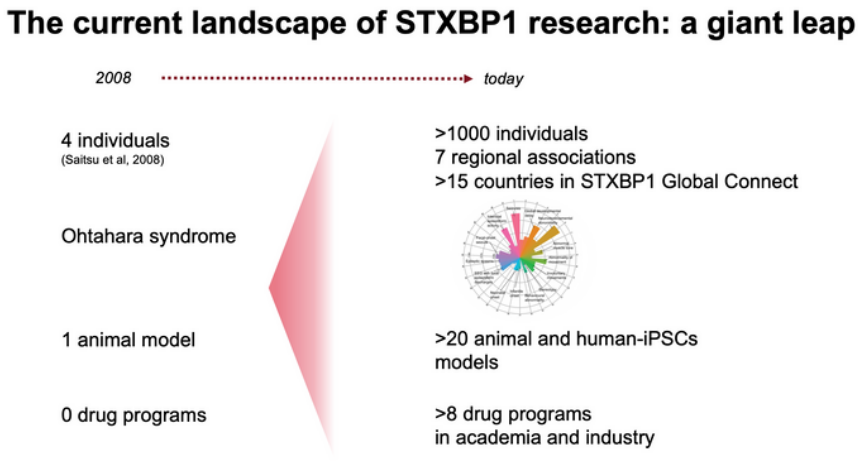
IMPACT REPORT 2022

STXBP1 Disorders

FROM OUR PRESIDENT

CHARLENE SON RIGBY
PRESIDENT & MOM

STXBP1 has gone from a newly discovered disorder with four patients in 2008 to an activated and growing community collaborating with industry and academia on multiple therapy programs.



Adapted from Dr. Ganna Balagura

This is tremendous progress but we still have so much to do. In order for any of these drugs in development to become approved therapies, we need to determine how to measure improvement that matters in our children. Therefore this year, we deepened our focus and investment on clinical trial readiness.

Thank you for your support . We are excited about our accelerating progress, but our patients and families have an urgent need for path altering treatments, so we know we must go *fast forward*!

With Hope and Urgency,

Charlene Son Rigby

OUR MISSION

- Create awareness in the disorders associated with STXBP1 mutations
- Fund and Drive Research to accelerate discovery of a cure
- Provide families with tools to help them understand the disease & how to get involved
- Advocate to improve early detection
- Foster activism to help change policies in favor of orphaned diseases
- Improve the lives of our STXBP1 Family

2022 GOALS

- Support and expand preclinical research and clinical trial readiness
- Raise $2M by 2022 to fund our research priorities
- Build Community
- Create Ongoing Awareness to Support Research Engagement and Community Development
- Maintain operational transparency

2022 YEAR IN REVIEW

STXBP1 Disorders

With your support, we are advancing research to accelerate therapies. In addition, we are building community and supporting our families on this challenging journey

1ST

- STXBP1 CLINICAL TRIAL FOR FOR 4-PHENYLBUTYRATE, WITH INITIAL RESULTS REPORTED AT AMERICAN EPILEPSY SOCIETY MEETING
- DISEASE CONCEPT MODEL FOR STXBP1 PUBLISHED
- FDA LISTENING SESSION TO EDUCATE THE FDA ON STXBP1 & OUR COMMUNITY'S LIVED EXPERIENCES

