



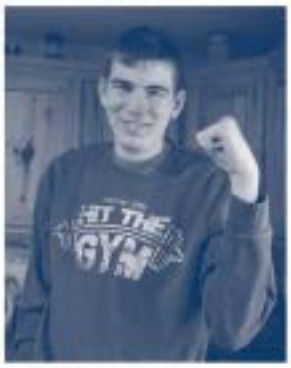
TBRS community












New Family *Welcome* Packet

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tip: **Download or print off the fact sheets and share with your doctors, therapists, and teachers!**

Donate

Welcome. We are so happy you found us!

Dear TBRS Community Friends,

Welcome to a place of hope, understanding, and relentless pursuit of knowledge. As a TBRS mom and as the Executive Director of the TBRS Community, I extend a heartfelt welcome to you and your family. You are now part of a unique family, one that understands the challenges and triumphs of living with Tatton Brown Rahman Syndrome (TBRS). Our mission is clear and steadfast: to support everyone affected by TBRS and to advance research toward interventions.

In the TBRS Community, you will find more than just support; you will discover a family you never knew you had. We recognize that living with a rare disease can be a solitary and daunting journey. That's why we strive to make our community a sanctuary where isolation turns into connection, and fear transforms into hope. Here, you are not alone. You are part of a family that celebrates each other's strengths and provides comfort during challenging times.

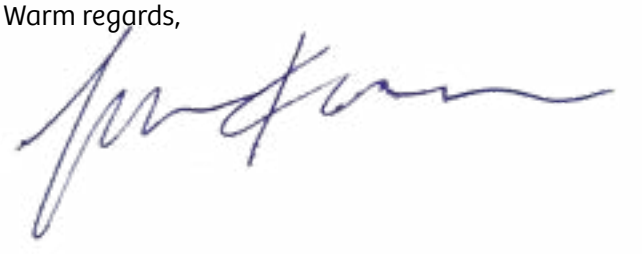
Our passion for supporting families is matched by our dedication to raising awareness and conducting impactful research. The TBRS Collaborative Research Network stands as a testament to this commitment. With over 200 researchers and clinicians, this network is a beacon of hope, driving forward our understanding of TBRS and related conditions. Every program, every research initiative we undertake is patient-focused, echoing the priorities and needs of our community members like you.

In our mission to advance research and interventions, we also encompass Heyn Sproul Jackson Syndrome (HESJAS) and other DNMT3A related disorders within our research program. We believe that by broadening our scope, we can accelerate our understanding and discovery of solutions that benefit our entire community. Together, we are stronger and more capable of unraveling the complexities of these conditions.

As you navigate through our program guide, you will see the breadth of what the TBRS Community has to offer. From support groups to educational resources, every aspect of our community is designed with you in mind. We encourage you to reach out, ask questions, and share your journey with us. Together, we are stronger, wiser, and capable of incredible feats.

Welcome to your new home, the TBRS Community. Here, you will find more than just friends – you will find a family that stands with you every step of the way.

Warm regards,



Our Vision

We envision a world where people affected by rare diseases, like TBRS, have a place to go for answers, support, treatments, and cures. It's as simple as that. Nobody should be left out when it comes to access to health and happiness.

The TBRS Community is turning this vision into reality for our families, while blazing a trail for all those impacted by rare diseases.

Jill Kiernan
Executive Director & Founder
jill@tbrsyndrome.org

New Family *Checklist*

- ☐ Join our private **Facebook Group** or our private platform, **TBRS Family Connect** to meet other families, share resources, and ask questions.
  - ☐ As part of our Regional Coordination Program, we have subgroups within the larger group, to meet the needs of non-English speakers and to provide more individualized support to different regions around the world.
- ☐ Subscribe to our quarterly **newsletter** to get the latest news and events in the Community.
- ☐ Check out our **YouTube channel** to take a peek into the lives of some of our diagnosed families. You can also view the latest presentations from our clinicians and researchers.
- ☐ **Participate in TBRS Research!** There are a lot of opportunities, and we encourage you to start with Count Me In for TBRS and the Patient Registry.
  - ☐ Count Me In for TBRS - Contact Registry (page 7)
  - ☐ Enroll in the TBRS and DNMT3A Patient Registry (page 7)
  - ☐ Patient Priority Survey (page 8)
  - ☐ TBRS Community Biorepository (page 8)
  - ☐ Clinical Research ID (page 8)
  - ☐ Citizen Health (page 9)
  - ☐ Brain Gene Registry (page 9)
- ☐ **Introduce yourself** to the Board of Directors and our Executive Director.
- ☐ Check out **events** and **news updates** on our website.
- ☐ **Get involved** with TBRS Community and volunteer.

tip: **Request a 1:1 meeting with Executive Director, Jill Kiernan, to introduce yourself, ask questions, and get to know the community.**

SCHEDULE HERE

We also have a private Facebook group (for families and individuals with TBRS).
https://www.facebook.com/groups/705487016188994

Newsletter: https://tbrsyndrome.org/blogs-newsletters

Website: tbrsyndrome.org

Email: info@tbrsyndrome.org

Guide to Programs:

Education and Outreach

Meetings with the TBRS Team

We can answer questions, point you to helpful resources, discuss TBRS research, and more. We love to get to know members of our community. https://calendly.com/jill-tbrs

Regional Coordination

Our Regional Coordination Program is recruiting leaders from communities and countries around the world to help provide local resources and support for TBRS families. We are stronger together!

