4th International KAT6A and KAT6B Conference

Boston, USA | April, 2023

Summary

This report is tailored for scientist, clinicians and families who have a child with KAT6A or KAT6B gene variations. The purpose is to:

- Provide a summary of the scientific sessions;
- Identify gaps and bottlenecks in current projects and the resources needed to overcome them;
- Propose a strategy to generate those resources.

ABSTRACT

The KAT6 Foundation organized the 4th International KAT6A and KAT6B Conference, which was a collaborative event centered around patients. The main objective of the conference was to strengthen international research on KAT6A and KAT6B and facilitate open discussions among families, clinicians, and researchers. It served as a platform for the KAT6 community to expand its network and for participants to establish connections with families and experts in the field. The event had a total of 200 registrants, including 60 families and 21 scientists from the USA and around the world.

Taking place in Boston, USA, the conference spanned a single day and covered a wide range of topics, such as personalized medicine, the role of iPSC cell lines, neuropsychological assessments, epilepsy, autism and its relation to KAT6A, special education, the KAT6A and KAT6B patient registry, and initiatives led by the KAT6 Foundation, such as the KATwalk.

During the conference, the KAT6 Foundation provided assistance to three research groups by creating a space for families to participate in research data collection. Additionally, the foundation organized consultation visits for families to meet experts in the field of KAT6A and KAT6B-related syndromes, namely Dr. Richard Kelley, Dr. Gabrielle Lemire, Dr. Andrew Zimmerman, and Dr. Jacqueline Harris.

KAT6 Foundation

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

Saylor Williams
Lab Manager, Serrano lab
Center for Regenerative Medicine
Boston University , USA

The KAT6 Foundation is a strong advocate for patient-focused research, with one of its key research themes being the establishment of an induced pluripotent stem cells (iPSCs) bank by the researchers at the Serrano Lab, located at the Center for Regenerative Medicine at Boston University. Ms. Saylor Williams at the annual meeting, helped families understand iPSCs by tackling three main questions - What are iPSCs?; What is an iPSC bank; and How will an iPSC bank will help the KAT6 Foundation?

What are iPSCs? - We might have heard about "stem cells", these cells have the ability to develop into other type of cells. iPSCs are similar to stem cells as they also have the ability to generate into other types of cells, however, they differ because iPSCs are sourced from individuals and then reprogrammed back in an embryo like state for them to differentiate in to other type of cells. This unique characteristics of iPSCs provides researchers with excellent opportunities to work with cells lines that closely reflect to the patient population.

What is an iPSC bank? - The goal of an iPSC bank is to collect as many samples as possible from patients with KAT6A or KAT6B gene variation. The broad and variable clinical manifestations exhibited by these genetic syndromes, highlights the need to bank many iPSC samples for researchers to work with a range of phenotypes. The first step in curation of KAT6A or KAT6B iPSCs is collection of a blood sample from individuals with these gene variations. Ms. Williams acknowledged that it can be stressful for some children to undergo blood draw and at Serrano lab the researchers are dedicated to make this step as comfortable as possible. From the blood sample, peripheral blood mononuclear cells containing genetic information are isolated to reprogram to iPSCs. These iPSC cell lines will be stored at Center for Regenerative Medicine at Boston University. The KAT6A and KAT6B iPSC bank aims to share these cell lines which can be differentiated to any type of cells with scientist across the world.

Scientific Sessions

At the Serrano lab, researchers are working on differentiating the KAT6A and KAT6B cells in to neurons and then brain organoids. Ms. Williams emphasized that these cell lines are the best we have in terms of reflecting the patient population.

The CReM has an open source biology policy which means that every resource that is generated at CReM for instance the iPSC cell lines at Serrano lab are open for sharing with researchers across the world. The CReM website hosts a CReM catalogue where all the cell lines are listed for scientists to use for their own research. Currently, the KAT6A or KAT6B cell lines are not listed in the catalogue as they are under development. At the last annual meeting, many children with KAT6A gene variation provided their blood sample to support the KAT6A iPSC data bank. Figure 1 shows the KAT6A variants samples collected by Serrano lab at the last annual meeting. The goal is to continue to collect KAT6A samples and this year onwards start collecting KAT6B samples as well. Ms. Williams extended a heartfelt thank you to all the families who participated in the blood draw for the KAT6A and KAT6B iPSC bank. She shared visuals of 2-4 months old brain organoids developed using patient derived iPSCs. The KAT6A and KAT6B iPSC data bank will support Serrano lab's goal to understand cortical neurogenesis in KAT6A/ KAT6B iPSC derived neuron models.

Scientific Sessions

Jacqueline Harris
Assistant Professor
Pediatrics, Neurology and Genetics
Kennedy Krieger Institute and John Hopkins
University School of Medicine, USA

Dr. Jacqueline Harris discussed neurodevelopmental research on KAT6A and KAT6B syndromes, which are epigenetic disorders. Epigenetics involves changes in gene expression without altering the DNA sequence. Dr. Harris focused on histone modification, specifically the acetylation of histones by the KAT6A and KAT6B proteins. These modifications impact the interaction between histones and DNA, affecting gene expression. Disruptions in these genes lead to developmental abnormalities, intellectual disabilities, and other health issues.

These disorders are classified as mendelian disorders, which are rare neurogenetic conditions involving disruptions in the epigenetic regulatory system. They can be categorized as writers, readers, erasers, or remodelers based on the specific function of the proteins involved in placing or removing epigenetic marks.

Dr. Harris discussed two types of mutations in the KAT6A gene: early truncating and late truncating mutations. Early truncating mutations occur at the beginning of the protein, resulting in only 50% of the protein being active, with one copy functioning normally and the other copy being inactive. Late truncating mutations happen towards the end of the KAT6A gene sequence, causing the protein to be cut or shortened. In non-truncating mutations, also known as missense mutations, there are small spelling mistakes in the gene code. These mutations lead to a change in one letter of the genetic code, resulting in the production of a different amino acid. Both KAT6A and KAT6B genes provide instructions for modifying histones.

