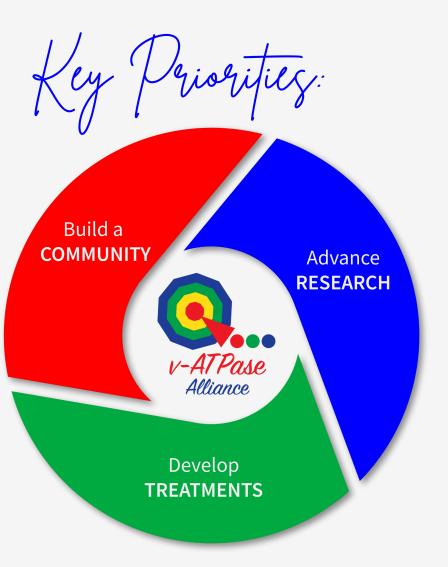
THE V-ATPASE VOICE



#MarchingForward

THE V-ATPASE VOICE



Build a COMMUNITY

Through sharing we will be able to empower each family with information to discuss with each care team.

Advance RESEARCH

Collect information and seek partnerships and support research to help define disease biology.

Develop TREATMENTS

Foster collaboration among researchers, drug developers and regulators to create tools and resources in therapeutic developments.

De art v-ATPase Alliance

#MarchingForward

THE V-ATPASE VOICE

SLUHLUO



Message from the Founders







Dear Supporters and Friends,

We hope this message finds you well. As the Founders of our rare disease nonprofit organization, we wanted to take a moment to share some exciting updates with you.

Behind the Scenes Efforts: Over the past several months, we have been hard at work behind the scenes. Our commitment to advancing rare disease research and supporting families affected by ultra-rare conditions remains unwavering. Here are some highlights of our efforts:

1. Introducing and Raising Awareness for v-ATPase Conditions: We participated in several conferences. including American Society of Gene and Cell Therapy, the Milken Institute 27th annual Global Conference, and the Ultragenyx Bootcamp. These events have Rare provided valuable platforms to raise awareness about v-ATPase conditions and engage with leaders in the rare disease space to discuss our research agenda, while providing opportunities to learn about tools, resources, and best practices to advance our mission. We are dedicated to staying informed and effective in our roles, and are proud to represent the v-ATPase Alliance these esteemed at gatherings.

- 2. Building a Strong Network: Establishing connections with other rare disease leaders, scientists, and researchers has been a priority. These networks allow us to share insights, collaborate on research, and advocate for better treatments and Through formal mentorship care. programs and many informal coffee chats other patient advocacy leaders, we have spread awareness about the Alliance and marched forward down the learning curve of best practices for our group.
- **3. New Partnerships:** We're thrilled to announce our recent affiliation with the Rare Epilepsy Network (REN). By joining forces with REN, we aim to amplify our impact and drive positive change within the rare epilepsy community. This partnership has already provided valuable insights, and we look forward to further collaboration with other member organizations.
- 4. A Recognized Resource for v-ATPase Families: We are excited to announce our inclusion in Epilepsy & Seizures 24/7 helpline database from the The Epilepsy Foundation of America. This recognition will help support inquiries about v-ATPase-related conditions and make it easier for those affected to reach out and learn more. We are honored for being part of the #1 trusted site for epilepsy and seizure updates.

Message from the Founders







Celebrating Ana Rita: We are immensely proud of Ana Rita, who has been selected participate the **FasterCures** in to LeadersLink leadership development program from the Milken Institute. This competitive 20-month program trains nonprofit leaders organizations conducting biomedical research, empowering them with invaluable professional leadership skills and networks. Her dedication and passion for rare disease advocacy inspire us all!

Urgency and Hope: As we work diligently behind the scenes, we recognize the urgency needed to tackle the challenges posed by v-ATPase disorders, and we are motivated by the memories of the children that we have lost in the past year. Advancing research and effecting change to avoid this outcome for other families drives us forward. Our goal is to find therapeutic approaches and develop concerted plans of care for all children affected by these conditions.

Thank you for your continued support. Together, we can make a difference in the lives of those facing rare diseases.

With Gratitude,

Ana Rita Moreira Luis Miguel Oliveira Kristin Anderson



Help us with our mission.

Donations go directly to research efforts that take us closer to a cure.

