

KAT6A News

The Newsletter of the KAT6A Foundation

What's happening in the KAT6A Foundation?

Since Our 501(c)(3) nonprofit organization was started in the end of 2017, the KAT6A Foundation has been very busy. Several dedicated parents from our Facebook support group have taken on leadership roles on various committees. We strive to help families coping with a KAT6A diagnosis by providing resources and support. To meet this goal, we are in the process of developing a registry and are working hard to make it the most useful tool to date for researchers and KAT6A families. Additionally, we are in the process of translating important information regarding KAT6A into various languages to better serve our international members. The KAT6A Foundation also aims to raise awareness of this rare disorder so that more individuals are diagnosed. We are proud that many new families have reached out to us via the website, fundraising page and support group.

An important part of our mission is to raise funds for research so that we can learn more about the KAT6A gene and find treatments. We have several research opportunities in the works and an exciting KAT6A mice study is underway in Australia. Read more about Dr. Arboleda's ongoing research on page 4.

WWW.KAT6A.ORG

Please visit the official website of the KAT6A Foundation, <http://www.kat6a.org>. We hope you will access the About KAT6A page to find valuable information regarding past and current research. Many questions you have are addressed in the FAQs tab. To date, 18 families have contributed to the Blog page. Thank you for sharing your stories! In our blog, you will read first hand accounts from KAT6A families who may be going through a similar experience as you. You will also find news articles and videos featuring our children and young adults. You can find out about upcoming fundraising and social events in our KAT6A community by visiting the Events page. There are also links on the webpage to our social networks: Facebook, Instagram and YouTube. Furthermore, you can help us raise money for research by encouraging your friends and family to visit our Donate page. The website is updated regularly, so please come back often and share it with your medical specialists and family members.

If you would like to contribute content to the website such as photos, a blog, fundraising event, FAQ, etc. Please send the details to Aimee Reitzen at aimee4fh@hotmail.com.

KAT6A Clinic Summary

On February 3, 2018, the first KAT6A clinic was held in Baltimore, Maryland, at the Kennedy Krieger Institute. Nineteen families attended and several more followed the clinic by livestream. We were pleased to have in attendance and as speakers Jacqueline Harris, M.D., Ph.D., Pediatric Neurologist from the Kennedy Krieger Institute in Baltimore, Hans Thomas Bjornsson, M.D., Ph.D., Director of Epigenetic and Chromatin Clinic and Assistant Professor of Pediatrics at Johns Hopkins Hospital in Baltimore, Jill Fahrner, M.D., Ph.D., Assistant Residency Program Director at Johns Hopkins Genetic Medicine Residency Program and Assistant Professor of Pediatrics at Johns Hopkins Hospital in Baltimore, and Richard Kelley, M.D., Ph.D., former Director of Division of Metabolism at Kennedy Krieger Institute in Baltimore and current researcher at the Division of Genetics and Boston Children's Hospital.

After a welcome by KAT6A Communications Director Brittany Green, Dr. Jacqueline Harris presented an overview of the KAT6A clinical syndrome. She explained that KAT6A is a histone modifier epigenetic disorder. This means that the gene function is changed, not the gene sequence, and it is influenced by the histone machinery. It is most often de novo, which means that the genetic change happens in the child and is not inherited from either parent. She reported that there are only a few documented cases, so not much is known about KAT6A syndrome. Researchers need more cases to study. However, there seem to be some features that are nearly universal and some features that seem to be related. Some of the universal features include hypotonia, feeding problems, congenital heart disease, eye or vision problems, skull abnormalities, distinctive facial features, and global developmental delay. Less common but probably associated features are small birth size, perinatal complications, seizures, specific behavioral features, sleep disturbances, immune system irregularities, dental abnormalities, hand abnormalities, and brain MRI abnormalities. She concluded by stating that current researchers learn most from the patients and their families and by drawing from information from other similar epigenetic syndromes.

Next, Dr. Kelley spoke about mitochondrial dysfunction in KAT6A. KAT6A affects metabolic protein absorption, and children with this disorder often have abnormal levels of certain plasma amino acids. Some that he mentioned were citrate, asparagine, and phenylalanine. Using common lab standards, amino acid levels often seem within normal range but a doctor who specializes in mitochondrial disorders uses a conversion scale to determine whether there is a mitochondrial disorder. Dr. Kelley has been working with several families to analyze plasma amino acid levels and then recommending parts or all of a mitochondrial cocktail that he has developed as treatment. Carnitine has been shown to potentiate chromatin opening, and Vitamin B5 helps the body break down carnitine, so these are often helpful to children with KAT6A. Several parents have documented developmental progress in their children who are taking carnitine and vitamin B5. Dr. Kelley is quite confident that carnitine is very beneficial to individuals with KAT6A.