Dr. Harris briefly discussed KAT6B syndrome, explaining that it is caused by a variant in one copy of the KAT6B gene, typically occurring spontaneously. This syndrome encompasses overlapping conditions such as Say-Barber-Biesecker-Young-Simpson syndrome (SBBYSS) and Genitopatellar syndrome (GPS), along with other related disorders. Intellectual disability and behavioral issues are commonly observed in all KAT6B and KAT6B-related disorders, but there is still much to learn about these conditions.

Scientific Sessions

Dr. Harris highlighted that KAT6A syndrome shares some neurodevelopmental characteristics with other similar epigenetic disorders, but it also has unique features. Common features include intellectual disability, a friendly disposition, and sleep issues. However, significant delays in expressive language/speech, oromotor dysfunction, craniosynostosis, and delays in motor skills are distinct to KAT6A gene variations. While motor skills may improve over time, certain skills like walking and fine motor skills lag behind.

Regarding intellectual disability, the majority of children with KAT6A gene variations fall into the moderate to severe range. Late truncating variants are associated with more developmental challenges compared to other types of variants. Behavioral issues are reported to be low in the KAT6A cohort, with strengths often seen in social and emotional domains.

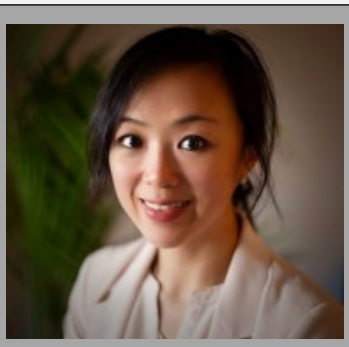
To summarize, early and late truncating mutations, as well as missense mutations, occur in the KAT6A gene. KAT6A syndrome has specific features such as delays in speech, motor skills, and craniosynostosis. Children with KAT6A gene variations generally experience intellectual disability, with late truncating variants having the greatest impact.

Dr. Harris highlighted that our understanding of the neuropsychological profile associated with variations in the KAT6A gene is incomplete. Specific strengths and challenges of individuals with these variations are not yet comprehensively known. Regular neuropsychological assessments and developmental monitoring were emphasized as important for children with KAT6A gene variations. Collaboration among educational and medical professionals is crucial for the well-being of these individuals.

The study conducted by Dr. Harris and her team focused on dimensions beyond IQ scores, including adaptive functions, sleep, and behavior. Surveys were conducted with 26 families having a child with KAT6A gene variation. Findings revealed significant impairments in adaptive function across the board. Surprisingly, there were low rates of behavioral issues observed, contrary to expectations. Sleep problems were prevalent in this population, with a higher proportion than reported in the literature (30-40%). Sleep challenges included multiple awakenings, restless sleep, enuresis (bedwetting at 7+ years), and daytime drowsiness. Over 60% of families sought advice or treatment for their child's sleep issues,

Scientific Sessions

Rowena Ng
Neuropsychologist
Kennedy Krieger Institute and John Hopkins
University School of Medicine, USA



Dr. Rowena Ng presented the findings of a study that focused on 15 children diagnosed with KAT6A syndrome. The participants included 2 with early truncating variants, 10 with late truncating variants, and 3 with missense variants. The main objective of the study was to report the non-verbal and cognitive profile of children with KAT6A gene variations. The aim was to gather information that could aid in developing more effective therapy and treatment plans, as well as providing guidance to families, clinicians, and researchers.

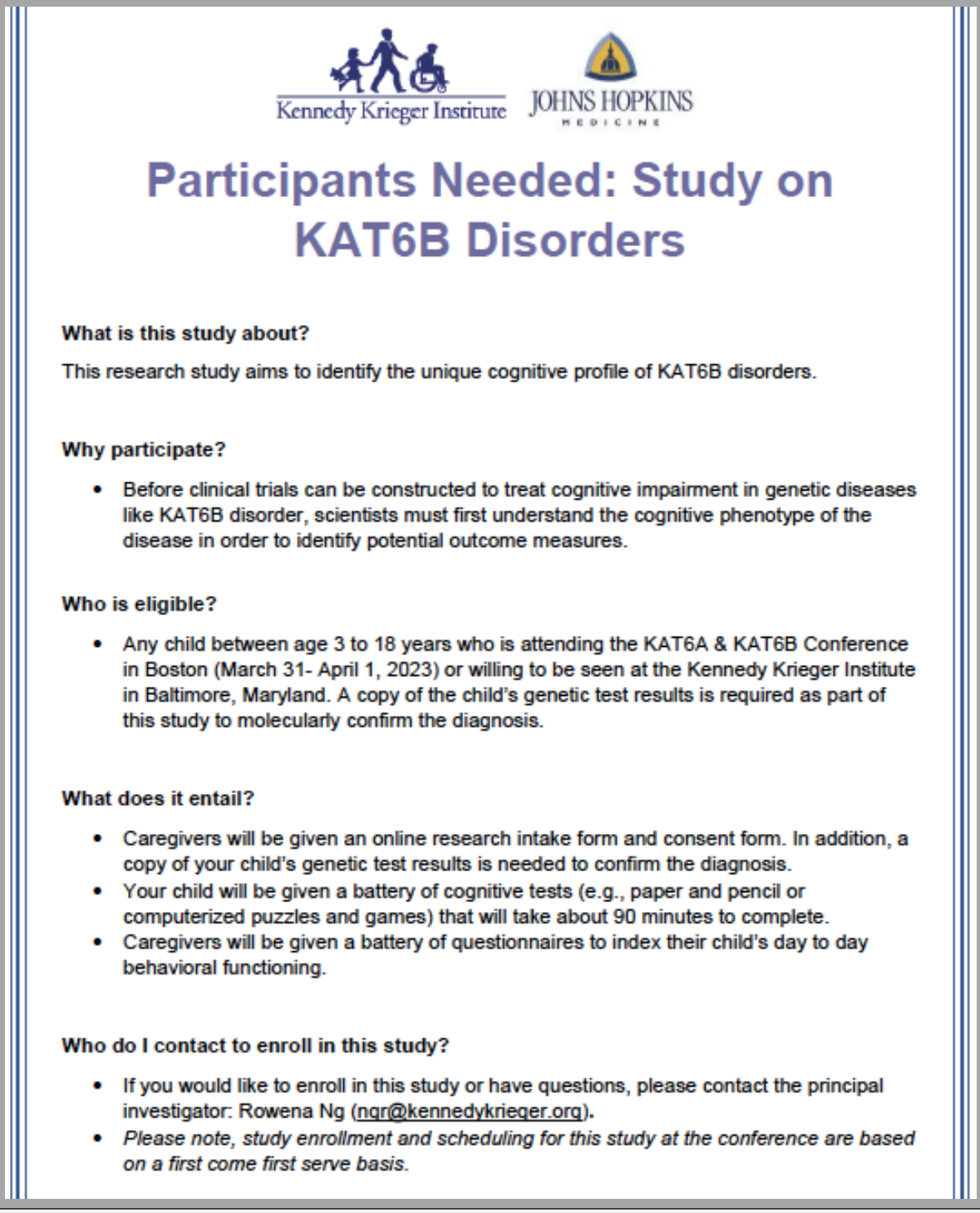
The study revealed that participants with missense variants tended to display relatively stronger non-verbal skills compared to those with truncating variants. However, within the truncating group, whether early or late, few differences were observed. When it came to receptive language, the results were more varied. Individuals with truncating variants generally had difficulties with comprehension of instructions, while vocabulary comprehension was similar across all variants.

