CTNNB1 Syndrome Newsletter

CSAW & ACCT Merger!

CSAW – CTNNB1 Syndrome Awareness Worldwide – and ACCT – Advancing CTNNB1 Cures and Treatments – have worked closely together on behalf of our community over the last several years. CSAW's focus has been on increased awareness of the Syndrome and connecting our families, and ACCT's has been funding meaningful scientific research.

Over that time our missions increasingly have overlapped: Awareness of CTNNB1 Syndrome has led to more research, more research has led to increased awareness, and the virtuous cycle continues. We realized that joining our organizations would enhance both missions while reducing administrative tasks, regulatory filings, and financial costs. It also would eliminate confusion among our families, our donors, and the research and medical communities that support us.

So, CSAW and ACCT have merged! Here's what to expect:

- We filed legal paperwork to create a combined organization as of Oct. 4, 2021.
- The new Board of Directors will comprise representatives from both CSAW and ACCT.
- Through 2021 we'll work on setting up the infrastructure for a unified organization. Until then, you can still reach us at any of our CSAW or ACCT emails, websites, or social-media outlets.
- Ultimately, donations to either legacy organization will be allocated in a budget to be determined by our new allied Board of Directors. Until then, you may continue to contribute to either CSAW or ACCT through our respective websites, Amazon Smile, and other donation portals.

We're excited to move into this new phase of serving our CTNNB1 Syndrome community. While it sounds complicated, our goal is to make this a seamless transition. We will let you know more details as we work them out.

Let us know what you think! Send us your ideas, and if you're interested in volunteering, let us know!

2nd Annual Research Conference Generates Excitement!

Last year ACCT and CSAW hosted the first annual CTNNB1 Syndrome Research Conference. We introduced our research team, Dr. Wendy Chung of Columbia University and Dr. Michele Jacob of Tufts University. They spoke about the importance of our registry and natural histories and described initial and upcoming research. There was excitement and optimism, but no results at that point.

This year's conference yielded positive research results, real excitement and reinforced our optimism!

2nd Annual Research Conference continued...

The following is a top-line summary of what we learned. If you would like more detailed information, the slides used on the YouTube presentation are available at www.curectnnb1.org.

Here's what we learned and how all of us in the CTNNB1 community can help advance our cause.

Research

Dr. Chung and Dr. Jacob, joined by Dr. Jonathan Alexander, a Post Doctoral Fellow at Tufts School of Medicine, presented to the community. Dr. Chung kicked off the presentation by reviewing the most recent data that families have contributed to our registry and natural history study through Simons SearchLight. The goal of our registry and natural history study is to collect detailed medical information and behavioral histories of patients that can be deidentified and then shared with qualified researchers from around the world.

The registry and natural history study are important to better understand how the syndrome develops over time and to identify common overlapping features of patients. This data, in turn, helps direct our research to develop therapies that target specific areas of concern in our community. Currently we have 130 registered families; 73 have submitted lab reports and 38 have completed medical-history interviews. This is a vast improvement from this time last year - but we can do better.

The exciting news is that the Simons Foundation has taken note of our community involvement and has graciously agreed to fund the development of several cell lines for us from donated blood from our community. These cell lines are an expensive and important next step in testing treatments for our community. Our increased participation in the registry will only help open more doors for outside grants as well as get more researchers and eventually pharma interested in investing in our community.

Dr. Jacob and Dr. Alexander then discussed the learning and motor assays conducted on our CTNNB1 syndrome mouse. Studies show reductions in beta-catenin levels, learning, and muscle strength, confirming the value of this mice model for in vivo tests of drug treatments to correct these changes. To date, two drugs have been tested on our CTNNB1 syndrome mice and one is yielding extremely promising results on both learning and motor skills in a young adult mouse! In a series of experiments, learning skills were increased close to the neurotypical mouse, and motor skills were significantly improved. It has been confirmed that the molecule intervention does indeed cross the challenging blood-brain barrier. This result is extremely promising for our community. Dr. Jacob will continue to test the drug intervention on mice at different ages with different dosing. We also have funded the testing of two additional drug interventions that target related neuro-pathways.

What's next for the successful drug? Preclinical testing on in vitro human cell models – pluripotent stem cell lines derived from neuro-typical skin cells differentiated into brain neurons, spinal motor neurons and skeletal muscle. Researchers at Tufts will delete one copy of the CTNNB1 gene in those cells, to replicate testing and compare results with data from the in vivo mouse results. That will enable testing of drug treatments in human-derived neurons and skeletal muscle – a critical step towards human clinical trials. The cells funded by the Simons Foundation will also be used for testing.