Continued support helps us to plan ahead, so please consider making a recurring monthly donation.





*v-ATPase*Patient Registry



It's Live!

We launched the first patient data collection program for v-ATPase-related disorders in partnership with Rare-X on March 19th, 2024. This milestone is the first step stone in our journey towards understanding and treating v-ATPase-related disorders.

The <u>v-ATPase Alliance patient Data Collection Program (DCP)</u> is a foundational study to create a robust open-access data set to speed scientific breakthroughs and life-changing treatments for our children. We aim to gain important information that may help in understanding how these disorders manifest, who is "at risk" of developing certain epilepsy and neurodevelopmental symptoms, who is not, and why, and we will follow people over time to learn how the disease progresses during its natural course. That information may lead to insights and tools that can help better diagnose, treat, and even cure this disease.

But we can't do it alone.



We need your enrollment and participation to gather important data from as many individuals as possible - remember we are a small population and therefore each participant has a huge impact on the robustness of the study. This is a tremendous task that our team is committed to supporting moving forward. The v-ATPase DCP study will set the foundation to establish Clinical Outcomes Assessments (COAs) and Clinical Endpoints. These consist of measurements or observations that reflect how a patient feels, functions, or survives, and outcomes that can be used to evaluate the effect of an intervention on participants in a clinical trial, respectively.



Patient Registry

The v-ATPase DCP is pivotal for our long-term success, enabling us to:

- Measuring Treatment Effectiveness: COAs and clinical endpoints provide objective measures to assess the effectiveness of a treatment or intervention. They help determine whether a new drug, therapy, or medical device produces the desired outcomes in patients.
- Understanding Patient Experience: COAs, particularly patient-reported outcomes, provide insights into the patient's perspective on their health status, symptoms, and quality of life. This patient-centric data is valuable for evaluating the overall impact of a treatment beyond clinical measurements.
- Regulatory Approval: Regulatory agencies such as the U.S. Food and Drug Administration (FDA) require evidence of clinical benefit, often demonstrated through COAs and clinical endpoints, for approving new drugs or medical interventions.
- **Comparing Interventions:** COAs and clinical endpoints facilitate comparisons between different treatments or interventions, helping healthcare professionals and patients make informed decisions about the most appropriate course of action.
- Monitoring Safety: Knowing what the disease looks like also helps with defining safety measures, which are crucial for assessing the risks associated with a treatment. Monitoring adverse events and safety endpoints helps ensure patient safety throughout the course of a drug testing.

Together we have the ability to build a vast and evolving engine of discovery that will funnel a wealth of insights, practical tools, and data directly into the hands of researchers and drug developers worldwide. The v-ATPase DCP holds the promise of reshaping the trajectory of v-ATPase research, guide clinical decision-making, and contribute to a healthier future for our children.

Sign up today and complete all the questionnaires from the comfort of your home.

Help us cure v-ATPase disorders.

Want to know more about the v-ATPase DCP? Watch our launching Webinar!

Also, feel free to use our Page by Page Guide with notes to help you guide through the setup and consent forms. PDF available here.

Ready to Start?





The Heroes Wall



Meet

In this issue we are sharing Peyton's story, as told by her mother, Elizabeth Milstead. The message she shares about advocating for your child, maintaining a positive outlook, and remembering to care for yourself are absolutely universal for any parent, but even more critical when you're raising a child with an ultra-rare disorder. Thank you for sharing your wisdom and encouragement with us, Elizabeth!

Our daughter, Peyton Grace, is currently 15 years old and lives in Becker, Minnesota. She has been facing developmental delays since she was younger. These delays have affected almost every aspect of her life, including sitting up, holding her head up, crawling, walking, and talking. Additionally, Peyton experienced staring spells, where she would stare off and be unresponsive until she would come out of it. Her neurologist at the time performed numerous EEG tests to check for seizure activity, but nothing was found. However, in October 2016, Peyton had her very first seizure, which marked the beginning of a series of changes. She subsequently experienced 60-80 seizures a day, every day, until we sought the help of the epilepsy unit to bring them under control with seizure medications. Around a year or two after her first seizure, we received a call from her neurologist and geneticist, informing us that they had identified Peyton's diagnosis as ATP6V1A genetic disorder. Shortly after, we discovered the Facebook group that led us to the Alliance. Peyton, despite her disorder, remains a vibrant and energetic girl who loves horse back riding, adaptive dance, bowling, and spending time with her friends. She is currently a freshman in high school and relies on her caregivers for all her daily needs, but she never loses her big smile and infectious energy wherever she goes.

