SHINE SYNDROME FOUNDATION

Fall 2022 Newsletter

October 2022

"Building community, research, family support, collaboration with medical experts, and determination to find a treatment - that is SHINE."

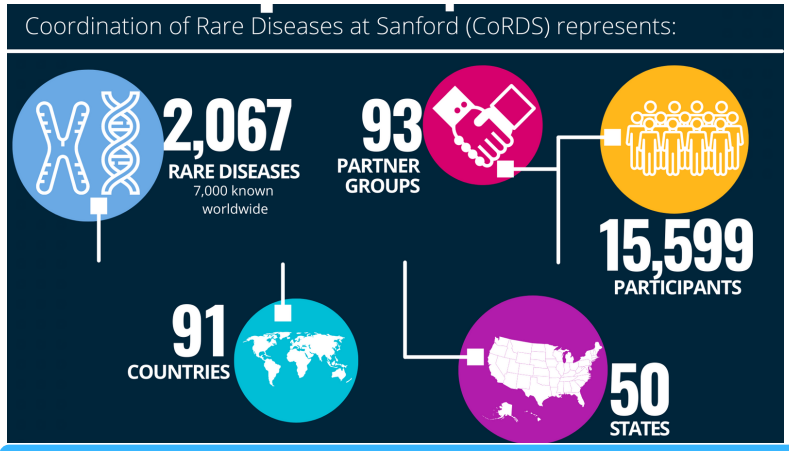
Thank you!

Wow! We are blown away by the support from our July sunSHINE Fundraising event. We had people sharing media content, tweets, videos, and donating from all over the world. We even got a news segment on WCPO in Cincinnati.

Our grand total raised during the month of July between the raffle and straight donations is $78,000 and we recently surpassed $90,000 in just over six months as a nonprofit. In addition to raising an incredible amount of funds, we also spread awareness of DLG4 and SHINE across the globe. Once again, we are amazed by what our foundation has been able to accomplish since earning nonprofit status in March of 2022. Thank you to every single person who helped us accomplish this huge goal.

This fall, we have some exciting things on the horizon. The funds used from the sunSHINE campaign will be used to hire Amanda Levy (see page 3 for a bio) for a 1-year position at the University of Copenhagen. We will be meeting monthly with Amanda and Dr. Tümer's team, providing regular updates to members about the project along the way.

We are looking forward to continuing on this journey with all our patient families and supporters. From the bottom of our hearts, thank you!

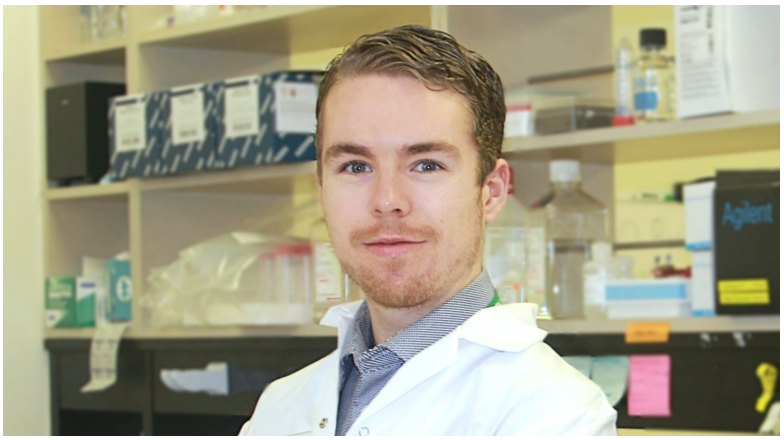


CoRDS is a centralized international patient database for rare disease.

Family To-Do Tasks

Please support these initiatives!

1. Visit www.shinesyndrome.org/registry to complete both Simons Searchlight and the CoRDS registry (coming soon). These are the best pathways to creating a natural history study of this disorder. The infographic to the left highlights information about CoRDS.
2. Submit photos to our SHINE Syndrome media bank so we can include your child when we post on social media.
3. Enter epilepsy information (Family FB Group)

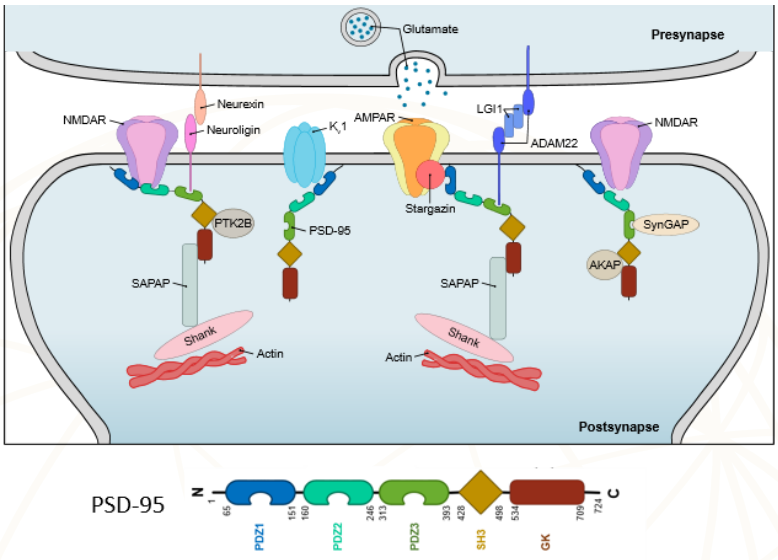


YouTube Informational Videos

Courtesy of MAB member, Alexandre White-Brown

Have you seen our YouTube channel yet? Thanks to Alexandre White-Brown from CHEO, we have a series of Informational videos covering different topics related to DLG4, variants, the PSD-95 protein, and more.