Advocacy

The TBRS Community participates in multiple rare disease advocacy opportunities, including the Rare Disease Diversity Council, Rare Disease Week on Capitol Hill, and more

Education & Outreach Series

The TBRS Community Education and Outreach Series are virtual meetings focused on different topics related to TBRS. Some of these meetings are recorded and can be found on the TBRS Community YouTube Channel.

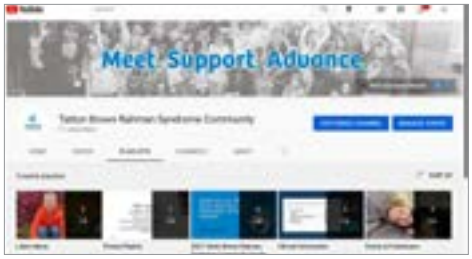
YouTube Channel

The TBRS Community has our own YouTube Channel! This is a great resource to learn more about TBRS by watching previous conferences and presentations from researchers.

- You can meet some of our featured families and share the videos with others who want to learn more about this rare disease.
- The channel is also a wonderful way to inform your doctors, specialists, therapists and teachers who work with your family and to spread awareness.

tip: **Did you know that you can sync the TBRS Community Google calendar to your online calendar so you don't miss any events?!**

Need help with this? Reach out to Kit: kit@tbrsyndrome.org



Check out our YouTube Channel for past recordings of the Family and CRN Conferences and to hear stories of some of our families!

Guide to Programs:

Family Support

Private Facebook Group

The Facebook group is a private and open forum for families and diagnosed individuals to connect with others. It includes updates on research, events, and news from families. Subgroups are available for international patients in a variety of languages and for caregiver-specific support.

TBRS Family Connect

TBRS Family Connect is a secure and private support community for patients, families, caregivers, and individuals impacted by TBRS. It's a place to access educational resources, stay informed about the latest news and research, and connect with others who share similar experiences. Whether you're looking for advice, support, or simply to connect with others, you'll find a welcoming space here.

Parent/Caregiver Virtual Support Group

The TBRS Community offers monthly virtual Support Groups for Parents/Caregivers. Attendees from around the world can participate. We create a safe place to share thoughts, feelings, and concerns without judgment. The meeting seems to take a different shape every time we gather—sometimes we focus on sharing resources or experiences, and we always seek to make everyone feel comfortable and supported.

Social Group for Diagnosed Individuals

Each month a wonderful group of individuals who are diagnosed with TBRS gather for our Social Group. We have a blast with activities that are requested by our group members. You may find us doing anything from dancing and joke telling to karaoke and rock painting. The group is ever evolving and always a fun time. There is no pressure to chat if you are feeling shy, and you don't have to participate in the activity if you would rather just talk.

Regional Meet-ups

The TBRS Community is encouraging and helping to plan regional in-person meet ups around the world. Please reach out if you are interested in organizing a meet-ups near you.

TBRS Cares

The TBRS Community sends care packages out to families in crisis.

For more information please visit our **website**, the **Facebook Group**, **TBRS Family Connect**, or email **info@tbrsyndrome.org** for more information.

"As I sat with my son to help him interact with the group and the trivia, his face was glowing. He communicated few words, but that hour will stay with me."

- Parent Zoe Wisnoski on a social group zoom

Guide to Programs:

Research Participation

The TBRS Community sponsors the full spectrum of research projects to advance our understanding of the syndrome and to accelerate the path to treatments. Our Community and Research Engagement Manager Kit Minor can answer questions and help you keep track of your progress along the way (kit@tbrsyndrome.org). We recommend starting with Count Me In for TBRS and the Patient Registry. Your participation is crucial to supporting people with TBRS!

Count Me In for TBRS

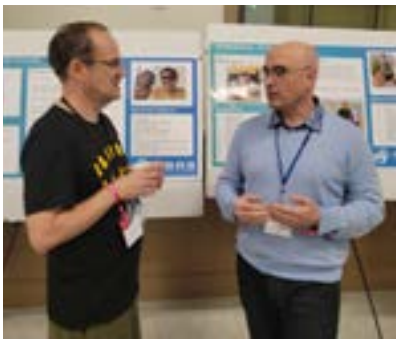
This is a list of contact info for patients and caregivers in our community. We do not share personal information without your consent, and this is an internal document used by TBRS Community staff to know how many individuals are in our community and how to reach them.

- You can choose to be contacted about studies and provide location data so we know where our patients are.
- This is important so we can best advocate for our global community!

