Issue 1
Summer 2017

Undiagnosed Diseases Network

Participant Engagement and Empowerment Resource (PEER)

Contents:

About the UDN

The Undiagnosed Diseases Network (UDN) is a research study that is funded by the National Institutes of Health Common Fund. Its purpose is to bring together clinical and research experts from across the United States to solve the most challenging medical mysteries using advanced technologies. Through this study, we hope to both help individual patients and families living with the burden of undiagnosed diseases, and contribute to the understanding of how the human body works.

About UDN PEER Group

By Teresa Locklear

The Participant Engagement and Empowerment Resource (PEER) group was founded in January 2017. The group consists of parents, patients, genetic counselors, and other medical support staff. Those that have a child with a rare disease often feel lost and alone. The PEER group was established to provide support for all those family members that have attended the UDN. We want to reach out to the doctors and genetic counselors to let them know more about the Undiagnosed Diseases Network. This network is so new that many don't know what all they do and how they work. We as parents feel lost when we don't have answers to what is happening to our child. The UDN is working hard to get those answers and we want to help support all those families.

PEER members at the in-person meeting in Boston, MA. Pictured (L to R): Kelly Schoch (UDN), Debbie Krieger, Ruby Owens, Emily Glanton (UDN), Liz Aronin, Jamie Mills, Ingrid Holm (UDN), Chad "Chad the Dad" Smith, Liz Worthington, Teresa Locklear, Anna Bican (UDN).

"Our Life with Quinn" – A Family's Story

By Jamie Mills

The first year of Quinn's life was like a rollercoaster ride, and nothing could have prepared us for what we would go through together. Liz and I were new parents, excited to welcome a beautiful baby boy into our family in the Fall of 2014. At first, things were normal (and great)! After 5-6 months, however, we realized that Quinn had stopped meeting new milestones. That's when the hits started coming: bilateral cataracts in his eyes that needed to be surgically removed; his first (major) seizure, which precipitated a hospitalization; diagnosis with microcephaly and delayed myelination in his brain; loss of appetite (due to anti-seizure medications), which resulted in a G-tube placement to ensure that he receives enough calories to grow. Within one year, our little boy had undergone four major surgeries and dozens of scans/tests, was on more medications than I've ever been on in my life, and had been hospitalized for a total of seven weeks. Our little boy had experienced so much pain and adversity in his short life! Even more crushing was the news that we received in December 2015 – the genetic testing available to us at the clinical level had yielded no diagnosis for Quinn's maladies.

Jamie and Liz with their son, Quinn

That's when we heard about the Undiagnosed Diseases Network (UDN) research program that was available at Duke University. After applying to the program, we were accepted into the study in May 2016. We met with Dr. Vandana Shashi and her excellent team of genetic counselors and clinical research coordinators, as well as other specialists, who re-evaluated Quinn and re-analyzed his genetic tests. The result of this work/research was remarkable: Quinn is one of seven individuals around the world with the same rare genetic mutation (NACC1). All of the children exhibited remarkably similar clinical presentations: in addition to the impairments described above, they share other similarities with Quinn, such as sleep disorders, periods of extreme irritability, hypotonia, and stereotypic hand movements.

Having a diagnosis for Quinn's disorder has been extremely significant for our family. We have since spoken with two families in the U.S./Canada that have children with Quinn's mutation, and it is remarkable to discuss similarities between the children. While we had been able to talk to other families with serious diseases, we feel that there was something incredible about speaking to a family with another "Quinn." The level of connection is simply deeper. In addition, learning that Quinn's maladies were caused by a genetic mutation that neither Liz nor I possessed gave us the comfort necessary to grow our family by one more member, without fear of passing on the NACC1 mutation to another child. Because of this, we welcomed Quinn's new baby sister Josie to our family in June 2017. And it's all thanks to the work of the UDN!

# The Model Organisms Screening Center (MOSC) at the UDN

By Shinya Yamamoto

The Undiagnosed Diseases Network has many moving parts: clinical sites that evaluate participants at medical centers, labs that perform genetic and genomic testing, a coordinating center, and research groups. One research group is the Model Organisms Screening Center, called the MOSC (pronounced like "mosque") for short. Researchers at Baylor College of Medicine and University of Oregon collaborate on the MOSC to tackle undiagnosed diseases at the next level. The MOSC's goal is to answer the following question: can we figure out what the genetic cause of the disease is by "modeling" human diseases in animals?

The Drosophila Core at Baylor College of Medicine

A "model organism" is a non-human species of animal that has been widely studied. Over the past century, genetic model organisms have taught us so much about human biology and what causes disease. Although these organisms (for example, yeast, nematode worm, fly, zebrafish, mouse) may look very different from us, fundamental biology and genes are quite similar in many ways. Experts in the MOSC use state-of-the-art genetic and genomic technologies to study fruit flies (the technical name is *Drosophila melanogaster*) and zebrafish. These animals are cost efficient, have short life-cycles, and genetic changes can be made to "model" a human disease condition. For example, the zebrafish has been particularly useful in genetic research about muscle disease because the embryos and larvae are completely see-through and the zebrafish body is quite muscular. If a genetic variant in a fruit fly or Zebrafish seems like it might be causing the disease, more studies can be done in mammals, such as a mouse.
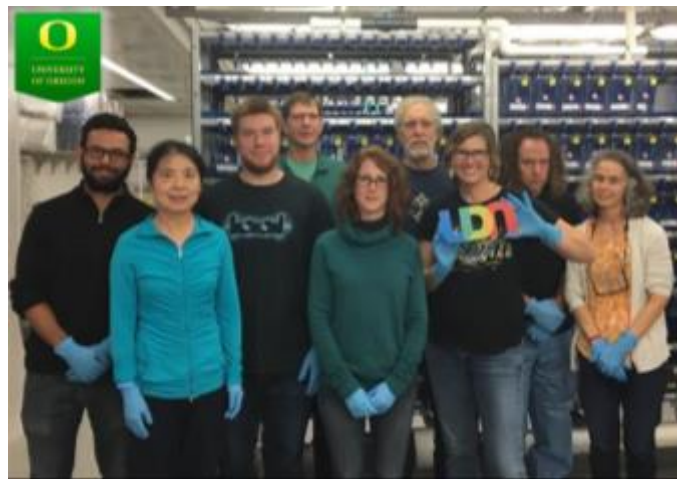
The Zebrafish Core at University of Oregon

When a diagnosis is not reached after a patient has had a thorough clinical and/or genetic evaluation, the MOSC gets called to action. The MOSC first performs a database search to learn more about the variant and try to find other patients with similar symptoms and genetic variants. Finally, experiments to assess gene and variant function are designed by MOSC researchers and are pursued in the Drosophila Core or in the Zebrafish Core.

Connect with a UDN PEER Family
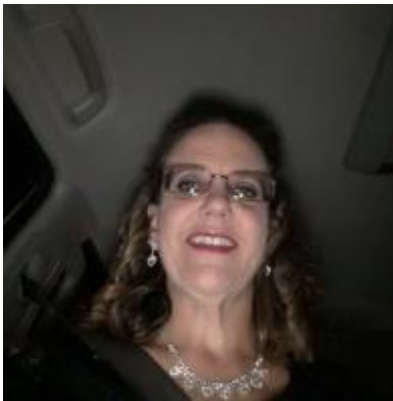
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