SUMMER 2024

PROPIONIC ACIDEMIA FOUNDATION

SEARCHING FOR A CURE HOPE FOR OUR CHILDREN

The Community Health Clinic
730 East North Street, Shipshewana, IN 46565

AGENDA

8:30-9:00 AM	Registration / Exhibits Open / Breakfast
9:00-9:15 AM	Welcome / Introductions
9:15-10:00 AM	Propionic Acidemia Overview
10:00-10:30 AM	Break – Meet other families and visit exhibitors
10:30-11:15 AM	Understanding the pathogenesis of cardiac complications in PA patients
11:15-12:00 PM	Diet and supplements in PA
12:00-1:00 PM	Lunch / Small Group Discussion
1:00-1:45 PM	Liver transplantation in PA, Kyle Soltys, MD, UPMC
1:45-2:30 PM	Heart transplantation in PA, Anthony Zaki, MD, Cleveland Clinic
2:30-3:00 PM	Break – Meet other families and visit exhibits
3:00-3:45 PM	New therapies / research in PA, Charles P. Venditti MD, PhD, NHGRI, NIH
3:45-4:00 PM	Wrap up – Questions

* Program subject to change

A limited number of no-cost Echocardiograms and EKGs for the patients and families with PA will be available. To schedule, contact Daniela at 717-925-8300.

Register online or mail in the registration form on page 11.

Gold Sponsor

moderna

Silver Sponsor

NUTRICIA

PA Registry

Help move research forward!

Participate in the Propionic Acidemia International Patient Registry.

For more information on joining the registry, or to update your information, go to www.paregistry.org

INSIDE

PROPIONIC ACIDEMIA FOUNDATION

ANNUAL REPORT 2023-2024

The Propionic Acidemia Foundation has expanded its reach for the year 2023-2024. PAF funded two new research projects with researchers not previously funded by the organization. Four different conferences were attended, all of which PAF attended and exhibited; three of those conferences Board President, Jill Chertow, presented. The number of families reached by PAF has increased.

Nine individuals ran in the New York City Marathon in November 2023 and raised $18,524 for PAF. Additionally, families and individuals impacted by PA held in-person and online fundraisers.

Impacts

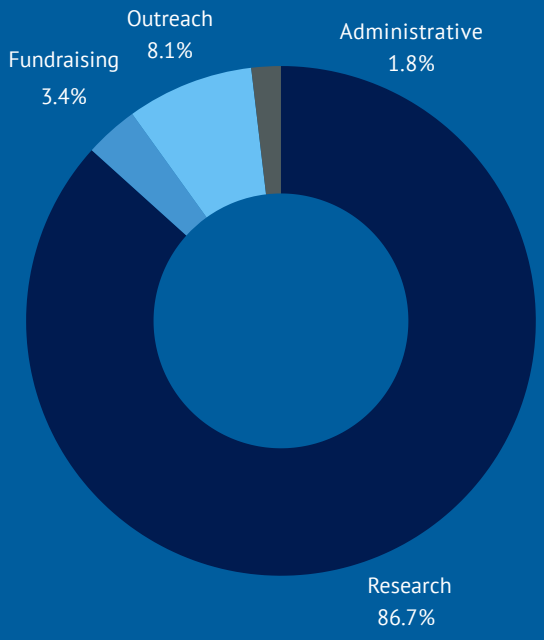
- A new grant for $46,000 awarded to Bart Bijnens, PhD, Universitat Pompeu Fabra (Barcelona, Spain), “Detailed Cardiac Functional and Electrical Phenotyping in Propionic Acidemia”
- A new grant for $50,000 awarded to Dr. Grant Mitchell, MD, CHU Saint-Justine (Montreal, Canada), “New approaches to understanding and treating propionic acidemia”
- Increased engagement across all media utilized (LinkedIn, Facebook, Instagram and e-mail)
- Attended and exhibited at Society of Inherited Metabolic Disorders (SIMD), 45th Annual Meeting, April 2024 in North Carolina, USA.
- Attended and exhibited at Genetic Metabolic Dietitians International (GMDI), Soaring to New Heights in Metabolics, April 2024 in North Carolina, USA.
- Presentation at Joint SIMD/GMDI day on Panel: Stronger Together: The Case for Support Clinic-Patient Organization Collaboration.
- In July of 2024, presented at The North America Rare Disease Summit in Illinois.
- *My Care Notebook & Emergency Handbook for Those with Propionic Acidemia/Methylmalonic Acidemia* are available to download.
- Attended & exhibited at the Illinois PKU and Allied Disorders Annual Meeting in Illinois.

