract and paid the first negotiated payment. As a community, we need to raise \$48,500 for the second and final payment. One of the primary reasons we were able to negotiate such a reasonable contract proposal was by using assets in existence. If you'd like your child's exact variant to be included in future research, there are many options. The best, easiest, and free option is providing a biospecimen sample for Simons Searchlight (US). We are also members at COMBINEDBrain and can also utilize their biorepository but there is a cost associated with this.

PROS

One of the reasons we chose to support this project is that Dr. Aqeilan will investigate AAV potential in both LoF and GoF variants to hopefully account for all possibilities.



Principal Investigator, Dr. Rami Aqeilan

research

CHEO, University of Copenhagen, Danish Epilepsy Centre, Cincinnati Children's



CHEO

The SHINE Syndrome Foundation is currently supporting a drug repurposing trial at CHEO under Dr. Alex MacKenzie and Dr. David Dymnt. At its core, drug repurposing has the potential to help increase PSD-95 production. One such drug is already being trialed in one of our patients, but a whole array of drugs are being tested on cell lines from members of our SHINE Community. Drug repurposing has the advantage of getting a potential treatment developed quickly because the drugs are already approved, tested, and known to be safe and effective. This is far enough along, that we expect preliminary results before this summer.

The University of Copenhagen and the Danish Epilepsy Centre

Researchers at the Danish Epilepsy Centre have finished their data collection. They plan to publish two studies. One will cover DLG4 patients who live with epilepsy. The second will encompass all DLG4 patients who contributed to the study. Amanda Levy, a Ph.D. student, and Dr. Tümer continue their studies of the missense variants and impacts on the protein



production of PSD-95. There is some speculation that some of the missense and potentially frameshift and nonsense at the very tail end of the gene may be GoF (Gain of Function). Two patient blood samples are en route to Denmark for RNA analysis.

Cincinnati Children's Hospital

The Hogenesch Lab at Cincinnati Children's Hospital in Ohio, USA has successfully used CRISPR-R to create six founder mice of a frameshift DLG4 variant. They will have enough to characterize in about four weeks and are studying the behavioral and sleep characteristics of the mice, as well as sending mice to other DLG4 researchers.



Have Questions about the
Research? Reach out:

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Or, visit our website:
www.shinesyndrome.org



Please stay tuned for updates. We will work to keep the community updated on the progress of these exciting projects as new information becomes available.

We thank you for your continued support and trust, as we work tirelessly to help this community that means so much to us all.

ARE YOU ALL IN? CLICK ON EACH ICON TO BEGIN!



ALL PATIENTS



ALL PATIENTS



U.S. PATIENTS ONLY

How Can Families Help these Efforts?

Participate in important natural history study and data collection

Create a fundraiser to help support the research efforts

Be a part of the research by submitting a biospecimen sample

EASY FUNDRAISING IDEAS

1. Create a Facebook Fundraiser for "DLG4 Synaptopathy "SHINE Syndrome." This is very easy to share with your personal connections and there are no fees associated with it.
2. Form a team for the first annual "Stroll for SHINE." Organize friends and family to have a walk/run in your town. Make your own route, get some donuts and post-race fuel, design shirts, and have fun honoring your rare warrior!
3. Play on your strengths! What are you good at? For some of us, it might be running a marathon, hosting a bake sale, speaking at a church or organization about your rare child, or holding a gala. No idea is too big or too small! If we can help in any way, please reach out to director of fundraising, Justin Neduchal at jneduchal@shinesyndrome.org.

Patient & Family Participation

We need ALL DLG4 patients involved to get to a clinical trial and treatment for our loved ones. Are you all in? Here is a checklist of things you can do as a DLG4 parent to get us there quicker:

- Complete all possible steps in Simons Searchlight
- Complete the CoRDS registry
- If in the US, enroll in Ciitizen and submit a biospecimen sample to Simons
- Help fundraise for these therapeutic options.

SHINE Star Seren



MEET SEREN

Seren is a curious, friendly, and loving little girl with a great sense of humor. She loves to play with her dolls, do craft activities, go swimming, and spend time in the great outdoors. She has a big brother whom she looks up to enormously.

She loves the idea of all animals but hasn't quite mastered loving them in the flesh, yet. She loves to sing and is learning to perform with our local inclusive theatre company. Her name means 'star' in Welsh, a somewhat fitting name for someone who shines so brightly to everyone she meets.