PERSPECTIVE

A MAGAZINE FROM THE TSC ALLIANCE

WINTER 2023 • VOLUME 154

Behind the diagnosis

COVER STORY | **PAGE 8**

Message from leadership

Welcome to our new Board Chair Bill Joseph. As another year begins, we are thrilled to report 2022 was full of several major accomplishments for the TSC Alliance®. First and foremost, and after a few difficult years, our organization was able to offer opportunities for the TSC community to once again gather in person – starting with the 20th Anniversary Comedy for Cure®, a few live locations in May for Step Forward to Cure TSC® and soon followed by the hugely successful 2022 World TSC Conference in Dallas. Each of these reinforced the TSC Alliance's commitment to ensuring everyone affected by TSC and their families have support – and hope – every step of the way.

As you'll read on page 7, the Tuberous Sclerosis Complex Research Program at the Department of Defense maintained its $8 million appropriation, in large part due to those of you who participated in the March on Capitol Hill or contacted your Senators and Representatives in other ways to urge their support of this federally funded program. Thank you for your year-long efforts to this initiative.

We also want to congratulate TSC Alliance Director of Research Gabrielle Rushing, PhD, and Director of Medical Affairs Ashley Pounders, MSN, FNP-C, who collaborated with Board Member Tanjala Gipson, MD, to write the first-ever article addressing the racial differences in TSC skin manifestations, which was published in *Therapeutic Advances in Rare Disease*. Thank you to those who participate in the TSC Natural History Database, whose information helped inform their writing. You can read more about it as well as other 2022 TSC research highlights on page 18.

We also want to salute outgoing Board of Directors members Sarah Chieffo and Margaret Cox. Sarah was instrumental in leading the TSC Alliance's government advocacy efforts during her tenure while Margaret was heavily involved in Outreach, Finance and Government Relations and starting a state government advocacy program in Alabama. Thank you both for your commitment. On page 3, you can learn more about our two new Board members, Jonathan Goldstein and Shafali Jeste, MD. Jonathan is the first TSC Alliance Future Leader to join the Board and brings an important perspective as a young adult with TSC. Dr. Jeste is a leader in TAND and autism research and will provide leadership in these critical areas for the TSC community.

We are excited to begin 2023 with several new initiatives on the horizon, including redesigning the TSC Alliance website and to begin planning for the organization's 50th anniversary in 2024. In addition, we will spend the year working a new five-year Strategic Plan, based on your input via our 2023 Constituent Survey. Please see this issue's back page to learn more and to participate.

The Constituent Survey is crucial for our planning efforts as we seek to enhance, improve and create new programs to benefit anyone affected by tuberous sclerosis complex. We urge you to take the online survey as soon as possible.

Of course, the TSC Alliance's work simply would not be possible without you and the community at large. We look forward to all the possibilities in 2023.

Kari Luther Rosbeck
President & CEO

Bill Joseph
Chair, Board of Directors

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If you have opinions, questions or articles for *Perspective*, we would like to hear from you. Please contact the managing editor to obtain a submissions form and guidelines.

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Perspective is published by the National Tuberous Sclerosis Association, Inc. d/b/a TSC Alliance, a 501(c)(3), charitable organization.

TSC Alliance welcomes new board members

The TSC Alliance is pleased to welcome two new members to our board of directors as of January 1, 2023 – Jonathan Goldstein and Shafali Jeste, MD. They will each serve three-year terms.

Jonathan Goldstein

Jonathan is an adult with TSC, who is a Strategy Manager at CVS Health, where he leads special projects for the Aetna Chief Marketing Officer and Marketing Leadership Team. He offers a broad background in strategic planning, public policy, marketing, healthcare management, behavioral health and program design and execution. Jonathan previously served in several volunteer roles at the TSC Alliance, including as a Future Leader; a member of the Equity, Diversity and Inclusion Task Force; and a non-voting member of the Outreach Committee. He is also National Co-Chair of CVS Health's CapAbilities CRG; a Cornell Alumni Admission Ambassador; Cornell's 5th Reunion Campaign Co-Chair; and a member of Cornell University's Council of Young Alumni Philanthropy. Jonathan hopes to use his experience as a patient advocate and as a strategist and operational leader to contribute to the Board's work and to help expand the reach of the organization's impact. He is also very passionate about government advocacy; diversity, equity, inclusion and belonging; and public policy. Jonathan lives in New York City.

Shafali Jeste, MD

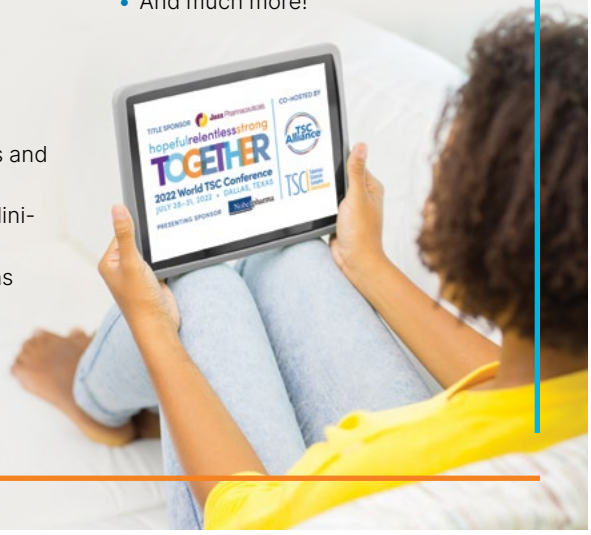
Dr. Jeste is Chief, Division of Neurology; Co-Director of the Neurological Institute; and Las Madrinas Chair at Children's Hospital, Los Angeles (CHLA). She has been engaged in research and clinical care for TSC since her residency in child neurology and has worked closely with families in designing TSC programs at Boston Children's Hospital, then UCLA and now CHLA. Dr. Jeste has a sincere appreciation for the importance of the partnership between the TSC Alliance and clinicians/researchers. She hopes serving on the Board will further strengthen these partnerships and also help strengthen the organization's medical and scientific efforts. Dr. Jeste currently serves on the TSC Alliance's Professional Advisory Board and the Board of the National Organization of Rare Disorders (NORD). She earned a bachelor's degree in philosophy from Yale University before gaining her medical degree from Harvard University. Dr. Jeste completed an internship, residency and fellowship in behavioral child neurology at Boston Children's Hospital. She lives with her family in Encino, CA.

Watch the 2022 World TSC Conference videos

Anyone can now watch videos from the last summer's 2022 World TSC Conference at *www.tscalliance.org/2022conferencevideos*. These videos include three general sessions, two general question-and-answer panels and three learning paths: large group lectures, panel discussions and specialty topics.

By accessing these free videos, you can learn more about:

- Global collaboration and the updated 2021 TSC consensus management and treatment guidelines
- Navigating the complexities for special needs care in TSC
- Using technology to your advantage
- Seizure types and treatments
- Surgical approaches for epilepsy in TSC
- TSC research updates
- Accessing early childhood services
- Genetics made simple
- Genetics, reproductive issues and impact on relationships
- LAM treatment options and clinical trials
- Skin and dental manifestations
- Transition into adulthood including employment and higher education
- Caregiver resources
- TSC-associated neuropsychiatric disorders, including ADHD, anxiety and autism
- Behavioral interventions and overview of medications
- Kidney issues and treatment options
- Gene therapy
- And much more!



Nobelpharma
Title Sponsor

TSC Alliance

STEP FORWARD to cure TSC®

2023 Step Forward to Cure® TSC Global Virtual Walk-Run-Ride

The TSC Alliance is proud to announce Nobelpharma America as the 2023 National Title Sponsor of the Step Forward to Cure TSC® program. Step Forward to Cure TSC is the TSC Alliance's largest annual fundraiser and awareness event.

Plan now to join us as we celebrate our 21st Anniversary of Step Forward to Cure TSC Global Hybrid Walk-Run-Ride with a month-long series of in-person and virtual walks, runs and rides starting April 15 and concluding with our world-wide celebration the weekend of May 20-21, 2023. **Register today at *www.stepforwardtocuretsc.org*.**

Tentative event schedule*

April 15, 2023	Fishers, IN
April 29, 2023	Nashville, TN
April 30, 2023	Renton, WA
May 6, 2023	Orlando, FL
	Rock Hill, SC
May 13, 2023	Salt Lake City, UT
	Liverpool, NY
May 20, 2023	Irwindale, CA
	Carrollton, TX
May 21, 2023	West Chester, PA
	Kansas City, KS
	Tulsa, OK
	Cincinnati, OH
	Rockville, MD

**All dates are subject to change. Please check www.stepforwardtocuretsc.org for the latest details.*

Registration is free, with fantastic prizes and contests available. All registered participants who raise $25 or more are automatically entered to win a Grand Prize that will be randomly selected during the Wrap-Up Rally on Sunday, May 21. *You need not be present to win!*

In addition, the Step Forward to Cure TSC Virtual Auction will be held from May 10 to 14. If you'd like to make an in-kind donation today, please contact Lauren Perry at *step4tscauction@tscalliance.org* for more information.

Questions?

Please contact Gail Saunders, Director, Community Programs, at *gsaunders@tscalliance.org* with any event-related questions.

National sponsors

Nobelpharma	MARINUS PHARMACEUTICALS	Jazz Pharmaceuticals
LivaNova Health innovation that matters	NEURELIS	UPSHER-SMITH Partners in Health Since 1919
SpecialCare a special needs program developed by MassMutual	Ovid Therapeutics	bridgebio hope through rigorous science

22nd Annual Comedy for a Cure®

Plan now to join us **Sunday, April 2**, at the **22nd Annual Comedy for a Cure®** to help us create a future where everyone affected by TSC has what they need to live their fullest lives. Since 2002, this TSC Alliance signature national event has harnessed the power of laughter to raise critically needed funds for the fight against TSC.

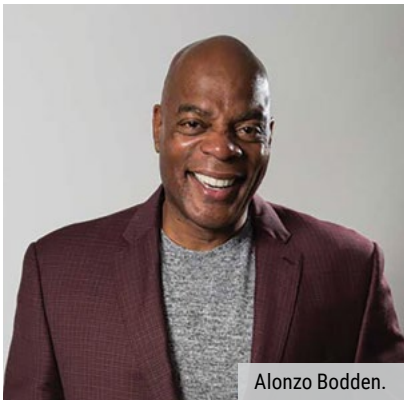
This year's event starts at 5 pm at AVALON in Hollywood. A pre-event cocktail reception begins with red carpet arrivals, hors d'oeuvres and an active silent auction, followed by a tasty dinner and a presentation of our honorees. The night concludes with an exciting live auction and dynamic comedic performances.

Comedy for a Cure brings together top comedians and entertainers to raise funds for those impacted by TSC. Since its inception, this event has raised more than $5.5 million toward finding a cure for TSC, providing support and information to anyone impacted by the disease, funding necessary research and increasing awareness.

This year's event will feature international comic sensation Russell Peters, who will headline the evening, and special guest star Alonzo Bodden, a prior grand prize winner of NBC's *Last Comic Standing*. We are grateful to our Comedian Committee members – Jim O'Heir (Chair), Shane Brady, Mo Collins, Kate Flannery, John Henson, Wendy Liebman, Melissa Peterman, Craig Shoemaker and Alex Skuby – who volunteer their time to ensure we present a great show.

Comedy for a Cure also provides a platform to highlight and honor those who have made significant differences in our fight against TSC, including the Holmes Family and Jim and the late Andrea Maginn.

Russell Peters.



Alonzo Bodden.

The **Holmes Family** will receive the **Courage in Leadership Award**. Lesley and Alex blazed a trail and found a treatment that saved their daughter, Seraphina, from a heart tumor that they were assured was going to kill her at or shortly after birth. Thankfully, Lesley and Alex were not going to let that happen, and four years later they continue to blaze a trail to find a cure for TSC as a family.