In terms of social cognition patterns, similarities were observed among the participants, but those with truncating variants reported more concerns related to autism spectrum disorder. These concerns encompassed social cognition, social motivation, and reduced repetitive behaviors. Parents of children with KAT6A syndrome, regardless of variant, reported similar difficulties with executive functioning in their daily lives.

It should be noted that the study faced limitations due to the limited number of individuals with early truncating and missense variants in the cohort. Therefore, further research with a larger sample size is necessary to draw more definitive conclusions. The study also highlighted the importance of utilizing adaptive neurocognitive tools, as individuals with sensorimotor impairment may face challenges when engaging with standard assessment procedures.

Scientific Sessions

The study did not explore whether individuals with KAT6B disorders would exhibit similar or distinct neurobehavioral patterns. To address this gap, a separate neuropsychological evaluation was conducted at the annual meeting by Dr. Harris and Dr. Ng, involving a total of 18 children with KAT6B gene variations.



Kennedy Krieger Institute JOHNS HOPKINS MEDICINE

Participants Needed: Study on KAT6B Disorders

What is this study about?

This research study aims to identify the unique cognitive profile of KAT6B disorders.

Why participate?

- Before clinical trials can be constructed to treat cognitive impairment in genetic diseases like KAT6B disorder, scientists must first understand the cognitive phenotype of the disease in order to identify potential outcome measures.

Who is eligible?

- Any child between age 3 to 18 years who is attending the KAT6A & KAT6B Conference in Boston (March 31- April 1, 2023) or willing to be seen at the Kennedy Krieger Institute in Baltimore, Maryland. A copy of the child's genetic test results is required as part of this study to molecularly confirm the diagnosis.

What does it entail?

- Caregivers will be given an online research intake form and consent form. In addition, a copy of your child's genetic test results is needed to confirm the diagnosis.
- Your child will be given a battery of cognitive tests (e.g., paper and pencil or computerized puzzles and games) that will take about 90 minutes to complete.
- Caregivers will be given a battery of questionnaires to index their child's day to day behavioral functioning.

Who do I contact to enroll in this study?

- If you would like to enroll in this study or have questions, please contact the principal investigator: Rowena Ng (nqr@kennedykrieger.org).
- *Please note, study enrollment and scheduling for this study at the conference are based on a first come first serve basis.*

Scientific Sessions

Richard I Kelley
Pediatrician and Biochemical Geneticist
USA

During the open forum focused on KAT6A and KAT6B metabolism, Dr. Richard I Kelley provided insights into the metabolic abnormalities associated with these genes. He specifically discussed the abnormal metabolism of amino acid-derived nitrogen, which was indicated by elevated plasma levels of citrulline and asparagine. Dr. Kelley emphasized the importance of examining the amino acid profile in the blood, as these levels are regulated by mitochondria. By investigating the amino acid profile, a better understanding of mitochondrial function can be gained.

One notable finding highlighted by Dr. Kelley was the deficiency of citric acid, which plays a significant role in intestinal motility and serves as a major energy source. In individuals with KAT6A mutations, citrate levels were notably reduced, indicating mitochondrial dysfunction. Moreover, systemic methionine deficiency was observed, which can contribute to bone marrow failure. The distorted amino acid metabolism not only leads to primary metabolic abnormalities but also causes secondary deficiencies in B-vitamins such as pyridoxine. Additionally, mitochondrial free radical damage and lactic acidemia were associated with these metabolic dysfunctions.

Dr. Kelley discussed various aspects of treatment discovery, which commence with the identification of key mitochondrial metabolites and amino acids that are deficient in individuals with KAT6A and KAT6B mutations. Plausible treatment options were explored, highlighting the importance of closely monitoring the efficacy of these interventions to further comprehend the cellular biochemistry of individuals with KAT6A and KAT6B gene mutations. Ongoing investigations aim to evaluate the effectiveness of these treatment approaches in improving outcomes for individuals affected by KAT6A and KAT6B syndromes.