It is incredibly exciting to see that research has accomplished so much in such a short time. But there is much left to do to create real-world treatments for our children. The key? Funding and families.

Funding and Families

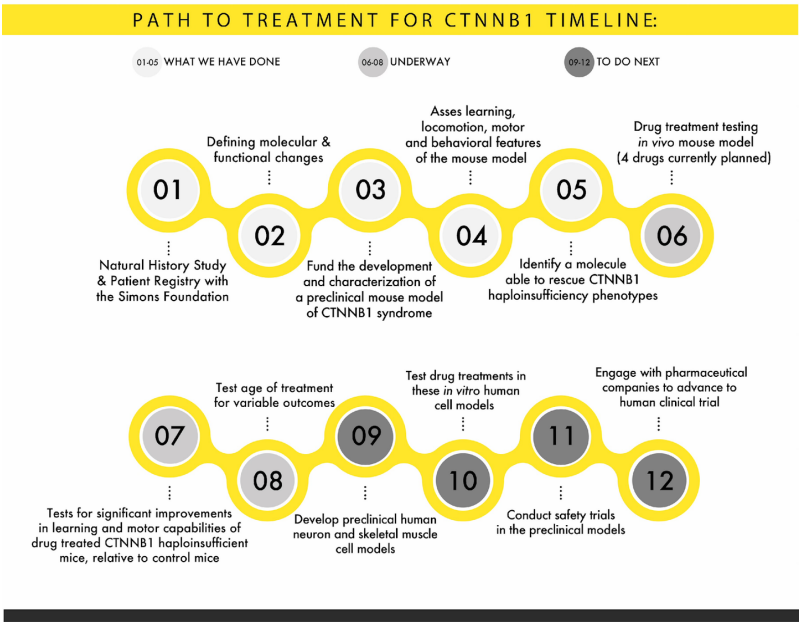
In less than three years, ACCT has raised almost $260,000 for research. The number of donors has almost doubled, reflecting a significant increase in community-based fundraising, amplified by corporate matching programs and Amazon Smile. Importantly, ACCT has kept expenses to less than 3% of total revenues. Especially encouraging was Dr. Jacob's announcement at the Conference of a first-time grant from NIH for CTNNB1 Syndrome research.

So with those great results from our funders, what's the biggest obstacle to developing treatments to help our children?

The bad news is, it's us.
The good news is, it's us.

We – the CTNNB1 Syndrome families – hold the key to finding effective treatments for our children.

We can raise money for research, but that won't do much good without robust information about our children and the Syndrome. Of the 130 children who have been registered on the CSAW registry as of July, 2021, only 38 have completed medical history interviews. (This is especially important because researchers need information on older children, who are represented in significantly greater numbers on the CSAW registry than the Simons.) Research will be successful in direct proportion to the complete data we provide via a patient registry and natural history studies.



Please enroll in Simons Searchlight registry and natural history study!

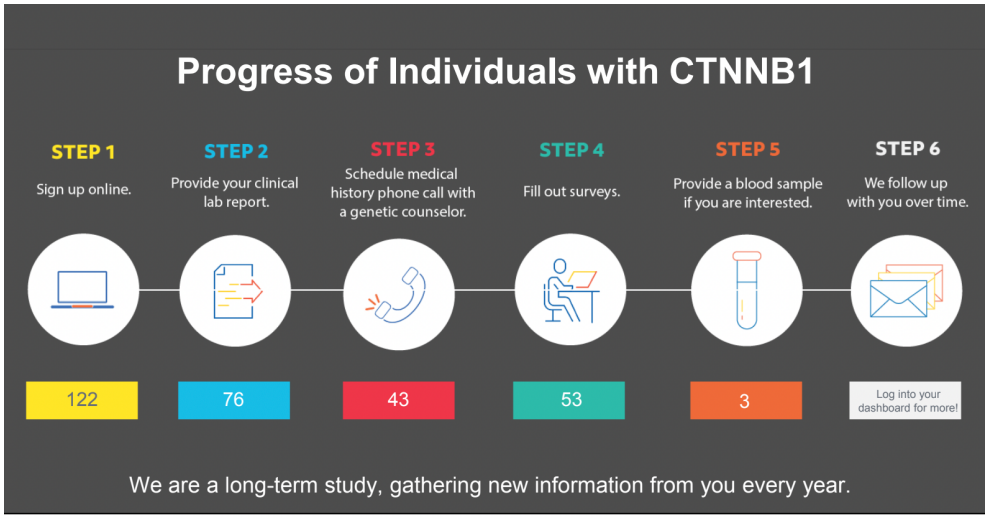
Our Registry and Natural History Study are hosted by Simons Searchlight and overseen by Dr. Chung. She and Dr. Jacob are working together to collect patient data to establish a baseline for clinical trials.