Jim Maginn and the late Andrea Maginn will be honored with the **TSC Champion Award**. Papa Jim and Grandma Buckeroo have been ardent supporters of the TSC Alliance for more than two decades, ever since their twin granddaughters, Abigail and Amelia, were diagnosed. With their help, the TSC Alliance implemented a research platform to de-risk drug development to bring new treatments more quickly to those, like their granddaughters, living with TSC. Andrea's dream was to help change the course of TSC for those living with TSC today and for generations to come, and Jim is determined to make her dream a reality.

The Holmes Family.

Although this year's event will not be broadcast virtually, you can still be involved by donating an auction item, soliciting a potential sponsor or increasing awareness by sharing the event on social media using #comedyforacure and @tscalliance.

Visit *www.comedyforacure.org* for sponsorship opportunities, tickets and more information. You may alco contact April Cooper at *acooper@tscalliance.org* or Anne Wolfe at *awolfe@tscalliance.org* with any questions.

Andrea and Jim Maginn (front row).

Other community campaigns

31st Annual Cookin' Up a Cure

Hosted by Pam Sztukowski
October 30

Congratulations on hosting the 31st Annual Cookin' Up a Cure event in memory of Joey Holuboey and **raising $5,000**.

Cookin' Up a Cure.

Luminate the Night.

Luminate the Night

Hosted by Karen Johnston, Mary Ann Lamb and Heather Harden
December 12-19

Congratulations to the TSC Alliance of the Carolinas on hosting its third annual community fundraiser, Luminate the Night. This year, the event **raised more than $19,000** to benefit the TSC Alliance. The participating families line their streets, driveways and walkways with luminaries, which consist of a battery-operated tea light candle placed in 2-3 inches of sand inside a white paper bag. A special thanks to organizers David and Karen Johnston, Mary Ann Lamb, Heather Harden and a host of volunteers.

Wrap Up for TSC

Hosted by Daniel Molina, Michael Arcari and Jaxson Vogel
December 16-17

Congratulations to Danvers High School seniors Daniel Molina, Michael Arcari and Jaxson Vogel for hosting Wrap Up for TSC, which **raised $2,001**. These amazing young leaders reached out to the TSC Alliance with a vision to host a gift-wrapping fundraiser as their Distributive Education Clubs of American (DECA) project. DECA is an organization that prepares emerging leaders by helping them learn skills in marketing, management, finance and entrepreneurship. A special thank you to Meghan Beaulieu, DECA teacher; Adam Federico; Danvers High School Principal; and numerous volunteers.

Wrap Up for TSC.

TEAM TSC
TRAIN • SWEAT • CONQUER

The TSC Alliance had a dedicated group of four runners who put in a lot of training hours outside of their full-time jobs to run on our behalf in the TCS NYC Marathon on November 6. Special thank you to Dr. Peter Crino, Immediate Past Chair of the TSC Alliance Board of Directors and Head of the University of Maryland TSC Clinic; Chip Burkhalter, also on the TSC Alliance Board of Directors as our Government Relations

Dr. Peter Crino.

Chip Burkhalter.


Bridget Lucas and Jenny Kuehn.

Chair, who ran his second consecutive TCS NYC Marathon for his son Bear; Jenny Kuehn, a pediatric cardiology nurse who was running for her daughter Louise; and finally, Bridget Lucas who ran to support her sister Jenny and niece Louise. These wonderful group of runners **raised a staggering $27,121** to help advance the mission of the TSC Alliance.

We were also grateful to have Celia Mastbaum and Liz Buchsbaum host the annual Rooftop Celebration on Saturday before the marathon. All the runners and their families attended the catered luncheon with some New York City-area community members to help celebrate Team TSC. It was a wonderful time to connect with the runners, their family and the local NYC TSC community. We are looking forward to 2023!

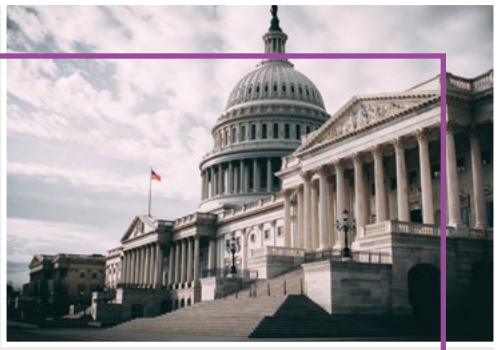
If you are interested in joining Team TSC in 2023, please visit *www.tscalliance.org/team-tsc/* to submit an interest form.

Facebook Donations/Birthday Fundraisers

September 1 to November 30, 2022
Raised: $11,922

Thank you for supporting the TSC Alliance on your birthday or special occasions.

Government advocacy



Congress clears $8 Million for TSCRP in FY23

On December 23 in the closing days of the 117th Congress, Congress approved a massive fiscal year 2023 (FY23) Consolidated Appropriations Act, which included $8 million in FY23 funding for the Tuberous Sclerosis Complex Research Program (TSCRP) at the Department of Defense (DoD). With this achievement, the total lifetime appropriation for the TSCRP now exceeds $113 million!

As in past years, our success in securing this vital funding can be attributed to the TSC Alliance's annual March on Capitol Hill and ongoing advocacy by our community. Additionally, the TSCRP has enjoyed strong bipartisan support in both chambers of Congress. Earlier this year, bipartisan "Dear Colleague" letters were circulated by Representatives Jamie Raskin (D-MD) and Markwayne Mullin (R-OK) in the House and Senators Martin Heinrich (D-NM) and Kevin Cramer (R-ND) in the Senate. The House letter was signed by 205 Representatives and the Senate letter was signed by 35 Senators.

The TSC Alliance is looking forward to continued success in the 118th Congress (2023-2024), which convenes January 3, 2023. We are looking forward to working with two newly elected Senate champions: Markwayne Mullin (now a Senator from Oklahoma) and Eric Schmitt (R-MO), who is the father of a child with TSC.

NIH receives significant funding increases in FY23

The Consolidated Appropriations Act enacted on December 23 also increased funding by $2.5 billion for the National Institutes of Health (NIH), to $47.5 billion in FY23. The bill also provides $1.5 billion new funding for the new Advanced Research Projects Agency for Health, or "ARPA-H," an increase of $500 million above the FY22 funding level. NIH makes important investments every year in TSC research, and ARPA-H is a promising new source of funding for discovering new therapeutics and cures for rare diseases like TSC.

Join our Government Action Team

If you'd like to get involved in this year's March on Capitol Hill, scheduled for March 1, please join our Government Action Team by visiting wwww.tscalliance.org/actionteam or emailing *grc@tscalliance.org* today.

The Ewing family.

Cover Story

Behind the diagnosis

BY ALEXANDRA EWING

Richard Albert Ewing, fifth in a long line of Richard Ewings, was born in Nashville in 2003. He was diagnosed with tuberous sclerosis complex (TSC) early on. At about 10 weeks old, he fell off his changing table and landed softly in a wicker trash basket. Of course, being new parents and needing to be sure, we rushed to the ER and sat waiting for them to take a look at him. Soon, they came in and told us he probably just had a bruise on his brain, but we could take him home. Nope, we said, that is not happening until you do a CT scan. We were so insistent they finally gave in.

That was when everything changed. We were told we should confirm their suspicion he had TSC. As fate would have it, it was then we learned our brother-in-law was lifting partners with Dr. Paul Rossman, who helped develop the diagnostic criteria for TSC. So off we went to Boston when Richard was four months old to get confirmation of what we already knew in our hearts was true.

We were told if we could get him to one year old with no infantile spasms, his trajectory would be much better. But that's not how life works is it? At 6 ½ months, Richard started having infantile spasms. At the time, there was no TSC clinic in Nashville, nor any neurologists who were that familiar with it. The young doctor we initially saw may as well have thrown a dart at the drug chart on the back of his door. He chose a drug

that, had he done any research at all, he would have discovered is completely ineffective against infantile spasms and was actually contraindicated as we learned with a simple Google search. He also told us Richard would probably end up being not much more functional than a vegetable.

Of course, we weren't going to accept that outcome and immediately tried to find a new neurologist. We wasted precious days on this search, while every day the damage increased. All his speech stopped cold. He became a different baby altogether. Through family connections, we got in to see a neurologist who at least had heard of TSC. We had the bad luck to have had Richard before Vigabatrin became the gold standard of care, before it was even approved by the FDA. And we were ill prepared. Not knowing we should have insisted on this, we accepted the existing standard of care, which was to put Richard on ACTH, or steroid therapy. He blew up like Violet in *Willy Wonka*, still cute but 25 pounds heavier. It took several weeks of giving him daily shots in the leg for the ACTH to do its job. But the damage was fairly apparent.

He would have two more rounds of seizures, absence seizures at 2 and complex partials at 6. Those were bubbling under the surface for 6 months before we finally realized what was happening because he had a seizure early one morning. We are luckier than many families in that Richard's second two seizure types were controlled fairly quickly and by then, the TSC clinic at Vanderbilt Children's had been established by Dr. Kevin Ess. It's not an exaggeration to say that this was a game changer for a lot of families in this region.

When Richard was about 10, we heard of a clinical trial to test the efficacy of Afinitor. Anecdotal evidence had shown it was controlling and reversing tubers and that there were suspected cognitive benefits as well. By then, we knew Richard had kidney tubers that were growing. We signed him up for the clinical trial, hoping his tuber growth would be halted or slowed and that the other ancillary cognitive benefits being tested might show up in him. For 11 months, we travelled up to Boston once a month to get blood drawn and in a few visits, do cognitive testing. They had hired a young woman straight out of her PhD program in child psychology. I have to say I've never met someone in a profession meant to interface with children who was less comfortable with children. She and Richard did not gel – she seemed unnerved by him, or perhaps by the assignment.

Her battery of questions was strange to say the least. One question my husband Rick and I would remember vividly was, "Richard, what is a shirt?" To say our son would not understand the nature of this question is an understatement. He just stared at her, not comprehending what she wanted him to say. In the end, she marked "no answer" and we moved on. At the end of

A young Richard and his dad Rick.

the study, she told us our son had an IQ of approximately high fifties and did not improve at all over the course of the study. When your child is only 10, with what you hope to be different possible trajectories in their life ahead of them, to hear this news is a bit devastating. The point of mentioning this, however, is really just to say these types of cognitive tests/questionnaires might well benefit from input from parents, who are definitely experts on their own children, if not also lay experts in this disease that has so many facets.

But the thing is, we didn't, and still don't, agree with her assessment. We think Richard's brain is like one of those old-fashioned televisions with rabbit ears you have to manipulate to get a good picture. He has more intelligence than he will ever be given credit for. For example, there was a moment around this time when I was trying to get him to get ready for school. He needed to go upstairs to put an item back on his bed, and I had already asked him several times. Finally he sighed loudly and stomped up the stairs. As he neared the top of the stairs, he began singing Bob Marley . . . "Get up, stand up, stand up for your rights." We were all struggling not to burst out laughing but knew in that moment we were right: there was so much more in his head than he could possibly share with the world.

If we think of all of our challenges, the biggest X factor is behavior – the TSC-associated neuropsychiatric disorders (TAND) aspects of this disease. Richard had a rough two years during the pandemic, with constant high anxiety, lack of sleep, self-injurious behavior and lashing out at us. This is what we will be working on in these next years to get him to the point where he can take advantage of resources out there. We'll also be looking to expand the resources available for Richard and for other families.

We're also in the midst of launching a YouTube channel that will go over a wide range of topics special needs families deal with a goal to help other families with information, ideas, hope and the knowledge they aren't alone, which is especially important for families getting a new diagnosis. We also want to give back to the community by participating in ongoing research to the extent we can. Richard just gave a blood sample to add to the TSC Alliance's Biosample Repository. We'll make sure to participate where we can with the hope we can spare families in the future from having to go through the things we and others we know have gone through.

