KAT6 Foundation

KAT6A KAT6B HANDBOOK

TABLE OF CONTENTS

1
Our Story

2
KAT6A & KAT6B Syndromes

3
Features of KAT6

4
Newly Diagnosed

5-6
FAQs

7
Of Special Concern

8
Supporting Families

9
Driving Research

OUR STORY

The KAT6A Foundation was founded in 2017 by a handful of parents of children identified with mutations on their KAT6A gene. At the time, there were fewer than 50 known KAT6A cases. In the span of 5 years, our numbers have expanded to over 370 known KAT6A cases worldwide. In 2020, the KAT6A Foundation began fostering connections with the KAT6B community and in 2022, we formally became the KAT6 Foundation, an organization devoted to understanding mutations in both KAT6A and KAT6B genes. Today, there are more than 500 known cases of KAT6 syndromes worldwide, and we expect our numbers to continue to grow.

We are the only 501(c)(3) nonprofit organization founded to support the international KAT6 community.

OUR MISSION

The KAT6 Foundation supports individuals and their families who are living with KAT6A and KAT6B syndromes around the world. We advance scientific research aimed at developing treatments, and spread awareness of KAT6 syndromes so they can be more easily identified, treated, and studied.

JOIN US

We hope that you will reach out to us if your family member was diagnosed with KAT6A or KAT6B syndrome. We empathize with your daily challenges and are here to support, educate, and learn from you.

Find our support group on Facebook. We have many international KAT6 families connecting every day. They will be your greatest resource.

KAT6A & KAT6B SYNDROMES

KAT6 syndromes are ultra rare diseases resulting from mutations in KAT6 genes. KAT6 genes are known as epigenetic regulator genes such that they open our DNA to make the right genes available at the right time for our bodies to function properly. Like thread in a spool, the DNA inside our cells is tightly wrapped. The timing of when our DNA becomes unraveled, to allow our genes to perform their function at the right time, is critical to their development. Therefore, KAT6 genes do not just serve one small role, rather, they control the function of a wide variety of genes across our chromosomes.
Studying KAT6A and KAT6B gene function will increase our overall knowledge of multiple systems in the body to unlock the possibility for greater health for all.

Children with KAT6 syndromes will carry a wide range of challenges as every case is unique. Some individuals will require much more support, while others' health and developmental delays may be mild. Scientists cannot yet fully explain this variability, however there is some evidence that the location of the mutation on the genes is a strong determinant of the severity of the symptoms. This is called genotype-phenotype correlation.

DIAGNOSING THE POPULATION

KAT6 syndromes are a result of genetic mutations that occur early in embryonic development. Typically, KAT6 mutations are de novo, which in Latin means "from the beginning; anew". In the context of genetics it means they are not inherited from a parent but are rather completely new to the family's genealogy.
Originally, these genetic mutations could only be identified through a costly DNA sequencing test known as Whole Exome Sequencing, which is not available in many parts of the world and often not covered by insurance. More recently, KAT6A and KAT6B mutations have been added to a less extensive test known as the Intellectual Disability NGS Panel. Because KAT6 mutation characteristics can be classified under larger umbrella diagnoses, such as autism, cerebral palsy, or global developmental delay, it is possible people with these mutations are being overlooked. Even when these tests are an option, many healthcare providers are not informed enough about rare genetic diseases to ask for them nor provide them as an option. The KAT6 Foundation aims to create more awareness of KAT6 syndromes so that more patients can receive appropriate testing and earlier and accurate identification.

As of 2022, there are fewer than 600 people diagnosed with KAT6 syndromes. As these tests become more available, we expect these numbers to significantly increase.

FEATURES OF KAT6

KAT6A Other names for this syndrome or gene: Arboleda-Tham syndrome, Lysine (K) acetyltransferase 6 A, MOZ, MYST3

KAT6B Other names for this syndrome or gene: Genitopatellar syndrome (GPS), lysine acetyltransferase 6B, MORF, MYST4, Ohdo syndrome, Say-Barber-Biesecker-Young-Simpson (SBBYS)