NEW STXBP1 FOUNDATION BOARD OF DIRECTOR MEMBERS, JARED BARNUM & CRISTINA BRENNAN

FLOURISH ART AUCTION & FUNDRAISING CAMPAIGN

$1.24M RAISED

TO FUND CLINICAL TRIAL READINESS & NATURAL HISTORY STUDIES

Move to Cure STXBP1 Disorders

300+

PARTICIPANTS FROM AROUND THE WORLD MOVING IN THE ANNUAL MOVE TO CURE STXBP1 EVENT

DEBUT OF STXBP1 GLOBAL CONNECT WITH 15 COUNTRIES REPRESENTED

STXBP1 Global Connect

STXBP1 SUMMIT+ RESEARCHER & FAMILY MEETING IN PHILADELPHIA

LAUNCHED SCIENCE SATURDAYS SERIES WITH JIM, OUR SCIENTIFIC DIRECTOR

27 PATIENT STEM CELL LINES

- 15 IN SIMONS SEARCHLIGHT
- 2 IN THE NEW STXBP1 FOUNDATION BIOREPOSITORY

SIMONS SEARCHLIGHT

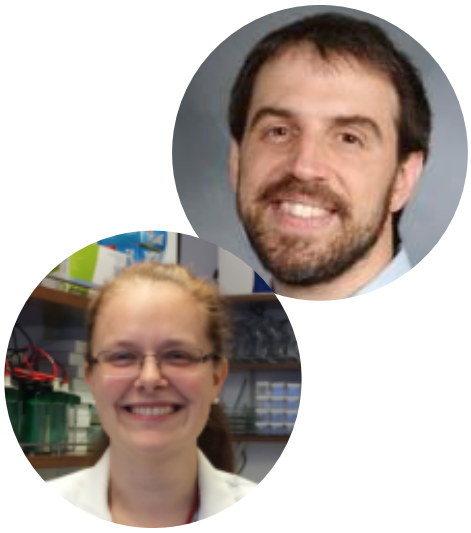
Driven by science. United by hope.

ciitizen | INVITAE | RARE-X

125 PATIENTS ENROLLED IN CIITIZEN NATURAL HISTORY STUDY & LAUNCHED RARE-X NATURAL HISTORY STUDY

2022 RESEARCH NEWS

Scientific research is core to accelerating therapies and one day a cure for STXBP1 disorders.



CLINICAL TRIAL FOR 4-PHENYLBUTYRATE COMPLETED

The first clinical trial with a therapy targeting the STXBP1 protein completed in 2022! Initial results were shared at the American Epilepsy Society Meeting in December.

Launched in 2021, this clinical trial was run at Weill-Cornell by Zach Grinspan, MD, MS. We thank Jacqueline Burre, PhD and her team for their foundational work to identify 4-phenylbutyrate as a possible therapy for STXBP1 disorder.

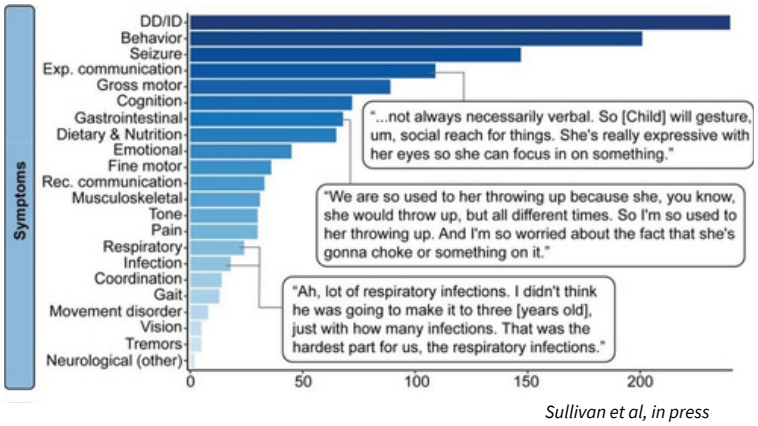
4-phenylbutyrate is an FDA-approved drug for urea cycle disorders. Drug repurposing is a strategy for therapy development where potential therapies can get to patients faster because safety studies were already completed as part of the original drug approval.

This clinical trial was funded by grants from the ODC's Million Dollar Bike Ride - Lulu's Crew Team STXBP1, and Clara Inspired. In addition, the STXBP1 Foundation and Clara Inspired provided a Patient Assistance Fund to cover unreimbursed medical and travel expenses.

STXBP1 DISEASE CONCEPT MODEL

The first disease concept model for STXBP1-related disorders has been developed! Disease concept models capture the relationship between symptoms, concerns, and impact on patients. Documenting this in a rigorous way supports measuring what matters to patients when evaluating potential therapies. These measurements are called "endpoints" in clinical trials.

This STXBP1 disease concept model is a critical step in our clinical trial readiness work.



Sullivan et al, in press

Thanks to Katie Rose Sullivan and the Children's Hospital of Philadelphia team for this pivotal work. The STXBP1 Foundation provided $50,000 funding for this project, with support from Capsida Biotherapeutics.

2022 FUNDED RESEARCH

The STXBP1 Foundation works with multiple collaborators and stakeholders to support and drive research to accelerate development of therapies for our patient community. We are thrilled to list these recipients of the grants and research funding awards that deliver on our mission to fund and drive research that will accelerate the discovery of a cure for STXBP1 disorders.