Lastly, as we go through this journey to get our children the best care we can and to find a cure, we do become quite well versed in the disease and should be listened to. Luckily, I'm not shy about sharing my opinions and did so fairly liberally with the research team up in Boston. My hope is if more of us give honest feedback, we'll be able to create better research programs that remember the importance of injecting humanity and compassion into the process.

Richard Ewing.

Harness the power of your IRA

Your IRA is a tool that helps you save for your retirement years. And, when retirement comes, your IRA also provides a smart way to support the organizations you care about most. When you give through your IRA, you not only help continue the mission of the TSC Alliance® Endowment Fund, you protect your hard-earned savings from taxes and qualify for benefits in return.

How it works

If you are 70½ or older, you can transfer *any amount* up to $100,000 per year directly from your IRA to a qualified charitable organization such as ours.

The benefits

Along with making an immediate impact at the TSC Alliance, your IRA charitable rollover gift (also often referred to as a qualified charitable distribution or QCD) benefits you as well.

- You pay no income taxes on the gift. The transfer doesn't generate taxable income or a tax deduction, so you benefit even if you don't itemize your tax deductions.
- Beginning in the year you turn 72, you can use your gift to satisfy all or part of your required minimum distribution.

Note: It is important that your gift passes directly from your IRA to the TSC Alliance Endowment Fund. If you withdraw the amount first, your gift will count as income and be taxable.

On Medicare or Social Security?

Making a gift through your IRA may decrease the amount of Social Security that is subject to tax and lower your Medicare premiums.

You can make a bigger impact than you ever imagined—while receiving benefits in return. To learn more about giving through your IRA, contact Lisa Moss, Vice President, Donor Relations, at (301) 562-9890 or *lmoss@tscalliance.org* today for help finding the perfect way to leave a lasting legacy.

The information in this article is not intended as legal or tax advice. For such advice, please consult an attorney or tax advisor. Figures cited in any examples are for illustrative purposes only. References to tax rates include federal taxes only and are subject to change. State law may further impact your individual results.

Current TSC research and clinical studies

A clinical study (also called clinical research or a clinical trial) is a research study using human volunteers designed to determine the safety and effectiveness of a drug, biologic (such as a vaccine), device (such as a pacemaker) or other treatment or behavioral intervention. Interventional trials determine whether experimental treatments or new ways of using known therapies are safe and effective under controlled environments. Observational trials address health issues in large groups of people or populations in natural settings.

The following clinical studies are currently recruiting participants. Choosing to participate in a clinical trial is an important personal decision. It is often helpful to talk to a physician, family members or friends about deciding to participate in a clinical trial.

TSC-STEPS

Why are we doing this study? Epilepsy is very common in infants diagnosed with tuberous sclerosis complex (TSC) and often very difficult to treat. This study tests if sirolimus, a medication used in older children and adults with TSC, is safe and effective in preventing epilepsy in infants with TSC before seizures have a chance to start.

What: The purpose of this research study is to learn more about the safety and efficacy of early sirolimus treatment to prevent or delay seizure onset in infants diagnosed with tuberous sclerosis complex (TSC), a genetic disorder where epilepsy is common.

Who: Infants 0 to 6 months old who are diagnosed with TSC and have no history of seizures may be eligible to participate. The infant also cannot have been treated with anti-seizure medications before enrolling.

Compensation: There is no compensation for your participation in this study. However, there may be limited travel funding available.

How many study visits are required? Each participant will have 7-8 study visits over 2 years. Some study visits can be done via telemedicine.

Where can I participate in the study? There are currently 8 study sites in the United States.

For more information, visit www.clinicaltrials.gov (identifier NCT05104983 or contact Molly Griffith at *info@tscsteps.org* or (513) 636-9669.

Baby Talk in TSC

Why are we doing this study? Our team is investigating how TSC impacts a baby's speech. The study is focused on examining the vocalizations and early language of infants with TSC.

What: In this study, we will obtain and analyze recordings of your child's babbling and speech. The majority of the recordings will be obtained in your home using a small recorder placed in your child's clothing (home recordings). In some cases, recordings will be obtained in an office/laboratory setting either at the University of Memphis or at Le Bonheur Children's Hospital. We will also give speech and language tests, ask you to complete developmental questionnaires, and we will analyze neurodevelopmental tests that are often completed as a part of clinical care for TSC.

Who: Your child must be a newborn to 36 months old.

Please contact us if you're interested in participating in our study, please contact Principal Investigator Tanjala Gipson, MD, at (901) 287-7337.

TSC MRI Study

Why are we doing this study?: Researchers at Johns Hopkins are seeking participants for an MRI research study where information will be collected to develop a new non-invasive imaging technique that will help us understand the biochemical factors affecting seizure activity and cognition in TSC.

What: MRI scan to take pictures of your brain (approximately 60 minutes). For participants with TSC, a separate session of up to 2 hours for a neuropsychological test.

Who can join? You are eligible if:

- You are a healthy volunteer
- You are a patient with TSC
- You are between the ages 6-30 years old

Compensation: Participants will be compensated $50 after completion of the study.

Location of Research: Kennedy Krieger Institute (KKI), 707 North Broadway, Baltimore MD 21205

To learn more information about this study, contact Mehreen Nabi at *tsc-mri@jh.edu*.

Autism Spectrum Disorder (ASD) and Intellectual Disability (ID) Determinants in TSC

Developmental Synaptopathies Consortium

Why are we doing this study? The goal of this study is to gain a better understanding of autism spectrum disorder/ intellectual disability (ASD/ID) in individuals with TSC so that effective treatments and interventions for ASD/ID can be found.

What: Participation in this study will involve up to three visits over the course of up to three years. Each visit includes a physical/neurological exam and behavioral testing. Visits may include a blood draw. *Virtual visits are an option.* Summary scores of your child's behavioral testing will be provided to you.

Who can join? Individuals 18 months and older are eligible to participate if they have been diagnosed with TSC and autism spectrum disorder and/or intellectual disability.

Compensation: There is no cost to participate in this study, and there will be no financial compensation for participation in this study.

Location of Research:

- Boston Children's Hospital (Mustafa Sahin, MD, PhD)
- Cincinnati Children's Hospital Medical Center (Darcy Krueger, MD, PhD)
- University of Alabama at Birmingham (Martina Bebin, MD)
- University of California at Los Angeles (Rajsekar Rajaraman, MD)
- University of Texas at Houston (Hope Northrup, MD)
- Stanford University (Brenda Porter, MD)

To learn more information about this study, please contact the appropriate site contact:

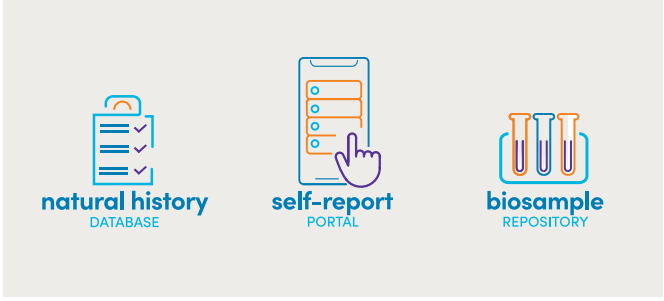
- Jeilo Gauna (Stanford), *jgauna@stanford.edu*
- Alexis Rodriguez (Houston), *alexis.rodriguez@uth.tmc.edu*
- Adrienne Victory (Cincinnati), *adrienne.victory@cchmc.org*
- Jessica Krefting (Birmingham), *jessicakrefting@uabmc.edu*
- Emine Arcasoy (Boston), *emine.arcasoy@childrens.harvard.edu*
- Angela Martinez (Los Angeles), *angelamartinez@mednet.ucla.edu*

TSC Natural History Database, Biosample Repository and Self-Report Portal

The TSC Alliance® is committed to supporting inclusive participation in research on TSC. If you or a loved one are interested but concerned about any aspect of these projects, please contact us to discuss potential flexibility. Participation in research enables improved care and treatments for patients of all backgrounds, so you can be a part of creating better care for the TSC community. Participation is voluntary, and you may opt out at any time.

The purpose of these initiatives is to accelerate research on TSC biology and drug development with the long-term goal of improved clinical care. We aim to do this by collecting information about people with TSC over their lifetime and collecting biosamples from people with TSC.

The purpose of your participation in the Self-Report Portal is to help the TSC Alliance and TSC researchers better understand the perspective of those affected by TSC so that we can begin to track changes and measure improvement in areas most important to you. Currently, we have questions related to TSC-associated neuropsychiatric disorders (TAND) and epilepsy in the portal.



Please note: As of December 1, 2022, you do not have to be a participant in the Natural History Database/Biosample Repository project to participate in the Self-Report Portal.

What results have come from the projects?

Sample distribution to researchers began in 2018. To date, portions of **1,897 samples** have been distributed to **40 distinct researchers for 47 distinct projects**.

One publication using brain tissue from the repository has been published. Two publications using cell lines have been published. You can find links to these on our webpage!

15 publications have been published using Natural History Database data. You can find links to these at www.tscalliance.org under the Researchers/Biosample Repository tab.

15 Seed Grants (funds up to $20,000) have been distributed to researchers to utilize Biosample Repository samples.

Marinus Pharmaceuticals **utilized plasma samples in a pilot study** that was completed prior to the initiation of a Phase 2 clinical trial of ganaxolone for epilepsy in TSC. This study is now in Phase 3.

If you are interested in participating in these projects or have questions, please email *biosample@tscalliance.org.*

Seizure Tracker: Data Sharing with the TSC Alliance

seizuretracker.com®
be aware. track it.

The TSC Alliance and Seizure Tracker™ have a data-sharing partnership wherein Seizure Tracker™ users can elect to share their patient-reported seizure and treatment data with the TSC Alliance and connect these data to medical information they provide to the TSC Natural History Database and any biosamples they choose to contribute. This information can be used to assess how epilepsy features compare within the TSC population, across other epilepsy subtypes, and to other measured TSC features within research studies.

How to get started with Seizure Tracker™

1. Go to *www.SeizureTracker.com* to learn more about the free diary system.
2. Set up a free account and start tracking.
3. Visit iTunes or Google Play to download the Seizure Tracker mobile app.
4. Enable the Alexa skill (Amazon voice control) to record seizures hands free.
5. Record your seizures, rescue medication, and VNS magnet swipes as they happen.
6. Use the extensive reporting features of SeizureTracker.com to share data with your care team. Retrospective reporting is also enabled.
7. Empower the TSC research community by contacting the TSC Alliance to let them know you would like to connect your Seizure Tracker data to the TSC Natural History Database.

Nobelpharma America supports Rare Disease Day and the TSC community

In anticipation of Rare Disease Day on February 28, 2023, Nobelpharma America is proud to continue its relationship with the TSC Alliance® to help drive awareness about the challenges faced by people with facial angiofibroma due to tuberous sclerosis complex (TSC).

Few people understand what it is like to live with a rare disease. Nobelpharma America looks forward to learning from the TSC community. The company appreciates that Rare Disease Day is a platform to engage with the community and raise awareness among the general public and policymakers about how these conditions impact people's everyday lives.

"Rare disease day inspires us to fulfill our mission," says Yoshiki Kida, President and CEO of Nobelpharma America (NPA). "We take a patient-first approach. Our organization is focused on providing therapies for medical conditions with limited or no treatment options. We believe that we have a societal obligation to help improve the lives of people living with rare diseases."

Each year Nobelpharma America reaffirms its commitment to advancing science in rare diseases and supporting the communities it serves. This year for Rare Disease Day, Nobelpharma America will continue to drive awareness and engagement through social media outreach, events, news, and other related programs.

