January 2022 Newsletter

Dear members of the SHANK2 community,

Welcome to the first edition of the SHANK2 Foundation semi-annual newsletter! Less than a year ago, when the challenges of having a family member with a SHANK2 disorder were exacerbated by the COVID-19 pandemic, neither of us would have guessed that just a short time later we would be part of a community that understood the sense of isolation, uncertainty, exhaustion, and, yes, joy, derived from having a child with a rare genetic disease.

Since we launched the SHANK2 Foundation six months ago, our goal was to bring together families, researchers, clinicians and biotech companies in order to achieve our mission to improve the quality of life for individuals affected by SHANK2 disorders. While we have a long way to go, our community is growing, our database of information on SHANK2 patients is expanding, and SHANK2 research is underway. We hope that the creation of the SHANK2 Foundation has provided you with a sense of community and a sense of hope.

Here's a recap of what we've done since the launch.

DATA COLLECTION

We have developed a three-tiered program to gather data on SHANK2 disorders. The information gained from this effort is necessary to initiate research, develop treatments and, ultimately, find a cure. All the data is de-identified and protected by strict privacy practices and is only accessible to researchers with the families' permission.

Patient Registry

Comprised of a demographic section, a general developmental profile, and five patient information surveys, the patient registry serves to help researchers interested in studying SHANK2 identify common traits and developmental patterns of SHANK2 patients. Gradually our database is expanding. Over twenty individuals are currently registered.

Here are a few things we've already learned from the registry:

- All our kids have:
  - Language delays
  - Gross and/or fine motor issues, ranging from minor to moderate
  - Low response to pain

- Most of our kids:
  - Get speech and occupational therapy
  - Are overactive (but not hyperactive)
  - Have an autism diagnosis (additionally, many are diagnosed with ADHD and/or IDD)
  - Have mild to moderate hypotonia
  - Are in inclusive classrooms
  - Have sensory processing differences (primarily tactile, sensory seeking)
  - Have few health problems beyond neurodevelopmental issues (some have digestive problems)

- The #1 priority for parents and caregivers is to improve our kids' ability to communicate

Phenotyping Study

Mount Sinai *Seaver Autism Center for Research and Treatment*

The Seaver Autism Center at Mount Sinai in New York City, founded by Dr. Joseph Buxbaum, a prominent neurodevelopmental disorder and autism researcher, has designed a study for the SHANK2 Foundation to identify the traits observed in SHANK2 patients in order to better understand the role pathogenic SHANK2 variants play in human development. Information gathered through assessments conducted by Dr. Buxbaum's team will complement the data collected in the patient registry. In order to begin the study, we need ten affected individuals who meet the criteria to participate, including a diagnosis of a de novo SHANK2 variant through genetic testing and residence in a home where English is spoken.

Standardized Physical Evaluations

Many doctors attending to our kids are unfamiliar with SHANK2 disorders and how to best treat affected patients. Dr. Yong-hui Jiang, a renowned SHANK2 expert and the Chief of Medical Genetics at Yale University Medical Center, is conducting standardized and thorough examinations for families and caregivers able to travel to New Haven, Connecticut. Dr. Jiang will use the findings of these exams to enhance the body of data collected in the patient registry and phenotyping study.

RESEARCH

Two SHANK2 research projects are currently underway. While the studies are not yet completed, preliminary findings have been reported.

MIT Mouse Model Study

Since 2018, Dr. Guoping Feng, a distinguished SHANK2 scientist and the Associate Director of the McGovern Institute at MIT, as well as his team at the Feng Lab have been studying animal models to understand the functional consequences of SHANK2 variants found in human patients. Using CRISPR genome-editing technology, the lab has created mice with the exact variants found in an individual with a SHANK2 disorder. Electrophysiological analysis of these mice has indicated that one of the SHANK2 variants in question significantly disrupts synaptic functioning in a region where SHANK2 protein is found. The research team is currently evaluating how this synaptic dysfunction affects behaviors in these mice.