Patient Registry

The TBRS Community has developed a Patient Registry in partnership with the National Organization for Rare Disorders (NORD). The registry is a series of surveys that ask about the quality of life, medical history, and development of people diagnosed with **TBRS, Heyn Sproul Jackson Syndrome (HESJAS), and other DNMT3A-related disorders.**

- It is important that all families contribute to the registry as it is an invaluable tool to help us further our understanding of TBRS and advance research so we can move toward identifying treatments, improving medical care, and formulating educational, social, and daily living supports.
- This secure, anonymized database helps clinicians and scientists fully understand TBRS and identify opportunities for research.



"Because of the contributions from TBRS families to our research projects, we know so much more about this syndrome."

Shown here, a family member and researcher collaborating together at the TBRS Summit to enhance their studies based on our contributions.

Guide to Programs:

Research Participation

Patient Priority Survey

The Patient Priority Survey asks about research priorities from patients' and caregivers' perspectives, so that we can fund research that matches your priorities and encourage a patient-driven research agenda in our Collaborative Research Network. This survey was created by the Overgrowth Syndromes Alliance (OSA), and organized by the TBRS Community and Malan Syndrome Foundation with the goal of finding treatments for overgrowth intellectual disability disorders.

- The survey can be completed by patients or caregivers. Contact us with accessibility needs.
- We have zoom meetings with patients who need assistance filling out the survey if needed.
- This is important so we make sure that TBRS research is benefiting patients in the most important ways!

TBRS Community Biorepository

People affected by TBRS and their family members can donate blood, urine, skin cells, and other tissues. These can be used by researchers to understand the science behind TBRS and to accelerate the development of treatments.

- Researchers apply and go through an advisory board to make sure they are researching TBRS and are going to return results to families.
- This is important so that we can get research moving quicker on TBRS!

Clinical Research ID (CRID)

The Clinical Research ID (or CRID) is a unique number that is used to connect patient samples to other research! The patient / caregiver can create this ID without using any personal information, and then it connects these samples in a de-identified way!

- This way, scientists will be able to see Registry data and have a sample for the same patient without knowing any identifiable information, offering researchers a very powerful and informative data set to accelerate research.
- The CRID is required for the Biorepository, but it is optional for the Patient Registry.

"Families have the best knowledge of TBRS - it's so important we share our experiences with doctors and researchers so they can get us the answers we need."

Biorepository collections from the TBRS Summit were critical to our researchers' findings

Guide to Programs:

Research Participation

Citizen Health

Citizen Health is a program that allows patients and/or caregivers to have access to ALL MEDICAL RECORDS! When you sign up with Citizen Health, you give them permission to go to all of your previous hospital systems and clinics to collect this information in one easy place! Many parents have also said that they end up getting back documentation that they have never seen before!

- Additionally, with Citizen Health you are able to choose to share anonymized versions of your medical documents with research! (including our Patient Registry!)
- This is important because it gives researchers a large amount of anonymized information to learn from.

Brain Gene Registry

The Brain Gene Registry is similar to our Patient Registry, but it looks at MANY neurodevelopmental (brain) disorders at the same time to find similarities in symptoms and treatment opportunities. This is run by many academic organizations across the US, including Washington University and Children's Hospital of Philadelphia (to name a few).

- This can help us find insights between disorders and potential similarities that can be used in clinical trials in the future!

? For questions or more information about our research programs, please contact our Contact Community and Research Engagement Manager, Kit Minor: kit@tbrsyndrome.org

Importance of Participating in Research

Participating in research means **real results** for individuals with TBRS! TBRS patients participating in research have already helped scientists to:

- Better understand the features and clinical findings of TBRS
- Estimate the risk of cancer in TBRS
- Make it easier to diagnose patients with TBRS
- Develop research models from patient samples
- Begin learning how TBRS affects the brain
- Create screening guidelines for management

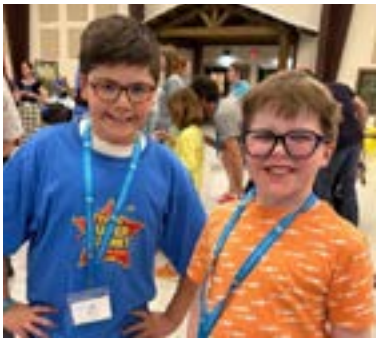
We can also answer patient questions using data from the Patient Registry! From this information, we have learned that cardiac issues, aortic root dilation, seizures, vision and hearing problems, and mental health problems are more common than previously reported.

Guide to Programs:

TBRS Summit

2026 Summit and Future Meetings

In-person Summits are held every other year, alternating with virtual summits every other year. Additionally, we plan meet-ups around the world, because nothing can replace getting together in person. The 2026 Summit was held March 19-22, 2026 at Morgan's Wonderland Camp in San Antonio, Texas. The venue included the first ever fully accessible camp for people of all needs. The Summit included family programming, scientific programming, activities for diagnosed individuals and families alike, cabin-style housing, food and fun!