As always, Nobelpharma America looks forward to supporting individuals, families and friends living with rare diseases, and encouraging others to join in this endeavor!

Meet the 2023 TSC Alliance Future Leaders

The TSC Alliance® Future Leaders Program is a group of individuals ages 17 through 27, including young adults with TSC, siblings of someone with TSC or other relatives of someone with TSC who are dedicated to building community leadership skills through volunteerism. The Future Leaders Program is committed to empowering young adult leaders through mentorship, volunteer services and grassroots advocacy to help develop community-minded change makers and leaders.

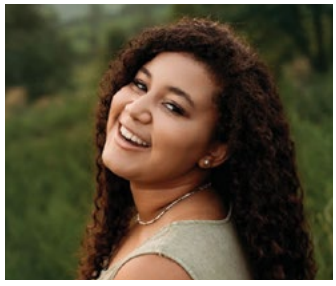
Meghan Nazareno, Arlington, Virginia

What is your primary connection to TSC? Adult with TSC.

What interested you in the Future Leaders Program? Working with other people interested in grassroots community building and advocacy within the TSC community makes me want to be part of the Future Leaders Program. I still have so much to learn from others and so much to learn about TSC.

What do you hope to gain from the Future Leaders Program? I hope to gain a better understanding of TSC and a better understanding of others' experience with TSC. Additionally, I am excited for the potential of meeting other young adults in a collaborative environment where we can all learn from each other.

Kylee Watts, Elberfeld, Indiana



What is your primary connection to TSC? Sibling of an individual with TSC.

What interested you in the Future Leaders Program? I am most interested in learning more about TSC and ways to fundraise. I have never met anyone who has heard about TSC before my family started to spread awareness and would love to find people my own age affected by TSC and learn their stories.

What do you hope to gain from the Future Leaders Program? I would love to gain a better understanding and gain a platform to advocate for TSC. I hope the Future Leaders Program can point me into the right direction for TSC advocacy and allow me to bring more awareness to my campus and hometown.

Anna Galvin, Oregon House, California

What is your primary connection to TSC? Adult with TSC.

What interested you in the Future Leaders Program? I am looking to find others my age with TSC. I have always enjoyed working with others, and I hope to help and meet more people.

What do you hope to gain from the Future Leaders Program? I hope to learn from others with experience with TSC and improve my knowledge of what can be done to continue to understand TSC. Also, it will be a chance for me to use my leadership skills by collaborating and sharing ideas.

Rebecca Fleming, Wexford, Ireland

What is your primary connection to TSC? Adult with TSC.
What interested you in the Future Leaders Program? As a young adult becoming more open with my TSC, I wish to become more involved. Moreover, I have an interest in rare diseases and hope to become a genetic counseling student with a focus on this area, especially TSC.

What do you hope to gain from the Future Leaders Program? I hope to gain experience in advocacy, and I also want to get more involved in TSC research. I value communication highly in helping families understand so they can voice their needs and concerns as well as gain leadership skills.

Rebecca Berger, Boca Raton, Florida

What is your primary connection to TSC? Adult with TSC.

What interested you in the Future Leaders Program? As an individual with TSC, I would like to become more involved with the TSC community as well as educate others about this disease.

What do you hope to gain from the Future Leaders Program? I'd like to become more involved in the TSC Alliance. I'd like to gain exposure to planning walks and perhaps other events involving the TSC community.

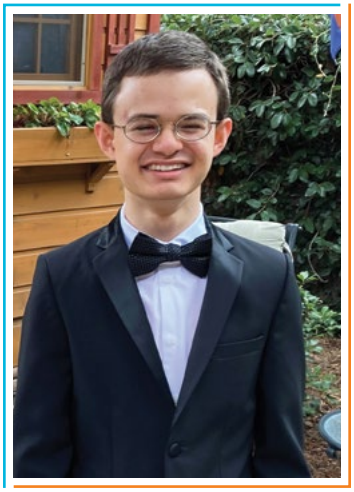
Sara del Valle, Odessa, Florida

What is your primary connection to TSC? Sibling of an individual with TSC.

What interested you in the Future Leaders Program? I want to help my sister and other individuals with TSC get a better quality of life. Also, I would like to help other siblings of individuals with TSC to network so we can share experiences and have a place to connect.

What do you hope to gain from the Future Leaders Program? I want to learn more ways to find a cure for TSC, increase awareness and raise research funds so we can eventually say "there once was a condition called TSC."

Bao Heffron, Irvine, California



What is your primary connection to TSC? Adult with TSC.

What interested you in the Future Leaders Program? I want to be able to work with others with TSC and learn from them. I would like to network with others and explore who I am and what I can do.

What do you hope to gain from the Future Leaders Program? A better understanding of how I can help others like me accomplish our goals.

Sydney Turner, Syracuse, New York

What is your primary connection to TSC? Sibling to an individual with TSC.

What interested you in the Future Leaders Program? Being a part of this program will allow me to connect with other individuals who are impacted by TSC as well as others who have watched their loved ones go through life with TSC.

What do you hope to gain from the Future Leaders Program? I hope to gain new experiences, participate in volunteer opportunities and meet other people who understand what it is like to have a sibling or loved one who is affected by TSC.

2022 TSC research review

The TSC Alliance® stimulates, coordinates and drives research toward a cure for TSC while improving the lives of those affected. Since 1984, the TSC Alliance has invested more than $34 million into TSC research projects through grants and contracts:

- $20.1 million in research grants
- $7.9 million into the Preclinical Research Consortium
- $4.8 million into the Natural History Database and Biosample Repository
- $1.3 million into the Clinical Research Consortium

TSC research grants

Most TSC Alliance research grants support focused projects enabling investigators to develop innovative ideas into preliminary data capable of garnering funding from larger organizations such as the NIH and TSCRP.

In 2022, the TSC Alliance awarded grants to the following researchers, each of whom is an early career researcher as defined by the NIH. This investment will foster the next generation of TSC researchers.

Wong Family Foundation Research Grant:

Ian Wenker, PhD
Research Assistant Professor, University of Virginia
Project Title: "Mechanisms of seizure-induced death of TSC model mice"
Lay Summary: Most tuberous sclerosis complex (TSC) patients suffer from TSC-associated neuropsychiatric disorders and epilepsy, for which no effective treatment is available. TSC is a genetic disorder caused by DNA mutations in either one of the two TSC genes. These DNA mutations result in defective TSC-RNA which causes loss of functional TSC-protein. Although the ultimate dream is to correct such mutations directly in the DNA, we now have the ability to get very close to that: correction at the level of RNA. Here, we propose to explore the use of antisense oligonucleotides (ASOs) as an innovative approach to treat TSC. ASOs can readily and safely enter neurons, which makes their use in particularly interesting for treatment of brain pathophysiology.

We will design and test ASOs that are aimed at either increasing functional TSC protein or reducing RHEB protein, a protein that becomes hyperactive when TSC is mutated. (Aim 1). Using TSC patient-derived induced pluripotent stem cells (iPSCs), which can be differentiated to relevant brain cell types, we will assess whether these ASOs can reverse the cellular and molecular TSC phenotype (Aim 2). The most promising ASOs will be tested in a mouse model for TSC-associated epilepsy, to provide in vivo proof-of-principle for the therapeutic use of ASOs in TSC (Aim 3). We expect that this research will facilitate future exploration of innovative TSC treatments and improve patient-derived cellular models of TSC to be used for that purpose.

Research Grant:

Uchenna Unachukwu, PhD
Associate Research Scientist, Columbia University Medical Center
Project Title: "Defining the pathogenic role of neural crest cells in tuberous sclerosis complex"
Lay Summary: Tuberous sclerosis complex (TSC) remains an incurable disease that forms benign tumors in multiple organs. The source of cells forming these tumors and biochemical mechanisms they employ have not been conclusively determined limiting effective therapies. We recently published findings that neural crest cells (NCCs), a multipotent stem cell, are associated with the kidney tumors in a mice model of TSC disease. Following analysis of these NCCs, we identified expression of a known cancer-causing gene, secreted phosphoprotein 1 (Spp1). Furthermore, the SPP1 protein was found to be exclusively expressed in TSC mice kidney tumors, kidney and lung lesions, and blood serum obtained from LAM patients but not in healthy samples. Therefore, in this proposal, we will test the hypothesis that Tsc2 and Spp1 mutations in neural crest cells cause TSC tumorigenesis. In Specific Aim 1, we will utilize gene editing technology to knockout Spp1 and Tsc2 genes in neural crest cell lines and determine the effects on tumorigenic characteristics of the NCCs. In Specific Aim 2, we will generate a novel inducible Wnt-1-Cre mouse model that fluorescently labels maturing NCCs and induce Tsc2 gene mutations in the NCCs at different developmental timepoints. These experiments will enable us to monitor and biochemically analyze tumor development caused by pathogenic NCCs and reveal new insights and disease-causing mechanisms for TSC disease to identify new therapeutic targets translatable to the clinic.

Postdoctoral Fellowship:

Annelot Clementine Mathilda von Esbroeck, PhD
Postdoctoral Researcher, Erasmus MC
Project Title: "Investigating ASO therapy for TSC-associated neuropathophysiology"
Lay Summary: Most tuberous sclerosis complex (TSC) patients suffer from TSC-associated neuropsychiatric disorders and epilepsy, for which no effective treatment is available. TSC is a genetic disorder caused by DNA mutations in either one of the two TSC genes. These DNA mutations result in defective TSC-RNA which causes loss of functional TSC-protein. Although the ultimate dream is to correct such mutations directly in the DNA, we now have the ability to get very close to that: correction at the level of RNA. Here, we propose to explore the use of antisense oligonucleotides (ASOs) as an innovative approach to treat TSC. ASOs can readily and safely enter neurons, which makes their use in particularly interesting for treatment of brain pathophysiology.

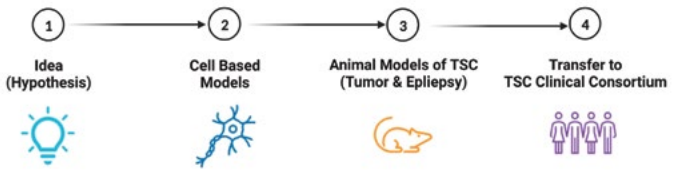
We will design and test ASOs that are aimed at either increasing functional TSC protein or reducing RHEB protein, a protein that becomes hyperactive when TSC is mutated. (Aim 1). Using TSC patient-derived induced pluripotent stem cells (iPSCs), which can be differentiated to relevant brain cell types, we will assess whether these ASOs can reverse the cellular and molecular TSC phenotype (Aim 2). The most promising ASOs will be tested in a mouse model for TSC-associated epilepsy, to provide in vivo proof-of-principle for the therapeutic use of ASOs in TSC (Aim 3). We expect that this research will facilitate future exploration of innovative TSC treatments and improve patient-derived cellular models of TSC to be used for that purpose.

Additionally, in 2022 the TSC Alliance continued supporting the following researchers:

- **Research Grant:** Nicola Alesi, MD, PhD: "Role of TFEB in the pathogenesis and therapy of TSC kidney manifestations" (Brigham and Women's Hospital)
- **Research Grant:** Gerta Hoxhaj, PhD: "Defining the genetic factors that mediate purine signals to the TSC network" (UT Southwestern)
- **Research Grant:** Philip Iffland, PhD: "Amino acid modulation as a therapeutic strategy for TSC-associated epilepsy" (University of Maryland School of Medicine)
- **Keith Hall Memorial Research Grant:** Oded Volovelsky, MD, PhD: "Targeting the Endocannabinoid System in TSC-induced kidney disease" (Hadassah Medical Center, Israel)
- **Postdoctoral Fellowship:** Katarzyna Klonowska, PhD: "Polyclonal somatic mutations drive TSC tumorigenesis" (Brigham and Women's Hospital)

TSC Preclinical Consortium

The preclinical consortium encourages collaboration between a multidisciplinary team of researchers, including clinical researchers. The consortium facilitates drug testing in cell and animal models of TSC. The compounds that prove efficacious and safe are referred to the TSC Clinical Research Consortium to consider for clinical testing. The consortium is currently characterizing a ***Tsc1* mouse model with autism-like behaviors** and a ***Tsc2* mouse model of epilepsy** in collaboration with Mustafa Sahin, MD, PhD. In addition, **a model for lymphangioleiomyomatosis (LAM)** is scheduled to be added in collaboration with The LAM Foundation and Nishant Gupta, MD.