Check out our YouTube channel here.



PSD-95 and the synapse - PDZ1-3, SH3 and GK are different domains of PSD-95. Only some of the proteins and receptors binding to PSD-95 are shown in the figure *(Adapted from Levy et al. 2022, the figure is subject to copyright).*

Current Research Plan

Presented by our Danish Research Team: Zeynep Tümer lab and PhD student Amanda Levy) (Copenhagen University Hospital), Kristian Strømgaard lab and Jakob-Barsley Sørensen lab (University of Copenhagen)

Synapses (the tiny gaps between nerves) are essential structures for the transmission of nervous impulses in brain circuits, and the PSD-95 protein, encoded by the *DLG4* gene, plays a central role in the structure and function of excitatory synapses through binding to several proteins residing both in the cell and on the cell membrane.

Different types of *DLG4* variants can affect the function of PSD-95, but we still do not know, how an abnormal protein (or less protein) can result in the symptoms observed in the affected children (or adults). It is crucial to understand the underlying molecular and cellular mechanisms to design/plan effective treatment strategies.

We hypothesize that loss-of-function variants (i.e. frameshift or nonsense variants) will lead to reduced amount of PSD-95 in the synapses, and increasing it will ameliorate symptoms; meanwhile, we do not know how the missense variants will exert their effects.

In our research, we will assess the effect of different types of DLG4 variants on the structure and function of the synapses. Our main approach is to make synthetic DNA molecules (vectors) representing the variants, introduce the vectors into mouse neurons and investigate the effects of the variants using diverse state-of-art methods including high-resolution imaging, electrophysiology, and protein interaction studies. These cell models can also be used to investigate whether a drug can correct the dysfunction observed. As a first step we plan to use FDA-approved drugs, as these can immediately be translated to the clinics and treatment.

Building our DLG4 Dream Team – Introducing the Newest Members of the SHINE Scientific and Medical Advisory Board

Introducing Erick Sell

An epileptologist from CHEO

Dr. Sell follows two patients with SHINE Syndrome. He is a pediatric neurologist working at CHEO, Ottawa since 2008. He did training in pediatric neurology and pediatric epilepsy at the Hospital for Sick Children in Toronto, Canada. His work involves predominantly looking after patients with genetic neurodevelopmental and epileptic encephalopathies.

Meet Amanda Levy

University of Copenhagen

Amanda Levy is a molecular biologist and geneticist currently employed as a Ph.D. student in Dr. Tümer's lab. Amanda's research focuses on the genetic and functional mechanisms of rare neurodevelopmental disorders, particularly SHINE syndrome, and she has written a review on the association between neurodevelopmental disorders and PSD-95 and its interaction partners.

Meet Kristian Strømgaard, Ph.D.

University of Copenhagen

Kristian Strømgaard obtained an MSc degree in Chemical Research from University College London, and continued as a Ph.D. student in medicinal chemistry, part-time at the Danish pharmaceutical company H. Lundbeck.

He did a postdoc at Columbia University (New York), and shortly after, he was appointed H. Lundbeck Professor at the age of 36 to establish research in Chemical Biology. He won the 'Teacher of the Year' award from the Faculty of Pharmaceutical Science (Univ. Cph.) in 2009.

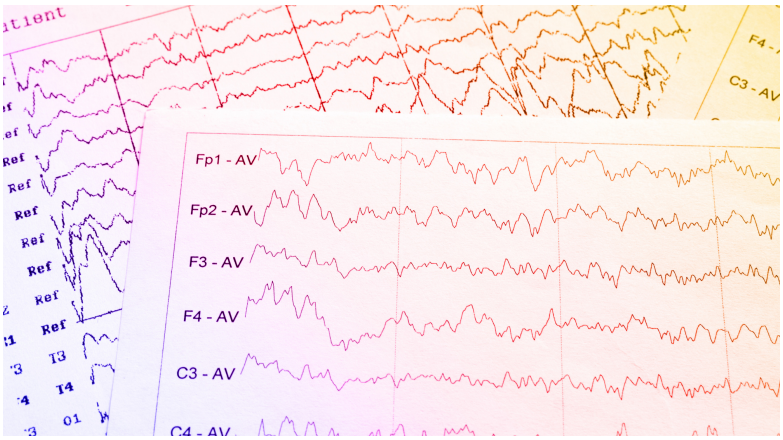
In 2012, he co-founded Avilex Pharma, where he developed inhibitors of PSD-95 (DLG4) as a novel treatment for stroke, and successfully brought the lead compound AVLX-144 through Phase 1 clinical trials. In 2014, he was appointed Director of the Center for Biopharmaceuticals, where he headed a research center on peptide and protein engineering. Recently, he was a visiting professor at Harvard Medical School (Boston) to explore medical research and innovation.