Peyton primarily uses a wheelchair to get around, but she also has a lift system at home to navigate the stairs, uses a walker, and has the assistance of caregivers. However, over the past couple of years, we've noticed that when Peyton is able to walk, she tends to walk on the outer sides of her feet, which has worsened even with the use of AFO orthotics. This past fall, we met with Peyton's orthopedic doctor to discuss potential options and determine the best course of action. We started with x-rays of her feet and followed up with a gait and motion lab at Gillette Children's in St. Paul, Minnesota. The purpose of the study was to measure Peyton's movements and muscle activity while she walks, which lasted around 3 hours. We then waited for the results before sitting down with the orthopedic surgeon to discuss the findings. We decided that surgery was necessary if we wanted Peyton to continue walking, as the skin on the sides of her feet would eventually break down and the tissue would deteriorate. The surgery, performed on the soft tissue, involved lengthening her calf muscle, tibialis anterior transfer, and posterior tibialis lengthening, and was scheduled for March 4th, just a few days after Peyton's 15th birthday.

The Heroes Wall





The surgery left Peyton unable to put any weight on her feet for 5 weeks, during which she had casts on both feet and relied heavily on her caregivers for every need, including getting around the house, changing, getting dressed, and bathing with bags covering her casts to keep them dry. We are currently 6 weeks post-surgery and Peyton is undergoing an intensive 10-day inpatient rehabilitation program at Gillette Children's Rehabilitation. She has been receiving PT twice a day, OT twice a day, therapeutic recreation therapy, and music therapy every day except Sundays. Our goal for Peyton is to ensure she is comfortable on her feet, enhance her durability, and build up her resilience and endurance before discharge.

When you are first faced with the role of being a caregiver for your child with disabilities, it's only natural to have lots of questions. Any new parent has lots of questions regardless, and changing your perspective to accommodate your child with a disability certainly adds more. To me, being a caregiver to my daughter Peyton is everything. It's not just being a parent, but also an advocate, a friend, and a fighter for your child. It has every high and every low known to mankind. We as their caregivers know them inside and out, better than anyone else, so we are the ones that NEED to stand up for them to ensure their wants and needs are being met. This includes everything from their daily activities and education, needs for therapists and visits with specialty doctors, and creating a healthy lifestyle for them to live in.

Some words of wisdom that I have for other parents going through this themselves"stay positive." Children are highly intuitive and can often sense their parents' emotions.
The stability of a parent's mood leads to the stability of the child's emotional
environment. It may be difficult, and of course we are all human, but stay positive!
Lastly, take care of yourself too. We do everything for our children, especially the child
we are caregiving for. If we want to be able to continue to do that for years to come,
we MUST find time to take care of ourselves. Through this journey, I have found long
distance running and yoga to be my best stress relievers. It is completely ok to take
time for yourself!





v-ATPase Alliance and other patient-driven foundations exist because rare diseases don't get enough attention from government and funding agencies for driving biomedical research, due to their low prevalence. However, epidemiological research clearly shows that rare diseases currently affect at any point in time 3.5% - 5.9% of the worldwide population, equivalent to a conservative estimate of 300 million people worldwide. Rare diseases are a public crisis and yet little to no orchestrated effort from governments exist to tackle them. And the most frustrating part is that the problem is not one of technological innovation, but an economic one instead. The technologies exist - we have an unprecedented capacity to survey the genome and find the genetic culprits causing these diseases, we have the ability to generate stem cells and gene editing tools to create the necessary models for pre-clinical drug development, and we have the ability to develop personalized therapies with tools like genetic therapies that are within our arsenal now. What we don't have is funding to build such models, screen therapies, conduct toxicology studies and build the pre-clinical package that leads to real drugs getting into the clinic.