> **"We went eager to meet people who could relate to us and we could learn from. The doctors, geneticists, TBRS staff, volunteers, and information knocked it out of the park."**
>
> - Katie Brennan, Parent and TBRS Summit attendee

Guide to Programs:

Collaborative Research Network

The TBRS Community Collaborative Research Network (CRN) is at the forefront of transforming research and treatment for TBRS. With over 200 clinicians and researchers united in their mission, the network harnesses a patient-centered research agenda to make strides in understanding and treating TBRS. By utilizing research tools provided by the TBRS Community, the CRN accelerates research and ensures that each project aligns with our comprehensive research roadmap. Witnessing the collaboration and dedication of the CRN is truly inspiring, as it propels partnerships to create impactful solutions for those affected by TBRS.

Research Roundtables

The TBRS Community began holding Research Roundtables for scientists in 2023 to ensure that we know about all up-to-date research efforts and can direct this information to our patient community. We also use this platform to inform our research community on patient priorities and TBRS Community activities and initiatives, and form working groups on specific topics like developing diagnostic, surveillance, and treatment guidelines.

These Roundtables provide a collegial space for researchers to discuss unpublished research, share resources, and collaborate.

Scientific Advisory Panel at the 2023 Summit

Guide to Programs:

Collaborative Research Network

Meet our Scientific and Medical Advisory Committees

Our Scientific and Medical Advisory Committees provide expert leadership on research efforts and clinical care.















Pictured Left to Right:

Harrison Gabel Washington University in St. Louis

William Gibson, University of British Columbia

Timothy Ley, Washington University in St. Louis

Joseph Malak, Bambini Pediatrics

Rachel Rau, Baylor College of Medicine

Marwan Shinawi, Washington University in St. Louis

Kate Tatton-Brown, St. George's University Hospital

Ayala Touy, Novartis/Baylor College of Medicine

Serge McGraw, University of Montreal

Rosanna Weksberg, University of Toronto

Laura Lavery, Rice University

Katherine King, Washington University Medicine

Vicken Totten, Emergency Medicine/TBRS Parent

Marçal Pastor Anglada, University of Barcelona/ TBRS Parent

Irene Valenzuela, Vall d'Habron Hospital

Additional members:

- Kit Minor
- Kerry Grens
- Jill Kiernan
- Keren Shtiegman

Get *Involved!*

Volunteer Teams

Make an Impact! Volunteer efforts are the driving force behind the TBRS Community. Each contribution, big or small, accelerates our progress towards supporting those affected by TBRS. Whether it's fundraising, planning events, advocating, or something else, your unique skills can make a real difference. Join us and help us move faster towards a brighter future for the TBRS community. The TBRS Community has four Teams and volunteers have many opportunities to contribute based on their skills and interests! For more information, email info@tbrsyndrome.org.

Fundraising and Development Team

The Fundraising and Development Team is responsible for coordinating fundraising events, identifying grant and sponsorship opportunities, and designing fundraising campaigns. Available positions include: Thank You Caller, Thank You Letter Writer, Family Fundraiser Coordinator, Grant Prospector, Grant Writer, Sponsor Seeker, and Campaign Writer.

Regional Coordination Team

The Regional Coordination Team is responsible for providing resources and TBRS Community information to diagnosed individuals and families in their region, as well as welcoming new members and planning local events. Available positions include: Regional Coordinator, Meet-Ups Host, Caring Ambassador, and Social / Support Group Facilitator.

Social Media Team

The Social Media Team is responsible for creating TBRS content, developing posts, and identifying photos for media use to promote engagement and awareness of TBRS and the TBRS Community. Available positions include: Photo / Video Content Scout, Reel Maker, Content Writer, and Storyteller.

Advocacy and Policy Team

The Advocacy and Policy Team is responsible for attending advocacy events, sharing stories with lawmakers and media, advising on DEI efforts, and hosting events to raise awareness of TBRS. Available positions include: Advocate, Media Contact Specialist, DEI Advisor, and Awareness Event Host.

> **"Volunteering for the Community has been incredibly rewarding. I get to donate my time to a wonderful organization while making a direct impact on advancing research and programs for TBRS that will ultimately benefit my daughter."**
>
> - Erin Rooker, TBRS Marketing Director and Volunteer of the Year, 2023

About the *Community*

Board of Directors

The TBRS Community Board of Directors is passionately committed to finding effective treatments and individualized support for those affected by TBRS. Their actions are driven by a common goal: to ensure that every person impacted by TBRS experiences the best possible health and happiness. They all volunteer their time to help make our Community a success!

Kacee Richter, *President*

Kerry Grens, *Vice President*

Zoe Wisnoski, *Secretary*

Tim Bernier, *Treasurer*

Erin Rooker, *Marketing Director*

Monica Bejano, *Board Member*

Robert Thibodeau, *Board Member*

Community Staff

Led by Executive Director and Founder, Jill Kiernan, our TBRS Community is supported by these three amazing staff. We are so thankful for all of their hard work and dedication.

Jill Kiernan, *Executive Director and Founder*

Jill is the Founder and Executive Director of the TBRS Community and Co-Founder of the Overgrowth Syndromes Alliance. She advances research and collaboration across rare diseases while ensuring families remain at the center of the organization's work as a TBRS mom.