Dr. Bjornsson was the last speaker and he spoke about Mendelian disorders of the epigenetic machinery and therapeutic possibilities. He has been studying a disorder very similar to KAT6A called Kabuki Syndrome. They are both epigenetic disorders of the histone machinery. Dr. Bjornsson is studying a mouse model of Kabuki syndrome and has been able to gain much needed

information, including some effects that can be reversed using drugs targeting the epigenetic machinery. He also feels that carnitine is likely a good therapeutic treatment for KAT6A.

He would like to be able to build KAT6A related data based on seeing more patients with KAT6A. He summarized by emphasizing how rare KAT6A is and that in order to assist in further research, the KAT6A Foundation needs to participate in research by donating results, samples and joining studies, as well as promote research by raising funds to help any interested lab get preliminary data to attract NIH funding. We can also continue to organize meetings and clinics such as this one and continue to increase awareness about KAT6A in the world.

The meeting concluded with some time for the families to meet, share information, and speak individually with the doctors. For those present as well as those families who were listening to the live feed, this first get-together was stimulating, rejuvenating, and gave us hope for our children's future.



KAT6A Fundraising

The KAT6A Foundation hosted an online t-shirt fundraiser in February, which raised \$2065.56. We have several family members of KAT6A individuals hosting birthday fundraisers on Facebook with all proceeds going to the KAT6A Foundation. In addition we have raised over \$15,000.00 via online donations and checks mailed directly to our foundation.

The Foundation now has silicone fundraising bracelets on hand for anyone that is interested in selling them. Please contact Jessica Vogland via Facebook messenger if you are interested.

You can also help us raise funds by shopping on <http://www.smile.amazon.com>. For your first time shopping, make sure to select KAT6A Foundation Inc. as your charity to support. It will save our charity to your account for all future purchases.

If you'd like to get involved with fundraising, please join our KAT6A Foundation Fundraising and Awareness Group on Facebook. <https://www.facebook.com/groups/1924074790952872/>

Dr. Valerie Arboleda's KAT6A Research



On March 1, 2018, Dr. Francis Collins, the Director of the National Institutes of Health (NIH) dedicated his blog posting to Dr. Valerie Arboleda's research on KAT6A. This blog post provides great visibility for our community and the KAT6A Foundation, and is a very good summary of her research plan.

It is important to recognize and thank all of the families who supported the Children's National Race For Every Child over the past several years. It was funds you raised for those events that supported her initial research. This research provided the early findings that helped her win the NIH grant that will help sustain this research going forward. So congratulations to all of you for helping further KAT6A research. And thank you for your continued support of our new KAT6A Foundation as we continue to raise funds to support future research.

Below you can read "NIH Director's Blog" posted on [https://directorsblog.nih.gov/2018/03/01/creative-minds-looking-for-common-threads-in-rare-diseases/ - more-9725](https://directorsblog.nih.gov/2018/03/01/creative-minds-looking-for-common-threads-in-rare-diseases/-more-9725)

Creative Minds: Looking for Common Threads in Rare Diseases

Posted on March 1st, 2018 by [Dr. Francis Collins](#)

Four years ago, Valerie Arboleda accomplished something most young medical geneticists rarely do. She helped discover a rare congenital disease now known as KAT6A syndrome [1]. From the original 10 cases to the more than 100 diagnosed today, KAT6A kids share a single altered gene that causes neuro-developmental delays, most prominently in learning to walk and talk, plus a spectrum of possible abnormalities involving the head, face, heart, and immune system.

Now, Arboleda wants to accomplish something even more groundbreaking. With a 2017 NIH Director's Early Independence Award, she will develop ways to mine Big Data—the voluminous amounts of DNA sequence and other biological information now stored in public databases—to unearth new clues into the biology of rare disorders like KAT6A syndrome. If successful, Arboleda's work could bring greater precision to the diagnosis and potentially treatment of Mendelian disorders, as well as provide greater clarity into the specific challenges that might lie ahead for an affected child.

A Mendelian disorder arises from a change in a single gene and follows the accepted patterns (dominant, recessive, X-linked, or mitochondrial) of genetic inheritance. There are an estimated 7,300 Mendelian disorders, and many are exceedingly rare [2].