But in all fairness despite the limited funding, an even bigger issue is the inability to access the available funding. FY2023 NIH budget was \$47.7billion. Rare diseases got ~\$6.8 billion. But only academic researchers have access to that funding. Patient advocacy groups are laser focused on filling the research gaps that are needed to de-risk therapeutic development for the conditions they represent, yet they are not even allowed to competitively apply for a piece of the pie. Should \$3B be put aside for patient advocacy groups focused on drug development at a baseline of \$3M research budget *each* we would see more therapeutics hitting the market than ever before. We know our diseases better than most of the doctors, the Facebook groups are years ahead of most of the published natural history studies, we are the coordinators of the researchers, and you will never find more motivated relentless groups.

On February, 29th, the Rare Disease Day, many groups came together to advocate for this change in many different federal institutions, including the White House. We would like to share with you the testimony of Nasha Fitter, co-founder and CEO of the FOXG1 Research Foundation, a patient-driven foundation dedicated to cure the FOXG1 Syndrome, as a testimony that embodies this sentiment and makes its case. - video link.

It's time for us to collectively turn awareness into action. Join us in advocating for change. Reach out to your elected officials, raise your voice for patient-driven research, and demand equitable access to funding for rare disease therapeutics. Together, we can ensure that patient advocacy groups like ours have the resources needed to accelerate research, develop life-changing treatments, and improve the lives of our children. Stand with us, because every voice counts.

HAWKE FALOON In Memorian

It is with our deepest sadness that we share that our v-ATPase community lost another warrior earlier this month. Hawke Faloon was born in 2018 and diagnosed with ATP6V1A Encephalopathy shortly after. He lived in Indiana with his two brothers and loving parents, Brynne and Jon, who were incredible caregivers and advocates for his needs throughout his life. He touched all of our hearts with his bright smile and the most beautiful hair! No family should have to lose a child, and we are emboldened more than ever to push our mission forward and urgently expedite research in our quest to find treatments for our children. We need the time, talents, and treasures of our global community to help us in this endeavor. If you feel led to make a donation in honor of Hawke, or by volunteering your time to the organization, please click here:

DONATE



After announcing the launch of the Alliance at the beginning of the year, our small but mighty community has absolutely risen to the challenge of engaging with our mission and sharing our message worldwide to raise awareness of v-ATPase disorders. We are thankful for all the ways in which these patient families and their communities have supported our efforts! It takes a village, and we have the best!

Dr. Kasia Goljanek-Whysall, Professor and Vice Dean at University of Galway, and her daughter, Niamh, participated in Ireland's "I am Number 17" campaign to raise awareness for rare diseases and the benefits of early diagnosis. She is a champion for diversity and inclusion, and her daughter's rare diagnosis of ATP6VOA1 has led her to become an even greater researcher and advocate for people living with rare diseases.

Read about the I am Number 17 campaign here: www.iamnumber17.ie

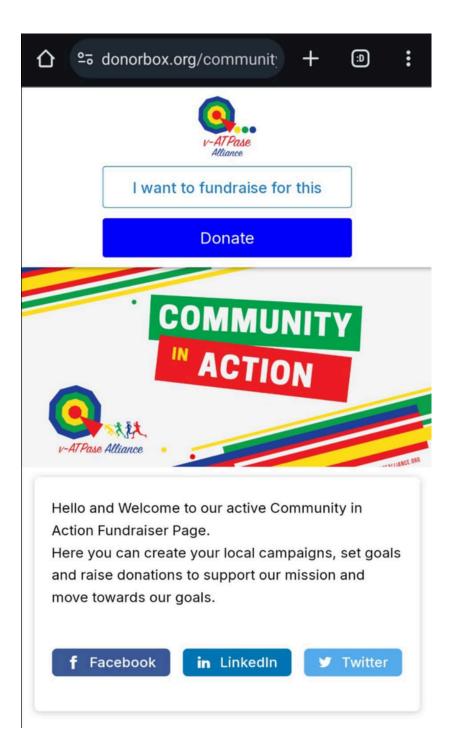


In February we launched a large campaign for Global Rare Disease Day, held each year on the last day of the month. This year was extra special as it fell on Leap Day – the rarest date on the calendar! Our families and friends participated in our first fundraiser and sported the "Care About Rare" Alliance t-shirt, held awareness events at school, took a polar plunge in icy waters, and even inked a brand new zebra tattoo!



We also activated our Community in Action Fundraising <u>web resource</u>, which allows anyone and everyone to fundraise on behalf of the v-ATPase Alliance.