This year, two new industry members joined the consortium with a total of **10 active industry members** at the end of the year. The consortium tested seven unique compounds in 2022, raising the total tested to 63 since 2016. Many compounds will enter preclinical testing, though only some will advance to clinical testing, due to lack of efficacy and/or safety. Excitingly, there are partners seeking clinical trials for their compounds in 2023-2024. Looking forward, we have already **contracted nine experiments with three companies to evaluate their drugs in preclinical models** and are actively cultivating three new industry members.

TSC Biosample Repository and Natural History Database

The TSC Alliance built the TSC Biosample Repository to accelerate research into why TSC is so variable among individuals and how we might determine which individuals respond better or poorly to certain treatments. Samples in the repository are linked to detailed clinical data in our TSC Natural History Database and are available to qualified researchers worldwide. As of December 1, 2022, the Natural History Database contained **2,546 participants** enrolled across 21 TSC clinic sites and the TSC Alliance.

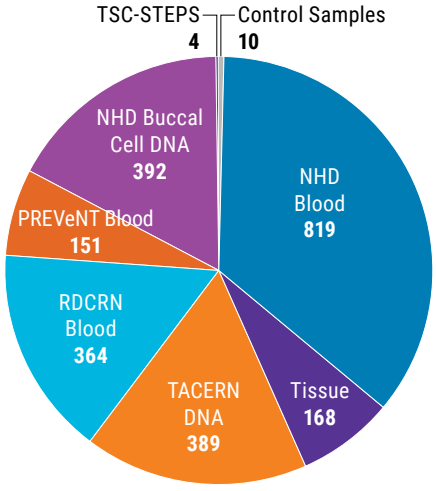
Current sites include:

1. Boston Children's Hospital, Boston, MA (Mustafa Sahin, MD, PhD)
2. Children's Hospital Colorado, Aurora, CO (Susan Koh, MD) [database only]
3. Children's National Medical Center, Washington, DC (William McClintock, MD)
4. Cincinnati Children's Hospital Medical Center, Cincinnati, OH (Darcy A. Krueger, MD, PhD)
5. Cleveland Clinic, Cleveland, OH (Ajay Gupta, MD)
6. Le Bonheur Children's Hospital, Memphis, TN (Sarah Weatherspoon, MD)
7. Loma Linda University Medical Center, Loma Linda, CA (Stephen Ashwal, MD) [database only]
8. Herscot Center for TSC at Massachusetts General Hospital, Boston, MA (Elizabeth A. Thiele, MD, PhD)
9. Minnesota Epilepsy Group, PA, Roseville, MN (Doug Smith, MD)
10. New York University Langone Medical Center, New York, NY (Josiane LaJoie, MD)
11. Nicklaus Children's Hospital, Miami, FL (Paula Schleifer, MD)
12. Texas Scottish Rite Hospital for Children, Dallas, TX (Steven P. Sparagana, MD)

13. Université de Montréal Sainte-Justine, Montreal, Canada (Philippe Major, MD)
14. Université de Montréal, Montreal, Canada (Mark Keezer, BA, BSc, MSc, MDCM, PhD)
15. University of Alabama, Birmingham, AL (Martina Bebin, MD, MPA)
16. University of California Los Angeles (UCLA), Los Angeles, CA (Rajsekar Rajaraman, MD)
17. University of Chicago, Chicago, IL (James Tonsgard, MD) [database only]
18. University of Iowa, Iowa City, IA (Michael Ciliberto, MD)
19. University of Pennsylvania, Philadelphia, PA (Katherine Nathanson, MD) [database only]
20. University of Texas Health Science Center, Houston, TX (Hope Northrup, MD)
21. Washington University, St. Louis, MO (Michael Wong, MD, PhD)
22. TSC Alliance, Silver Spring, MD (remote consenting and mobile sample collections, Gabrielle Rushing, PhD)

Samples are housed at and distributed from the Van Andel Institute in Grand Rapids, Michigan, under control of the TSC Alliance. Research projects utilizing biosamples are expected to lead to new hypotheses regarding biomarkers, mechanisms for new treatment approaches, risk-factors, or genetic modifiers. These discoveries could make clinical trials more efficient and lead to drug development or new directions of research and larger projects funded by the National Institutes of Health (NIH), Department of Defense's Tuberous Sclerosis Complex Research Program (TSCRP) or other sources.

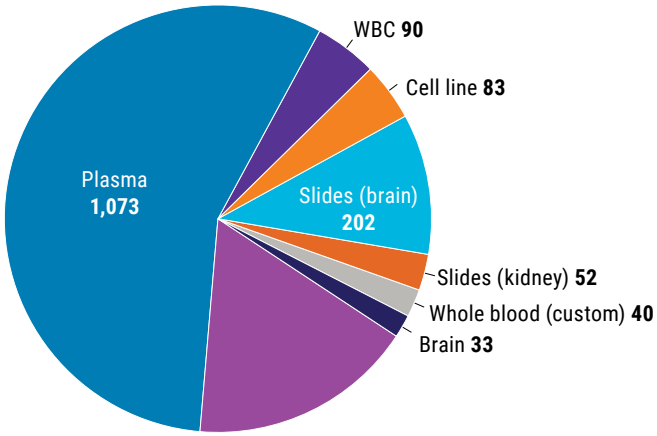
The Biosample Repository continues to add diversity in types of samples. Ultimately, this valuable resource will help lead the way for predictive and personalized care. As of December 1, 2022, the Biosample Repository has acquired **2,297 blood, buccal (cheek) swab or tissue samples**. Our mobile phlebotomy initiative enables anyone with TSC to participate in the Biosample Repository regardless of where they receive medical care. To date, we have acquired **356 blood samples via mobile phlebotomy**.



In 2022, **four publications** using TSC biosamples and/or TSC natural history data were published including two utilizing TSC cell lines, one utilizing buccal (cheek) swab biosamples, and two utilizing NHD data.

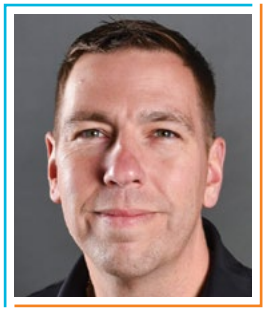
One publication focused on **racial disparities in TSC**. The TSC Alliance's Director of Medical Affairs Ashley Pounders, MSN, FNP-C, and Director of Research Gabrielle Rushing, PhD collaborated with Tanjala Gipson, MD (Le Bonheur Children's Hospital) to highlight differences in skin manifestations between races in individuals with TSC and the potential effects of these differences on diagnosis and care. The aim of the publication was to identify differences in TSC skin features between Black and White individuals to raise awareness in TSC clinics and the TSC community. In addition, the data provide insight into how these differences can affect the timing of TSC diagnosis and subsequent treatment regimens. By highlighting these potential disparities, we hope to ensure improved timing in diagnosis and treatment regimens for all affected by TSC in the future. The TSC Alliance thanks all of the families who provided photos for this publication. To read the results in full, please see Ashley J. Pounders*, Gabrielle V. Rushing*, Sonal Mahida, Bareng Aletta Sanny Nonyane, Emily A. Thomas, and Rabiah Sundus Tameez. Racial differences in the dermatological manifestations of tuberous sclerosis complex and the potential effects on diagnosis and care (2022) Ther Adv Rare Dis 3: 1–16. doi.org/10.1177/26330040221140125

In 2022, portions of **620 of these samples** were shared with **12 different researchers**, and since inception, portions of **1,897 samples** have been distributed to **40 distinct researchers for 47 distinct projects**.



We recently selected awardees for **four biosample seed grants** totaling $59,324 that will increase the utilization of our current inventory and advance scientific discoveries. The awardees are Dr. Dave Feliciano, Dr. Mark Hester, Dr. Geoff Owens, and Dr. Amina Jouida. Read more about their collaborators and projects below.

Dave Feliciano, PhD



Associate Professor, Clemson University, Department of Biological Sciences

Project Title: A Subependymal Giant Cell Astrocytoma Cell Atlas

Impact Statement: The short-term impact is we will provide the TSC community with a single cell resolution atlas of SEGAs that allows for determination of cellular composition, cellular level comparisons of transcriptomes,

and inference of cellular origins of SEGAs. A hallmark of TSC is activation of the protein kinase mTOR1. mTOR inhibitors are a frontline treatment for TSC but have limited efficacy. Major limitations to these drugs (rapamycin and rapalogs) are that their effects are reversible, are subject to resistance, may not effectively eliminate neurological manifestations and have side effects including immunosuppression. Most relevant is that treatment with rapalogs is a life-long sentence because treatment cessation allows SEGA regrowth. The long-term impact is that studying the cell types, origin, and transcriptomic signatures that will infer cellular events altered in SEGAs will allow for the future therapeutic targeting of cellular vulnerabilities to irradicate TSC tumors.

Mark Hester, PhD and Alecia Biel, PhD

Assistant Professor, Nationwide Children's Hospital, Abigail Wexner Research Institute, Institute for Genomic Medicine (Hester) and Postdoctoral Researcher, The Research Institute at Nationwide Children's Hospital (Biel), Columbus, Ohio

Project Title: Understanding Molecular Mechanisms of Blood Brain Barrier Deficits in TSC

Impact Statement: Over half of epileptic TSC patients have seizures that cannot be completely controlled by medication. There are many factors that contribute to drug-resistance among these patients, but calcification of cortical tubers is one of the best-known, which is thought to be related to blood-brain barrier integrity. Nevertheless, our understanding of molecular mechanisms leading to cortical tuber calcification is limited. Therefore, this proposal seeks to define and delineate the relationships among pericyte-associated BBB dysfunction and drug resistant epilepsy in TSC patients.

In the short term, we expect this project will provide a deeper understanding of the natural disease history of TSC in regard to cortical tuber calcification and development of drug-resistant epilepsy. It will also provide new insights into molecular changes occurring in brain perivascular cells in the setting of TSC1/TSC2 deficiency. In the long term, we expect to use the findings from this project to bridge into deeper mechanistic studies of cortical tuber calcification, which will be critical in designing therapeutics that target this pathology. Funding this study will allow us to bridge into a larger research project aimed at modulating brain calcification using molecular tools and therapies in mouse and brain organoid models. We will then be well-positioned to test directly the effects of calcification on seizure phenotypes in TSC. Additionally, given the multi-organ involvement of TSC, the findings of this study may help in understanding the underlying mechanisms of calcification that cause dysfunction in other organs such as the kidney.

Geoff Owens, PhD (Project Scientist), Aria Fallah, MD (Assistant Professor), Rajsekar Rajaraman, MD (Assistant Professor), Julia Chang, PhD (Study Coordinator)

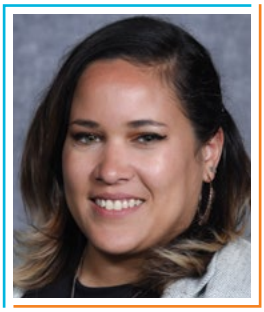
Institutional Affiliation: UCLA David Geffen School of Medicine, Departments of Neurosurgery and Neurology

Study Title: Does everolimus significantly alter the T cell repertoire in TSC patients?