The presentation concluded with an open forum, providing an opportunity for further discussion and exchange of ideas on this topic.

Scientific Sessions

Andrew Zimmerman
Pediatric Neurologist
UMass Chan Medical School
Massachusetts General Hospital
Worcester, USA

Dr. Andrew Zimmerman presented an overview of clinical findings and research related to autism spectrum disorder (ASD), specifically focusing on its application to KAT6A and KAT6B. With over 38 years of experience working with individuals on the autism spectrum, Dr. Zimmerman highlighted the significant increase in ASD diagnoses over the years. In 1987, the prevalence of ASD was only 0.05%, whereas by 2020, it had risen to 2.8% of the population. This increase is attributed partly to improved recognition and understanding of the disorder. Furthermore, the patient population has become more diverse, with ASD being identified in individuals from various backgrounds. ASD is known to have a complex genetic basis, involving the interaction of multiple genes and environmental influences.

ASD is a diverse range of conditions characterized by a collection of symptoms. It was first described by Lou O'Connor at John Hopkins in 1944 and has since been recognized as a syndrome. Dr. Zimmerman emphasized that even years later, there is a need for assistance in diagnosing patients, as evident by speech therapists seeking help. The field of autism research aims to identify the genetic causes underlying the disorder, as approximately 40% of ASD cases can be explained by genetics. Additionally, prenatal factors contribute to about 20% of cases, while environmental influences may account for approximately 40%. Clinical features commonly associated with autism include developmental delays in speech and motor skills, intellectual disability, learning disabilities, difficulties in social communication, attention deficit hyperactivity disorder (ADHD), anxiety, sleep issues, gastrointestinal problems, and seizures.

Autism is often associated with various genetic syndromes, and notable differences have been observed between individuals with autism linked to a known genetic cause and those where the genetic cause remains unidentified. Recently, the KAT6A gene has been identified as being associated with autism spectrum disorder (ASD), while no such information is available for KAT6B.

Scientific Sessions

Persistent deficits in social communication and social interaction

- Deficits in social-emotional reciprocity.
- Deficits in nonverbal communicative behaviors used for social interaction
- Deficits in developing, maintaining, and understanding relationships.

Restricted, repetitive patterns of behavior, interests, or activities, as manifested by at least two of the following:

- Stereotyped or repetitive motor movements, use of objects, or speech
- Insistence on sameness
- Highly restricted, fixated interests
- Hyper or hyporeactivity to sensory input

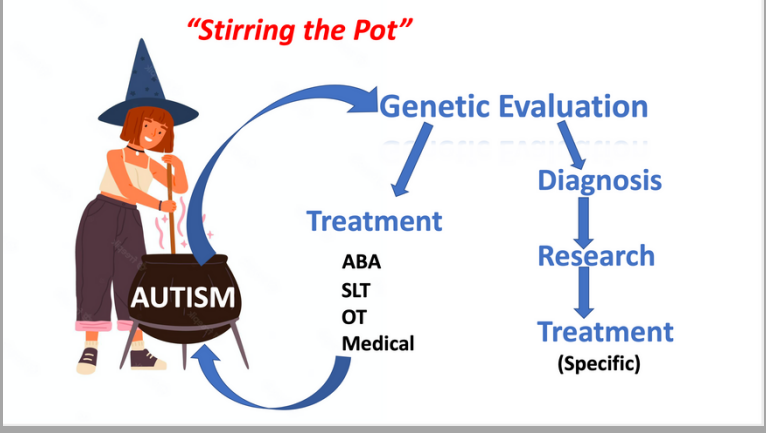
Dr. Zimmerman discussed several environmental factors that have been linked to autism, including advanced parental age, prematurity, and prenatal drug exposure to substances such as valproic acid and terbutaline. The economic burden of caring for individuals with ASD is significant, with estimated costs of $40,000 to $60,000 per year and a lifetime cost of $3.2 million, resulting in a total estimate of $126 billion per year. Comorbidities such as anxiety, depression, ADHD, bipolar disorders, and seizures are prevalent among individuals with ASD. Families also face challenges related to sleep disturbances and a range of gastrointestinal problems, including constipation, diarrhea, feeding difficulties, food allergies, and gastroesophageal reflux disease (GERD).

Autism is often associated with various genetic syndromes, and notable differences have been observed between individuals with autism linked to a known genetic cause and those where the genetic cause remains unidentified. Recently, the KAT6A gene has been identified as being associated with autism spectrum disorder (ASD), while no such information is available for KAT6B.

Dr. Zimmerman discussed several environmental factors that have been linked to autism, including advanced parental age, prematurity, and prenatal drug exposure to substances such as valproic acid and terbutaline. The economic burden of caring for individuals with ASD is significant, with estimated costs of $40,000 to $60,000 per year and a lifetime cost of $3.2 million, resulting in a total estimate of $126 billion per year.

Scientific Sessions

Comorbidities such as anxiety, depression, ADHD, bipolar disorders, and seizures are prevalent among individuals with ASD. Families also face challenges related to sleep disturbances and a range of gastrointestinal problems, including constipation, diarrhea, feeding difficulties, food allergies, and gastroesophageal reflux disease (GERD). Researchers worldwide have adopted various approaches to better understand autism, including exploring mitochondrial issues, immune system involvement, gastrointestinal tract abnormalities, and prenatal infections. Dr. Zimmerman presented a metaphorical cartoon illustrating how individuals with autism are placed into a pot, representing the autism category. Researchers and neurologists continue to "stir the pot" by evaluating patients, conducting genetic assessments, and seeking a better understanding of underlying causes. The goal is to pursue genetic diagnoses, as they contribute to an understanding of the underlying biology, facilitate research efforts, and ultimately lead to targeted treatments for autism.
r. Zimmerman shared an exciting news in the field of medical advancements for Rett syndrome: the FDA has recently approved trofinetide, now branded as Daybue, as a treatment option. This is a significant breakthrough after years of dedicated research. Trofinetide, a synthetic analog of insulin-like growth factor 1 (IGF-1) peptide, shows promise for individuals with Rett syndrome. However, it is worth noting that the treatment is quite expensive. The brain, known as the most complex organ in the human body, is followed closely by the gastrointestinal (GI) tract, which contains numerous nerve endings and transmitters, functioning as a "brain" within itself. The brain is composed of an astounding 10-15 quadrillion synapses.



