

SEARCHING FOR A CURE - HOPE FOR OUR CHILDREN

PARTICIPATION MATTERS

Every Contribution Makes a Difference



When our community participates, we create stronger support, advance research, and bring hope to every family affected by propionic acidemia.

SHARE YOUR STORY

Your experience with propionic acidemia matters. Sharing your story can help another family feel less alone, increase awareness, and help others understand what life with PA is really like.

Whether you share a diagnosis story, a personal experience, a milestone, or a challenge you have overcome, your voice can make a difference.

PARTICIPATE IN RESEARCH

Research depends on participation from individuals and families affected by PA. Studies help researchers learn more about the disease, its progression, complications, and the experiences of those living with it. Every participant contributes another piece to the puzzle. By participating when you can, you help build knowledge that may benefit future generations.

VOLUNTEER YOUR TIME

There are many ways to support the Propionic Acidemia Foundation. Volunteer at an event, help with awareness efforts, share information on social media, support fundraising, welcome a newly diagnosed family, or offer your skills and ideas.

*“Your voice matters.
Your experience matters.
Your time matters.”*

Together, our individual efforts become a stronger collective voice for everyone affected by propionic acidemia.

GET INVOLVED



Share your story



Participate in research



Volunteer your time



Spread awareness



Connect with another family

**YOU CAN MAKE AN IMPACT.
WE CAN MOVE PA FORWARD.**

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Research Awards

\$30,000 CONDITIONAL GIFT

Toward the Development of Safe Harbor Editing to Treat Propionic Acidemia (PA)

Principal Investigator: Charles P. Venditti MD, PhD, National Human Genome Research Institute, NIH

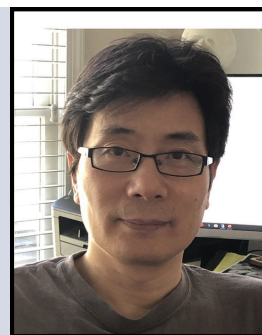


Propionic acidemia (PA) is a severe inborn error of metabolism caused by biallelic pathogenic variants in PCCA or PCCB, resulting in substantial morbidity and early mortality for patients despite current dietary and supportive therapies. This project will adapt a proven Albumin (Alb) safe-harbor editing strategy previously developed for methylmalonic acidemia [Schneller JL, Lee CM, Venturoni LE, Chandler RJ, Li A, Myung S, Cradick TJ, Hurley AE, Lagor WR, Bao G, Venditti CP. In vivo genome editing at the albumin locus to treat methylmalonic acidemia. *Mol Ther Methods Clin Dev.* 2021 Nov 11;23:619-632. PMID: PMC8634044<<https://pmc.ncbi.nlm.nih.gov/articles/PMC8634044/>>], using an AAV-based platform to deliver a therapeutic PCCA donor vector and a CRISPR/Cas9 cassette designed to target the Alb initiator codon. We hypothesize that targeted insertion of a functional PCCA transgene into the Alb locus will provide durable hepatic PCCA expression sufficient to restore propionyl-CoA carboxylase activity, reduce toxic metabolite accumulation, and improve survival and disease phenotypes in PA mice. Our strategy leverages the strong endogenous Alb promoter to drive immediate therapeutic expression from episomal AAV genomes while enabling durable expression through targeted integration into the Alb locus, with integration efficiency enhanced by CRISPR/Cas9-mediated genome editing. Successful completion of this work will define the feasibility, efficacy, and safety of Alb-based genome editing to treat PA and provide the broad foundation for future clinical translation of genome editing to treat organic acidemias.

\$50,000 NEW RESEARCH GRANT

Targeting gut microbiome and alternative propionyl-CoA disposal pathways through diet to improve outcomes in propionic acidemia

PRINCIPAL INVESTIGATOR: Guofang Zhang, PhD, Duke University



Propionic acidemia (PA) is a rare inherited metabolic disorder in which the body cannot properly process certain nutrients, leading to the accumulation of toxic metabolic compounds. Current treatment relies primarily on restricting dietary protein and providing supplements such as L-carnitine. Despite these approaches, many individuals with PA continue to experience serious long-term complications.

This new research project, led by Guofang Zhang, Ph.D., at Duke University, explores a new dietary strategy targeting an underappreciated source of metabolic stress: the gut microbiome. Gut bacteria produce propionate, primarily from dietary carbohydrates, and our preliminary studies indicate that microbiome-derived propionate may be a major contributor to the buildup of harmful propionyl-CoA in PA.