COMMON TRAITS

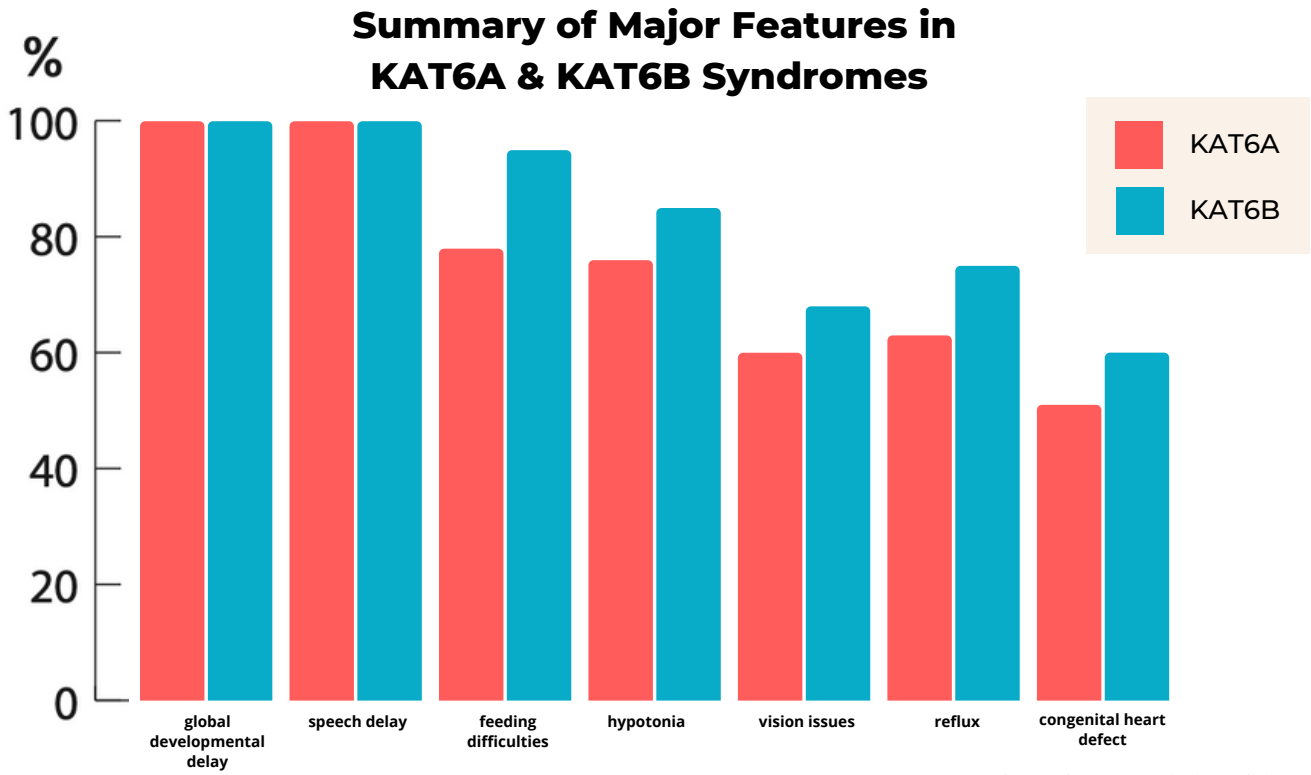
Affecting greater than 50% of diagnosed individuals

- global developmental delay (physical and/or cognitive)
- intellectual disability
- significant speech and language delay
- congenital heart defects
- distinct facial features
- feeding difficulties
- vision problems
- gastrointestinal problems including reflux and constipation
- hypotonia
- microcephaly
- sleep disturbances (KAT6A)
- problems with hips or knees (KAT6B)
- growth problems (KAT6B)
- genital anomalies (KAT6B)

LESS COMMON TRAITS

Affecting fewer than 50% of diagnosed individuals

- endocrine conditions such as hypothyroidism
- respiratory problems
- skull abnormalities
- cortical visual impairment
- autism spectrum disorder
- sensory processing disorder
- genital anomalies (KAT6A)
- seizure disorders
- kidney problems
- dental anomalies
- hearing impairment
- ADHD
- frequent infections (KAT6A)
- growth problems (KAT6A)
- problems with hips or knees (KAT6A)
- fractures (KAT6B)



Kennedy J. et al "2019 Genetics in Medicine"
Yabumoto M. et al "2021 Molecular Genetics & Genomic Meidicine

NEWLY DIAGNOSED?