Scientific Sessions

Notably, in autism, there have been remarkable findings related to brain overgrowth, particularly in male infants, which is associated with macrocephaly (larger head size). Differences in neuroanatomy have been observed between children with autism and typically developing children, including reorganization failures and patchy disorganization in neonates and children with autism. Resting EEG studies in adults have shown diffuse, short-range connections, while functional connectivity studies using MRI have been conducted in toddlers. These investigations aim to deepen our understanding of autism spectrum disorder and its neural underpinnings.
In toddlers with ASD, connectivity issues are observed in the back of the brain rather than the frontal lobe, where most connections typically occur. Research focuses on understanding how therapy can impact connectivity in ASD. Potential causes and drug targets include mitochondrial dysfunction, chronic neuroinflammation, oxidative stress, and environmental toxins. The website Spectrum News covers literature on the autism spectrum and recently highlighted a study emphasizing the crucial role of family groups in advancing autism research. Families require more support from researchers to maximize their valuable contributions. ASD is often accompanied by associated conditions such as sleep difficulties and gastrointestinal problems. ASD involves a range of symptoms and its prevalence is on the rise due to improved recognition and understanding of its biological underpinnings. The exact genetic and environmental causes of ASD remain unknown.

Scientific Sessions

Xiang-Jiao Yang
Professor
Goodman Cancer Institute
Department of Medicine
McGill University

Dr. Yang delivered a presentation on the origin of genetic diseases, focusing on the case of syndromic intellectual disability. The title of the presentation was inspired by Charles Darwin's famous book, "Origin of Species," highlighting the role of mutations as the root cause of many diseases. Even a single nucleotide change can have a profound impact, completely halting the production or activity of a protein. These spelling mistakes, or mutations, can occur during the replication process, which is the main source of random or de novo mutations.

Dr. Yang discussed a study conducted on acute myeloid leukemia, where a mutation was identified involving a chromosome translocation in a gene called MOZ, now known as KAT6A. The background research explored the identification of MOZ and MORF during the study of acute myeloid leukemia and how these genes are linked to lysine acetyltransferase. Dr. Yang's early work in the 2000s demonstrated the essential role of both histone and lysine acetyltransferases in brain development. The presentation touched upon key processes in protein synthesis, such as acetylation and propylation, with a particular focus on the involvement of KAT6A and KAT6B genes in these processes. These two genes encode catalytic enzymes within the function of the BRPF protein.

The BRPF protein is of utmost importance in the development of vital brain structures, including the hippocampus, gyri, and sulci. It also plays a role in the blood system, as its loss can lead to bone marrow failure. In the context of syndromic intellectual disability, the causative mechanism lies in de novo mutations occurring in the BRPF1 gene. This protein activates the KAT6A and KAT6B proteins, which receive instructions from BRPF1 to acetylate histones. Understanding the origin of mutations is crucial to improve our ability to diagnose at the molecular level, which in turn facilitates the development of targeted therapeutics and interventions.

Scientific Sessions

This knowledge is invaluable for families affected by rare genetic variations, as it helps them make informed reproductive decisions.
Dr. Yang concluded the presentation with a heartfelt message to the families, acknowledging their strength and resilience as an inspiration to him personally.

Scientific Sessions

John Gaitanis
Hasbro Children's Hospital,
Rhode Island, USA

Dr. John Gaitanis delivered a comprehensive presentation on seizures and epilepsy. The audience gained an understanding of the various types of seizures observed in the KAT6 population and their medical assessment. Seizures were defined as transient clinical events resulting from abnormal cortical neuron activity, while epilepsy was described as the occurrence of recurrent, unprovoked seizures. Within the KAT6 population, approximately 9% of patients (7 out of 76 cases) experienced epilepsy. Seizures were classified as either partial or generalized, with partial seizures further categorized as simple or complex based on their specific characteristics (motor, sensory, autonomic, and psychic). Generalized seizures encompassed absence, myoclonic, clonic, tonic, tonic-clonic, and atonic seizures. Notable seizure types reported in the KAT6 population included complex partial seizures, absence seizures, staring episodes, and Jeavons epilepsy, which involved absence seizures and eye myoclonia.

Dr. Gaitanis presented three case reports of children with KAT6A gene variations who had a history of seizures. The first case involved an infant with focal and generalized seizures during early infancy, which subsequently improved without intervention by the age of 3. The child also experienced exaggerated startle reflex syndrome triggered by unexpected noises. In the second case, epilepsy began at 3 months of age, manifesting as daily right hemiclonic seizures during sleep. At the age of 11, the child exhibited bilateral tonic seizures and episodes of "loss of awareness." The third case involved seizure onset at 5 months, characterized by clusters of symmetric spasms. Based on these reported cases, two themes related to epilepsy in KAT6 gene variation emerged. These themes included the presentation of infantile spasms during infancy and generalized epilepsy with absence seizures during childhood.

Scientific Sessions

The diagnosis of epilepsy involved a comprehensive approach, including obtaining a medical history, conducting a physical examination, performing an electroencephalogram (EEG), and utilizing magnetic resonance imaging (MRI). Differentiating the type of epilepsy was crucial as each type exhibited distinct treatment response and prognosis, making accurate classification based on clinical and EEG criteria essential.