Because of their rarity, Mendelian diseases might seem like an unlikely match for Big Data tools. But as researchers have grown more adept at sequencing genomes and finding rare mutations, several recent studies have suggested that genes and pathways involved in many Mendelian disorders may also be involved in more common disorders [3-4].

Continued...

Arboleda, a researcher at the University of California, Los Angeles (UCLA), is now starting to look at Mendelian disorders from an oligogenic, or multi-gene, construct. While a rare, single-gene mutation may exert its most devastating impact on one biological pathway, she suspects such mutations can also have ripple effects that disrupt genes that control other biological pathways, including ones involved in more common diseases and traits.

To test this hypothesis, Arboleda will study a condition that she knows well: KAT6A syndrome. The syndrome is triggered by a mutation that usually arises spontaneously in the *KAT6A* gene during early development and is expressed in almost all cell types. The gene essentially encodes a master control switch: an enzyme that helps unwind certain parts of a chromosome, allowing gene-transcribing proteins access to blocks of genes to modify their expression levels as needed.

Arboleda has already collected skin cells from several kids with KAT6A syndrome and, for the first time, is using genomic tools to profile how a mutated *KAT6A* gene alters transcription across the genome. She's using a technique called RNA-seq to generate the global gene-expression data and ChIP-seq to monitor the activity of proteins that bind to DNA to influence gene expression. Arboleda and her team will use this information to identify the many biological pathways that appear to be affected by the *KAT6A* mutation.

Then comes another challenge: using Big Data tools to search for similarities between the genomic profiles of KAT6A kids and those of kids with common disorders that display some features similar to KAT6A. Such disorders include autism spectrum disorder, congenital heart defects, craniofacial defects, and immunodeficiencies.

For these analyses, Arboleda will turn to the rich body of data generated by the more than 2,500 genome-wide association studies (GWAS), [Genotype-Tissue Expression \(GTEx\)](#), and [Encyclopedia of DNA Elements \(ENCODE\)](#). She'll use these tools to search for genetic variations that control gene expression in ways that are reminiscent of KAT6A syndrome and which are associated with risk for common disorders. Arboleda wants to see which of these variations might also influence some of the symptoms associated with KAT6A syndrome.

According to the young UCLA researcher, all of this effort will be worthwhile if she can help the families of kids with KAT6A syndrome, whom she regards as priceless partners in her research endeavors. It's a sentiment that resonates with me and the many other NIH-funded scientists who are working so hard to find cures for rare diseases, especially as we celebrate the 11th annual Rare Disease Day at NIH today.

References:

[1] [De novo nonsense mutations in *KAT6A*, a lysine acetyl-transferase gene, cause a syndrome including microcephaly and global developmental delay](#). Arboleda VA, Lee H, Dorrani N, Zadeh N, Willis M, Macmurdo CF, Manning MA, Kwan A, Hudgins L, Barthelemy F, Miceli MC, Quintero-Rivera F, Kantarci S, Strom SP, Deignan JL; UCLA Clinical Genomics Center, Grody WW, Vilain E, Nelson SF. *Am J Hum Genet.* 2015 Mar 5;96(3):498-506.

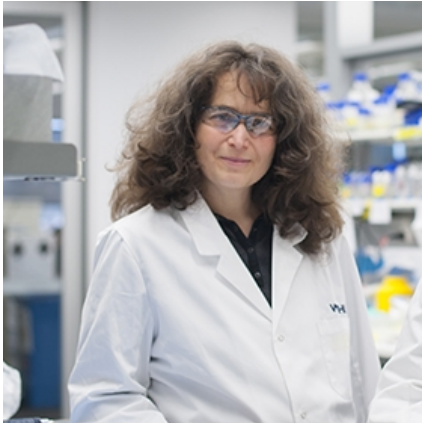
[2] [Centers for Mendelian Genomics uncovering the genomic basis of hundreds of rare conditions](#). Benowitz S, National Human Genome Research Institute, August 6, 2015.

[3] [A nondegenerate code of deleterious variants in Mendelian loci contributes to complex disease risk](#). Blair DR, Lyttle CS, Mortensen JM, Bearden CF, Jensen AB, Khiabani H, Melamed R, Rabadan R, Bernstam EV, Brunak S, Jensen LJ, Nicolae D, Shah NH, Grossman RL, Cox NJ, White KP, Rzhetsky A. *Cell.* 2013 Sep 26;155(1):70-80.