Impact Statement: We are investigating the potential involvement of T cells in the development of seizure intractability. Everolimus, which is approved for the treatment of SEGAs, has been found to reduce the seizure burden in some TSC patients. The therapeutic effect of the drug was achieved at blood levels that are comparable to those used in trials to prevent rejection of transplanted organs. This indicates that everolimus may be immune suppressive in treated TSC patients, which could account in part for its therapeutic effect on seizure frequency. Sequencing T cell receptors in blood collected from TSC patients with seizures before and after receiving EVL may answer this question.

Our proposed sequencing of samples from the TSC Alliance's Biosample Repository will provide critical preliminary data for a competitive grant application to the NIH and to the Department of Defense's TSC research program. The potential involvement of adaptive immunity in TSC has not been thoroughly explored; our research may launch new possibilities for detection, monitoring and treatment of intractable epilepsy in children with TSC.

Amina Jouida, PhD



Postdoctoral Researcher, University College Dublin, Conway Institute of Biomolecular and Biomedical Research, Dublin, Ireland

Project Title: The role of circulating serum exosomes in epithelial-to-mesenchymal transition and the premetastatic niche in lymphangioleiomyomatosis (LAM).

Impact Statement: This project will demonstrate the utility of exosomes as potential diagnostic and prognostic tool in LAM patients. Exosomes may provide biological information which allows a more comprehensive assessment of the evolving disease and the possible response to targeted therapies. Importantly the assessment of serum exosomes is non-invasive and thus referred to as liquid biopsy. Early diagnosis will not only help reduce mortality, and cost of patient care but also improve prognosis, prolong survival, and quality of life of patients.

TSC Alliance welcomes new Research Project Manager

In 2022, the science team welcomed Liz Cassidy, MPH, as Research Project Manager, reporting to Director of Research Gabrielle Rushing, PhD. Liz brings experience as a clinical trials coordinator including data entry, research study consent procedures, and biospecimen processing. Liz is also fluent in Spanish, which will be helpful in many aspects of TSC Alliance research projects.

"I'm so thrilled to be a part of the TSC Alliance and working with such an inspirational group of community leaders and advocates," said Liz. "My passion in research has developed throughout my career into bringing my research into the hands of the community, where I thrive to help bring science closer to finding a cure for chronic illnesses like TSC. I hope that in being the new Research Project Manager, I can help our community feel comfortable getting involved in the research opportunities like the Natural History Database and the Biosample Repository, as well as help create a seamless process for our coordinators and participants at our many sites throughout the country."

"I am also hoping to bring my background in Maternal and Child Health to research at the TSC Alliance, where I can help with research initiatives and educational resources focusing on how TSC affects women throughout the lifespan," she continued. "Finally, I am particularly excited to be working with Gabrielle and the other wonderful staff involved in the TSC Alliance."

Whole Genome Sequencing (WGS) project update

In 2021, thanks to a generous donation from Julian and Janice Gangolli, the TSC Alliance

On the horizon: innovative research

Biomarker Innovation Workshop

Thanks to a recent gift from the Ramesh and Kalpana Bhatia Family Foundation, the TSC Alliance has created "Anya's Accelerator" to focus on furthering translational research on TSC-Associated Neuropsychiatric Disorders (TAND). The TSC Alliance will host an Innovation Workshop focused on TAND Biomarkers April 26-27, 2023, in Silver Spring, MD. More than 25 key opinion leaders, including Dr. Mustafa Sahin, Dr. Darcy Krueger, Dr. Anna Jansen and Dr. Shafali Jeste, will paticipate.

PREVeNT trial results

The Preventing Epilepsy using Vigabatrin in Infants with TSC (PREVeNT) trial's last study visit will take place in January 2023. We eagerly anticipate the results of this trial in Spring of next year. The central hypothesis of this Phase IIb trial, supported by a $7 million grant from NINDS, is that early identification of electroencephalography (EEG) biomarkers and early treatment versus delayed treatment with vigabatrin in infants with tuberous sclerosis complex (TSC) will have a positive impact on developmental outcomes at 24 months of age. It would also prevent or lower the risk of developing infantile spasms and refractory seizures. This preventative approach would be expected to result in more favorable long-term cognitive, behavioral, developmental, and psychiatric outcomes and significantly improve overall quality of life. In addition to promoting awareness of the trial among the TSC community to enhance enrollment, the TSC Alliance is collecting blood samples from participants in PREVeNT for the Biosample Repository.

2023 International TSC Research Conference

The 2023 International TSC Research Conference, being hosted September 7-9, 2023, in Washington, DC, convenes basic and clinical researchers interested in TSC and related disorders, including epilepsy, autism, cancer and rare diseases with related features. Through collaboration of participating senior and junior researchers and trainees, the conference enables opportunities to accelerate research to improve health care and quality of life for individuals with TSC and beyond. The 2023 International TSC Research Conference aims to inspire new approaches in research by connecting trainees and researchers, especially those from underrepresented groups in research, to the latest developments related to TSC research.

The program also fosters connections and conversations to promote collaborative research to address unmet medical needs of those affected by TSC. The conference will include an Early Career Researcher Symposium, to engage trainees and early-stage investigators around issues unique to their career stage, including discussions on data sharing practices, poster presentations, feedback on presentation skills, and overall exposure to broader research opportunities (e.g., industry, patient advocacy) in the field of TSC.

conducted a small pilot study using DNA from 20 blood samples in our Biosample Repository to demonstrate the feasibility of this approach. Samples that had not been previously analyzed were sent to the Translational Genomics Research Institute (TGen) for WGS. Continued funding support from the Gangolli family permitted an additional 48 samples to be sequenced in 2022, totaling **68 samples since inception**. WGS is an important step toward understanding the relationship between genetic variants and their impact on disease.

This initiative supports clinical validation of variants found via WGS in either the *TSC1* or *TSC2* gene at GeneDx, and genetic results are offered back to participants along with a genetic counseling session free of charge to the family to help them better understand their unique TSC diagnosis and provide valuable information for future decision making such as family planning. Our current genetic counseling partner is Kate Richardson, MS, CGC at University of Texas Health Science Center at Houston.

Genetic results are one of the most requested pieces of data from the Natural History Database. We hope to grow this project to complete WGS on 500 samples and offer the data to TSC researchers to better understand the variability observed in people affected by TSC, which may lead to predictive and personalized care. Rather than having many researchers at different institutions undertake this type of sequencing, the TSC Alliance can accelerate this process by coordinating and funding WGS on hundreds of DNA samples and sharing those data with multiple researchers.

The Gangolli family continues to support the WGS initiative and has been joined by the Watts and Frost families. As a result, we look forward to more results from this exciting research in 2023.

TSC Alliance earns highest ratings from watchdog organizations

The TSC Alliance® recently earned the highest rankings from four watchdog organizations: Charity Navigator, Candid, GreatNonProfits and Better Business Bureau.

The TSC Alliance now has a **4-Star Rating** from **Charity Navigator**, the world's largest and most trusted nonprofit evaluator. Charity Navigator's third-party accreditation validates our organization's operational excellence. In addition, this rating designates the TSC Alliance as an official "Give with Confidence" charity, indicating our organization is using our donations effectively based on Charity Navigator's criteria.

Candid (formerly Guidestar) recently confirmed the TSC Alliance has once again earned its **Platinum Seal of Transparency**. The Candid seal is the highest possible rating and indicates we exceed nonprofit industry standards. This exceptional designation sets us apart and demonstrates our trustworthiness to the public.

GreatNonProfits just added us to its **2022 Top-Rated List**. This rating is especially important because it's based on TSC community input.

Finally, the TSC Alliance has **met all 20 Standards for Accountability** of the **BBB Wise Giving Alliance Program**.

These milestone achievements for the TSC Alliance couldn't have happened without you and your support. Your trust and support help us make a difference for the individuals and families we serve.

Thank you for being an integral part of our mission to find a cure for tuberous sclerosis complex while improving the lives of those affected.

TrustTSC: Treating uncontrolled seizures in tuberous sclerosis complex

A Phase 3 clinical trial

BY IAN MILLER, MD, VICE PRESIDENT OF CLINICAL DEVELOPMENT, MARINUS PHARMACEUTICALS

Antiseizure medications (ASMs) are the mainstay of treatments for seizures caused by tuberous sclerosis complex (TSC), which occur in approximately 85%[1,2] of affected individuals. Yet, despite the availability of three ASMs specifically indicated for TSC-associated seizures, as well as numerous conventional ASMs prescribed based on seizure type, seizures remain treatment resistant in many patients. Non-medication options for refractory seizures include surgical removal of cerebral TSC lesions (tubers) or other brain tissue where seizures originate, vagus nerve stimulation, a ketogenic diet, or participation in a clinical study of an investigational ASM.

Investigational medications are evaluated first in a laboratory setting to establish experimental evidence of safety and effectiveness, an important step to ensure that a medication is appropriate for entry into human studies. The first human (Phase 1) trials are performed in a small number of healthy volunteers before proceeding with larger studies in patients. Phase 1 studies provide initial evidence of safety and appropriate dosing of an investigational medication. These are followed by Phase 2 studies in which the participants are those with the medical condition for which the drug is being considered. These studies provide information on potential effectiveness in patients, further evidence on the medication's safety, and on the optimal dose. An investigational drug then moves into larger Phase 3 studies in which patients typically receive either the active treatment or a placebo. In most Phase 3 studies, neither the patient nor the study physician and staff are aware of whether an individual is receiving the drug or a placebo, i.e., these are *double-blind* studies. Phase 3 trials provide the pivotal data used to support regulatory approval and involve hundreds or even thousands of patients. The hope is to find new treatment options that could benefit patients. The process of demonstrating that a treatment is safe and effective takes years but has resulted in three new treatments for seizures associated with TSC over the past five years. The ASMs everolimus, cannabidiol, and fenfluramine have all been shown to be safe and effective and are now part of the standard of care for TSC-associated seizures.

One of the newest clinical trials is evaluating the investigational medication, ganaxolone, as a potential treatment for seizures associated with TSC. Ganaxolone has a chemical structure that is similar to allopregnanolone, a substance normally produced in the brain and other organs. Allopregnanolone modulates the activity of $GABA_A$ receptors which results in inhibition of the firing of brain neurons, thereby preventing their excessive activation. In epilepsy, there is an imbalance in the level of excitation relative to inhibition of neurons. Therefore, increasing the inhibitory activity regulated by GABA can reduce the excessive brain activation which underlies the occurrence of epileptic seizures.

Based on the results of a Phase 3 clinical trial, ganaxolone oral suspension was approved by the U.S. Food and Drug Administration (FDA) in March 2022 for the treatment of seizures associated with CDKL5 deficiency disorder in patients two years of age and older under the brand name ZTALMY® CV.[3]

A Phase 3 clinical trial, the TrustTSC study, is ongoing to evaluate ganaxolone for the treatment of seizures associated with TSC. The TrustTSC study is a double-blind clinical trial in which study participants will receive 16 weeks of treatment with either ganaxolone or placebo and has a planned enrollment of 162 patients.

TrustTSC is currently being conducted at more than 70 sites globally with additional countries being added. The trial is open to individuals with uncontrolled TSC-associated seizures who are 1-65 years of age (some non-U.S. countries require participants to be at least two years old) and who meet the qualifications for study entry. Interested individuals with TSC, or the parents or caregivers of someone with TSC, can find more information about the study and a list of study sites at www.*TrustTSCtrial.com*. Travel support is available for individuals who do not live near a study center location.

