SCN2A RELATED AUTISM & EPILEPSY

FAMILIESCN2A FOUNDATION

WWW.SCN2A.ORG

2020 Q4 is finally here...Scroll on down to see what we've been up to!

We are excited to announce another 2020 Action Potential Grant!

ACTION POTENTIAL GRANT AWARDEE

EDUARDO PÉREZ

Cleveland Clinic / Genomic Medicine Institute

★ $50,000 – Research Grant

★ Integrating clinical and genetic variables to model SCN2A variant pathogenicity and outcomes

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For more on this year's A/P Grant projects and to learn about future grant opportunities from the FamilieSCN2A Foundation, please click here.

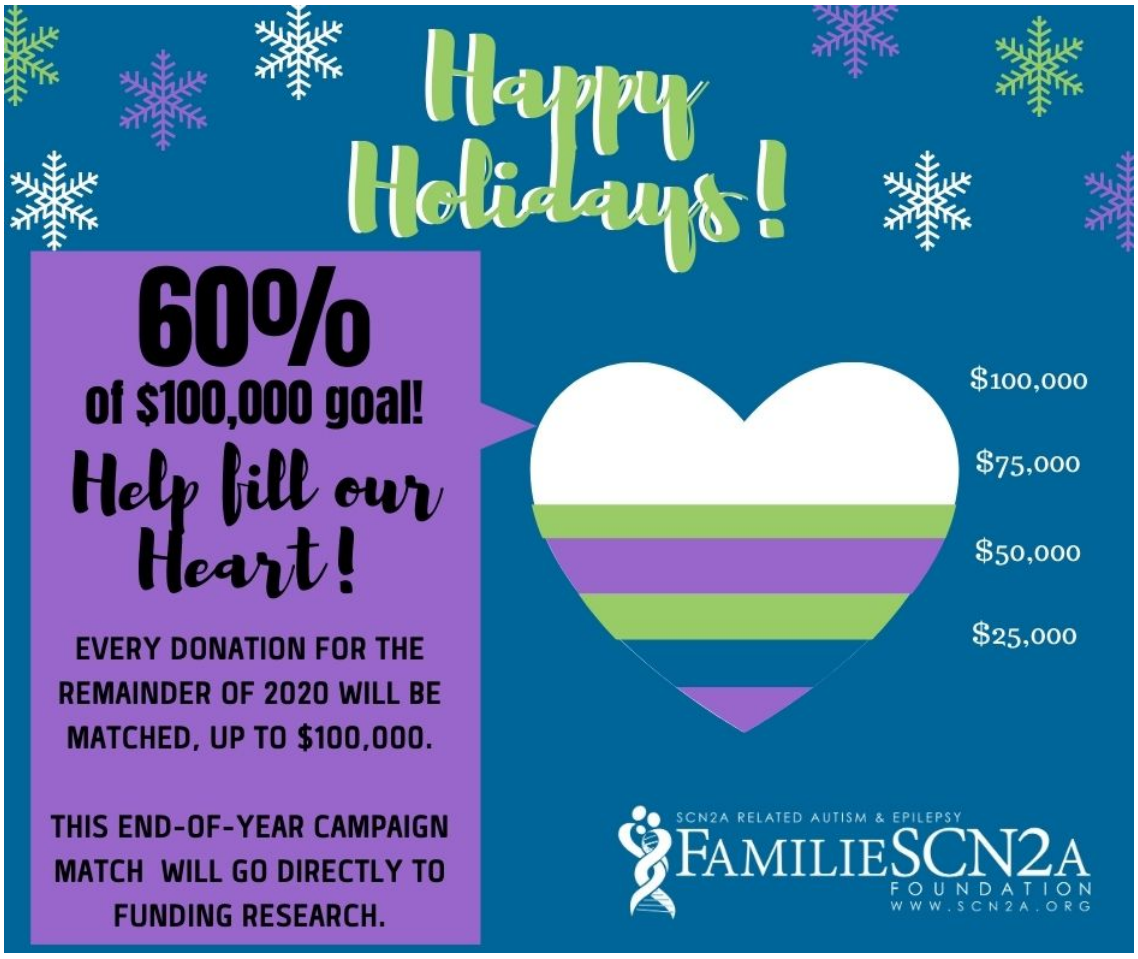
We are grateful to our many donors who make this research possible!