Kit Minor, MPH, *Community and Research Engagement Manager*

Kit leads community and research engagement initiatives, working with researchers, clinicians, and families to advance TBRS research. She coordinates scientific programming, supports the Collaborative Research Network, and develops resources that address the community's highest priorities.

Róisin DeBonis, *Development and Communications Manager*

Róisin is a communications and development professional with experience in nonprofit fundraising, disability support services, project management, and creative storytelling. She helps strengthen donor engagement, expand community support, and communicate the organization's mission with authenticity and impact.

Jamie Cannon, *Community Experience & Engagement Coordinator*

Jamie brings expertise in community engagement, event planning, stakeholder relations, and operations management. A former Community Liaison Officer at U.S. Embassies worldwide, she helps strengthen connections, coordinate programs, and create meaningful experiences for TBRS Community members.

Colette Corry, *Family and Friends Support Group Co-Lead*

Colette lives in New York City with her husband and son, Luke, who has TBRS. An educator with experience supporting students of all abilities, she is dedicated to fostering connection, understanding, and support among families in the TBRS community.

Jenny Graham-Beeson, *Family and Friends Support Group Co-Lead*

Jenny is a Board Certified Behavior Analyst, advocate, and mother of four whose youngest son has TBRS. Drawing on both professional and personal experience, she helps create a supportive environment where caregivers can connect, learn, and share experiences.

RTW Foundation, *Rare Disease Science Advisor*

Through its Rare Disease Advisory Program, RTW Foundation provides scientific and strategic guidance to the TBRS Community. The foundation partners with rare disease organizations to strengthen research efforts, build capacity, and accelerate progress for patients and families.

Tatton Brown Rahman Syndrome
Fact Sheet

Tatton Brown Rahman Syndrome (TBRS), also referred to as *DNMT3A* Overgrowth Syndrome, is a rare genetic disease caused by variants in the *DNMT3A* gene. There is a wide range of medical issues associated with TBRS but most individuals have a few unifying characteristics:

- **Overgrowth:** TBRS causes children to grow rapidly, and adults with the syndrome are often largely above average in height and weight. Head circumference is also often increased in size (this is referred to by doctors as macrocephaly).
- **Intellectual Disability:** Some individuals have severe cognitive impairment, while others have a mild or moderate disability.
- **Facial Features:** Thick, lowset, horizontal eyebrows, large front teeth, and narrow eye openings are subtle yet distinctive characteristics of people with TBRS. Facial features typically become more recognizable in the teenage years.

TBRS was first described in 2014, and although doctors continue to identify more individuals affected by the syndrome each year, it remains extremely rare, with around 450 people known to have been diagnosed as of 2025. Physicians are still learning about the full spectrum of conditions associated with TBRS. In addition to having the three characteristic features of overgrowth, intellectual disability, and recognizable facial features, some individuals additionally present with **autism, joint hyper-mobility, low muscle tone, kyphoscoliosis, seizures, behavioral and mental health disorders, heart defects, hearing and vision concerns, sleep apnea, early puberty, and blood disorders. There is also evidence to suggest patients have an increased risk of developing cancer, mainly thought to be leukemia.**

There is no cure for TBRS. The needs of individuals with TBRS vary greatly—some are able to live independently with minimal aid, while others require lifelong intensive support and medical care. Because of this variability, it is important to gather a thorough assessment of each person's specific needs and for **families to participate in the Tatton Brown Rahman Syndrome (TBRS) and *DNMT3A* Patient Registry.**

The Gene

The protein produced by the *DNMT3A* gene is involved in a process called DNA methylation, which helps cells determine which genes are turned on or off. Although all cases of TBRS involve mutations or deletions in DNMT3A, the location of the mutation in the gene is not the same for all individuals, with most patients having a unique mutation or deletion of their own.

It appears that most mutations arise from spontaneous changes in the gene (called de novo mutations), rather than mutations inherited from the person's parents. Some individuals may have inherited the *DNMT3A* variant from a parent who has TBRS or does not have TBRS. In the latter case, this is because the mutation can sometimes occur later in development and therefore be present in only certain types of cells (this is called mosaicism). Individuals with mosaicism could have a mutation in *DNMT3A* in sperm or eggs, also called the germline, and therefore possibly pass it down to their children.

Mutations in *DNMT3A* that cause TBRS are heterozygous, meaning they are only on one of the two copies of the gene that each person has. Because each parent provides one copy of a gene, someone with TBRS has a 50 percent chance of having a child with the genetic mutation. Genetic counseling is important to help clarify the inheritance pattern of TBRS.