The study will investigate whether a modified ketogenic diet—low in carbohydrates and higher in fat—can reduce propionate production by the gut microbiome while also helping the body dispose of propionyl-CoA through alternative metabolic pathways. The research will define the optimal balance of carbohydrates, protein, and fat and determine whether these metabolic changes can also be observed in humans. Ultimately, this work aims to guide the development of safer, more effective dietary therapies and lay the foundation for future clinical trials for individuals living with PA.

Haven Mae's Story

We welcomed Haven Mae into this world on October 14th, 2024. She is our fourth child and everything from those first few days were normal and similar to the births of our other children.

We left the hospital three days later but received a terrifying phone call at home the following morning from the state.

They asked if our baby was breathing and conscious but would not tell us anything going on. We had a regular visit with the pediatrician already scheduled so we went straight to their office. The doctor evaluated Haven and said she looked well, when the hospital then called and asked us to come to them (2 hours away). We asked the pediatrician what was going on but all he said was that he was asked to see if she had signs of acidosis or hyper ammonia. We then got to the hospital where they confirmed she was stable but did take more bloodwork to narrow down her diagnosis since she set off 3 of the newborn screenings; propionic acidemia, methylmalonic acidemia, and cobalamin disorder. Although her c3 was very high, everything else in her new bloodwork was relatively normal.

In disbelief, I also asked for genetic testing which came back showing she has two VUS mutations.

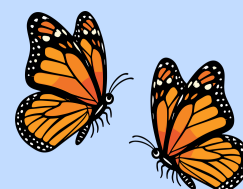


We also got enzyme testing done for her. Learning and navigating such a complex and devastating diagnosis so rapidly and expectedly was one of the hardest parts in those early days. Haven is now 21 months old and doing great. She is a happy toddler who loves to play with her siblings. She is on a restricted diet that we are still adjusting to, as well as expanding for her.

The trickiest part is navigating the toddler stage in relation to food while she tries to exercise control and independence. She loves movies, dancing and singing songs. Her favorite thing to do is collect the eggs from our chicken coop every morning and get slobbery kisses from our dog. She tries to keep up with her big brothers outside, and loves playing with baby dolls and coloring with her sister. She has a big personality already and her siblings adore and encourage it. My hope for Haven is that we properly navigate this and find the best balanced diet for her that she can not only enjoy but that will nourish and protect her. I pray for wisdom and guidance over all of the medical professionals treating Haven and all of our sweet babies, that their treatment plans preserve and protect their little minds and bodies as best we can so they may live the beautiful and joyful lives they deserve.



Share your story!
Spring Newsletter Deadline is March 1st.
Email paf@pafoundation.com



2025-2026 ANNUAL REPORT



Our focus this past fiscal year has been on increasing outreach to families impacted by Propionic Acidemia, funding promising research projects, distributing educational materials to families, collaborating with other rare disease organizations, and exhibiting and attending conferences.

- Organized the PA Family Day in November 2025, in Wheeling, IL.
- Exhibited and attended the PKU Organization of IL and Allied Disorders Low Protein Annual Meeting in November 2025 in Rosemont, IL.
- Partnered with HCU Network America, MSUD Family Support Group, and EveryLife Foundation for Rare Diseases on the Advocacy Webinar Series - "Advocacy 101 - What is advocacy and How you can get involved" and "Advocacy 101: Tell your story - Drive Change" in March 2026
- Exhibited and attended the Genetic Metabolic Dietitians International (GMDI) Conference in April 2026, in St. Louis, MO.
- Attended the American Society of Gene + Cell Therapy (ASGCT) 2026 Annual Meeting and the Annual Meeting of the Accelerating Medicines Partnership® Bespoke Gene Therapy Consortium (AMP® BGTC) in May 2026, in Boston, Massachusetts.
- Exhibited and attended the Society for Inherited Metabolic Disorders (SIMD) 2026 Annual Meeting in Rio Grande, Puerto Rico in May 2026.
- Attended the Rare Organic Acidemias Research (ROAR) Consortium Kick-off meeting in May 2026, in Houston, TX.
- Awarded a \$50,000 grant to Dr. Michael J. Wolfgang, at the Johns Hopkins University, Baltimore, Maryland for the research project "Mechanisms of Disease in Propionic Acidemia."
- Awarded a \$50,000 grant to Dr. Guofang Zhang, Duke University, Durham, North Carolina, for the research project "Targeting the Gut Microbiome and Alternative Propionyl-CoA Disposal Pathways Through Diet to Improve Outcomes in Propionic Acidemia."
- Awarded a \$30,000 Conditional Gift to Dr. Charles P. Venditti, at the National Human Genome Research Institute part of the National Institutes of Health, Bethesda, Maryland for research project "Safe Harbor Editing to treat Propionic Acidemia."

