6th International KAT6A and KAT6B Conference

Baltimore, USA | June, 2025

Summary

This report is designed for scientists, clinicians, and families with a child affected by KAT6A or KAT6B gene variations. Its purpose is to:

- **Summarize the scientific sessions**
- **Identify gaps and bottlenecks in current projects and outline the resources needed to address them**
- **Propose a strategy to generate these resources**
- **Outline the next steps to support the KAT6 Foundation's mission**

By addressing these points, we aim to advance understanding and support for individuals with KAT6A or KAT6B gene variations.

ABSTRACT

The KAT6 Foundation organized the **6th International KAT6A and KAT6B Conference,** a collaborative event centered around patients. The main objective was to strengthen international research on KAT6A and KAT6B and facilitate open discussions among families, clinicians, and researchers. The conference provided a platform for the KAT6 community to expand its network and establish connections among families and experts in the field. The event had 210 registrants, including 58 families and 20 scientists from the USA and around the world.

Held in Baltimore, USA, the one-day conference covered a wide range of topics, including personalized medicine, the role of iPSC cell lines, neuropsychological assessments, generation of accurate animal models to study KAT6 gene variations, advocacy, the KAT6A and KAT6B patient registry, and initiatives by the KAT6 Foundation, such as the KATwalk.

During the conference, the KAT6 Foundation assisted three research groups by facilitating family participation in research data collection. This year, the foundation also hosted three workshops for families on speech, advocacy, and a round table with Dr. Kelley. These workshops were highly praised for providing opportunities to learn and practice new skills and brainstorm various topics related to the health of children with KAT6A and KAT6B gene variations.

Scientific Sessions

Natacha Esber
Director of Science and Research
KAT6 Foundation

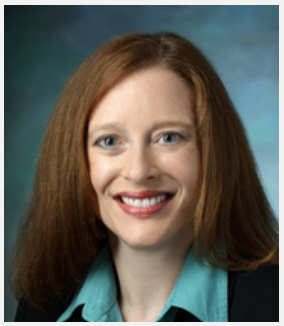
Jordan Muller
Chairperson
KAT6 Foundation Board

Dr. Natacha Esber, Director of Science and Research at the KAT6 Foundation opened the scientific session by highlighting the importance of studying KAT6A and KAT6B gene variations and driving therapeutics research to support children and families affected by these disorders.

Mr. Jordan Muller, Chairperson of the Board of the KAT6 Foundation, moderated the scientific presentations.

Scientific Sessions

Dr. Jill Fahrner MD, PhD
Molecular and Epigenetics Researcher
Kennedy Krieger Institute
John Hopkins Medicine
Baltimore, USA



Introduction

Dr Jill Fahrner provides an insightful exploration of KAT6 syndromes within the broader category of Mendelian disorders of the epigenetic machinery (MDEM). Drawing on her clinical and research experience at Johns Hopkins, she weaves together both bedside and bench perspectives, highlighting the clinical diversity, shared molecular mechanisms, and emerging therapeutic avenues for this group of disorders.

Overview of Mendelian Disorders of the Epigenetic Machinery

MDEMs are genetic conditions caused by pathogenic germline variants in genes that encode key components of the epigenetic system. These genes are functionally categorised into four main groups: writers, which are enzymes responsible for placing epigenetic marks such as acetylation or methylation on DNA or histones; erasers, which remove these marks; readers, which recognise and interpret the marks to influence gene activity; and remodelers, which physically alter chromatin structure to regulate access to the DNA. Together, these components maintain the dynamic regulation of gene expression essential for normal development and cellular function.

Role of KAT6A and KAT6B in Epigenetic Regulation

KAT6A and KAT6B are "writer" genes that add acetylation marks to histones, thereby enabling a more open chromatin structure and promoting gene expression. A loss of function in these genes leads to an imbalance—tipping the scale towards gene silencing. However, Dr Fahrner emphasises that the pathophysiology is not always straightforward; there may be different mechanisms at play, even within the same gene group.

When these "writer" functions are impaired, the chromatin state is altered, leading to widespread disruptions in gene expression. This imbalance results not only in direct gene silencing but also in indirect downstream effects due to misallocation of chromatin-modifying proteins elsewhere in the genome.

Scientific Sessions

Direct and Indirect Effects on Gene Expression

At Johns Hopkins, Dr Fahrner directs a multidisciplinary clinic for individuals with MDEMs. Over a five-year period, the clinic saw 432 patients—more than half from outside Maryland and spanning three continents. Among them, 153 had confirmed epigenetic conditions with pathogenic variants in 26 different genes, most commonly in "writer" genes.

The clinic's team includes geneticists, neurologists, genetic counsellors, and neuropsychologists. They offer diagnostic evaluations and tailored care plans, while also conducting research to better understand these rare conditions.