With our clear focus on therapy development clinical trial readiness, in 2022 we funded biomarker and therapy development, extended evaluation and monitoring of patients for the 4-phenylbutyrate trial, and supporting clinical sites.

RECIPIENT	FUNDING	PROJECT DESCRIPTION
Baylor College *Dr. Charles Chen*	$20,000	Biomarker Development in Mouse Model
Weill-Cornell *Dr. Zachary Grinspan*	$50,000	Phenylbutyrate for STXBP1 - 1 Year Follow-Up Evaluation for Clinical Trial
Colorado Children's *Dr. Scott Demarest*	$60,000	Neurogenetics Multidisciplinary Clinic
CHOP *Sarah Ruggiero*	$50,000	Genetic Counseling
Probably Genetic	$15,600	AI-based Patient Identification and Sequencing

In addition, the following researchers have been awarded grants through the Orphan Disease Center Million Dollar Bike Ride Program from Lulu's Crew Team STXBP1.

RECIPIENT	FUNDING	PROJECT DESCRIPTION
Baylor College *Dr. Mingshan Xue*	$80,070	Novel Mouse Model for STXBP1
Weill-Cornell *Dr. Jaqueline Burre*	$80,070	Small Molecule Therapy Development with Mouse Model

Learn more about all of these projects at our website.

CLINICAL TRIAL READINESS

With multiple potential medicines in development across gene therapies, antisense oligonucleotides and small molecule drugs, we are at an exciting and promising time for STXBP1 therapeutic development. We must quickly develop clinical trial readiness to maximize the likelihood of successful clinical trials. Here we highlight several of the foundation's Clinical Trial Readiness initiatives.

FDA LISTENING SESSION

On April 12, 2022, the STXBP1 Foundation held its first Listening Session with representatives from the U.S. Food and Drug Administration (FDA). The goal was to provide the FDA with a broad overview of the lived experience of people with STXBP1-related Disorders, the requirements for daily caregiving of affected individuals, and treatment priorities. Key discussion points were the spectrum of symptoms, and that STXBP1 should not be looked at as solely a seizure disorder, and the large unmet medical need for STXBP1 therapies.

ELECTRONIC MEDICAL RECORD STUDY

STXBP1 Foundation has sponsored a natural history study with Ciitizen. So far, medical record data is being collected for 125 STXBP1 patients across hospitals and medical providers. The first presentations on this rich data set have provided a detailed profile of patients, helping prepare for prospective natural history studies.

Children's Hospital Colorado

COLORADO CHILDREN'S NEUROGENETICS CLINIC

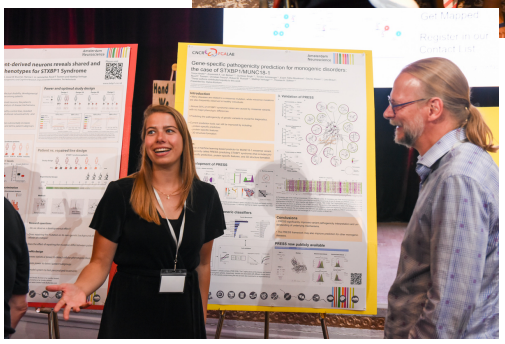
In January 2022, the STXBP1 Foundation launched a Neurogenetics Multidisciplinary Clinic at the Children's Hospital Colorado in partnership with three other rare disease organizations. Dr. Scott Demarest and Dr. Margarita Saenz are the co-Directors of the clinic. The clinic provides coordinated care where patients are able to be seen by multiple providers in a single visit including neurology, physical therapy, occupational therapy, rehabilitation therapy, developmental pediatrics, and special care. Through this clinic, we are expanding clinical expertise for STXBP1 to support better clinical care, and to prepare for clinical trials.

ORCA
Observer-Reported Communication Ability Measure

ORCA COMMUNICATION MEASURE

The STXBP1 Foundation has been working with Duke and COMBINEDBrain to evaluate a new measure of communication ability called ORCA. Communication has consistently been ranked by families as a top impactful symptom for STXBP1. The initial phase of the study has been completed, and the ORCA holds promise to be a more effective measure for our patients.