My child was just diagnosed, what medical steps should I take?

- It is recommended that every individual diagnosed with a KAT6 gene mutation should see a cardiologist to rule out any structural heart problems.
- Monitoring weight gain in infancy is important. Feeding difficulties and reflux are common and may need significant medical support by a gastroenterologist. Your GI doctor can help manage constipation to prevent possible bowel obstructions and emergency medical care.
- It is also important to have vision assessed by a specialist and monitored yearly since eye problems occur in 60% of known cases.
- If your child experiences recurrent infections, discuss with your providers an immunology workup.
- KAT6B patients should have kidney and thyroid function tested.
- Consider undergoing a sleep study if signs of sleep apnea or sleep dysfunction.
- Other tests to consider include an abdominal ultrasound, audiology evaluation, and brain MRI. Discuss these tests with your child's pediatrician.

CONNECT WITH OTHERS

"Before receiving my son's diagnosis of KAT6A I thought we were alone in this journey. The sleepless nights, the GI issues, the surgeries, the unknowns were overwhelming, to say the least. After joining the KAT6 community and Facebook support group, I finally felt like there was hope, relief, and comfort in knowing we were certainly not in this by ourselves. The commonalities of our children blew me away and the insight and advice from parents have helped to guide many difficult decisions and have led us in the right direction for others. The work of the KAT6 Foundation is by far the most important research and education of our lives. There is no better way for us to support the foundation than through fundraising efforts that directly impact our son."
-Katie

JOIN THE KAT6A/KAT6B PATIENT REGISTRY

Our KAT6A/KAT6B Patient Registry launched in 2019 through the National Organization of Rare Diseases (NORD). It is the first longitudinal study of KAT6 syndromes. Our registry collects valuable data about many aspects of KAT6 syndromes, enabling researchers to understand the full range of KAT6 characteristics and to identify areas for additional studies. Most importantly, the KAT6 Foundation owns the data we collect, which allows us more control around directing research and sharing information. The KAT6 Foundation also analyzes our patient registry data and shares it with our patient families on the *Facebook* support group, helping families better understand and support their loved ones.

Register at https://kat6a.org/registry/

FAQs

What is the likelihood that I could have another child with KAT6A or KAT6B?

In de novo KAT6A and KAT6B gene mutations, there is a 2% risk of the syndrome reoccurring for the same parents. Very occasionally the genetic mutation can be found in some of the cells of one of the parents, this is called 'gonadal mosaicism'. In such cases, it is possible to have further children with this condition. In rare instances, KAT6 gene mutations are inherited. In these cases, there is a 50% chance that any offspring will inherit the genetic mutation. For this reason it is recommended for families wanting to have more children to speak with a genetic counselor.

What is the life expectancy for KAT6A and KAT6B individuals?

We are collecting data through the KAT6A/KAT6B Patient Registry in order to conduct a longitudinal study. Currently, the oldest individual diagnosed with KAT6A is in his 50's, and the oldest with KAT6B is in her 40's. We will learn more about the progression of KAT6A and KAT6B as more cases are identified and followed over time.

Will my child learn to talk?

Most KAT6 individuals have language delays. Yet, there's a wide range in language ability. Some children are nonspeaking and communicate through signs, body language or adaptive technology. Others are verbal teens and adults despite language delays as young children. Many parents report that their children have better receptive language than expressive language.

Where are individuals diagnosed with KAT6 living around the world?

Individuals have been identified in at least 40 different countries. Many caregivers connect via our support group and WhatsApp internationally. Our Foundation can provide translated materials at your request.

FAQs

What treatments are available?

Currently doctors are treating the symptoms related to KAT6A and KAT6B on an individual basis, but there is no medication for KAT6 syndromes specifically. Your child may require medication to help control constipation, acid reflux, behavioral issues, seizures, sleep disturbances, and other health problems caused by the gene mutation.

Many parents have observed benefits from vitamins and supplements including:

l-carnitine, pantothenic acid, coenzyme Q10, Vitamin E, Vitamin C, Cytra-3 and others. You can learn more about these supplements by watching Dr. Richard Kelley's presentation from our 2022 Conference. It is essential to consult your child's physician before starting anything new.