Clinical Information

Doctors familiar with TBRS recommend meeting with the following clinicians:

- **Cardiologist:** Recent findings show that over half of individuals with TBRS are affected by cardiac conditions, such as valve abnormalities, cardiomyopathy, or aortic root dilation—all of which may develop or worsen over time. It is important for families to discuss cardiac monitoring with their care team, including establishing a baseline echocardiogram and scheduling regular follow-ups to track any changes related to the heart valves, aorta, or heart muscle.
- **Physical therapist, speech therapist, occupational therapist:** For young children, states' Early Intervention programs can screen for eligibility. Older children may access these services through the school district, and adults, through their medical insurance or local adult services programs.
- **Geneticist and genetic counselor:** To coordinate care and screenings, and keep families updated on new developments with the diagnosis
- **Neurologist:** Registry findings suggest that more than half of patients have experienced a seizure, and a large portion of the population presents with neurological conditions. Assessment and surveillance of these conditions are strongly recommended.
- **Hematologist/Oncologist:** A low threshold should be adopted for investigation of potential symptoms of leukemia and other blood conditions/cancers.
- **Dermatologist:** Skin checks are recommended due to the presence of melanoma cases in children and young adults. Abnormal skin biopsies have also been seen in some children.
- **An orthopedic physician, audiologist, ophthalmologist, urologist, pulmonologist, dentist, psychiatrist, or behavioral therapist** should be consulted if specific issues arise.

Cardiac

While not all TBRS patients have a heart condition, these conditions have been seen in a large portion of the population. Over half of individuals in the TBRS and *DNMT3A* Patient Registry have been diagnosed with a heart condition or structural abnormality. Among the most serious concerns is aortic root dilation, which can be progressive and may lead to life-threatening complications such as dissection or rupture. Other reported heart issues include atrial or ventricular septal defects, patent ductus arteriosus (PDA), mitral valve abnormalities, cardiomyopathy, and arrhythmias.

Routine cardiac evaluations—including baseline and follow-up echocardiograms—are recommended starting in childhood. Referral to a cardiologist should be considered for all individuals with TBRS. For more details and the most up-to-date guidance, *please see detailed cardiac information in the **Appendix 1,** attached.*

Blood Disorders and Cancer Risk

Because *DNMT3A* plays a key role in regulating cell growth and DNA methylation, individuals with TBRS may have an increased risk for certain cancers. More research is needed into this subject, but surveillance is recommended for these conditions. At least eight individuals with TBRS have been diagnosed with blood cancers such as acute myeloid leukemia (AML), lymphoma, and other hematologic malignancies. These cancers have occurred in both children and adults. Some individuals have also developed solid tumors,

including melanoma, central nervous system tumors, and other rare cancers. Skin checks and awareness of symptoms such as persistent fevers, unusual bruising, or frequent infections are recommended.

There are currently no formal screening guidelines, but families may consider discussing symptom monitoring and occasional baseline blood testing (such as a Complete Blood Count, or CBC) with their healthcare team. For a more detailed summary of reported cases and surveillance tips, please *see detailed hematology/oncology information in **Appendix 2,** attached.*

Resources

Website: www.tbrsyndrome.org **Email:** info@tbrsyndrome.org

Public Facebook page: https://www.facebook.com/dnmt3aovergrowthsyndrome/

Private Facebook group for families and providers:
https://www.facebook.com/groups/705487016188994/

Registry: https://tbrsregistry.iamrare.org/

Ostrowski PJ, Tatton-Brown K. Tatton-Brown-Rahman Syndrome. 2022 Jun 30. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK581652/

Totten V et al. Arterial aneurysm and dissection: toward the evolving phenotype of Tatton-Brown-Rahman syndrome. J Med Genet. 2024 Aug 29, 61(9): 870-877.

Zebrauskiene D et al. Aortic disease and cardiomyopathy in patients with a novel DNMT3A gene variant causing TBRS. Clin Epigenet. 2024, 16(76).

Disclaimer: The TBRS Community provides this information to support informed clinical decision-making. This fact sheet is not a substitute for medical advice, and we do not provide recommendations for specific treatment. Please consult a qualified healthcare professional for individual medical care.

Updated: *June 2025*

Tatton Brown Rahman Syndrome (TBRS) Cardiac Care and Surveillance Fact Sheet

Background

Tatton Brown Rahman Syndrome (TBRS) is still a relatively new genetic condition, and research is ongoing. The surveillance recommendations published in GeneReviews in 2022 will need ongoing updates as new findings emerge. This fact sheet provides clinicians and families with the most current information by incorporating unpublished data from our TBRS and *DNMT3A* Patient Registry (with over 200 participants) and the latest published research.

Overview of TBRS and Cardiac Concerns

TBRS is a genetic condition caused by pathogenic variants in the *DNMT3A* gene. TBRS is associated with overgrowth, intellectual disability, joint hyper-mobility, hypotonia, obesity, behavioral/psychiatric problems, kyphoscoliosis, seizures, and a variety of other clinical features.

Cardiac Phenotype in TBRS

Individuals with TBRS may exhibit various cardiovascular manifestations, with aortic root dilation being a significant concern reported in multiple cases. Congenital heart defects, including atrial septal defects (ASD), ventricular septal defects (VSD), and patent ductus arteriosus (PDA), have also been observed, though their frequency is still being studied. Less commonly, individual cases of mitral valve prolapse, dilated cardiomyopathy, and arrhythmias have been reported. The increasingly recognized cardiac involvement among individuals with TBRS highlights the need for routine cardiac surveillance.