Up-to-date information on the latest in SCN2A research!
Virtual Series is now available to all at www.scn2a.org/hope.html

Rx: Hope Virtual Series

FAMILIESCN2A FOUNDATION

We Value Your Feedback



Please consider a heartfelt donation to help us reach the full potential of this generous $100,000 matching opportunity. Funding TWICE the research will accelerate cures for SCN2A disorders. Give here or text SCN2A to 4-4321. Thank you!

Thank you to everyone who participated in the 2020 SCN2A Warrior Challenge. We had 314 registrants and **40** teams. Special SHOUT OUT to Ryan Beckman and Jamie & Mark Tuminello for taking the lead on organizing the event which raised over $27K. This year, those funds have been matched to bring the total to over $54K! Check out more photos from the WC.

We hope you will join in the fun next year...October 2021!

Anne Berg, PhD, has been a friend of FamilieSCN2A since our first conference at her home base, Lurie Children's Hospital in Chicago (2016), and we are excited to have her leading our Clinical Trial Readiness Study. We caught up with Anne, who is also a research professor at Northwestern Medicine, to talk about why the CTRS is critical in positioning SCN2A for clinical trials. But first, how did we get to this point? Well, Anne has had a role in that as well…and if you watched her RX: Hope Virtual Series presentation you've already got an idea of the expertise she brings to the table.

In order to have a successful clinical trial for a drug or biologic (such as gene therapy) we must demonstrate to the US FDA (Food and Drug Administration) that it is not only safe and effective but that the outcomes, or endpoints, of the treatment are measurable and desirable in the patients. For SCN2A, particularly in cases where there is Developmental Epileptic Encephalopathy, it's important to get the measurement tools right so that changes, even small ones, can be demonstrated effectively. Submitting a candidate treatment to the FDA is a multi-step process; gathering and interpreting data is a key requirement at several points along the way. And that's what Anne does so well.

Rare disorders are challenging because it's hard to get a large number of patients together to study. The Foundation partnered with Simons Searchlight in 2015 to start the very first SCN2A registry. Simons studies genetic neurodevelopmental conditions associated with Autism and they have collected a rich dataset of patient reported developmental and medical points across 147 single genes and 20 copy number variant disorders. Simons ensures that these data are high quality and are made freely available to qualified researchers. Another invaluable role Simons plays in collecting and distributing data is the biobank where they have blood and saliva and are in the beginning stages of creating cell models for the patients registered. Having access to this type of data has increased both the quantity and quality of research in SCN2A.

We recently signed Anne on to do an in-depth analysis of the Simons data and the resulting paper is now published (click on SCN2A in the news).

"The people at Simons were amazing to work with and the results were helpful to us in demonstrating the need for more precise measurement tools for our population."

The Simons data gave us an overall picture of what kids with SCN2A look like in terms of their medical history. Some important points stood out such as the large number of cases with vision problems which is extremely helpful to know. Interestingly, the subcohort without epilepsy is almost as severely impaired which puts the focus on the underlying cause: the SCN2A gene mutation. The Simons survey was also important in that it put commonly reported SCN2A co-morbidities (such as gastrointestinal issues and cortical visual impairment) into real numbers, i.e. more key data.

SCN2A is a large gene with many variants causing a range of issues from early onset epilepsy to autism and, often, both. It will take more than one 'cure' to cure SCN2A disorders and precision medicine will be at the forefront. The big goal of precision medicine is to treat all aspects of a disease in an individual and not just suppress the symptoms; to ameliorate the burden of the disease itself. The big question is how to *measure* improvement in those varied aspects of the disease. Many randomized clinical trials use a tool called the Vineland Adaptive Behavior Scales. However, the biggest take-away from the Simons data is that most of the Vineland scores for SCN2A patients were so low that the measurement is simply not useful in all areas.

"It's like asking a cell biologist to use a yardstick to measure microns," according to Dr. Berg.