MISSION: The Propionic Acidemia Foundation is dedicated to finding improved treatments and a cure for Propionic Acidemia by funding research and providing information and support to families and medical professionals.

VISION: To create a future where Propionic Acidemia can be prevented, and any affected individual can be cured and live a productive life.

FINANCIAL STATEMENT

Expenses

Programs: Research & Outreach

\$135,523

Fundraising

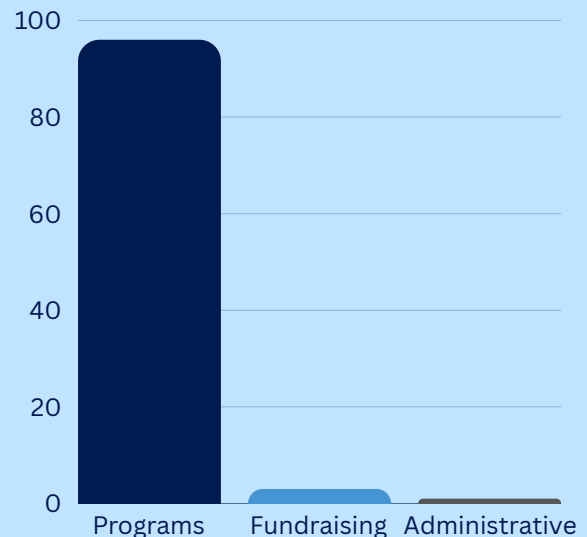
\$3,922

Administrative

\$1,913

Total Expenses

\$141,358



Income

Donations

\$128,836

Interest Income

\$ 23,418

Total Income

\$152,254

Cash Assets 8/01/2025

\$505,073

Cash Assets 7/31/2026

\$515,969

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Gene Therapy Trial for Propionic Acidemia - Mayo Clinic

OPEN FOR ENROLLMENT

David Deyle, MD and Michael Barry, PhD have recently opened their clinical trial titled, “Phase 1 Study of Intravenous Administration of a Serotype rh.10 Replication Deficient Adeno-associated Virus Gene Transfer Vector Expressing the Human Propionyl-CoA Carboxylase cDNA to Individuals with Propionic Acidemia.”

The purpose of this research is to evaluate the safety and potential benefit of gene therapy for propionic acidemia. Active participation in the study takes approximately 52 weeks and includes 3 nights in the hospital for your gene therapy and 10 in-person visits to Rochester, MN. There will also be a total of 13 home health visits during the first year. During these visits, patients will be evaluated through blood draws, urine collection, physical examinations, nutritional evaluations, developmental assessments, quality-of-life questionnaires, and cardiac evaluations. Participants will receive the viral vector through a single IV administration and monitored for safety. Compensation will be provided for all on-campus visits to assist with expenses to participate in this study.

Participants in this study may not see any health benefits. However, the benefits of gene therapy for propionic acidemia could reduce complications of propionic acidemia including poor feeding, irritability, low blood sugar, high levels of ammonia in the blood, and episodes where the body has trouble maintaining normal balance causing illness.

Key inclusion and exclusion criteria (see study team for detailed criteria):

Inclusion criteria	Exclusion criteria
Age six months to 2 years of age on the day of infusion.	Safety lab results outside of acceptable study range performed as part of screening visits.
Confirmed diagnosis of propionic acidemia with biallelic PCCA gene mutations.	Active viral infection (includes HIV, Hepatitis B or C).
Diagnosis of neonatal-onset propionic acidemia with a documented episode of decompensation.	Previous liver transplant. Grade 3 or 4 heart failure.
Parents or legal guardians must give consent for their child's participation.	Previously received gene therapy or messenger ribonucleic acid (mRNA) treatments for PA.