[4] [Properties of human disease genes and the role of genes linked to Mendelian disorders in complex disease aetiology](#). Spataro N, Rodríguez JA, Navarro A, Bosch E. *Hum Mol Genet.* 2017 Feb 1;26(3):489-500.

Advancing KAT6A Research

Dr. Anne Voss



We are proud to announce that Dr. Anne Voss at Walter & Eliza Hall Medical Institute (WEHI) in Melbourne, Australia will begin to test experimental treatments in KAT6A mice. She has been studying KAT6A and the KAT6B related protein in mice for many years now. Meg Salisbury is acting as a consumer for her research and Dr. Richard Kelley is a collaborator on the project. Initially, she will be looking at the effects of carnitine and valproic acid on markers of biochemical dysfunction with potential research to follow.

Anne is very open and warm. She is eager to learn about our children and assist us in any way that she can. She will hold a conference call with our support group on May 7th to answer any questions you may have about her research and for her to ask any questions of us that she may have to help direct her research.

<https://www.wehi.edu.au/people/anne-voss>

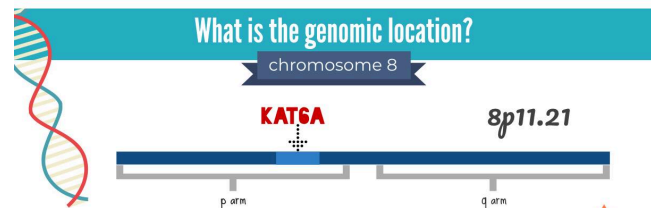


KAT6A Infographic

KAT6A

gene

<p>Alternate names: MOZ, MRD32, MYST3, MYS T-3, ZNF220, RUNXBP2, ZC2HC6A</p>	<p>Associated Conditions: Autosomal dominant intellectual disability 32</p>
--	---



The "genomic location" tells us where to find the gene on a chromosome.

What to expect?

Features associated with KAT6A gene changes:

- Intellectual Disability/Developmental Delay
- Autism Spectrum Disorder
- Epilepsy or Seizures

Donations Needed

We are compiling a list of durable medical devices and gently used speech aids that your children have outgrown so that these items can be passed on to other KAT6A individuals. Please contact Lindsey Geiger via Facebook messenger if you can help support this cause.



Awareness Video

We are still looking for photos and videos of our kids for the KAT6A awareness video. These are the types of photos/videos we are looking for:

- 1) Those beautiful loving moments
- 2) Showing one of the best KAT6A traits – their happy and cheeky nature
- 3) Achievements
- 4) The tough stuff - hospital stays, tough therapy

If you have any you would like to share please send them to Meg Salisbury.

Upcoming Events

Conference Call with Dr. Voss- KAT6A Mice Study

May 7 @ 6:00pm EST

The link to the conference call will be posted on the support group.

Dalton Graham Run

July 22 @ 9:00 am

*Middletown Elks 2179, 251 Church St
Belford, NJ 07718 United States*

KAT6A Walk to Find a Way

September 15

Raleigh, NC, United States

Stay tuned for more details including information about "Virtual Walks" that will place this day around the world.

Visit www.kat6a.org to read more about these scheduled events and to stay up to date on what may be coming to your area.

Social Media

Please like/follow/subscribe to us on social media.

Facebook

<https://www.facebook.com/kat6afoundation/>

Instagram

<https://www.instagram.com/officialkat6a/>

Youtube

<https://www.youtube.com/channel/UCPJcgZbhqzGZq0k2VRIn9LQ>



This custom photo frame created by Vera Moura was used on Facebook by many to bring awareness to KAT6A.

We are eager for your help and to hear your ideas. If you'd like to get involved with the foundation and help on one of our committees, we welcome you to join our KAT6A Foundation Fundraising and Awareness Group today. <https://www.facebook.com/groups/1924074790952872/>

Noteworthy Achievements

Each quarter we'd like to celebrate recent accomplishments by KAT6A individuals. We also want to recognize and thank families who have gone above and beyond to raise awareness about our very rare syndrome in their communities.



Cullen, age 13, competed in a Special Olympics swim meet in South Carolina. He swam the 25m breast stroke and the 25m freestyle. Breast stroke is his favorite! He placed first in breast and fifth in freestyle.

John competed in the Special Olympic field trials in March and qualified for the Oklahoma State competition.

Eight-year-old Peter's literature entry recently won the Reflections PTA Artist for his school, then his county, and the statewide competition for New York.