Dr Fahrner notes that intellectual and developmental disabilities are present in 100% of patients with MDEMs evaluated, ranging from mild cognitive impairment to profound intellectual disability. Although the chart illustrating this data did not display correctly during her talk, she reiterated the significance of neurodevelopmental impacts in this patient group.

Current Management is Symptomatic

Currently, treatment options for KAT6A, KAT6B, and other Mendelian Disorders of the Epigenetic Machinery (MDEMs) are limited to symptomatic management. Standard care typically involves early intervention through developmental therapies, special education support, and the use of communication aids. Patients also undergo routine screenings to monitor for associated conditions, including cardiac, vision, gastrointestinal, and hearing issues, as well as sleep studies and brain imaging when indicated. However, there are no existing therapies that address the underlying epigenetic abnormalities, underscoring a critical and unmet need for targeted treatment approaches.

A New Therapeutic Concept: Rebalancing Chromatin States

Dr Fahrner introduces an emerging therapeutic approach focused on restoring chromatin balance by pharmacologically targeting the opposing components of the epigenetic machinery.

For example, if a “writer” like KAT6A is defective, one strategy may be to inhibit the opposing “eraser” enzyme. This could help rebalance the chromatin state and normalise gene expression.

Such strategies take advantage of the fact that unlike DNA mutations, epigenetic marks are reversible and can be targeted by small molecule drugs. Some such compounds already exist, originally developed for cancer or other diseases, and may have repurposing potential for MDEMs.

Scientific Sessions

Proof-of-Concept from Weaver Syndrome Research

Dr Fahrner's lab explored a novel therapeutic approach using a mouse model of Weaver syndrome, a distinct Mendelian disorder of the epigenetic machinery caused by pathogenic variants in the EZH2 gene—a "writer" enzyme responsible for placing the H3K27me3 repressive mark. The mutant mice exhibited phenotypes consistent with the human condition, including excessive somatic growth, heightened osteoblast activity, and upregulation of genes involved in bone formation. To counteract the effects of the defective writer enzyme, the team treated the mice with GSK-J4, a small molecule inhibitor targeting the opposing "eraser" enzyme. This intervention successfully normalised osteoblast function. Furthermore, RNA sequencing demonstrated that treatment with GSK-J4 reversed gene expression changes in 97% of the genes affected by the EZH2 mutation, suggesting significant therapeutic potential. The next phase of this research involves testing the treatment in vivo to assess its effectiveness across the whole organism.

Concluding Thoughts

Dr Fahrner concluded her presentation by emphasising three key takeaways. First, KAT6 syndromes are part of a wider group of Mendelian disorders caused by dysfunction in the epigenetic machinery. Second, although these are genetic conditions, their impact extends across the genome through disrupted epigenetic regulation, leading to complex neurodevelopmental and multisystem manifestations. Finally, she highlighted the potential for targeted therapies that modulate epigenetic marks—offering a promising direction for future treatments that go beyond symptom management and address the root molecular mechanisms of these disorders.

Scientific Sessions

Jacqueline Harris
Pediatric Neurologist

Rowena Ng
Pediatric Neuropsychologist

Kennedy Krieger Institute & John Hopkins School of Medicine
Baltimore, USA

Overview and Objectives

Dr. Harris and Dr, Ng provided a comprehensive overview of KAT6A and KAT6B syndromes, focusing on their genetic and epigenetic aspects, clinical features, cognitive and behavioral phenotypes, and recent research findings. The primary objectives were to discuss these syndromes from both genetic and epigenetic perspectives, highlight Mendelian disorders of the epigenetic machinery (chromatinopathies), and examine the clinical and genetic manifestations of these disorders.

Part 1: Presented by Dr. Jacquiline Harris

Dr. Jacquiline Harris opened the presentation by introducing the KAT6A and KAT6B genes and outlining their biological roles. She explained that both genes are involved in histone acetylation, a process critical for chromatin remodelling and gene transcription. Mutations in these genes disrupt normal gene expression during development, leading to syndromic neurodevelopmental delays. Dr. Harris then summarised the cognitive and developmental profiles observed in children with KAT6A and KAT6B-related disorders, drawing primarily from clinical observations and caregiver-reported assessments. Key features include global developmental delay—typically moderate to severe across motor, language, and cognitive domains—and significant speech and communication difficulties, with expressive language often more affected than receptive. While some individuals are non-verbal, others rely on augmentative and alternative communication (AAC). Intellectual disability is common, with varying levels of severity, and many children experience motor impairments such as hypotonia, delayed milestones, and coordination difficulties. Behaviourally, individuals often display a friendly and social demeanour, though some also experience anxiety, hyperactivity, or repetitive behaviours.