If you are interested in learning more or have questions about recruitment, please contact the study team at RSTCGResearch@mayo.edu



David Deyle, MD



Michael Barry, PhD

ROAR Consortium Receives NIH Funding

We are excited to share that the Rare Organic Acidemias Research (ROAR) Consortium has received NIH funding as a new consortium within the Rare Diseases Clinical Research Network (RDCRN). For the first time, a national research network is dedicated specifically to studying rare organic acidemias, including propionic acidemia (PA), methylmalonic acidemia (MMA), isovaleric acidemia (IVA), glutaric aciduria type 1 (GA1), and cobalamin C disease (CblC).



ROAR brings together families, advocacy organizations, clinicians, and researchers across the United States with a shared goal of improving the lives of people living with these rare disorders. Over the next five years, the consortium will study the long-term effects of these conditions, support the development of new treatments, and help prepare the community for future clinical trials.

Patient and family voices are at the heart of ROAR's mission. Working closely with advocacy partners, including the Propionic Acidemia Foundation, the consortium will ensure that community priorities help guide research and education efforts. Families can also participate through the ROAR Registry, a free and secure way to learn about research opportunities and stay connected with the consortium. The launch of ROAR is an important step forward for the organic acidemia community and creates new opportunities to advance research, improve care, and build hope for the future.

Learn More

- ROAR Consortium: <https://roar.rarediseasesnetwork.org/>
- RDCRN: <https://www.rarediseasesnetwork.org/>

Funding Acknowledgement: The ROAR Consortium is supported by the NIH through NICHD, NCATS, and NHGRI.



ROAR Kickoff Meeting
Houston, Texas
May 25-27th

Nash's Story



Nash was diagnosed with PA, at Children's National hospital, shortly after he was born and after an intense and extreme early onset. After spending several days non-responsive and with climbing ammonia numbers, we knew from his first weeks that a liver transplant was the best option to give him the fullest life possible. While we were well-informed on the risks of transplant, the priority for us to protect his brain became our non-negotiable and we chose to list him on the national registry before he was 3 months old.

The months of waiting for a liver were a blur of feedings around the clock and isolating to prevent any controllable chance of illness. In addition to hoping for a match from the registry, several close relatives pursued living donor evaluation and, ultimately, Nash's dad, Nick, was a match. Nash received a portion of Nick's liver at 5.5 months old through the MedStar Georgetown pediatric liver transplant program.

The transplant was successful (though not without complications and many more months of hospital time), and now, at 2.5 years post-transplant, Nash is thriving. He is a vibrant, extraordinary little man with a jocular sense of humor and an infectious smile.

While managing PA and a liver transplant are never without sacrifice and risk, we are so grateful for the care and support Nash has received and have no doubt of the big, beautiful life he will lead. He is obsessed with dinosaurs, his big brother, Remy, and playing outside. He shows us daily what it is to find joy in the simplest of things and embodies resilience in the face of hardship. He is the greatest illustration of what it is to live life to the fullest and we cherish him, and his example, every day.

We are grateful for this community and are always open to supporting and swapping stories with other families whose lives have been impacted by PA.

Roberto's Story

My name is Keylith Margarita Vásquez Díaz, and I am Roberto Josemiguel's mother. We live in Chachapoyas, in the Amazonas region of Peru. Roberto was born on September 23, 2016, and is currently approaching his tenth birthday. He is the second of my three children. Roberto was born via C-section at 37 weeks of gestation. During his first few months, we noticed his development was slower; however, we initially thought every child has their own pace. He was late to hold up his head, experienced excessive drooling, and—at approximately nine months of age was diagnosed with muscle hypotonia. From then on, he began physical therapy three times a week.

When he was one year and four months old, he had a seizure that was not accompanied by a fever. Due to this episode, he was rushed to another region, where he was diagnosed with epilepsy and prescribed Valprax, a medication he took for about two months. At the time, we were unaware that a metabolic disorder might be involved. We now believe that episode may have been related to a metabolic decompensation.

As he grew, Roberto faced increasing difficulties in motor, cognitive, language, behavioral, and social interaction areas. Consequently, we consulted various specialists, and at age three, he was diagnosed with Level 2 Autism Spectrum Disorder. He also developed marked food selectivity; for a time, he would accept only three foods and completely rejected meat and other sources of animal protein.

Since he was very young, he has received physical, occupational, speech, behavioral, and learning therapies. Thanks to his effort and constant support, he has made significant progress. However, he still requires support and supervision in various daily activities, as well as assistance with his education, communication, learning, and the development of his autonomy.