During the evaluation for participation, the study site team will interview the patient or parent for a detailed history of seizures and medications. If the seizure and medication history indicate the required degree of insufficient responsiveness to antiseizure medications, the physician or another medical professional on the team will provide complete information about the study, conduct a physical and neurologic examination, and perform some diagnostic tests including an EKG and blood work. If the patient is eligible to enter the study, the patient or parent/caregiver will track seizures in an electronic diary while taking their current medications. Those who continue into the treatment phase of the study will be randomly assigned to receive either ganaxolone oral suspension or a placebo oral suspension. As discussed

above, the patient, their family/other caregiver and the study site physician and staff will not know whether the participant's study treatment is ganaxolone or placebo.

The blinded study treatment will continue for 16 weeks, during which there will be visits to the study site for interim assessments of seizures, diagnostic blood work and other tests. Additionally, the physician and study team will ask whether there have been any side effects from the study treatment. Although this occurs at study visits, the patient should notify the study team at any time if they think they might be experiencing a side effect.

In addition to evaluating the effect of ganaxolone on seizures, the study will also explore whether there are improvements in other domains. For example, sleep problems are significant for many with TSC, and the TrustTSC clinical trial will assess the effect of ganaxolone on sleep quality, as well as looking at whether there have been any improvements in mood, behavior or quality of life.

Those completing the double-blind phase and meeting certain criteria, have the option to enter a long-term extension, during which all study participants will receive treatment with ganaxolone. There is no blinding of treatment in the extension study.

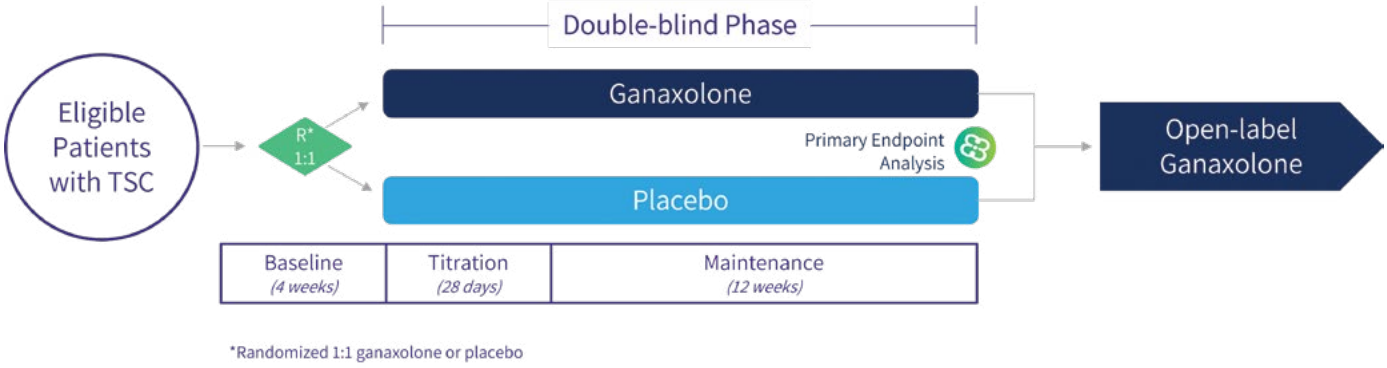
Once the double-blind part of the study is complete and the data has been analyzed, an application will be submitted to the FDA to request approval of ganaxolone for the treatment of seizures associated with TSC. The whole process from study completion to FDA approval can take up to two years. We are hopeful the results of the TrustTSC study will demonstrate a clinically relevant reduction in TSC-associated seizures, and that the trial will pave the way for providing a novel and efficacious treatment option.

1 TSC Natural History Database Consortium in Epilepsy and Neurodevelopmental Comorbidities in Tuberous Sclerosis Complex: A Natural History Study Feb 4, 2020, DOI: https://doi.org/10.1016/j.pediatrneurol.2019.12.016

2 Kingswood et al. Orphanet Journal of Rare Diseases (2017) 12:2 DOI 10.1186/s13023-016-0553-5

3 ZTALMY (ganaxolone) oral suspension CV prescribing information. Radnor, Pennsylvania, USA. Marinus Pharmaceuticals, Inc.; December 2022.

TrustTSC study design

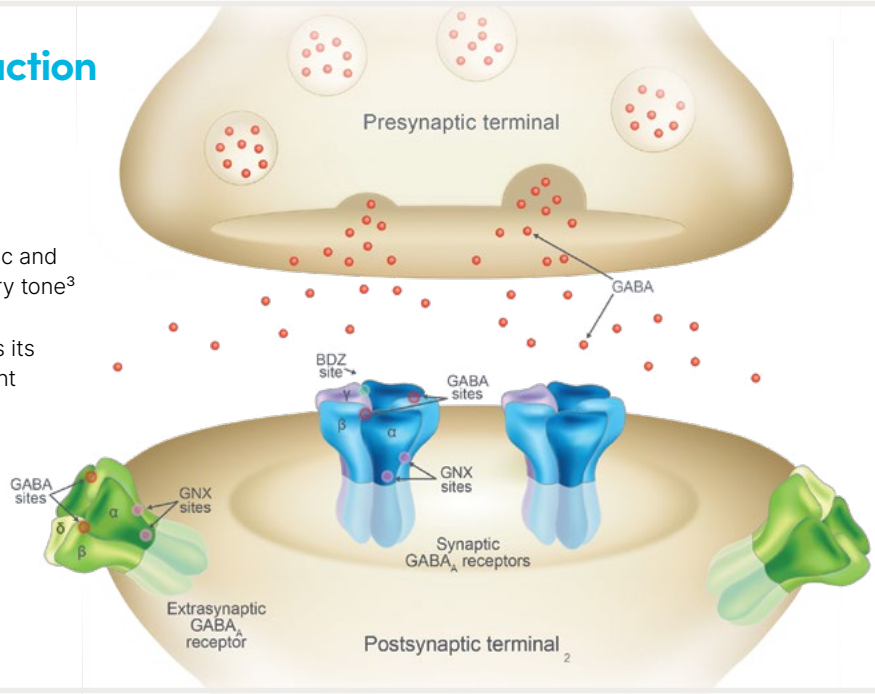


Ganaxolone mechanism of action

Ganaxolone has been shown to target a binding site on $GABA_A$ receptors that is distinct from the benzodiazepine site[1]

Ganaxolone has been shown to bind to both synaptic and extrasynaptic $GABA_A$ receptors to maximize inhibitory tone[3]

The precise mechanism by which ganaxolone exerts its therapeutic effects is unknown, but its anticonvulsant effects are thought to result from positive allosteric modulation of the gamma-aminobutyric acid type A ($GABA_A$) receptor in the CNS.



1 Nohria V, et al. Neurotherapeutics. 2007;4(1):102-105.

2 Reddy DS, et al. Trends Pharmacol Sci. 2016;37(7):543-561.

3 Chuang SH, et al. J Pharmacol Exp Ther. 2018;365(3):583-601.

Honorariums (September 1 – November 30, 2022)

You can honor a friend or family member for an important occasion with a gift to the TSC Alliance®. It is a wonderful way to send a birthday or anniversary wish, or congratulations for retirement, a job well done, graduation etc. Please include the name and address of the individual being honored so that acknowledgement of your kind donation can be sent. TSC Alliance cards are also available if you would like to make a gift in honor of family, friends or colleagues. To receive tribute cards, contact Justin Martucci, Development Systems Manager, at (240) 638 4643 or *jmartucci@tscalliance.org.*

Tribute(s) for Alana Alexander
Ms. Samantha Kopp
Tribute(s) for Rebecca Anhang-Price
Mr. Daniel Silverberg
Tribute(s) for Nicholas Antonio
Mrs. Kimberly Osborn
Tribute(s) for Bladen D. Arndt
Dr. and Mrs. James B. Sims
Tribute(s) for Wyatt Atkinson Pruce
Ms. Rachel Nolzahn
Tribute(s) for Parker C. Beebe
Mr. Ryan Beebe
Tribute(s) for Ethan C. Bennett
Mr. and Mrs. Matt Jorski
Tribute(s) for May Bracy
Mr. Randy Cover

Tribute(s) for Chloe Bredeson
Dr. and Mrs. James B. Sims
Tribute(s) for Molly Britt
Mrs. Mary Lucett
Tribute(s) for Ireland R. Burress
Mr. B.L. Burress
Mr. and Mrs. Cody N. Clyman
Mr. and Mrs. Keith Smith
Ms. Shirley J. Smith
Zion Community Church of God
Tribute(s) for Isaac Burt
Mr. and Mrs. Tom Burt
Tribute(s) for Emilie T. Busel
Mr. and Mrs. Harry C. Meyer
Tribute(s) for Marley Castrantas
Mr. Jonathan Albin
Ms. Felicia Lundrigan

Tribute(s) for Rachel Castrantas
Anonymous
Tribute(s) for Frank Cenna
Mr. and Ms. Dean Edmundson
Dr. Paula Schauble
Tribute(s) for Jaclynn J. Cobbs
Ecolab
Tribute(s) for Elliot Cohen
Rachel and Joshua Wojnilower
Tribute(s) for Elijah Cole
Dr. and Mrs. James B. Sims
Tribute(s) for April L. Cooper
Mr. Justin Martucci and Mrs. Paula Reichel
Tribute(s) for Landon Cox
Mr. and Ms. Robert Moss
Tribute(s) for Dr. Peter B. Crino
Anonymous
Mr. and Mrs. William Joseph
Tribute(s) for Deborah A. Cummings
Dr. and Mrs. James B. Sims
Tribute(s) for Layla D
Ms. Jessica L. Wiles
Tribute(s) for Nick D'Antonio
Mrs. Kimberly Osborn
Tribute(s) for Law Davis
Dr. and Mrs. James B. Sims
Tribute(s) for Alexandra Donato
Ms. Yaeko Ito
Tribute(s) for Levy Dragoun
Ms. Svetlana Ioffe
Tribute(s) for Kelly Duncan
Ms. Val H. Auboil

Tribute(s) for Jeremy Elias
Dr. Carol Hoffman
Tribute(s) for Grace Englebert
Kimberly-Clark
Tribute(s) for Hailey Fisk
Anonymous
Tribute(s) for Tyler J. Gates
Mr. and Mrs. George Delano
Tribute(s) for Tristan Goetz
Mr. Wilma T. Lyton
Tribute(s) for Helen Gottschall
Mr. Leonard Goodman
Tribute(s) for Eden Grafft
Chubb Charitable Foundation
Tribute(s) for Harper Hemphill
Ms. Laurie Hall
Tribute(s) for Matthew Hillier
Mr. and Mrs. Anthony J. Russo

Introducing the 2023 Regional TSC & LAM Conference Series

The TSC Alliance® and The LAM Foundation will join together once again to co-host four Regional TSC & LAM Conferences in 2023 aimed at individuals with TSC and or LAM and their caregivers. Sites will include:

- Alabama
- Colorado
- Washington
- Washington, DC

These one-day conferences will feature local leading researchers and clinicians specializing in TSC and lymphangioleiomyomatosis (LAM). They will also include networking opportunities to meet other families and individuals from the area.

Topics will include sessions across the lifespan of TSC and LAM, including:

- Research updates, including upcoming clinical studies and trials for TSC and LAM
- Behavior and mental health
- LAM
- Genetics
- Women's Health Issues
- Seizure types and treatments
- Kidneys
- Skin

People in each region will gather to attend these conferences to make stronger connections with peers, researchers and clinicians in their community. Families and individuals who live with TSC and LAM, professionals who work with them and extended supporters will use the meetings to learn more about current treatment options, basic and transitional research and clinical trials and to spend time with other people affected by TSC and LAM. These conferences will also allow the TSC Alliance and The LAM Foundation to reach newly diagnosed families, identify new constituents and provide resources and support.

More information, including exact dates and locations, will be available soon so be sure to check *www.tscalliance.org/2023conferences* to stay updated.