So, it's up to you. If your child has CTNNB1 Syndrome, what can you do?

It's a simple process, but we know the hard part for our parents is just finding the time. We're here to help make it as easy as possible. Here's what you need to do.

- Create your account at https://research.simonssearchlight.org/account/create.
- Send in your child's genetic test report.
- Talk to the genetic counselor to discuss your child's medical history and development.
- Complete your online survey including annual updates.
- You can email Simons with any questions (coordinator@simonssearchlight.org) and can request a blood collection kit if located in the U.S.

[NOTE: Your child's information will be deidentified but can be reidentified (with your permission) if he or she is recruited for a clinical trial.]



SIMONS SEARCHLIGHT

Other steps families can take to help:

- Complete the Voice of the Community survey.
- Participate in the blood drive to make stem-cell lines for in vitro models. (US families are especially needed while COVID protocols continue to slow international transport.)
- Volunteer for in-person evaluations.

The news from this year's Research Conference was undeniably good. But there is much work still to do, and time is our most valuable asset. Please help create the foundation we need to continue making progress for our children!

Connecting With Each Other

The usual challenges of parenting are compounded for parents and primary caregivers of children with needs that are special. The restrictions due to the COVID pandemic made things harder for many. But we've also seen how powerful connecting virtually can be. So our creative and compassionate families have come up with some ideas to help us help each other.

- The Parents' Place Moms and Dads sometimes need a place to go to for guidance and support. We want to provide help with the many challenges our parents face, such as coping with the emotional demands of full-time caregiving, advocating for appropriate school interventions and accommodations, and knowing what we need to do to be ready for when our children turn 18. If you have something you would like to share or a topic you would like to write about, please let us know. We would love as many people to be a part of this as possible. We want to hear from you; someone will always relate to your experience! We are also going to get back to highlighting families each week in the Family Spotlight. If you would like to be a part of either of these please reach out to Annie at annie.wood@ctnnb1.org.
- Meetups The burden of stress is great for parents of children with needs that are special. Fear, worry, guilt, isolation, grief, and depression are all common. Often the most beneficial support parents receive is from other parents, so our goal is to get back to in-person meet ups as Covid restrictions allow. We need volunteers to help organize these events in different regions. If you are interested in helping to plan a meet up in your area, contact Annie at annie.wood@ctnnb1.org.
- CTNNB1 Grandparents and Family Facebook Page For many good reasons, the CTNNB1 Facebook page for parents is private – only parents are admitted. But we've all heard from other family members – including many grandparents – who yearn to understand more about their family's situation. So we also set up a FB page for Grandparents and Family of CTNNB1 children. It also is private, so if you have someone who would like to join, they will have to request permission at the page (link above). There already are 123 (very pleased) members.

CTNNB1 Moms Rally for Our Kids!

- When CTNNB1 mom Effie Parks got the diagnosis for her son, Ford, she felt the isolation and fear most parents face at the beginning of that journey. She found solace and community in listening to podcasts by others with children who have special needs, but there weren't many, and she soon ran out of new shows to listen to. Her solution? Start her own podcast! So on Oct. 31, 2019, Effie launched Once Upon a Gene, a podcast dedicated to creating, expanding, and connecting everyone in the rare-disease community - patients, parents, doctors, researchers, therapists, teachers, family, friends - anyone who has an interest in any rare disease. And now, less than 3 years later, Effie won the WeGo Health Best in Show Award for Once Upon A Gene! WeGo Health is the world's largest network of over 100K Patient Leaders, working across virtually all health conditions and topics.

CTNNB1 Moms Rally for Our Kids! (cont.)

Their network collaborates with pharmaceutical and life sciences companies, agencies, consultancies, startups and all types of organizations across healthcare. So, not only is this a remarkable achievement for Effie, but it raises our CTNNB1 community profile as well. Congratulations to Effie, and thanks for your work on behalf of all of us!

- Špela Miroševič, from Slovenia, is mother to her 2-year-old son Urban. Špela is also a psychotherapist and a biopsychologist, working as a researcher at the Medical University Ljubljana. When Urban was diagnosed with CTNNB1, she decided to create an EU non-profit organization, CTNNB1 Foundation, dedicated to advancing ongoing research on CTNNB1 Syndrome. She is writing a systematic review on published literature and is communicating with ACCT, as well as researchers around the world in an attempt to best help children affected with this syndrome. Congrats to Špela - having an ally in the EU helps keep our community a truly global effort!