In 2021 he was awarded the University of Copenhagen Innovation Award and appointed Novo Nordisk Foundation Distinguished Innovator, and has taken out >15 patents, which have led to the establishment of 3 biotech companies. Dr. Strømgaard has particular experience with studies of PSD-95, where he since 2006 has worked on developing ligands that perturb PSD-95 and engaged in molecular levels studies of the structure and function of PSD-95 and interacting proteins.

CoRDS Registry Launch

Visit www.shinesyndrome.org/registry

CoRDS is our second patient registry and is completely specific to SHINE Syndrome and DLG4. Information is available on our website, www.shinesyndrome.org/registry.
The CoRDS registry is extremely important in developing a natural history study of this disorder. This can be completed online or a paper copy can be requested. This will be available in November, so check our FB group and website for a launch date!



Epilepsy Research Project

Rikke Møller, Guido Rubboli, and Benedetta Kaspian, neurologists at the Danish Epilepsy Centre, are studying epilepsy in DLG4 patients. They are requesting patients' neurologist(s) names and email addresses, as well as permission to request or collect EEG tracings. Even if your child does not have epilepsy, they may still be interested in contacting your child's neurologist and collecting any raw EEG data. Please see the Google Sheet in the private family FB group to contribute your child's information. The team will reach out to the patient's neurologist on your behalf, though you may be asked to collect and send EEG tracings.

RAREis Grant Recipient

Awarded $5,000 to create a media awareness video

In July, Horizon Therapeutics announced that our foundation was awarded a $5,000 grant to use to create an awareness video about SHINE Syndrome. We are highlighting one doctor and five patient families to raise awareness and use for future fundraising endeavors, as well as a final last slide showing all our SHINE patients. Thank you to everyone who submitted a photo. Filming has wrapped up and we hope to reveal the video in November!

SHINE Star - Sebastian

Meet 6yo Sebastian from London, UK

Sebi is a very sweet and gentle boy. Sebastian has low muscle tone, hypermobility, is nonverbal, and struggles to communicate his basic needs. When he was little he loved vocalizing nursery rhymes and playing the piano, but later he lost this interest. He now loves the water. He is anxious but loves hugs and kisses. His parents have not lost hope that one day Sebastian will be able to talk and communicate and have tried many therapies over the years. They are hoping science and research will find an answer as soon as possible.

DLG4 Registry Goals

Patient Registry	Simons Searchlight	CoRDS	Danish Epilepsy Centre Project
Purpose	To collect information that will be used to compare DLG4 to other neurodevelopmental disorders connected to ASD	CoRDS is a DLG4-specific patient registry that will be used to create a natural history study of this disorder.	This study is specific to DLG4 patients **with epilepsy** to study neurologist clinical data and raw EEG tracings.
Family Tasks	Enroll, upload your child's genetic report, complete developmental surveys, schedule and complete a medical history interview, and submit a blood sample.	Enroll, upload a medical report (optional), give consent, and complete survey	Complete Google Sheet with diagnosis and neurologist's name and email.
Time Commitment	1-2 hours	1-2 hours	5-10 minutes
More Information	**ENROLL**	Launching this Fall!	Enroll in the Family FB Group
Contact Person	Courtney Roche SHINE Director of Patient and Family Engagement croche@shinesyndrome.org		

Fall Fundraising Campaign

We will continue fundraising for future research opportunities and the integration of our foundation into the larger rare disease community. Thanks to the DLG4/SHINE community's generosity, we have plans to fund:

- A full-year salary for Amanda Levy
- One nonsense variant mouse model
- One frameshift variant mouse model
- A mini-documentary about the disorder to raise awareness and generate revenue.

Donations can be made anytime:

- Online: www.shinesyndrome.org/takeaction
- Venmo: @shinesyndrome
- Hosting a FB Fundraiser for DLG4 Synaptopathy/SHINE Syndrome
- By Check:
  - SHINE Syndrome Foundation
    4906 White Blossom Blvd.
    Mason, Ohio 45040

REGISTRY INCENTIVES

Simon's Searchlight:
Amazon gift cards of varying amounts per completed survey. These are available for all Amazon country platforms. These incentives are provided by the Simons Foundation and are available to everyone who participates. (Click on the image above to go to Simons).

CoRDS:
The SHINE Syndrome Foundation will be providing raffle item incentives for all families who complete the CoRDS registry. Please check for updates in the family Facebook group for registry availability, raffle dates, and incentives provided by our foundation. This registry should roll out in November 2022.

QUICK Links

Shop Bonfire

Donate @Venmo

Find us on Amazon Smile!

Partner with us for Community Rewards!