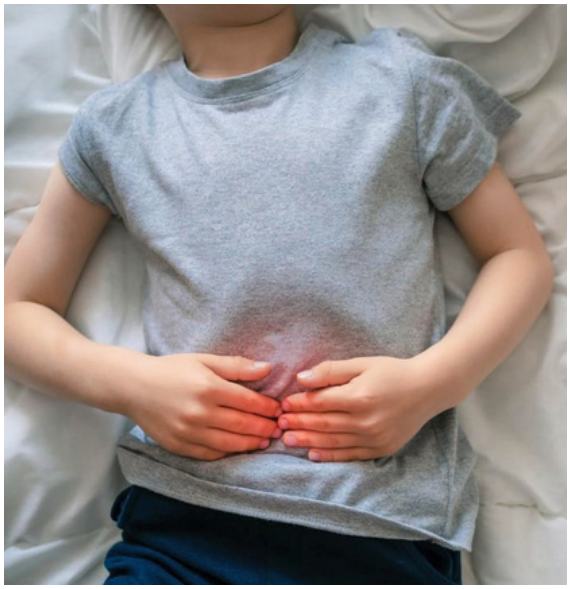
What therapies will benefit my child?

Every individual is different, but many in the KAT6A and KAT6B communities receive a wide variety of therapies as children to aid in their development.

- Physical therapists help improve gross motor development, which is typically delayed in our children due to abnormal muscle tone, motor planing difficulties and poor coordination.
- Occupational therapists work on fine motor activities required for daily living.
- Speech therapists work with our children in developing speech production, receptive language, signs and vocalizations. Many children have apraxia and struggle with the motor planning required for fluent speech. PROMPT speech therapy is highly recommended.
- Feeding therapists work with children with feeding difficulties. Many KAT6 children have feeding delays due to hypotonia and acid reflux, and others have structural damage that requires feeding tubes.
- Orthopedic intervention can be beneficial to patients with contractures, clubfoot, or hypotonia. Your child may benefit from specialized orthotics.
- Vision therapy is beneficial for individuals with Cortical Visual Impairment (CVI) or strabismus.
- Special education accommodations will likely be required for your child. Individuals with KAT6 have a wide range in intellectual ability, so it is impossible to predict how your child's needs will need to be met in school. Early intervention programs may offer a special educator starting at birth if cognitive delays are present.
- Various alternative therapies may benefit your child, such as: aquatic therapy, music therapy, sensory therapy, sound therapy, voice therapy, hippotherapy, and biofeedback.

OF SPECIAL CONCERN:

BOWEL OBSTRUCTIONS IN THE KAT6 POPULATION



Parents of a child with a KAT6 variant are the first to recognize when the one they care for is in distress and needs medical care. People with KAT6 syndromes may quietly tolerate increasing pain until it has become severe and may show no signs of a bowel obstruction until it has progressed to a serious degree. Obstructions can happen again and again and can strike at any age. An obstruction can quickly go from serious to dangerous.

Low motility in the gut means weak contractions of the muscles that mix and propel contents in the gastrointestinal tract. When weak contractions fail to keep intestinal contents moving, this is ileus — not a blockage but a slow-down or stoppage.

If the bowel contents sit too long, they can begin to ferment and decay, with potentially serious results. If it does not eventually start moving on its own, it may respond to non-invasive treatments such as stimulants taken orally or a rectal enema. But if there is a physical barrier to continued movement, the problem can quickly become life-threatening.

During gestation, when a portion of the developing intestinal tract fails to move properly into place in the baby's abdomen, it Is known as a malrotation. This is an anatomical defect and one that must be suspected if problems arise after birth. If it causes repeated interference in normal digestion or leads to an obstruction, then it can become a serious problem.

When a loop of intestine and the membrane that holds it in place twist around each other like sausage links, this causes an obstruction called a volvulus. Trapped intestinal material, already partially digested, continues to break down though, and some contents may be ejected as diarrhea or gas, while most of it will remain and swell the gut.

A person suffering a volvulus, who enters emergency surgery soon enough, may still lose part of the intestinal tract in surgery. Without emergency surgery a volvulus is almost certain to be fatal. A growing pocket of gas can be detected on successive x-rays, but not if the physician is treating the patient for a suspected food allergy or diagnosing tantrums due to anxiety.

A volvulus is a rare occurrence in the general population, but among the KAT6 population it seems common enough to be of serious concern.
It appears now that untreated bowel obstructions are the leading cause of death among children affected by KAT6 syndromes.