Tribute(s) for Christy Hobart Shapiro
Mr. Michael Grossman
Tribute(s) for Ty Hurst
Mr. and Mrs. Matthew Moberly
Tribute(s) for Hannah Jeffers
Mr. and Mrs. Keith A. Gaskill
Tribute(s) for Avery Jodoin
Chris Latvala Campaign
Mr. and Mrs. Donald Sheldon
Tribute(s) for Morgan Johns
Ms. Lynda J. Gresham
Mr. and Mrs. Mark Waters
Tribute(s) for Annie Johnson
Mrs. Shonnie Johnson
Tribute(s) for Thomas Kijak
Mr. and Mr. Michael Kijak
Tribute(s) for Dan F. Klein
Mr. Robert Riker
Tribute(s) for Jay Lamb
Ms. Jane Weathers
Tribute(s) for Oliver Lanier
Ms. Anne K. Lanier
Tribute(s) for Brianna LaVoun
Mr. and Mrs. Edward V. Capoziello
Tribute(s) for Louis Letendre
Ms. Deborah S. Fischer
Tribute(s) for Isabel Madison
Mrs. Diane McSwain

Tribute(s) for James J. Maginn
Ms. Sally Oxley
Tribute(s) for Olivia R. Malatesta
Mrs. Barbara Malatesta
Tribute(s) for Matthew Mastbaum
Mr. and Mrs. Neil Cooperstein
Tribute(s) for Colin McKiernan
Mr. and Mrs. Charles Leffler
Tribute(s) for Diane McSwain
Dr. and Ms. Michael Greenberg
Tribute(s) for Liam Meece
Ms. Katie Sappington
Tribute(s) for Hank Meinart
Anonymous
Tribute(s) for Ethan Merriman
Mrs. Lorraine Houchin
Tribute(s) for Ellie Miller
Mr. Brian Ruttenberg
Tribute(s) for Lindsey Miller
Mr. Brian Ruttenberg
Tribute(s) for Parker Moody
Mr. and Mrs. Ben Ficklen
Tribute(s) for Ashlyn Moore
Anonymous
Hamilton Southeastern Jr. High School
Tribute(s) for Lisa M. Moss
Mr. Landon Cox III
Tribute(s) for Lauren Niemeyer
Mr. and Mrs. Michael Niemeyer

Tribute(s) for Hayley Noakes
Mr. and Mrs. Dwayne Hittie
Tribute(s) for James E. Oliver
Mrs. Mary J. Oliver
Tribute(s) for Allison Parker
Mr. and Mrs. Brian N. Belanger
Tribute(s) for Mary Ann Pastori
Mr. and Mrs. David Scroggins
Tribute(s) for Nicholas Patton
Mr. and Mrs. Kevin Patton
Tribute(s) for Paige Pfeiffer
Mr. and Mrs. William F. Pfeiffer
Tribute(s) for Hillary Poche
Mr. and Mrs. David Rauch
Tribute(s) for Matthew E. Price
Mr. Daniel Silverberg
Tribute(s) for Jaylin Pruitt
Dr. and Mrs. James B. Sims
Tribute(s) for Anthony Rasavage
Mr. and Ms. Mark Rasavage
Tribute(s) for Emma Roche
Anonymous
Mr. and Ms. Thomas Roche
Tribute(s) for Kristine Ross
Ms. Kelly S. Ross
Tribute(s) for Kori Rothweiler
Mr. and Mrs. Lawrence F. Fisher
Tribute(s) for Ryder Schalich
Ms. Kasey Schalich

Tribute(s) for Madalyn Scherer
Mr. and Mrs. Joseph D. Garvey
Mrs. and Mr. Barbara Schneider
Tribute(s) for Mary Ann Scroggins-Pastori
Mr. and Mrs. Gerald E. Nerheim
Tribute(s) for Erika Seward
Mr. and Mrs. Gregory J. Guzley
Mr. and Mrs. Paul Seward
Tribute(s) for Benjamin Shapiro
Mr. Michael Grossman
Tribute(s) for Henry P. Shapiro
Mr. Michael Grossman
Tribute(s) for Christopher S. Sherman
Mrs. Joan Williams
Tribute(s) for Josh Sims
Anonymous
Mr. Jeff Davis
Dr. and Mrs. James B. Sims
Tribute(s) for Meghan J. Sirinek
Mr. and Mrs. Robert Pfeiffer
Tribute(s) for Drew Sklarin
Mr. and Mrs. Melvin Nudelman
Tribute(s) for Emma Smith
Mr. and Mrs. George Corcoran
Tribute(s) for Lily Lowbridge Solise
Mr. and Mrs. Alexander Jamieson
Tribute(s) for Philip Swotkewicz
Mr. and Mrs. Frank Seiling

Tribute(s) for Seth R. Taylor
Ms. Abbey Taylor
Tribute(s) for Benjamin Theis
Mr. Paul Thomas
Tribute(s) for Tyler J. Trapp
Ms. Gail A. Spitzer
Tribute(s) for Gabriel Tripp
Ms. Katie Tripp
Tribute(s) for Emily Un
Mr. Ricky Un
Tribute(s) for Heather Wachter
Mr. and Mrs. Ronald D. Wachter
Tribute(s) for Jay P. Wareham
Mr. and Mrs. Craig S. Wareham
Tribute(s) for Meghan G. Weingarth
Mrs. Jennifer R. Schillig
Tribute(s) for Ilana Wiesel
Mr. and Mrs. Nachum Wiesel
Tribute(s) for Amanda Wiezalis
Mr. and Ms. Carl P. Wiezalis
Tribute(s) for Ashley Wiezalis
Mr. and Ms. Carl P. Wiezalis
Tribute(s) for Mia Wojnilower
Samuel Wojnilower
Tribute(s) for Alyssa Youmans
Mrs. and Mr. Jennifer Davenport
Ms. Marilyn Lembcke
Mr. and Mrs. Jose Ruiz

Memorials (September 1 – November 30, 2022)

Contributions are given to the TSC Alliance® at the request of family members in memory of their loved ones. We extend our sympathies to the family and friends of those memorialized below. These generous contributions support the progress of our mission to find a cure for tuberous sclerosis complex.

Tribute(s) for John K. Allison
Mr. and Mrs. Glen A. Call
Tribute(s) for Micah Amado
Mr. and Ms. Christopher Rosbeck
Tribute(s) for Christina Bardsley
Ms. Courtney Green
Tribute(s) for Jack Beard
Mr. and Mrs. Eugene Mehmert
Tribute(s) for Zach Bernosky
Mrs. Mary Kay Bernosky
Tribute(s) for Ted Bernstein
Anonymous
Tribute(s) for Jane Breyer-Friedman
Mrs. Faith M. Golden
Tribute(s) for Quinn Ramondetta Broome
Mr. and Mrs. Harry Broome Jr.
Tribute(s) for Heather J. Buntrock
ABM Janitorial Services
Tribute(s) for Bonnie Burress
Mr. B.L. Burress
Mr. and Mrs. Cody N. Clyman
Mr. and Mrs. Keith Smith
Ms. Shirley J. Smith
Zion Community Church of God

Tribute(s) for Sherrie Busel
Mr. and Mrs. Harry C. Meyer
Tribute(s) for Michael D. Carey
Mr. and Mrs. Sid Strong
Tribute(s) for Harry Chaifetz
Mr. and Mrs. Mel Chaifetz
Tribute(s) for Martha Chaifetz
Mr. and Mrs. Mel Chaifetz
Tribute(s) for Justin Chermack
Shannon Williams
Tribute(s) for Della Cohen
Mr. and Mrs. Douglas A. Proctor
Tribute(s) for Gertie Cohen
Anonymous
Tribute(s) for Steve Cohen
Mr. and Mrs. Douglas A. Proctor
Tribute(s) for Matthew Colby
Mr. and Mrs. Craig M. Colby
Tribute(s) for Dudley C. Conner
Ms. Jane A. Angle
Tribute(s) for Irene C. Davila
Ms. Robin Hoy
Tribute(s) for Raymond Ecker
Anonymous
Ms. Joan M. Doherty
Mr. Thomas Ecker

Ms. Cynthia A. Kopfman
Ms. Shelly Todd
Tribute(s) for Carol Eliason
Mr. and Mrs. James Butler
Tribute(s) for Gordon Ferrell
Ms. Patricia J. Ahonen
Ms. Jacquelyn L. Tossberg
Tribute(s) for Kate Gilmore
Mrs. Marilyn A. Gilmore
Tribute(s) for Gerda Imke
Ms. Diane Chellis
Tribute(s) for Linda Jarvis
Mrs. Faith M. Golden
Tribute(s) for Imogene Johns
Ms. Lynda J. Gresham
Mr. and Mrs. Mark Waters
Tribute(s) for Ken Johnson
Mr. James Norman
Tribute(s) for Lynne Katz
Ms. Michelle Morgan
Tribute(s) for Helen Larson
Mrs. Miriam S. Green
Tribute(s) for Ashley H. Mackie
Mr. David Brockman
Mr. and Mrs. Jimmie Graham
Mr. Rob Willis

Tribute(s) for Sherril Ann A. Malesky
Mrs. Audrey Malesky
Tribute(s) for Karl Marszalowicz
Anonymous
Tribute(s) for Ty Martin
Anonymous
Mr. and Mrs. James C. Williams
Tribute(s) for James W. McAlevey
Mr. and Mrs. Bruce Fitzmaurice
Tribute(s) for Patricia Porter
Mr. and Mrs. Raymond A. Peterson
Tribute(s) for Tom Price
Anonymous
Ms. Susan Schmitz
Mr. D.A. Wytonick
Tribute(s) for Thorpe Richards
Ms. Miriam Brenner
Ms. Beverley M. Ciccarone
Ms. Terri Hall
Suzanne MacDonald Family Fund
Tribute(s) for Ryder Schalich
Anonymous
Tribute(s) for Larry Scheib
Colt Logistics LLC
Mr. Charles L. Horton
Ms. Pamela J. Johnson

Mr. and Mrs. James Minnis
Mr. and Mrs. Michael Smith
Mr. J.L. Stephens
Mr. Michael D. Walker
Tribute(s) for Jack Schmertzler
Mr. and Mrs. Mel Chaifetz
Tribute(s) for Regina Schmertzler
Mr. and Mrs. Mel Chaifetz
Tribute(s) for Stephen Schmertzler
Mr. and Mrs. Mel Chaifetz
Tribute(s) for Maureen Shea
Mrs. Eleanor Krauss
Tribute(s) for Mary Lou Smoot
Mr. and Mrs. Thomas J. Greene
Tribute(s) for Maureen Stea
Anonymous
Ms. Elizabeth Gibbs-Romanowski
Ms. Kim Lonnborg
Tribute(s) for Donald C. Undercuffler
Mr. and Mrs. Donald Sheldon
Tribute(s) for Sam Von Lintel
Mr. Kevin Bittel
Tribute(s) for Darcy Young
Mr. and Mrs. William Joseph
Tribute(s) for Barbara Zipkin
Mr. and Mrs. Mel Chaifetz

8737 Colesville Road, Suite 400
Silver Spring, MD 20910 USA

The TSC Alliance needs your input

In 2023, the TSC Alliance will update our five-year strategic plan, so we are launching a comprehensive online Constituent Survey to assess what the organization is doing right, identify those things we can do better and lay the groundwork to ensure our planning efforts are on the right track.

The survey takes about 15-20 minutes to complete, and your input will be instrumental to ensure our efforts meet the TSC community's needs. As an incentive to participate, all participants who fully complete the survey will be entered into a drawing to win one of ten $50 Amazon gift cards.

You can make your voice heard online today by going to **www.tscalliance.org/2023survey** or clicking the QR code.

Please note: The survey is open until 12 a.m. (midnight) Eastern Time, Tuesday, March 14. If you experience any difficulties accessing the survey or have additional questions, please email Anne Wolfe at awolfe@tscalliance.org.