In 2024, together with other mothers of children with autism, we decided to pursue genetic and metabolic testing to better understand our children's needs. Initial results showed findings consistent with possible propionic acidemia. Furthermore, acylcarnitine tests revealed a persistent elevation of propionylcarnitine (C3).

In light of these results, Roberto began treatment in December 2024 with L-carnitine and coenzyme Q10,



alongside a diet low in animal-based protein. Following the start of treatment, we began to observe significant improvements in his language, comprehension, social interaction, and cognitive performance.

To obtain a definitive answer, a trio whole-exome sequencing test was performed in January 2026, analyzing samples from Roberto, his father, and myself. The results, delivered on July 29, 2026, molecularly confirmed that Roberto has late-onset propionic acidemia, identifying two variants in the *PCCA* gene. After many years of uncertainty, we finally understood that Roberto had not only autism but also a hereditary metabolic disorder.

Receiving this confirmation brought fear, sadness, many questions, and a new grieving process. However, this time it found a mother who was better prepared and willing to research and seek the care her son needed. Roberto has been evaluated by specialists in clinical genetics, cardiology, nutrition, and ophthalmology. To date, he has not required a transplant.

He currently continues oral treatment with L-carnitine and coenzyme Q10, as well as a special diet with strict control of animal-based protein intake. One of our main challenges is accessing specialized care and obtaining the metabolic formula he needs. We live far from Lima, and very few professionals in our region are familiar with propionic acidemia. This compels us to travel, seek specialists in other cities, and cover the costs of consultations, tests, treatments, and special dietary needs.

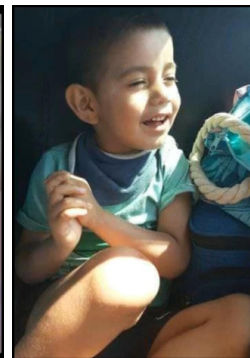
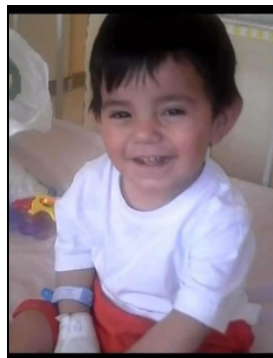
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Roberto's Story

continued from page 9

As a family, we hope that Roberto can receive ongoing multidisciplinary medical follow-up, access his metabolic formula, and maintain good metabolic stability, thereby avoiding future decompensations.

We also wish for him to continue making progress in his communication, learning, and autonomy, and to be able to develop his full potential with the appropriate support. Our greatest hope is for him to lead a healthy, safe, and happy life with the best possible opportunities.



Research Opportunity: Reproductive Healthcare

Patient and Caregiver Experience with Reproductive Healthcare for Adolescents and Young Adults with Inherited Metabolic Disorders

Dr. Jessica Gold from Northwell Health is conducting a research study about how young adults with inherited metabolic disorders (IMD) make decisions about contraception and pregnancy. This topic is very important because many young adults with IMD are now reaching adulthood, entering romantic relationships, and starting to think about starting families. The following survey should take about 10-15 minutes to complete. <https://redcap.link/OASRH>

For questions or to participate by phone, contact:

Jessica Gold, MD, PhD,

Dept: Medical Genetics, Northwell Health

Phone: 516-918-4800

Email: Jgold4@northwell.edu



Targeted gene editing of PCCA pseudoexon using CRISPR/Cas12a for potential therapy in propionic acidemia

Prof. Lourdes R. Desviat, PhD
Assoc. Prof. Eva Richard, PhD
Centro de Biología Molecular Severo Ochoa UAM-CSIC
Universidad Autónoma de Madrid, Spain

This summary highlights the key findings from a recently published research article (Alvarez et al. 2026), leveraging the expertise of our group in propionic acidemia (PA), RNA splicing and targeted genetic therapies. In this manuscript, we provide proof of concept for a potential treatment strategy for PA patients with certain mutations, by using the innovative gene editing CRISPR/Cas technology, the so-called molecular scissors capable of locating and precisely modifying a specific region of DNA. CRISPR-based gene-editing therapy has already been approved for certain diseases, with many additional applications currently being evaluated in clinical trials. The use of gene editing may in the future have a positive impact within the patient PA community.

Propionic acidemia is genetically heterogeneous, and can occur by deleterious sequence variation, in both genes PCCA and PCCB encoding both subunits of the propionyl-CoA carboxylase enzyme (PCC). In this work we have focused on a PCCA splicing variant.