When designing a clinical trial, it is critical to use appropriate assessment tools to accurately measure and demonstrate even small changes in a patients' abilities. A measurement should be able to show a range of abilities (hi-low-mid) and at different ages as ability levels change. A behavioral measure used in a trial for another rare disease failed to show a significant difference in outcome when taking the new drug. They used the wrong measurement scale. The FDA said 'no' to approval and that door was closed. There are no 'do-overs' with the FDA.

The 'Ability Study Survey' conducted earlier this year was a step in the right direction, as it directed us towards more useful testing instruments, such as the M-CHAT (Modified Checklist for Autism in Toddlers, a validated developmental screening tool for toddlers) that will give us relevant measurements for future trials. Now that we have useful measurement tools available, we can launch the SCN2A Clinical Trial Readiness Study to start collecting data that will be useful to

biotech and pharmaceutical companies who want to find better treatments and ultimately, cures, for SCN2A disorders.

Data Collection Models: Registry, Retrospective, Prospective

With more than 30 years in the field, Anne understands all too well the impact of rare epilepsies and autism on families. She knows it can be a burden for parents to have to fill out multiple surveys. The Simons registry was an important first step in collecting patient data and bio-specimens. It brought the SCN2A community and its data together in one place which created interest among both academic researchers and industry groups.

Natural history studies and registries are 'retrospective,' which is a great initial orientation to a condition. It involves going back through old records to get an idea of patients' history. However, it must rely on information collected 'as is' without knowing that someone in future might be looking at it, so it's not necessarily in a usable form for clinical trials. It's not granular, but it's relatively quick.

The CTRS has been designed 'prospectively.' We have involved multiple SCN2A stakeholders (researchers, industry, FDA) in creating questions that will give us the measurements we want, in the way we want them, under a specific protocol. It's very precise. It may take longer, but it is what we need to be ready for clinical trials. For instance, if a company has a drug that seems to work, a clinical trial will use a measure sensitive to the change it makes in the patient. Setting these measurement tools up in advance with the CTRS ultimately helps us all save time and resources. There will be a data use agreement as part of the patient's informed consent so that industry groups can have access to de-identified data and won't have to reinvent the wheel. This is the kind of collaboration that will expedite the path to cures for SCN2A related disorders.

We have partnered with Anne who has assembled an all-star team to implement the SCN2A Clinical Trial Readiness Study including:

- **Keith Coffman, MD**, Children's Mercy Hospital, Kansas City, MO. A pediatric neurologist specializing in movement disorders and dysautonomia.
- **Aaron Kaat, PhD**, Northwestern Feinberg School of Medicine. A psychometrician with expertise in adapting measurements for people with disabilities.
- **Erica Anderson, PhD**, Assoc. Professor of Psychiatry and Behavioral Sciences, Northwestern Feinberg School of Medicine. A neuropsychologist whose areas of research include neurocognitive functioning in pediatric epilepsy and disorders of autonomic regulation.
- **Gerry Nesbitt, Director**, Clirinx. An informatics innovator specializing in academic clinical research IT.
- **Abbie Van Nuland, MS**, Research Scientist, Lurie Children's Hospital, Epilepsy Center.

It's clear that she loves her work, but when Anne isn't elbow-deep in data, she might be found weaving on the loom she built by hand or practicing her French to keep in touch with family

abroad. And even though she now has to make an appointment at the pool, swimming a mile twice a week keeps her lifelong love of swimming alive.

"I am overwhelmed and humbled by the willingness and generosity of parents to participate in research. You truly inspire me." Anne Berg

CTRS Study Recruitment (Phase 1)

The goal is to recruit 100 patients

- **Everyone with SCN2A will be invited to participate in the screening survey for the CTRS study. Initially, we are focusing specifically on children with SCN2A related epilepsy who are between the ages of one and 25. If someone is not eligible right now, there will be an option to reconnect for the next phase of the CTRS.**
- **The first phase study language is English (use of an interpreter is acceptable) and the countries of residence involved are the US, Canada, England, Wales, Scotland and Ireland. There is a clinician-led interview portion which will involve a phone or zoom call with participants/parents.**
- **Once the study is determined to be appropriate for your child, you will schedule a time, at your convenience, to speak with a member of the research team who will walk you through the steps of the study and obtain your informed consent. There will be check-ins at 3 months, 6 months and 12 months (with gift cards for participation along the way).**