> **About 54% of the 200 patients in the TBRS and DNMT3A Patient Registry have been diagnosed with a heart condition or structural abnormality.**

Recent research has identified **aortic root dilation** as a significant concern in some individuals with TBRS. These studies have identified more than 15 cases of aortic dilation or dissection in individuals with TBRS, encompassing pediatric and adult patients. **The cases span from childhood to middle adulthood, and some patients experience rapid progression of aortic dilation.** The aortic root dilation is of varying degrees of severity and can be associated with other cardiovascular issues, including mitral valve abnormalities and arrhythmias. Dissection and rupture are potentially life-threatening complications, and emergency surgery for aortic dissection has been documented.

Key Takeaways for Clinicians

- Routine cardiovascular surveillance is essential for individuals with TBRS.
- Aortic root dilation can be progressive, emphasizing the need for regular echocardiograms starting in childhood.
- Referral to a cardiologist should be considered for all TBRS patients.
- TBRS is still a newly identified condition, and more data are needed to develop formal surveillance guidelines. The TBRS Community continues to collect and analyze data through its Patient Registry to support further research and clinical recommendations.

Surveillance Recommendations

The last updated surveillance guidelines for TBRS were published in GeneReviews in 2022 (**prior to the aortic dilation findings**) and can be found here: https://www.ncbi.nlm.nih.gov/books/NBK581652

The cardiac recommendations from GeneReview suggest (please see GeneReviews for complete information):

- **Recommended Cardiac Evaluations Following Initial Diagnosis:** Baseline echocardiogram to assess structural heart defects and aortic dilation
- ***Ongoing Surveillance Recommendations:*** Echocardiogram to assess aortic root indices: Ongoing surveillance to be determined by size of aortic root, advice of cardiologist, health care framework, and data from longitudinal studies

Recent Findings on Aortic Dilation in TBRS

Recent studies have identified 15 cases of aortic dilation or dissection in individuals with TBRS. Cases include both children and adults, with some experiencing rapid progression over time. Below is a summary:

Age of individual (years)	Description of aortic root dilation	Progressive (yes/no)
40	Near-complete ascending aortic dissection requiring emergency surgery	not known
16	Aortic dilation detected post-genetic diagnosis	Yes: rapid progression
10	Aortic root dilation detected during workup for severe pectus excavatum	Yes
39	Aortic root dilation at 44 mm requiring surgery	Yes
14	Mild aortic dilation with mitral regurgitation	not known
10	Aortic dilation	No
30	Aortic root dilation at 49 mm, with a history of mitral leaflet billowing	not known
16	Aortic root dilation with mitral regurgitation	not known
30	Aortic root dilation at 57 mm, requiring surgery	not known
34	Aortic root dilation diagnosed in adolescence at 35 mm	Yes
38	Diagnosed with aortic root dilation at 41 mm	not known
27 & father of unknown age	Father and son with *DNMT3A* variant; both had aortic dilation, mitral valve prolapse, and arrhythmia	not known
49	Ruptured iliac aneurysm requiring emergency stenting; subsequent complications	Yes
6	Enlarged aortic valve, progressed from 24 mm to 29 mm by age 10	Yes

Citations

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Tatton Brown Rahman Syndrome (TBRS) Blood and Cancer Fact Sheet

Overview

Tatton Brown Rahman Syndrome (TBRS), caused by pathogenic variants in the *DNMT3A* gene, is associated with overgrowth, intellectual disability, hypotonia, obesity, increased risk of malignancy, cardiac disorders, seizures, and other features. Because *DNMT3A* plays a key role in regulating cell growth and DNA methylation, researchers believe it may also contribute to an increased risk of developing certain cancers.

Tatton-Brown-Rahman Syndrome (TBRS) is still a relatively new genetic condition, and research is ongoing. The surveillance recommendations published in GeneReviews in 2022, will need ongoing updates as new findings emerge. This fact sheet is designed to provide clinicians and families with the most current information by incorporating unpublished data from our TBRS and *DNMT3A* Patient Registry (with over 200 participants) and the latest published research. As we continue to gather insights, we will update this reference sheet.

While it will take many more years and larger studies to fully understand cancer risk in TBRS, early findings suggest the importance of cancer surveillance—particularly for blood cancers like leukemia and solid tumors.

What We Know About Cancer Risk in TBRS

- **Leukemia and Other Blood Cancers:** Research has shown that individuals with TBRS may be at increased risk for **acute myeloid leukemia (AML), lymphoma,** and other hematologic malignancies. To date, at least 8 cases of hematologic cancer have been reported in individuals with TBRS. These cancers have appeared in both children and adults, with a **median age of diagnosis around ten years.**

- **Melanoma and Other Solid Tumors:** A recent publication reported the first known case of melanoma in an adult with TBRS, with genetic evidence suggesting that *DNMT3A* deficiency contributed to tumor development. Two additional melanoma cases have been reported in the TBRS Community, but are not published in the literature. There have also been rare reports of central nervous system and peripheral tumors.