Scientific Sessions

Dr. Harris presented preliminary data from neurodevelopmental assessments, including cognitive testing and adaptive functioning measures like the Vineland Adaptive Behaviour Scales, indicating overlapping but distinct profiles between the two syndromes—KAT6A being more frequently associated with significant speech delays, whereas KAT6B showed greater variability. She also highlighted how environmental influences and access to therapies significantly shape developmental outcomes, emphasising the importance of early intervention, speech therapy, and inclusive educational strategies, while acknowledging the limited research available due to the rarity of these conditions.

Part 2: Presented by Dr. Rowen Ng

Dr. Rowen Ng continued the presentation by delving deeper into the behavioural characteristics, caregiver experiences, and broader implications for ongoing support in individuals with KAT6A and KAT6B syndromes. She emphasised that although these conditions are individually rare, their impact on the quality of life for families is profound. Drawing on caregiver surveys and interviews, Dr. Ng highlighted the everyday challenges and lived experiences of those caring for affected individuals. She noted that social engagement is often a relative strength, with many children demonstrating affectionate and interactive behaviours. Adaptive functioning profiles typically show stronger skills in socialisation and daily living, while communication and motor domains are more impacted. Dr. Ng also pointed out common behavioural concerns, including sensory sensitivities, attention difficulties, and self-stimulatory behaviours such as hand-flapping and rocking. Some children may display features characteristic of autism spectrum disorder (ASD), though not all meet diagnostic criteria. She discussed emerging insights from functional assessments and classroom observations, noting that individualised support strategies—such as the use of augmentative and alternative communication (AAC) tools, structured routines to manage anxiety, and sensory integration activities—can contribute to meaningful developmental gains. Dr. Ng also highlighted the emotional and logistical burden on families, many of whom endure lengthy diagnostic processes and face a lack of targeted resources. She stressed the importance of peer support networks, multidisciplinary care, and educational advocacy in navigating these challenges. Concluding her presentation, Dr. Ng underscored the need for personalised approaches, given the variability in strengths and difficulties across individuals. She advocated for continued research efforts, including patient registries and longitudinal studies, to advance understanding and improve outcomes for those with KAT6A and KAT6B syndromes.

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Key Takeaways

KAT6A and KAT6B are rare neurodevelopmental syndromes resulting from mutations in chromatin-modifying genes, and are characterised by developmental delays, intellectual disability, and significant expressive language impairment. Although behavioural profiles vary, many individuals are socially motivated and may also display signs of anxiety, sensory sensitivities, or self-regulatory difficulties. Personalised therapy plans, including the use of augmentative and alternative communication (AAC), alongside multidisciplinary support, are critical in promoting developmental progress and improving quality of life. Families often encounter challenges in securing timely diagnoses, coordinating care, and accessing appropriate resources, highlighting the urgent need for greater awareness, clinical guidance, and tailored supports. This presentation offered a comprehensive overview of the current understanding of KAT6A and KAT6B syndromes and served as a call to action for continued research, enhanced clinical recognition, and strengthened community support for affected individuals and their families.

Scientific Sessions

Dr. Sandeep Sreerama
MD-PhD candidate
Center for Regenrative Medicine, Serrano Lab
Boston University, USA

The KAT6 Epigenetic Fingerprint: What KAT6 Blood Cells Reveal About Development and Disease

Dr. Sandeep Sreerama explored how blood cells from individuals with KAT6A and KAT6B syndromes provide unique insight into human development and disease. His research focuses on understanding the epigenetic fingerprint which includes the distinct patterns of histone modifications found in these individuals' cells. These patterns may illuminate how disruptions in chromatin regulation influence early development, neurodevelopmental outcomes, and disease progression.

Background and Research Aim

Dr. Sreerama began the presentation by outlining the scientific foundation of the study, highlighting the critical roles of the KAT6A and KAT6B genes in chromatin modification, particularly through histone acetylation. This process serves as a key regulatory mechanism for gene expression, functioning like an "on/off" switch for different parts of the genome. When mutations disrupt the normal function of KAT6A or KAT6B, the resulting misregulation of gene expression during development can lead to a wide range of cognitive, physical, and behavioral differences. The central aim of the research is to map the histone modification landscape—or "epigenetic fingerprint"—in individuals with KAT6 mutations using their blood cells. By analysing these patterns, the research team seeks to better understand how KAT6 mutations affect the development and function of blood and neural cells, create disease models that can be used to explore potential therapies, and identify biomarkers that could help predict the severity of symptoms or a person's likely response to treatment.

What Makes KAT6A/B Cells Unique?

Dr. Sreerama discussed how patient-derived blood cells, specifically Peripheral Blood Mononuclear Cells (PBMCs), offer a window into the body’s systemic epigenetic environment. By using fluorescent antibodies that bind to specific histone marks, his team could visualize and quantify differences in how genes are regulated in KAT6-mutant versus healthy cells.