Pre-mRNA splicing is a crucial cellular process that occurs after genetic information is transcribed from DNA into precursor messenger RNA (pre-mRNA). This pre-mRNA is initially synthesized as a sequence containing both coding regions (exons) and non-coding regions (introns). During pre-mRNA splicing introns are removed and exons are joined precisely, forming the mature mRNA that serves as a template for protein synthesis. The splicing process is executed by a complex molecular machinery called the spliceosome that recognizes specific sequences at the boundaries between introns and exons. Sequence variations in these regions or in auxiliary splicing regulatory elements (enhancers and silencers) disrupt this splicing process and can lead to diseases. In some cases, aberrant splicing can result from deep intronic variants activating or creating potential splice sites, which lead to the aberrant inclusion in the mature mRNA of intronic regions known as pseudoexons.

In this work we have focused on the deep intronic variant PCCA c.1285-1416A>G activating a pseudoexon which is included in the mRNA, resulting in the absence of PCCA protein and PCC activity. To correct this defect, we used the gene-editing tool CRISPR-Cas12a in a previously developed hepatoma cell model with the variant.



We tested several strategies to prevent the cell from incorporating the erroneous genetic information (pseudoexon) into the mRNA. The most effective approach was to abrogate the activating signal (enhancer) that triggers this mis-splicing event. As a result, partial recovery of normal mRNA, PCCA protein and PCC activity levels up to a therapeutic range were obtained.

The genetic editing strategy offers a potential advantage over other approaches such as the use of antisense oligonucleotides, which was previously explored for this same splice defect in a collaborative work with Prof. B.S. Andresen (Spangsberg-Petersen et al. Mol Ther Nucleic Acids 2023). While these treatments require repeated administration to maintain their therapeutic effect, gene editing could provide a more durable correction. However, these results have only been obtained in cellular models. Before any potential clinical application can be considered, it will be necessary to evaluate the efficacy and safety of this approach in animal models and to develop delivery systems capable of efficiently targeting affected organs.

Taken together, this work provides proof of concept that gene editing can correct hidden intronic DNA defects that disrupt cellular instructions and cause disease. Although the approach is still at an early stage of development and has so far been limited to cellular models, the findings open new possibilities for the treatment of PA and other genetic disorders caused by similar alterations.

We acknowledge the continuous support of the Propionic Acidemia Foundation and the essential role that patients and their families play in the research into this rare disease. We look forward to continuing to be part of the propionic acidemia research community advancing towards a better understanding and treatment of this rare genetic condition.

Reference: Álvarez M, Del Álamo JV, Richard E, Desviat LR. **Targeted gene editing of PCCA pseudoexon using CRISPR-Cas12a for potential therapy in propionic acidemia.** Molecular Therapy: Nucleic Acids 2026. <https://doi.org/10.1016/j.omtn.2026.102990>

Ways to Support PAF

Your time, voice, and generosity help move PA research and community support forward.

FUNDRAISE

Create a birthday fundraiser, #GivingTuesday campaign, or fundraiser simply because you want to help.

VOLUNTEER

PAF is always looking for volunteers to support events, awareness, fundraising, outreach, and family connection.

DOUBLE YOUR GIFT

Check with Human Resources to see whether your employer matches charitable donations or offers volunteer-hour grants.

GIVE STOCK

PAF accepts stock donations. Email paf@pafoundation.com with questions.

UPCOMING EVENTS

- 10/5 SIMD NAMA — Illinois • exhibiting and raising awareness
- 10/31-11/1 FALL PA FAMILY WEEKEND — New York (see below)
- 11/1 TCS New York City Marathon 2026
- 11/7 OH Families Fall Fest — Athens, Ohio • 2:00–6:00 PM

Dedicated gifts in honor and memory, Facebook fundraisers, and online giving also make a difference. Every dollar helps.



Save the date!
Fall Fest

Jackie O's Taproom
benefiting
Propionic Acidemia Foundation
Nov 7, 2026, 2:00–6:00
Details coming soon!



FALL PA FAMILY WEEKEND

AN AUTUMN GATHERING FOR OUR PA FAMILIES



SATURDAY • OCTOBER 31

Breakfast at 10:00 AM



SUNDAY • NOVEMBER 1

Post-Marathon Party at 7:30 PM

 **Manhattan, New York**

All PA families welcome!



RSVP: mlcotrinaPAF@gmail.com

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SEARCHING FOR A CURE HOPE
FOR OUR CHILDREN

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