Just click in the "I want to fundraise for this" and follow the steps to set up your own campaign and help us reach our goals.



Our first participant is Elizabeth Milstead, proud mother of Peyton, and an avid runner! She is running her 2nd marathon in Duluth, Minnesota next month. In the midst of an intense surgery and recovery period for Peyton, she is taking inspiration from her daughter and finding her own strength and resolve to train and run this race for a reason – to spread awareness for her rare disease and help raise money that will further research on v-ATPase disorders. Will you support Elizabeth's incredible efforts and make a donation today?

Community in Action - Elizabeth Milstead's Fundraiser

Additionally, if you or a friend or family member feel called to fundraise on behalf of the Alliance, please reach out and we can set up your own personalized fundraising page!



If you have an upcoming run or sporting event and want to help give visibility to the Alliance and v-ATPase disorders, please reach out and we can set you up with game day gear! We can't wait to see our shirts everywhere in the world!





MD TALKS



Ricardo Morcos, MD and Angel Aledo-Serrano, MD, PhD.

To help you and your loved ones navigate a life with v-ATPase genetic disorders, we are partnering with researchers, medical doctors, and health professionals to discuss v-ATPase-related disorders research and care through The v-ATPase Voice and other media outlets.

In this issue, Drs. Ricardo Morcos, MD, and Angel Aledo-Serrano, MD, PhD, physicians and epileptologists from the Instituto de Neurociencias Synaptia in Madrid, Spain, discuss the intricate genetic landscape of epilepsy. From navigating the diverse array of genetic variants to the enabling role of genetic testing in diagnosis and the promising future of personalized therapies, understanding the genetic underpinnings of epilepsy is a crucial piece of the puzzle to improve patient's lives and even provide a cure to this debilitating condition.

Navigating the Genetic Landscape of Epilepsy

In this issue, we're thrilled to delve deeper into the intricate world of genetic epilepsy, offering a comprehensive understanding that can empower your journey. Let's explore the complexities of genetics, the nuances of diagnosis, and the exciting future of epilepsy treatment.

Unraveling Genetic Epilepsy

Epilepsy, a diverse neurological condition, finds its roots in various factors. Genetic elements contribute significantly, accounting for around 60% of cases. These genes can influence critical aspects of brain development, disrupting the intricate balance between neural inhibition and excitability, leading to an increased susceptibility to seizures.

Understanding the types of genetic variants is essential for grasping the intricacies of genetic epilepsy. From single nucleotide variants (SNVs) to structural variants and nucleotide repeat expansions, each variant type can have different effects on gene function. This complexity adds layers to our comprehension of the condition.

Genetic Testing and Diagnosis

Genetic testing emerges as a powerful ally in the diagnosis of epilepsy, particularly for those with an early onset and associated neurodevelopmental challenges. Indications for testing are diverse, including early onset, a family history of epilepsy, or instances of unexplained drug-resistant epilepsy.



MD TALKS



Ricardo Morcos, MD and Angel Aledo-Serrano, MD, PhD.

Multiple genetic testing methods, such as gene panels and whole-exome sequencing, contribute to identifying different types of genetic variants associated with epilepsy. The interpretation of results is a collaborative effort involving geneticists and neurologists, ensuring a thorough understanding and providing comprehensive counseling for individuals and their families.

Treatment and Future Directions

The discovery of a genetic basis for epilepsy opens new avenues for tailored treatment strategies. Approximately 30-40% of cases can benefit from personalized approaches. Treatment decisions are increasingly influenced by the functional impact of the specific genetic variants. For instance, certain anti-seizure medications are selected based on the affected gene, showcasing the potential for precision medicine in epilepsy care.

Excitingly, the future holds promising therapeutic approaches, including gene delivery and editing. While not yet integrated into routine clinical practice, these "gene therapies" promise to revolutionize epilepsy treatment, offering the potential to alter the trajectory of the disease.

In Conclusion

Understanding the genetic facets of epilepsy represents a paradigm shift in our comprehension of the condition. Genetic testing stands out as a pivotal step in the diagnosis journey, providing valuable information that shapes various aspects of care. As personalized therapies advance, the epilepsy community can look forward to a brighter and more tailored future in the treatment landscape.

Remember, you are not alone. Your strength and resilience inspire us all.