These histone marks vary in intensity across cell types. Some marks (e.g. H3K27me3 or H3K9ac) are associated with gene repression or activation. In KAT6-deficient cells, the presence and distribution of these marks change, creating a unique cellular "fingerprint."
Through high-dimensional data analysis and clustering, the team was able to categorise PBMCs into various immune cell subtypes. Each cluster showed differences in histone marks — even among cells of the same lineage — suggesting that the impact of KAT6 mutations is widespread and context-dependent. In simpler terms, the mutation doesn't just impact one cell type; it alters how many different cells behave at the epigenetic level.

Development of Disease Models Using Stem Cells

To deepen their understanding of how KAT6 mutations influence development, Dr. Sreerama and his team reprogrammed blood cells from individuals with KAT6A or KAT6B mutations into induced pluripotent stem cells (iPSCs). These iPSCs mimic early embryonic cells and have the capacity to differentiate into any tissue type, including neurons and cardiac cells. This model enables researchers to study the effects of KAT6 mutations on early developmental processes, monitor epigenetic changes over time, and generate organ-like structures—such as brain cells—in the laboratory to more accurately model disease mechanisms. A key advantage of using iPSCs is their ability to serve as a renewable and widely distributable source of KAT6-specific cells, fostering collaboration across research groups and accelerating efforts to evaluate potential treatments using human-derived cellular models.

The Vision: From Fingerprints to Prognostics

To deepen their understanding of how KAT6 mutations influence development, Dr. Sreerama and his team reprogrammed blood cells from individuals with KAT6A or KAT6B mutations into induced pluripotent stem cells (iPSCs). These iPSCs mimic early embryonic cells and have the capacity to differentiate into any tissue type, including neurons and cardiac cells. This model enables researchers to study the effects of KAT6 mutations on early developmental processes, monitor epigenetic changes over time, and generate organ-like structures—such as brain cells—in the laboratory to more accurately model disease mechanisms. A key advantage of using iPSCs is their ability to serve as a renewable and widely distributable source of KAT6-specific cells, fostering collaboration across research groups and accelerating efforts to evaluate potential treatments using human-derived cellular models.

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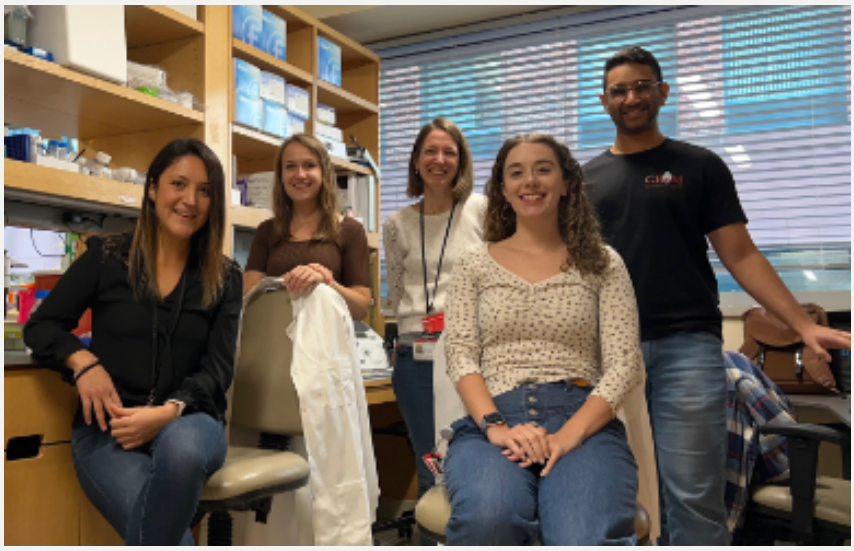
Challenges and Next Steps

Dr. Sreerama acknowledged that the research is still in its early stages, with several notable challenges ahead. One major hurdle is the rarity of patient samples, which limits the ability to conduct large-scale studies. Additionally, interpreting high-dimensional epigenetic data is inherently complex, requiring advanced analytical tools and expertise. There is also a pressing need to validate initial findings across larger and more diverse cohorts to ensure their reliability and generalisability. Despite these challenges, Dr. Sreerama emphasised the critical importance of advancing this research, highlighting the need for ongoing collaboration to expand access to samples, improve analytical methods, and ultimately accelerate the translation of scientific insights into meaningful clinical applications

Concluding Thoughts

Dr. Sreerama concluded with a message of hope and determination. He acknowledged the vital contributions of the KAT6 community — from families providing samples to researchers and clinicians pushing boundaries. The presentation reinforced the idea that although KAT6A/KAT6B syndromes are rare, they are incredibly powerful models for understanding gene regulation, development, and disease.

By combining patient-derived samples, stem cell modelling, and advanced epigenetic profiling, the team at Boston University is laying the groundwork for a future where diagnosis is quicker, treatments are personalised, and outcomes are significantly improved for individuals with KAT6 syndromes.