Key Takeaways for Families and Clinicians

- **Know the signs and symptoms of leukemia:** These include persistent fevers, fatigue, easy bruising, unusual bleeding (like nosebleeds or petechiae), pallor, swollen lymph nodes, or frequent infections.

- **Skin exams should be part of routine care.** Families should regularly check for new or changing moles or skin lesions, and a dermatologist may be helpful for ongoing surveillance.

- **No formal guidelines exist yet.** Surveillance decisions should be discussed with your medical team and may depend on age, personal and family history, and advice from specialists. As there is no good screening test for blood cancers, and there is no generally agreed-upon routine monitoring. Having a blood test called a complete blood cell count (CBC) done once when you are healthy and not having symptoms could be helpful to establish your normal baseline values. If any symptoms concerning a blood cancer occur, blood tests, including a CBC, should be done immediately. Some experts have suggested doing CBCs yearly, but no consensus has been reached.

Suggested Surveillance

These are not clinical recommendations, but areas to consider discussing with your healthcare provider:

Area of Concern	Suggested Screening Tool	Frequency	Notes
Blood cancers	Complete Blood Count (CBC)	Anytime symptoms develop	Have a routine CBC done to establish baseline values
Skin cancer	Skin check (self or clinical)	Monthly self-exams	
Yearly exams by your doctor, early referral to a dermatologist for any concerning lesion	Patients in the TBRS Community report precancerous skin biopsies, melanoma, and other skin cancers, even in early childhood, suggesting skin checks should be done regularly.		
Other solid tumors	Based on symptoms	No routine surveillance guidance exists	Referral as clinically indicated.

Research indicates that TBRS may predispose individuals to both hematologic (blood-based) and solid tumors. As of now:

- At least 8 individuals with TBRS have been diagnosed with hematologic cancers, including acute myeloid leukemia (AML), B-cell acute lymphoblastic leukemia (B-ALL), Hodgkin lymphoma, essential thrombocythemia, and T-lymphoblastic leukemia.
- These diagnoses range from early childhood to adulthood, with a median age of diagnosis around 10 years.
- One individual developed chronic multi-lineage cytopenias, which may represent a cancer predisposition or pre-leukemic condition.
- Three individuals have been reported with melanoma. One of these cases had lymph node metastasis, along with a previous rare tumor (dermatofibrosarcoma protuberans).
- There are also three reported cases of central and peripheral nervous system tumors, including medulloblastoma, pituitary adenoma, and ganglioneuroma.

Table of Published Cancer Cases in TBRS

Case #	Cancer Type	Age at Diagnosis	DNMT3A Variant	Notes	Source
1	Acute Myeloid Leukemia (AML)	12	R882C	NPM1, NF1, MYC mutations; remission after treatment	Ferris et al. 2022
2	B-cell Acute Lymphoblastic Leukemia	9	R882H	Alive; details of mutations unknown	Ferris et al. 2022
3	T-lymphoblastic Leukemia (post GNBL)	6 (GN), 6 (T-ALL)	R882H	Passed away; metastatic ganglioneuroblastoma prior to T-ALL	Balci et al. 2020
4	Chronic multi-lineage cytopenias	5	Y528X	Possible pre-leukemic condition	Ferris et al. 2022
5	AML	20	I310F	Received allogeneic transplant	Ferris et al. 2022
6	Hodgkin Lymphoma	27	Y735C	Treated with autologous transplant; alive	Ferris et al. 2022
7	Essential Thrombocytosis	34	R882H	Deceased	Ferris et al. 2022
8	AML	15	R882C	Co-mutation PTPN11T73I; alive 8 years later	Ferris et al. 2022
9	AML	12	Y735S	Alive 12 years later	Ferris et al. 2022
10	Melanoma (Stage IIIA)	34	F414fs (germline), R749C (somatic)	Also had prior dermatofibrosarcoma protuberans at age 20	Chen et al. 2023
11	Medulloblastoma	Child	Not specified	CNS tumor	GeneReviews
12	Pituitary adenoma	Child	Not specified	CNS tumor	GeneReviews
13	Ganglioneuroma (with T-ALL)	6	R882H	Reported as part of case #3 above	Balci et al. 2020

**Patient #10 has since passed away at 39 years old from metastatic melanoma.*

Importantly, additional cancers have been reported anecdotally by families in the TBRS Community Facebook group. These have not yet been included in the published literature.

Why Surveillance Matters

Because cancer risk in TBRS is not fully defined, **early detection** through symptom awareness and basic screening may improve outcomes. Several TBRS families have shared personal stories where early recognition led to timely care.

Additional Resources

- TBRS and DNMT3A Patient Registry: tbrsregistry.iamrare.org
- Hematologic malignancy risk: Ferris et al., Blood 2022
- Melanoma case study: Chen et al., Mol Case Stud 2023
- GeneReviews TBRS Entry: NCBI GeneReviews

Disclaimer: The TBRS Community provides this information to support informed clinical decision-making. This fact sheet is not a substitute for medical advice, and we do not provide recommendations for specific treatment. Please consult a qualified healthcare professional for individual medical care.