Treating seizures in children was discussed as a high priority to mitigate the risks associated with seizure-induced injury, prolonged seizures, sudden unexplained death in epilepsy, cognitive effects from frequent seizures, and overall quality of life. Dr. Gaitanis discussed a range of antiepileptic drugs and outlined the first-line treatment options based on the specific type of seizures. Additionally, he addressed the question of what could be done if medication failed, introducing non-medicated alternatives such as the ketogenic diet, vagal nerve stimulation, and epilepsy surgery.

Furthermore, Dr. Gaitanis highlighted the connection between epilepsy and autism spectrum disorders, noting that epilepsy occurs in 8 to 20% of children with autism, while autism is present in up to 30% of children with epilepsy. The co-occurrence of these conditions is more frequent when seizures develop within the first three years of life. Epilepsy diagnosis displayed two peaks, occurring either early, such as in cases of infantile spasms and Dravet syndrome, or later in life.

Despite the advancements in epilepsy research, there are still several unknowns that need to be addressed. These include better identification of individuals at risk of developing epilepsy, understanding the prevalence of EEG abnormalities in patients without seizures, assessing the impact of EEG abnormalities on developmental outcomes, and determining the optimal treatment options specifically for epilepsy in individuals with KAT6 gene variations.

Scientific Sessions

David Carlson
Assistant Superintendent, Special Education and Pupil Personnel Services

Mr. Carlson delivered a presentation from a school district's perspective on providing services to students with unique disabilities. The presentation outlined four strategic goals. Firstly, the academic goal aimed to advance learning for all students. Secondly, the social-emotional and ethical goal focused on supporting the development of social-emotional skills and ethical values. The third goal emphasized capacity building by investing in the skills, knowledge, and expertise of the community. Lastly, ensuring safety and promoting a safe and respectful environment for all students was identified as a crucial goal.

The presentation emphasized the importance of special education in offering free and appropriate public education while fostering a least restrictive environment. The concept of a least restrictive environment meant that children should have the maximum access to general education while always learning in an environment that minimizes restrictions. Various special education programs were discussed, tailored to individual students' strengths, developmental needs, and learning goals.

The least restrictive environment model aimed to have 60% of students spend 80% of their school day in general education classes. The integration of therapeutic services such as physical therapy (PT), occupational therapy (OT), speech and language therapy, and counseling was emphasized within the education model. These services were provided through individual sessions, group sessions, or consultation models, ensuring students received the necessary support.

Addressing the increasing prevalence of anxiety among students, Mr. Carlson dedicated some time to discussing the social-emotional needs of students. Efforts were made to acclimate these children to the school setting, and initiatives were implemented to support mental health.

Scientific Sessions

The Partnership for Safe and Healthy Youth Center was highlighted as a multidisciplinary team of experts who conducted family/youth guided meetings to assess the strengths and challenges of the entire family. This approach facilitated the determination of appropriate services, avoiding the need for families to navigate multiple agencies separately. Professional development workshops were provided for school psychologists and student assistance counselors, including mental health first aid training.

The presentation also introduced the Therapeutic Alternative Program (TAP), which offered short-term temporary support to students in crisis or those struggling to attend their regular school program. TAP included instructional support, daily counseling, family consultations, progress monitoring, and psychiatric consultations if necessary.

Transition planning was another crucial aspect discussed, which aimed to help students and families establish a vision for their future in terms of living arrangements, employment, and community participation.

Additionally, the presentation highlighted various useful assistive technologies and special education resources. These included tools like "Snap & Read," "Co-writer universal," "Google Read&Write," and the resource "Sora."

Overall, Mr. Carlson's presentation emphasized the school district's commitment to meeting the unique needs of students with disabilities through a comprehensive range of academic, social-emotional, and therapeutic support services, while also promoting a safe and inclusive learning environment.

Scientific Sessions

KAT6A Foundation Leadership Presentations

Bhawika Sharma Lamichhane
Postdoctoral Scholar
University of Utah, USA

Dr. Bhawika Sharma Lamichhane is a postdoctoral scholar at Stanford University and a research member of the KAT6 Foundation. Emile Najm, the CEO of the KAT6 Foundation, presented Dr. Sharma L.'s work on the KAT6A and KAT6B Patient Registry. This registry is a secure cloud-based platform developed to manage health information from families who have a child with KAT6A or KAT6B related syndromes. Its purpose is to provide participants with a centralized location to store and organize their KAT6 medical data. Additionally, the registry acts as a comprehensive database that enhances our understanding of various KAT6 related disorders. It enables researchers to identify patterns and trends, leading to new insights and potential areas of further study. By sharing information quickly and securely with researchers and clinicians, the KAT6A Foundation aims to guide the development of standards of care. Currently, there are 125 registered individuals out of the 396 known cases with KAT6A variants, while for KAT6B-associated disorders, only 6 confirmed cases out of 147 are present in the registry as of 2021. Dr. Sharma L. provided an overview of the registry's layout, which organizes health information into categories such as diagnosis, birth and family history, medical history, treatment, and quality of life. To streamline the process, families are advised to gather all necessary information before filling out the registry. The KAT6 Foundation actively engages with patients, using personalized emails and social media follow-ups to encourage participation in the registry. The registry can be accessed by families through the link Kat6a.iamrare.org. Researchers can request access to the de-identified data collected in the registry from the KAT6 Foundation.

Scientific Sessions

KAT6A Foundation Leadership Presentations

Karen Ginsburg
Chair, Fundraising Committee
KAT6 Foundation

Marjorie Weintraub
KAT6 Foundation

The KAT6 Foundation is dedicated to raising funds to support families and research. Ms. Karen Ginsburg, chair of the fundraising committee, and Ms. Marjorie Weintraub, a fundraising professional, recently presented the foundation's fundraising initiatives. Currently, the foundation hosts two major events each year: KATwalk in either spring or fall, and the Annual Appeal in December. To learn more about these events, families can visit the foundation's website.