Scientific Sessions

Ms. Zoe Goldstone-Joubert
Genetic Counseling Student

Dr. Paul Marcogliese
Biochemistry and Genetics Researcher

Rady College of Medicine, University of Mannitoba, Canada

Presentation title: Understanding the spectrum of KAT6A and KAT6B variants using fruit floes

Dr. Paul Marcogliese and Genetic Counseling MSc candidate, Zoe Goldstone-Joubert presented their work on Drosophila (fruit fly) models of KAT6A and KAT6B. The majority of the work uses the fruit fly as a “living test tube” to find out if the various KAT6A and KAT6B changes (ie variants) that patients have show differing impact when the human KAT6A and KAT6B variants are expressed in the fly. They hypothesized that since there is a wide range of clinical symptoms between patients with KAT6A and KAT6B disorders, the variants may have different mechanisms. This is what they found. They showed in the flies that KAT6A truncations (nonsense and frameshift) act differently from each other depending on where the truncation is in the protein. Surprisingly, all eight KAT6A missense variants tested acted as something called a gain-of-function. This is surprising as there is a wide assumption that the disorder is caused by loss of function. Truncations in KAT6B also varied in impact depending on the location of the truncation, while KAT6B missense variants seemed to mostly be loss of function. In parallel, the Marcogliese lab is selectively reducing the levels of the single KAT6A and KAT6B sister fruit fly called enok in developing and adult neurons. These flies have lifespan and motor deficits, and the lab is currently screening drugs to rescue these symptoms in the fly model. Further validation in the flies and confirmation in mammalian cells is needed, but the fruit fly offers a rapid system for testing patient-specific variant impact and may lead to precision medicine models.

Scientific Sessions

Ms. Paulina Varella Castillo
PhD Candidate
Dr. Xiang-Yao Zhang's lab, McGill University

Presentation title: A Highly Efficient Mutagenesis Method to Engineer KAT6 and Other Gene Variants for Functional Analyses.

In this presentation, Ms. Paulina Varela Castillo introduced a novel and efficient mutagenesis method designed to engineer patient-derived mutations in KAT6A, KAT6B, and other genes for use in functional studies. Her work aims to accelerate the study of rare neurodevelopmental disorders by improving the speed, accuracy, and scalability of DNA editing in the laboratory. As part of Dr. Xiang-Yao Zhang's lab at McGill University, which specialises in the study of epigenetic regulators, Ms. Varela Castillo has focused on developing tools to bridge the gap between molecular biology techniques and the clinical understanding of rare genetic mutations.

Background: Understanding KAT6 Mutations

Ms. Varela Castillo began with an overview of gene mutations, distinguishing between inherited and de novo variants. Most KAT6A and KAT6B mutations are de novo, meaning they occur spontaneously during early development and are not inherited from a parent. These mutations—ranging from single base changes (missense) to more severe alterations such as nonsense or frameshift mutations—can disrupt the structure and function of the KAT6A or KAT6B proteins, both of which are critical components of histone acetyltransferase complexes involved in chromatin regulation and gene expression.
Because these genes operate within larger protein complexes, a mutation in KAT6A or KAT6B can impact the assembly or function of the entire complex, leading to downstream effects on neurodevelopment. However, the clinical impact of many patient-identified mutations remains uncertain. Thousands of KAT6A/B variants are classified as "variants of uncertain significance" (VUS), meaning their role in disease is unknown. This presents a major barrier to diagnosis and treatment planning.

The Role of Site-Directed Mutagenesis

To address this, Ms. Varela Castillo presented site-directed mutagenesis as a powerful molecular biology tool that enables researchers to recreate specific patient-derived mutations in the lab. By introducing these mutations into DNA sequences with high precision, scientists can evaluate their functional consequences—such as whether they impair protein activity or disrupt interaction with other components of the histone acetyltransferase complex.
Traditionally, the gold standard for site-directed mutagenesis has been the QuickChange method, which relies on long complementary primers and the Pfu polymerase. However, this approach is slow, costly, and often unreliable—particularly when working with large DNA plasmids like those containing full-length KAT6A or KAT6B genes (over 12,000 base pairs). Generating a single mutation using this method can take weeks and may fail entirely.

Implications for KAT6 Syndromes Development of the P3 and P3A Methods

To overcome these limitations, Ms. Varela Castillo and her team developed two improved mutagenesis protocols: P3 and its enhanced version, P3A. These methods optimise PCR conditions, polymerase selection, and primer design to significantly increase editing efficiency and speed.
The key innovation in the P3A method is the use of primers with 3' overhangs, which improve the stability and reliability of DNA synthesis during PCR. By testing different polymerases, such as Q5 and SuperFi II (the most accurate commercially available enzymes), the team achieved up to 100% efficiency in generating precise mutations. This made it possible to rapidly introduce patient mutations into large plasmids in under a week—dramatically outperforming the QuickChange method.