Rarebase/*Function* Platform

The SHANK2 Foundation is one of fifteen rare disease advocacy groups participating in the newly launched *Function* Platform created by biotech company Rarebase. The Rarebase team is currently screening a library of 4,000 FDA-approved drugs to see if any could act as a treatment for SHANK2 disorders. By early Spring, Rarebase will be sharing an update on the project, including whether they have identified any promising candidates.

FAMILY SUPPORT

The SHANK2 community of families and caregivers is growing, and we have created two ways to meet and support one another.

Facebook Group

The SHANK2 Foundation private Facebook group provides a forum where members can engage in conversations about our kids, ourselves and anything SHANK2 related. Our Facebook group has grown to 34 members from 8 countries. A special thanks to Sarah Schmidt who does an outstanding job of facilitating weekly group conversations on various topics.

Zoom Meet-ups

On January 2nd, we held our first community "meet-up" to give families and caregivers a chance to meet face-to-face (virtually) and engage in relaxed and open conversation. Regular meetings will be scheduled to accommodate participants in varying time zones. Please join us for our next scheduled meeting on January 30th at 2:00pm EST.

SHANK2 DAY

On November 13, 2021 (in reference to the location of the SHANK2 gene at 11q13), we held our first annual SHANK2 day meeting (virtually) bringing together families, researchers, and clinicians. We are so grateful to the experts who educated us on topics related to SHANK2 disorders as well as the families and professionals who attended the conference. All the sessions were interesting and informative and, together, gave attendees a comprehensive background on the SHANK2 gene, its role in disease, the status of SHANK2 research, and offered help and hope for our kids and our families. If you missed the meeting, the recordings are posted to the foundation's Vimeo account. Contact us for a direct link and password to the recordings. We look forward to another productive meeting on November 13th, 2022!

ALLIANCES

We have joined a number of organizations who share our goal of helping individuals and families affected by rare diseases.

COMBINEDBrain

A consortium of patient advocacy foundations that meet monthly along with researchers, clinicians and biotech representatives to share knowledge in an effort to expedite clinical treatment development

JumpStart

As part of the Orphan Disease Center at the University of Pennsylvania, JumpStart guides patient advocacy groups through the process of developing programs and treatments for their communities

Global Genes

A forum where constituents of the rare disease community connect, exchange information and support one another

CureSHANK

A foundation seeking to further research and development for treatments of all SHANK disorders (SHANK1, SHANK2, and SHANK3)

We are in the early stages of joining forces with other family advocacy groups to develop a more efficient and effective way of finding individuals with our respective rare diseases, worldwide.

AND ALL THE REST

- In November 2021, the SHANK2 Foundation officially became a 501(c)(3), or a tax-exempt entity.

- In January 2022, we welcomed Alex Lanjewar to our board. Alex, is a candidate for a Ph.D. in neuroscience at the University of Southern California. She is investigating biological mechanisms that contribute to typical development of cognitive functions as a means to better understand how deficits seen in neurodevelopment disorders may arise. Her research focuses on the MET gene, which codes for a protein that indirectly interacts with SHANK2. Alex is well suited to support the SHANK2 Foundation's objective of accelerating research and treatment developments for individuals affected by pathogenic SHANK2 variants. Her academic and clinical experiences have prepared her to identify and analyze areas of research critical to finding treatments for SHANK2 disorders.

As we move forward, our short-term goals include:

- Finalizing talks for a biorepository
- Establishing a think-tank of SHANK2 researchers
- Exploring grant opportunities
- Creating a scientific advisory board

If you haven't already, please:

- Write to Tess Levy (tess.levy@mssm.edu) to determine your child's eligibility for the phenotyping study
- Sign up for the patient registry and/or complete the demographic, developmental and survey sections
- Visit our webpage to read some of the stories from members in our community (https://shank2.org/community/)

We are so grateful that each and every one of you has joined our community. Please feel free to reach out to either one of us with any questions, suggestions or concerns you may have. We look forward to a productive 2022!

Sincerely,

Polly and Ben

the SHANK2 foundation
https://shank2.org