COMMUNITY



STXBP1 SUMMIT+ MEETING

The STXBP1 Summit+ Family Meeting was held 19 - 20 August in Philadelphia. With over 300 in-person and 240 virtual attendees, we brought researchers, clinicians, and industry partners together with our family community for two action-packed days. The Research Roundtable was held on the first day, with over 80 researchers. 19 presentations spanned Key Clinical Updates, Clinical Trial Readiness, Preclinical and Therapy Development Updates.

The family agenda included clinical, research and therapy updates, birds of a feather tables and multiple social opportunities with other families and researchers.

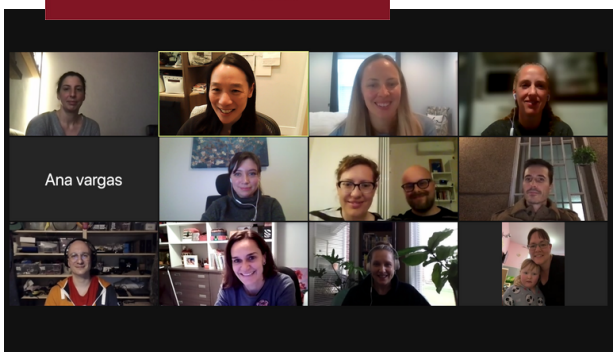
And, 100 biosamples were collected from patients and family members to accelerate STXBP1 research, including a study looking at metabolites in blood to identify potential STXBP1 biomarkers!

MOVE TO CURE

The 6th Annual Move To Cure STXBP1 Disorders event took place 24 - 25 September. We challenged the community to move with a purpose and help us take steps towards a cure! Together, we raised awareness of STXBP1 Disorders, fundraised for STXBP1 research, and had some great fun!

This year, we raised almost $65,000 for research, and 300+ people around the world participated.

COMMUNITY



STXBP1 GLOBAL CONNECT

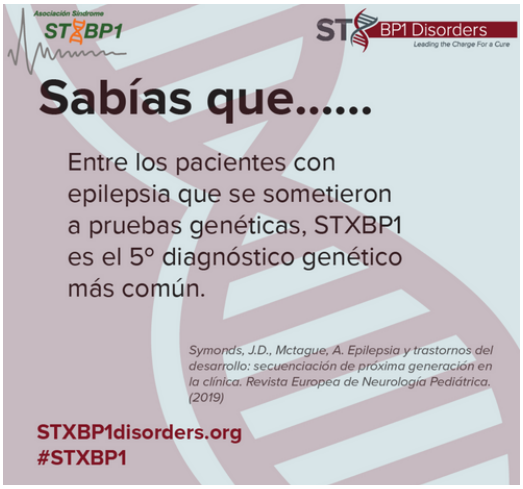
In August, we launched STXBP1 Global Connect, an affiliation of groups from around the world all chartered with improving the lives of patients afflicted with STXBP1 disorders.

STXBP1 Global Connect is growing fast and now includes 15 countries and 7 formal organizations: STXBP1 Foundation in the USA, Asociación Síndrome STXBP1 in Spain, STXBP1 Italia in Italy, Rare Smile in Israel, STXBP1 Syndrom in Germany, Associação STXBP1 Brasil, and STXBP1 France.

Together we are STRONG!

SEPTEMBER AWARENESS MONTH

September is STXBP1 Awareness Month! Why September? The STXBP1 gene is on the 9th chromosome and September is the 9th month of the year. We promoted awareness all month with community spotlights, Did You Know cards, and a social media campaign. Did You Know cards are now available in English, Spanish, Dutch, Portuguese and German!