Application to KAT6 and Beyond

Using these methods, the team successfully engineered 10 different KAT6A mutations with an average success rate of 80%., and 9 KAT6B mutations with a success rate of up to 96%.
These variants were introduced into mammalian expression vectors and tested in human cells to assess whether they caused functional disruptions—such as impaired histone acetylation—using antibody-based detection of histone marks.

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Importantly, Ms. Varela Castillo highlighted that the utility of the P3 and P3A methods extends well beyond KAT6. Her lab has already applied the technique to over 20 expression vectors, covering more than 100 mutations across diverse genes, including epigenetic regulators like KAT8 and P300, as well as viral genes such as those encoding the SARS-CoV-2 spike protein. The methods are also adaptable to vectors with high GC content and can support cassette mutagenesis, allowing for large DNA insertions, deletions, or fragment replacements without relying on CRISPR or recombination systems.

Concluding Thoughts

In closing, Ms. Varela Castillo highlighted three key takeaways from her presentation. First, the P3 and P3A mutagenesis methods provide fast, reliable, and cost-effective alternatives for generating patient-derived gene variants, particularly in large and complex DNA constructs such as those involving KAT6A and KAT6B. Second, these techniques enable researchers to investigate the functional impact of rare genetic variants with greater efficiency, supporting clinical interpretation and the advancement of personalised medicine. Third, this work plays an important role in bridging the gap between basic scientific research and clinical diagnostics, contributing to a deeper understanding and improved treatment strategies for rare genetic disorders.

Scientific Sessions


Ms. Beth Woodbury


Ms. Amy Young


Ms. Susan Hartung


Ms. Sue Carpenter

KAT6 Foundation Advocacy Committee

Presentation title: KAT6 Parents Also Known as Professional Advocates

Introduction

The KAT6 Foundation Advocacy Committee delivered a powerful and heartfelt presentation addressing the critical importance of advocacy in the lives of families raising children with KAT6A and KAT6B syndromes. Committee members, including Beth Woodbury, Amy Young, Susan Hartung and Sue Carpenter, shared personal experiences and practical strategies for advocating in medical, educational, and legislative settings.

Medical Advocacy

The Advocacy committee emphasised the importance of being prepared, staying organised with medical paperwork, and speaking up respectfully but firmly to secure proper care. Beth shared a personal story of her adult son's traumatic hospitalisation, which underscored the need for parents to adapt their advocacy as children transition into adult care. Her experience highlighted the importance of requesting appropriate wards, support staff, and continued involvement in decision-making.

Educational Advocacy

Families were provided insights on educational rights and navigating the Individualised Education Program (IEP) process. The advocacy committee explained how to initiate a psychoeducational assessment, understand the timelines involved (e.g. 60-day evaluation windows), and participate meaningfully in IEP meetings. They stressed the value of having an advocate—someone to act as a second set of eyes and voice—to ensure that school districts provide all entitled services. The group encouraged families to document everything, ask questions, and, when necessary, escalate to mediation or due process.

Scientific Sessions

Multiple families shared experiences of schools denying essential services, such as speech therapy, and how persistent advocacy and legal action led to successful outcomes. Their stories illustrated that while advocacy can be exhausting and emotionally taxing, it is essential for securing the support children need to thrive.

Policy and Legislative Advocacy

The final section focused on systemic advocacy, particularly related to disability funding and Medicaid. One parent, who has spent decades supporting disability communities, described how advocacy at the state and local government levels helped protect funding that enables individuals with disabilities to live independently in the community. By sharing personal stories with policymakers and showing the value of community-based services, the advocacy efforts successfully prevented major budget cuts. She encouraged all families to engage with their legislators, personalise their stories, and make their voices heard.

Key Takeaways

The Advocacy committee reinforced several key messages: parents are their child's most powerful advocates, and being prepared, persistent, and informed can significantly impact the support and services their child receives. The committee highlighted the importance of using personal stories as compelling advocacy tools, capable of influencing both educators and policymakers. They also emphasised the value of community—sharing experiences and supporting one another strengthens collective efforts and fosters resilience. The KAT6 Foundation Advocacy Committee closed by encouraging families to speak from the heart, keep thorough documentation, and never hesitate to ask for help, reminding everyone that only those walking the same path can truly understand the daily challenges of raising a child with a disability.

Shared Journeys

Lusia Langi
Sibling Bonds

Lusia shared a heartfelt account of her deep bond with her younger brother Cannon, who was diagnosed with the rare KAT6A gene variation, alongside severe autism and speech apraxia. Despite Cannon being nonverbal and having complex support needs, Lucia describes a loving and intuitive relationship built on patience, shared routines, and mutual understanding. She reflects on their upbringing together, recalling how Cannon's diagnosis brought challenges but also immense joy, growth, and resilience into their family. Lusia emphasises how Cannon communicates affection in his own unique ways—through hugs, shared smiles, and physical closeness—and how she has always strived to be a safe, loving presence for him. As she transitioned to college, Lucia remained connected through FaceTime calls, bedtime stories, and songs, ensuring that their bond remained strong despite the distance. She acknowledges that while she has supported Cannon through his milestones, it is Cannon who has shaped her into a more empathetic, patient, and grounded person. Their relationship is defined not by disability, but by unwavering love, mutual care, and the powerful connection between siblings.