Communication problems are common with the KAT6 population as is a high tolerance for pain. Children and adults with KAT6 syndromes, especially those who can't tell us that something hurts or where it hurts, need to be monitored continually for lack of gut movement. Doctors need to trust what we are telling them, and so our information must be reliable. By educating ourselves, paying close attention to the signs our child gives us, and making sure we communicate consistently and accurately with medical providers, we can be our child's best advocates.

SUPPORTING FAMILIES

BRINGING FAMILIES TOGETHER

The KAT6 Foundation is the official sponsor of the International KAT6A & KAT6B Conference. We have hosted three conferences in conjunction with Johns Hopkins in Baltimore, Maryland. The goal of the annual conference is to solidify KAT6A and KAT6B research internationally. Each conference enables open dialogue between families, clinicians, and researchers and provides a platform for the KAT6 community to expand its network.

EMPOWERED GRANTS

Empowered Grants provide funding for the purchase of assistive equipment, devices, and technology, as well as a variety of therapies for individuals diagnosed with KAT6 syndromes. Assistive equipment and technology can enable individuals to participate more fully in society, care for themselves, reach educational goals, build stronger connections, improve communication, and attain social and emotional growth.

Since 2020, we have awarded more than 50 grants to KAT6 individuals living in the US and internationally. Each grant reward is for US $600.

Visit https://kat6a.org/empowered-grant/ for a full set of guidelines and to download an application today.

KAT6 ADVOCACY

Our advocacy team helps caregivers navigate the educational and medical systems to make informed decisions and obtain optimal services and care for their child.

The team is a great resource for families transitioning from education to adult services. They assist families in understanding the process and rights of students with Individual Education Plans and help parents interpret evaluative reports and their implications.

DRIVING RESEARCH

THE KAT6 FOUNDATION PROUDLY FUNDS AND SUPPORTS INTERNATIONAL RESEARCH BY CONNECTING FAMILIES TO CURRENT RESEARCH STUDIES.

- **David Geffen School of Medicine**, USA - stem cell research on KAT6A and KAT6B, which continues to develop (2017 – present)
- **Technion Institute**, Israel - multiplex analyses of the molecular pathophysiological mechanisms underlying KAT6A and KAT6B syndromes (2018 – present)
- **Walter and Eliza Hall Institute of Medical Research**, Australia - KAT6A and KAT6B mice studies are underway with the future goal of potential treatments being tested (2018 – present)
- **Murdoch Children's Research Institute**, Australia - international speech study on KAT6A and KAT6B individuals (2019 – present)
- **Chan Zuckerberg Initiative**, USA - the KAT6 Foundation was chosen as part of the Chan Zuckerberg Initiative: Rare as One Network — a group of 30 patient-led organizations that are accelerating research and driving progress in the fight against rare disease (2020 – present)
- **Centro Andaluz de Biología del Desarrollo (CABD)**, Spain – a study of precision personalized medicine in KAT6A Syndrome (2020 - present)
- **Center for Regenerative Medicine (CREM)**, USA - the KAT6 Foundation and collaborators have established the first patient-derived induced Pluripotent Stem Cells (iPSC) bank for KAT6A and KAT6B variants (2022 - present)
- **Kennedy Krieger Institute**, USA – pilot study of Cognition and Neurobehavior in KAT6A Syndrome (2022 – present)
- **Rare Diseases: Models & Mechanisms Network (RDMM)**, Canada- the first study involving fly models to investigate the neurological implications of KAT6A and KAT6B gene mutations (2022 - present)

Learn more about this groundbreaking research and how to become involved at kat6a.org/funded-projects/

KEY RESOURCES

KAT6A Fact Sheet by Centre for Genetics Education
KAT6A Syndrome Report by NORD
KAT6A Syndrome: Genotype–Phenotype Correlation in 76 Patients with Pathogenic KAT6A Variants

KAT6B Disorders
Novel Variants in KAT6B Spectrum of Disorders Expand Our Knowledge of Clinical Manifestations and Molecular Mechanisms

KAT6 Foundation

KAT6 Foundation
3 Louise Drive
West Nyack, NY 10994-1911
EIN # 82-3118535

www.kat6foundation.org
Email: support@kat6a.org

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