The upcoming KATwalk in 2023 will be the fourth since the foundation's establishment in 2017, with a goal of raising $150,000. Last year's KATwalk raised $165,000 and was one of the most successful fundraisers. Karen and Marjorie's message to families was, "The KAT6 Foundation is your foundation, and we need your help in developing a donor network, writing grants, and organizing annual events."

Fundraising efforts are ongoing throughout the year, and the Fundraising Committee is seeking volunteers to accelerate their efforts. The KATwalk can be hosted in either a virtual or in-person format, and the foundation supports both options. The KAT6A Foundation also establishes regional captains across the world, such as in Easter, Mid-West and Western USA, Australia, Netherlands, UK, Germany, Israel, and Canada, to support families interested in hosting a KATwalk event. The foundation manages detailed reporting of registrants and donations. Karen emphasized that both formats are powerful, and families can choose the format that is easiest and most enjoyable for them.

Scientific Sessions

KAT6A Foundation Leadership Presentations

This year, the KAT6 Foundation plans to focus on corporations and foundations for the annual appeal, seeking funding for specific initiatives. Marjorie shared that a targeted and personal ask is an effective way to fundraise. Marjorie and Karen often work with families to set up Zoom calls with potential donors who show interest. They also mentioned that if families know someone, whether an institution or an individual, who might be interested in becoming a donor, the KAT6 Foundation can provide a 10-slide overview for families to share within their community.
Anyone can participate in fundraising, making it an excellent way to support the foundation.

Scientific Sessions

KAT6A Foundation Leadership Presentations

Karen Ginsburg
Chair, Fundraising Committee
KAT6 Foundation

Alexa Elkins
KAT6 Foundation

It was inspiring to have a mother-daughter duo provide a snapshot of their life with KAT6A in their presentation titled "KATTalk." The daughter, Alexa (Lexi), is a 14-year-old girl with a KAT6A gene variation. She was diagnosed with KAT6A when she was 8 years old.
During their talk, Lexi's mom, Karen, candidly shared the upsides of having a KAT6A gene variation. Lexi is incredibly friendly and has a remarkable ability to remember the names of people and characters she's come across or read about. She has a joyful personality, which is fantastic. At school, Lexi actively participates in a newsletter called "The Apple." However, there are also some challenges that come with her condition, such as social skills, handwriting, balance, and focus. But with the help of AFOs (ankle-foot orthotics), braces, speech therapy, occupational therapy, physical therapy, and oro-motor therapy, Lexi is making progress.
Lexi is a huge music lover and has an impressive Spotify playlist with 2564 songs. She can tell you the name of each artist and song version in her playlist. Her memory for songs and singers is amazing. Lexi also enjoys reading, especially the Harry Potter series, and she keeps a diary where she writes down her thoughts. She's also a big fan of movies and has a unique talent for remembering the names of the cast members by watching the credits. She loves telling stories and incorporates her favorite characters and actors into her own imaginative tales.

Scientific Sessions

KAT6A Foundation Leadership Presentations

What's really heartwarming is that Lexi has formed a close bond with her babysitter's dog, even though she was initially scared of it. She also loves being in the water and, after years of swimming lessons, she can now swim independently. Lexi's achievements are a testament to the hard work and dedication of her family, as well as the support of the KAT6 community, researchers, and everyone involved in helping these children.

Scientific Sessions

KAT6A Foundation Leadership Presentations

Amy Young
Parent of a child with KAT6A gene variation
Volunteer, KAT6 Foundation

Susan Hartung
Board member, KAT6 Foundation

The KAT6 Foundation is a parent advocacy group and constantly strives on empowering and educating families on how to effectively advocate for children with KAT6A or KAT6B gene variations. Susan Hartung and Amy Young have a long association with the KAT6 foundation. Susan has a 37 year old son with KAT6A and a 33 year old daughter with Autism. Susan has been a strong advocate for disability services for over 30 years. After Amy's son was diagnosed with KAT6A in 2016, she became passionate about supporting families in the KAT6 Community and began working with the heads of the Foundation to learn about the extensive process of creating the first ever KAT6A/KAT6B patient registry to assist in research for these rare diseases.

Susan and Amy presented on tools for effective advocacy with a key note that "every parent or guardian has the right (and obligation) to advocate for their child." The KAT6 Foundation hosts an advocacy committee to support families on advocacy, gather resources and help hem become the most effective parent advocated possible.

Since both KAT6A and KAT6B gene variation are rare genetic syndromes, at times doctors, teachers and service providers may not be familiar with this syndrome. Susan and Amy advised parents to carry the KAT6 handbook for medical appointments and print out extra copies to leave with them.

Scientific Sessions

KAT6A Foundation Leadership Presentations

Susan and Amy emphasized the importance of families engaging in active listening and continuous learning, while maintaining a deliberate focus on their child's long-term goals. They highlighted the value of appreciating the support of others and embracing diverse communication methods to effectively convey their message. Additionally, they encouraged families to form partnerships with individuals who share similar perspectives, as well as those with differing viewpoints, demonstrating an open-minded approach that facilitates considering various positions and responding thoughtfully to issues. They stressed the significance of resilience in bouncing back from negative feedback and actively involving the public and stakeholders. Ultimately, they underscored the need for families to prioritize collaboration and recognize its pivotal role in achieving collective objectives.

It is important for families to learn about their state's law regarding disability education as this may differ from state to state. However, every family is entitled to Child Find. Child Find means that schools have a legal duty to evaluate children impacted by disability. To ensure effective advocacy for their child, parents should follow these general "good practice" guidelines. They should begin by requesting FERPA (Family Educational Rights and Privacy Act) to protect their child's educational records. Keeping a journal to document dates, subjects, and details of all communication, whether phone calls, appointments, meetings, or informal discussions, is highly recommended. Organizing all relevant records such as IEPs, meeting invitations, evaluations, meeting notes, and progress reports in a binder or online folder is essential. Written communication with school personnel is crucial and should be documented. If parents decide to enlist the help of an outside advocate, they should review the current IEP (Individualized Education Program) Plan and prepare a list of questions and concerns. Even if they choose not to hire an advocate, it is advisable to compile such a list before an IEP meeting to discuss with the school team.