Shared Journeys

Lusia Langi
Resiliency in a Life of Unknowns

Kristen courageously shared her life story—a journey marked by complex medical challenges, resilience, and the unconditional bond with her twin sister, Kim. Born six and a half weeks premature, Kristen faced significant difficulties from the start, including hypotonia, feeding issues, and failure to thrive. Her early years were filled with countless medical appointments, therapies, and surgeries—from gastrointestinal procedures to open-heart surgery and treatments for juvenile myositis, a rare autoimmune condition she developed as a teenager. Despite these challenges, Kristen remained determined to live a full life. She began speech therapy at a young age—initially nonverbal, she didn't speak her first words until the age of six—and has continued therapy ever since. Kristen's twin sister played a critical role in her development, often sensing her needs before Kristen could express them herself. Though their abilities differ significantly—Kim now lives independently and trains horses professionally—Kristen finds joy and purpose in volunteering, spending time with her dog, and staying connected to Kim through shared activities like horseback riding. Kristen's story is a powerful testament to strength, perseverance, and family support in the face of rare genetic disorders.

Research, Fundraising and Patient Registry

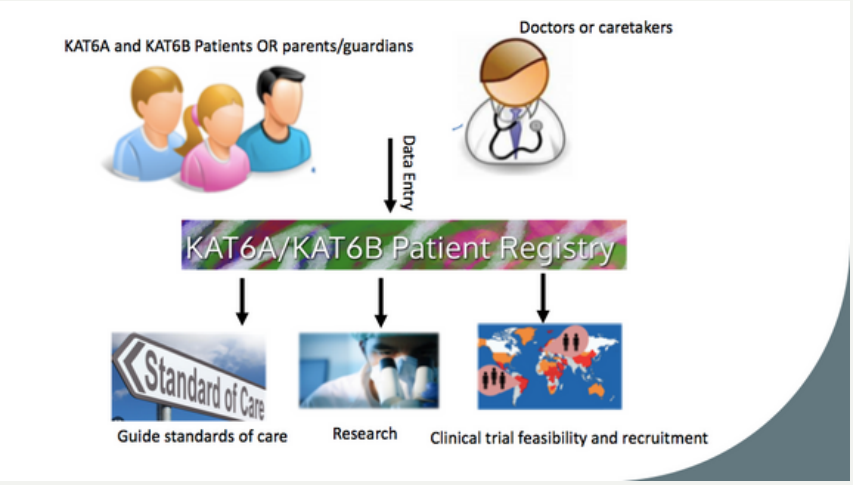
Jordan Muller
Chairperson

Aimee Reitzen
Director, Marketing & Communication

Jordan shared an update on the Foundation's research strategy, highlighting a major milestone: for the first time, the KAT6 Foundation issued a public Request for Proposals to the research community. This decision was made possible by the steady growth in fundraising and community support over the past eight years. The RFP resulted in 11 submissions, from which seven high-quality research projects were selected for funding based on alignment with strategic priorities and budget capacity. These studies represent both KAT6A and KAT6B conditions and range in length from one to three years.

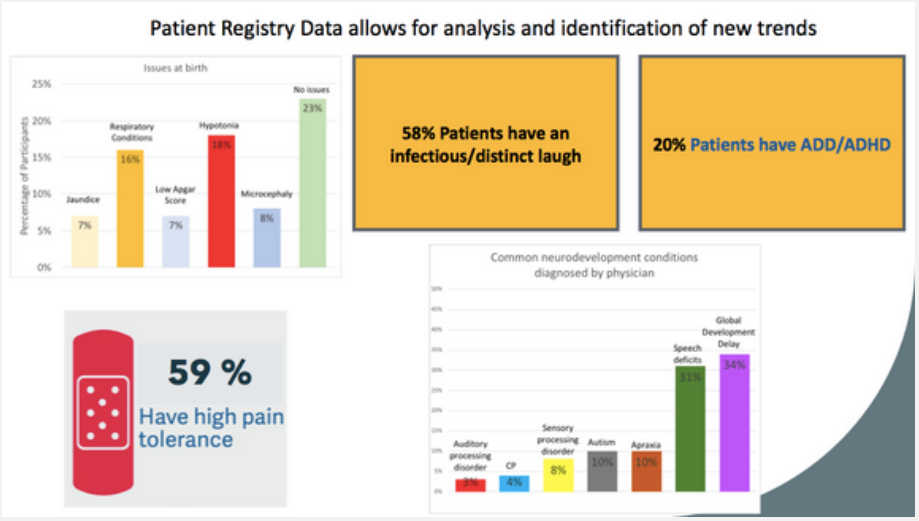
Aimee spoke passionately about the critical role of fundraising in sustaining the Foundation's mission. She thanked families and supporters who have participated in KATWalks and annual appeals, which together raised over $476,000 in the previous year. Donations fund research, therapy grants, assistive technology, the annual family conference, and administrative costs. This year marks the 8th annual KATWalk, with options for both in-person and virtual participation. A new T-shirt design will allow teams to customise with their city or name, adding a fresh element to the campaign. Aimee also emphasised the importance of the annual appeal, which surpassed expectations last year. Personal outreach, strategic donor engagement, and community events—like local restaurant nights or marathons—are all encouraged. A newly formed grant committee is also pursuing institutional funding, while families are encouraged to volunteer their unique skills to support the Foundation's goals.