Kind Regards from Madrid, Ricardo Morcos, MD and Angel Aledo-Serrano, MD, PhD. Instituto de Neurociencias Synaptia, Madrid, Spain.

Key bibliography:

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Classroom



The patient's journey with a v-ATPase disorder usually starts (or better said it's acknowledged) when a person receives a genetic report with a positive result for a v-ATPase gene. But there is quite a lot of information in these reports and understanding them can be both crucial and complex for families navigating this diagnosis. Besides the positive or negative result, these tests offer insights into the molecular underpinnings of a patient's condition. However, deciphering them requires more than just a basic understanding of biology.

Today, we will explore the components of a genetic report, understanding its contents to empower patients and their families with the knowledge they need to navigate their journey with a v-ATPase disorder.

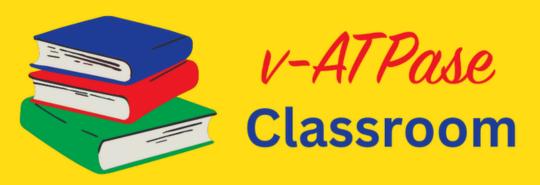
Unfortunately, v-ATPase associated genes are not yet included in common genetic panels or newborn screening tests for faster diagnosis, and therefore more sophisticated analysis are needed in order to detect these genetic alterations. Thus, typically one finds a v-ATPase diagnosis after performing a whole exome sequencing (WES) analysis, a powerful genetic test used to analyze all the regions of the DNA in an individual's genome that code for functional proteins in the cells - known as the exome - where most of the disease-causing variants exist.

Whole exome sequencing may provide several types of genetic information, including:

- Single nucleotide variants (SNVs): Point mutations involving the substitution of one nucleotide for another within the coding region of a gene.
- Insertions and deletions (indels): Small insertions or deletions of DNA within coding regions, which may disrupt gene function.
- Splice site variants: Mutations that affect the junctions between exons and introns, which can alter mRNA splicing and gene expression.
- Copy number variants (CNVs): Large-scale duplications or deletions of genomic segments, including exonic regions, which can lead to gene dosage imbalances and disease.

Although the format or language of the report may differ slightly, typically a genetic report will contain the following information exemplified here for a SNV:

Next Page





Gene	Coding DNA	Variant	Zygosity	Mode of Inheritance	Inherited From	Classification
ATP6V0c	C.448 C>T	p.(L150F)	Heterozygous	Autosomal Dominant	De Novo	Pathogenic Variant

Let's dive into the components of this report and explore the different possibilities.

Gene identifies the v-ATPase gene affected.

Coding DNA and Variant report the alterations that occurred at the DNA and Protein levels respectively. These alterations are typically represented using a standardized format known as the Human Genome Variation Society (HGVS) nomenclature, and common possibilities for variant representation include:

- Substitution (SNV):
 - c.448 C>T: A substitution of cytosin (C) with thymine (T) at nucleotide position 488 in the coding DNA sequence.
 - o p.L150F: Amino acid change from leucine (L/Leu) to phenylalanine (F/Phe) at position 150 of the protein.
- Insertion (INS):
 - o c.456_457insT: Insertion of a thymine (T) nucleotide between positions 456 and 457 in the coding DNA sequence.
 - o p.Glu78_Thr79insPro: Insertion of proline (Pro) between amino acid positions 78 and 79 of the protein.
- Deletion (DEL):
 - c.789_792delAGTC: Deletion of the AGTC nucleotides between positions 789 and 792 in the coding DNA sequence.
 - o p.Lys102del: Deletion of lysine (Lys) at position102 of the protein.
- Duplication (DUP):
 - c.234_237dupATCG:Duplication of the ATCG nucleotides between positions 234 and 237 in the coding DNA sequence.
 - o p.Ala56dup:Duplication of alanine (Ala) at position 56 of the protein.
- Frameshift Variant:
 - o c.345_346insG: Insertion of a guanine (G) nucleotide between positions 345 and 346, causing a frameshift mutation.
 - p.Pro78fs: Frameshift mutation resulting in a premature stop codon after position
 78 of the protein.