GIVING TUESDAY

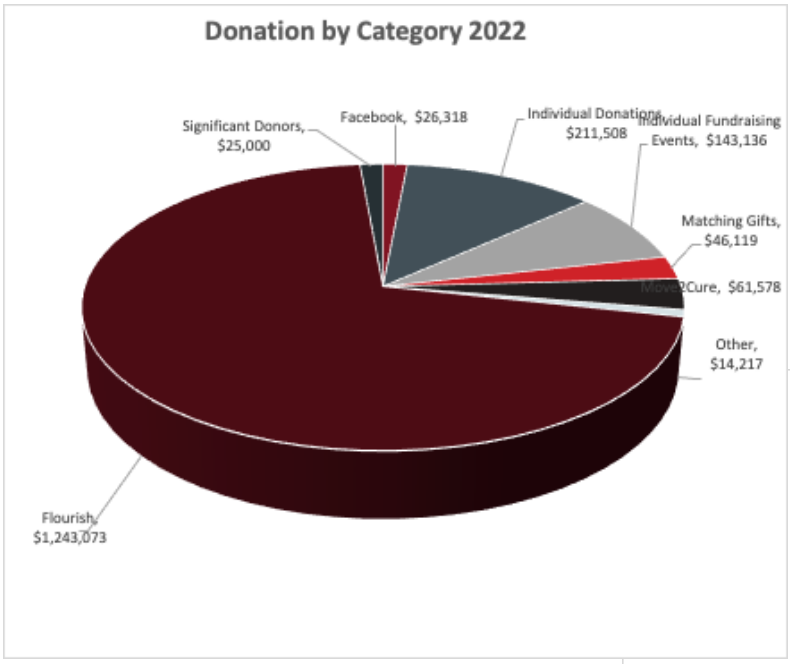
On Giving Tuesday our global community came together. Donors gave generously in honor of over 200 STXBP1 kids; supporting MORE research, MORE clinical trials, MORE days without seizures, MORE smiles, and MORE hope! STXBP1 grandparents and the Grands Society stepped up to the challenge. A grand total of $100K was raised from Giving Tuesday through end of 2022!

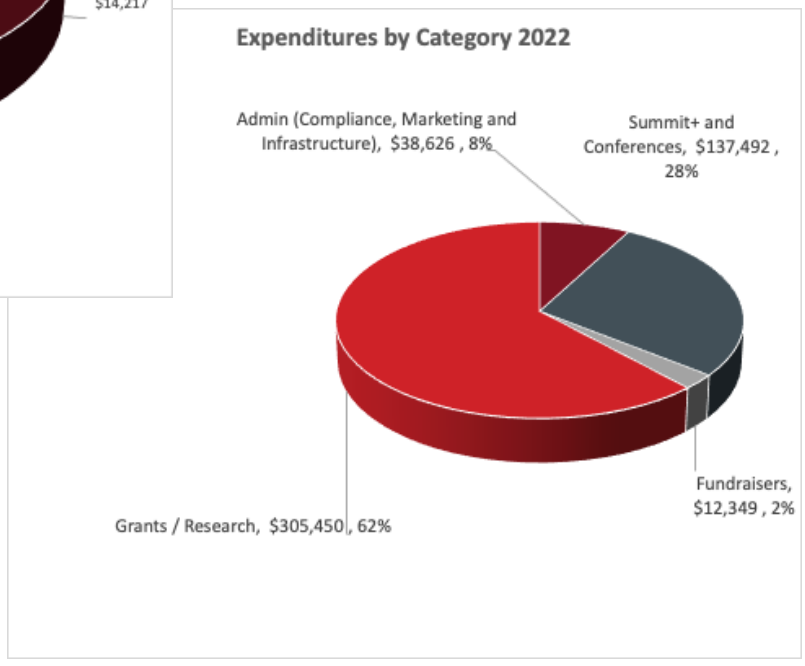
FINANCIALS & TRANSPARENCY

Another RECORD BREAKING year made possible by our incredible donors and families! In 2022 we broke the $1 million mark with a HUGE thank you to the Flourish campaign and the artists that supported this multi faceted campaign! This helped push us over the 2020 - 2022 goal that the STXBP1 Foundation raise over $2 million in 3 years! We did it!

In 2022 we were ELATED to bring our families back together for our first in person Summit+ since COVID impacted our ability to physically gather. Seeing all of the smiling faces of our STXers and their families ignited the passion in our researcher community as well as our board members! We continue to put our money where our mouth is with 90% of our annual expenditures funding grants and research as well as family support. About 10% of our costs represent administrative items and we strive to continue to minimize such costs to fall below the typical spend of charities that allocate about 75% to programming and 25% to administrative costs.

We look forward to capitalize on the groundwork we have laid in 2022 as we continue leading the charge for a cure! In 2023 we will embark on our greatest journey yet as we strive to Fast Forward STXBP1 and we couldn't do it without your support! Thank you for believing in our kids!!





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