Scientific Sessions

KAT6A Foundation Leadership Presentations

Prior to the meeting, parents should craft an opening statement to clearly articulate their concerns and aspirations for their child. Lastly, recording IEP meetings can be valuable for reference and ensuring accurate documentation.

Susan and Amy highlighted that up through age 22, services are an entitlement. In addition to advocating for services for children, Susan and Amy engaged in a discussion about the importance of advocating for services specifically tailored to adults with disabilities, which is a topic that receives comparatively less attention. They mentioned that up through age 22, services are an entitlement and according to federal law school must start transition planning at the age of 14. It is important for families to educate themselves on their stat's services. Some common points are - every state has an HCBS (Medicaid Home-and Community-Based Services waiver program. Through this program, states can help provide different services that allow those who need care to receive services in their homes or communities. Some states have Medicaid Autism Waivers. Most communities have local programs – recreation, respite, etc. They recommended families to visit medicaidwaiver.org, a website that list programs by state.

Susan and Amy acknowledged that the process of advocating for services can be overwhelming. They shared a few pointers, such as the significance of doctor's letters as strong forms of documentation. To save time, families can draft a letter and request the doctor to edit it on their letterhead. They also gave prominence to staying informed about lawmakers and funding authorities. In their presentation, they provided sample letters that have proven effective in advocating for their children. Moreover, Susan and Amy's presentation was enriched with valuable resources, relatable stories, and helpful personal experiences.

Scientific Sessions

KAT6A Foundation Leadership Presentations

Lindsey and Colin Blanch are the parents of three beautiful children. Their daughter, Audrey, who is 14 months old, was diagnosed with a KAT6A gene variation in June 2022. Like any other parents who have a child with a rare gene variation, getting a diagnosis was extremely tough. Lindsey and Colin were aware of Audrey's hypotonia as early as 2 months of age, and their medical team thought that was the only area of concern.

Determined to uncover the underlying cause of Audrey's hypotonia, Lindsey and Colin pursued numerous tests and investigations, anxiously seeking answers. The pivotal moment arrived when Lindsey vividly recalled the day she and Colin received the life-altering diagnosis through a poignant video call with their neurologist. However, the neurologist's limited knowledge about the KAT6A gene variation left Lindsey and Colin feeling overwhelmed and uncertain about Audrey's future.
It was during this period of waiting, filled with anxiety and unanswered questions, that Lindsey and Colin fortuitously discovered the KAT6 Foundation. Lindsey said that this remarkable organization proved to be an invaluable resource, providing them with compassion, support, and a wealth of information

The KAT6 Foundation has provided invaluable support to the Blanch family in various key ways following Audrey's diagnosis. Firstly, they found solace and a sense of belonging within the foundation's compassionate community. Lindsey and Colin were swiftly welcomed into a Facebook support group, gaining access to a network of individuals who understood their journey firsthand. Remarkably, their request to join the group was accepted on the very same day Audrey received her diagnosis. Alongside this, the foundation's CEO, Emile Najm, promptly provided Lindsey and Colin with essential resources to educate themselves about the KAT6A gene variation.

Scientific Sessions

KAT6A Foundation Leadership Presentations

This act of kindness ignited a glimmer of hope within Lindsey, as she discovered stories of other families whose children with the same gene variation were leading fulfilling lives. Overwhelmed with gratitude, Lindsey confided that she often revisits these messages, as they hold immense significance for her and Colin. The Blanch family considers themselves fortunate to be part of the KAT6 Foundation's global family, where they find understanding, empathy, and a shared journey with parents facing the ups and downs of raising children with rare gene variations. Lindsey shared that she learnt about a physical therapy intervention program on the KAT6 Foundation's YouTube channel to help Audrey with her hypotonia. The video was posted by another family, and Lindsey and Colin tried the program for Audrey who had a positive change in her motor skills after undergoing the program. This is just one example from many instances the KAT6 Foundation has been a useful resource as Lindsey and Colin make decisions about Audrey's care.

Secondly, the foundation has proven to be a treasure trove of experiences and advice for the Blanch family. Navigating the complexities of caring for a child with a rare gene variation often involves trial and error, learning on the fly, and continuous adaptation. In this regard, being able to draw upon the wisdom and insights of others who have traveled a similar path has been invaluable for Lindsey, Colin, and their journey with Audrey. The collective experiences and guidance shared within the foundation have empowered the Blanch family to provide the best possible care for their daughter, allowing them to face the challenges with greater confidence and resilience.

Lastly, in addition to the community and experiential support, the KAT6 Foundation has played a vital role in advancing scientific research and knowledge about KAT6A and KAT6B gene variation. Colin shared that it was extremely helpful to have access to all published research through the foundation's website, enabling them to deepen their understanding of these gene variations. Colin, especially during the early days of Audrey's diagnosis, found valuable resources on the foundation's webpage and YouTube channel. These resources empowered him and Lindsey to explore potential treatment options that were being investigated at the time. The foundation's unwavering commitment to promoting discovery and driving awareness has contributed to a growing body of evidence and facilitated coordination and funding for crucial research efforts.

Scientific Sessions

KAT6A Foundation Leadership Presentations

While the days following the diagnosis were filled with uncertainty, fear, and grief, Lindsey and Colin have discovered a profound sense of hope and joy through their connection with the KAT6 Foundation. They express sincere gratitude for the foundation's unwavering support, recognizing it as a beacon of light that accompanies them on their journey.

KAT6 Foundation

Thank you!