Monika Rammal, aunt to Eleanor, has gone above and beyond to raise awareness for KAT6A. As a teacher in Austria, she guided her students to create a breathtaking and inspiring video to raise awareness about KAT6A and to support her niece. Deservingly this project received the most online votes for the "Strong School Awards." Thank you Monika for being a talented and dedicated teacher, devoted aunt to Eleanor and advocate for all KAT6A families.

Several individuals have held personal fundraisers to support KAT6A research. Thank you Lindsey Geiger for supporting us through Scentsy, Brittany Green for orchestrating the "One of a Kind Leggings for One of a Kind Kids" Lularoe fundraiser, Kimberly Harvey-Chase for designing and selling KAT6A awareness bracelets and supporting us in a bake sale in Canada, and to Andrew Rankin for fundraising on behalf of our foundation as he participates in the New York Five Boro Bike Tour on May 6th.

The Green family hosted a KAT6A awareness booth at their local Children's Fair in Boone, North Carolina on April 21st. They also raised money for our foundation by selling KAT6A bracelets.

On April 22nd, in Thurgoona NSW, Australia, Ginger's grandfather helped raise funds for our foundation through his bicycle shop's inaugural event, Omloop Het Amogah! Thank you Washington Cyclisme for your support.

On March 11, Marc ran with his son, Pol, in the Zurich Marathon in Barcelona Spain along with some great friends, the Tremp Runners. Great job raising awareness for KAT6A and for giving Pol an unforgettable experience.



KAT6A Foundation Leaders

Board of Directors

Terri Fallis

Karen Ginsburg

Jordan Muller

Emile Najm

Shelby Rau

Aimee Reitzen

Meg Salisbury

David A. Woodbury

Chairperson

Jordan Muller

Chief Executive Officer

Emile Najm

Secretary

David A. Woodbury

Treasurer

Matt Salisbury

Communications

Director: Brittany Green

Family Services

Director: Tresh Crosby

Newsletter: Aimee Reitzen

Fundraising

Director: Jessica Vogland

Australia Region: Meg Salisbury

Science and Research

Director: Natacha Esber, MD

Registry Coordinator: Amy Young

Social Media

Director: Vera Simoes Moura

Facebook: Aimee Reitzen

Instagram: Miranda Lentine

Youtube: Jessica Levesque

Technical Advisors

Natacha Esber, MD

Susan Hull, MD

Luis C. Maas, MD

Andrew J. Rankin, PhD

Kenneth N. Rosenbaum, MD

Alain Verloes, MD, PhD

Web Master

Aimee Reitzen

Contact us at
support@kat6a.org
with any questions or
comments. We are
here to serve you.

KAT6A Providers List

Austria

Dr. Sara Baumgartner, A.Univ.-Prof. Dr. Daniela Karall, IBCLC Medical University of Innsbruck, Clinic for Pediatrics/Inherited Metabolic Disorders, Innsbruck, Austria

France

Alain Verloes, MD, PhD, Chief of the Department of Medical Genetics, “CRMR Anomalies Développement & Syndromes Malformatifs et Déficiences Intellectuelles de causes rares”, Robert Debré Hospital, Paris, France

Iceland

Hans Tomas Bjornsson, MD, PhD, starting June, 2018

International

Richard Kelley, MD, PhD, Former Director, Clinical Mass Spectrometry, Laboratory, Kennedy Krieger Institute Associate Professor, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD

United States of America

Hans Tomas Bjornsson, MD, PhD, Director of the Epigenetics and Chromatin Clinic at John Hopkins University, Baltimore, MD

Jill Fahrner, MD, PhD., Assistant Residency Program Director at Johns Hopkins Genetic Medicine Residency Program and Assistant Professor of Pediatrics at Johns Hopkins Hospital, Baltimore, MD

Jacqueline Harris, MD, MS, Assistant Professor of Neurology and Pediatrics Director, Center for Tuberous Sclerosis and Related Disorders, Kennedy Krieger Institute, Johns Hopkins Medical Institution, Baltimore, MD

Kenneth N. Rosenbaum, MD, Founder of the Division of Genetics and Metabolism, Rare Disease Institute, at the Children's National Medical Center, Washington, DC

Valerie A. Arboleda MD, PhD, Founder of the Arboleda Lab at UCLA, Department of Pathology and Laboratory Medicine, David Geffen School of Medicine, UCLA, Los Angeles, California. Dr Arboleda will arrange referrals to clinical genetic specialists at UCLA

KAT6A Photo Gallery



Send us photos of you raising awareness for the KAT6A Foundation and be featured in the next issue of KAT6A News.