Research, Fundraising and Patient Registry



Emile Najm
CEO, KAT6 Foundation

Emile presented an in-depth update on the KAT6A/B Patient Registry, launched in 2019 in partnership with the National Organization for Rare Disorders (NORD). The secure, cloud-based registry now includes data from 502 respondents globally, with 71% diagnosed with KAT6A and 29% with KAT6B. The registry collects detailed medical, genetic, and quality-of-life information across 12 surveys. This dataset is critical in identifying clinical trends, guiding standard of care, informing therapeutic development, and supporting clinical trial recruitment. Emile encouraged families to contribute data and keep their entries current, noting that researchers have already begun requesting de-identified data for studies. Future goals include publishing findings in scientific journals and forming a mortality review committee to better understand causes of death and disease progression in the KAT6 population. The registry continues to be a cornerstone of the Foundation's research and advocacy work.



“Freedoms of Speech” Workshop

Patricia Wilson
CCC-SLP, TSSLD
Otto Specht School

The "Freedoms of Speech" workshop was organized into several key sections, each addressing different aspects of speech and communication therapy through creative analogies.

I. **Communication:** This section covered the foundational principles of effective communication, setting the stage for the subsequent topics.

II. **Acrobatics Analysis:** Focused on individual abilities and presentations, this section explored the potential therapeutic approaches to improve communication skills, answering critical "why" and "how" questions.

III. **Juggling Programs:** Highlighted the importance of brain plasticity and the coordination of different systems necessary for effective communication.

IV. **Lion Taming:** Emphasized social and emotional regulation and activities designed to foster a growth mindset, reinforcing the belief "I am capable."

V. **Magical Acts:** Discussed systems integration, including sensory signs and communication developments that support brain changes, and motor planning for speech. This section analyzed various approaches such as PROMPT, ASL, and AAC.

The workshop provided a comprehensive overview of innovative techniques and strategies to enhance communication abilities in individuals, focusing on both the physiological and psychological aspects of speech therapy.

Available on YouTube

Conference Highlight Video created by Jeffrey Worden

- KAT6A KAT6B Patient Registry Update by Emile Najm CEO
- Fundraising for KAT6 Foundation by Aimee Reitzen, Director of Marketing and Communications
- Charting new paths Funded Research Initiatives for 2025 and beyond by Jordan Muller, Board Chair
- KAT6 Syndromes & Mendelian disorders of the epigenetic machinery Perspectives from the bedside and the bench by Jill A. Fahrner, MD, PhD
- Highly Efficient Mutagenesis Methods to Engineer KAT6 and Other Variants for Functional Analyses in vitro by Paulina Varela Castillo, PhD Student at Dr. Xiang-Jiao Yang's Lab
- The KAT6 Epigenetic Fingerprint, What KAT6 Blood Cells reveal about Development and Disease Course at Serrano Lab, by Sandeep Sreerama, MD PhD Candidate
- Understanding the spectrum of KAT6A and B variants using fruit flies by Zoe Goldstone-Joubert, BSc and Paul C Marcogliese, PhD
- Cognitive and Behavioral Features of KAT6A and KAT6B Disorders by Rowena Ng, PhD and Jacqueline Harris, MD, MS
- Welcome to the 6th International KAT6 Conference 2025 by Dr Natacha Esber
- Sibling Bonds by Lusia Langi, Content Creator and NCAA Athlete

KAT6 Foundation's Next Steps

The KAT6 Foundation aims to continue supporting and empowering families with children affected by rare diseases. In terms of research, the foundation plans to fund more trials aimed at creating animal models to study KAT6A and KAT6B gene variations, as well as support additional clinical trials focused on treatment and drug efficacy. The foundation is committed to sustaining its initiatives, such as the KATwalk, the Empower grant, and the annual meeting, all of which are vital for raising funds and resources for the community. Additionally, the foundation seeks to build a strong advocacy team to further its mission and amplify its impact.

KAT6 Foundation

Thank you!