*v-ATPase*Classroom



Gene	Coding DNA	Variant	Zygosity	Mode of Inheritance	Inherited From	Classification
ATP6V0c	C.448 C>T	p.(L150F)	Heterozygous	Autosomal Dominant	De Novo	Pathogenic Variant

- Splice Site Variant:
 - c.678+1G>T: Mutation at the +1 position of intron 678, affecting the canonical splice donor site.
 - c.123-2A>G: Mutation at the -2 position of intron 123, affecting the canonical splice acceptor site.
- Large Rearrangements
 - c.123_456dup: Duplication of a large segment of DNA spanning from nucleotide position 123 to 456 in the coding DNA sequence.
 - c.789_890del: Deletion of a large segment of DNA spanning from nucleotide position 789 to 890 in the coding DNA sequence.

Zygosity refers to the genetic composition of an individual with respect to a specific genetic variant. Typically varies between "Heterozygous" when one allele carries a variant, while the other allele is wild-type; "Compound heterozygous" when two different variants or mutations are present on each allele; "Homozygous" when both alleles carry the same variant or mutation; and "Hemizygous" when only one gene copy is present due to deletion or absence of the other copy.

Mode of Inheritance refers to the pattern in which a genetic condition is passed down from one generation to the next within a family. The possibilities for mode of inheritance typically include:

- Autosomal dominant when the genetic condition is caused by a mutation in one copy of a gene.
- Autosomal recessive when the genetic condition is only caused when mutations exist in both copies of a gene.
- X-linked dominant when the genetic condition is caused by a mutation in a gene located on the X chromosome, and it typically affects both males and females.
- X-linked recessive when the genetic condition is caused by a mutation in a gene located on the X chromosome, and it typically affects males more severely. Affected males inherit the mutated gene from their mothers, who are typically carriers but do not show symptoms.
- Y-linked when the genetic condition is caused by a mutation in a gene located on the Y chromosome.





*v-ATPase*Classroom



Gene	Coding DNA	Variant	Zygosity	Mode of Inheritance	Inherited From	Classification
ATP6V0c	C.448 C>T	p.(L150F)	Heterozygous	Autosomal Dominant	De Novo	Pathogenic Variant

Inherited from indicates the origin of a genetic variant or mutation observed in an individual. It may have maternal or paternal inheritance or the variant might be de novo (new mutation), indicating that the variant arose spontaneously in the individual and is not inherited from either parent, which is the most common in v-ATPase genetic disorders.

Classification categorizes the genetic variants based on their potential impact on protein function and association with disease. A genetic variant may be classified as "Pathogenic" when the variant is known or predicted to cause disease or dysfunction based on strong evidence from functional studies, population data, or clinical observations; "Likely Pathogenic" when the variant is likely to cause disease or dysfunction based on available evidence but requires further validation or clinical correlation to confirm its pathogenicity; "Benign" when the variant is unlikely to cause disease or dysfunction and is considered part of normal genetic variation within the population; "Likely Benign" when the variant is likely to be benign based on available evidence but requires further validation or clinical correlation to confirm its benign nature; or "Variant of Uncertain Significance" when the variant has unclear significance, meaning its impact on protein function and association with disease is uncertain - VUSs require further investigation, functional studies, or additional evidence to determine their clinical significance.

In addition to Whole Exome Sequencing (WES), v-ATPase disorders can also be identified with Whole Genome Sequencing (WGS) tests, which cover the entire DNA sequence inclusive of the DNA coding region covered in a WES test. The report and nomenclature in a WGS test are comparable to a WES.

In cases where a v-ATPase genetic alteration occurs due to large insertions or deletions in specific chromosomal regions encompassing v-ATPase genes, a diagnosis may also be obtained by performing a Whole Genome Chromosomal Microarray, also known as Chromosomal Microarray Analysis (CMA). This is a high-resolution genetic test used to detect abnormalities in the chromosomes' structure allowing for the detection of gains, losses, or rearrangements of chromosomal segments in the genome.

Understanding your genetic report can empower you and your family with tools to navigate your v-ATPase disorder journey more effectively, fostering informed decision-making and personalized care.





Our Mission



We need your support!

Finding cures to diseases is a long road.

Each action you take will help us move towards our goals.

We need you to be involved.

Here is a short list of quick actions you can take:





Unite Families

Advance Scientific Research

Raise Awareness

CONTACT US

www.vatpasealliance.org @vatpasealliance

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