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



Research Grants & Registry	$108,882
Outreach Conferences, & Educational Material	$10,114
Fundraising	$4,269
Administrative	$2,346
Total Expenses	$123,551

Income

Cash Assets 8/1/2023	$438,080
Cash Assets 7/31/2024	$460,486

Donations	$119,441
Interest Income	$26,516
Total Income	$145,957

Board of Directors

Jill Chertow, President
Brittany Smith, Treasurer
Angela Waits, Secretary
Maria L. Cotrina
Susan M. Weaver
Veronica Lopez, emeritus

Propionic Acidemia Foundation

PO Box 151
Deerfield, IL 60015-4421
1-877-720-2192
www.pafoundation.com

EMILY'S STORY

45 minutes. A short and smooth delivery, following the easiest pregnancy known to man.

Emily was born on September 7th, 1999. Complete with all five fingers and toes, we had no warning of what was to come. She was seemingly perfect— my husband and I, a physician and dentist, were confident in our ability to care for our first child.

The short period between the Tuesday night she was born and the Thursday night we brought her home was a haze. Emily's angelic beauty clouded my senses and coupled with the excitement of becoming a first-time mother, it was easy to dismiss early issues. Nurses quelled all of my concerns, they knew I was nervous. I can't blame them, I was. We noted that she was not feeding well in the nursery. I remember attempting to breastfeed, but she was not interested. My complaints about Emily's tight lips were brushed off with assurances of relax and breastfeeding takes time. I felt like I was doing something wrong. Nevertheless, I stifled my anxiety and brought her home.

When we arrived home Thursday evening, I opened a small hospital-sized bottle of Similac and fed her. I instantly felt better knowing that she had something in her system. *Relax, these things take time* repeated in my mind like a mantra. I was finally starting to believe the nurses.

Within an hour Emily vomited the formula right back up. I changed her and settled her back into the bassinet beside our bed. None of this sat right with me, but I was exhausted from the delivery only two days prior. I continued to push away my anxious thoughts and decided that she just fed too quickly.

I woke up around 5 am the next morning and immediately checked Emily's diaper. After all, a healthy baby should have a wet diaper by now. Right?

Her diaper was completely dry and my heart began to race as I connected the dots. She never cried for

a feeding. Something is *wrong*. I lifted a floppy baby from the bassinet and her eyes remained shut. Terror set in. I called the pediatrician and he told me to race her to the ER, *it must be sepsis from the delivery*.

My mom took us to the North Shore LIJ. As we pulled up to the ER, we were met with a swarm of doctors, nurses, residents, and security guards waiting for *my sick baby* to arrive. They pulled her from the car seat and rushed her into the hospital, while simultaneously stripping off her clothes. I ran alongside the chaos begging for reassurance: *will she be okay?* Doctors were kind but honest: *we don't know*.

We shortly learned her ammonia level was 1400, the normal value for a newborn is under 40. My husband quickly rushed over, leaving behind a waiting room full of patients, his daughter was the only patient that could not wait. He joined me in the Pediatric ICU only to find Emily on a respirator. She had been dialyzed multiple times to reduce the ammonia levels.

The doctors did not believe Emily would survive through the night that Friday, September 10th. We were urged to sign a DNR. But, my husband flat-out refused. He proceeded to open every single medical textbook he had on our bed that night and spoke to every physician friend from all over the world. One dear friend, Dr. Sunita Khetrapal, a pediatric geneticist from the Children's Hospital of Philadelphia (CHOPS), advised us to return to the ICU and tell them to feed Emily. Dr. Kehtrapal explained that our (cont. PAGE 5)

EMILY (CONT. PAGE 4)

baby was in a state of starvation 3 days post-delivery. She was breaking down muscle mass and releasing amino acids. Unable to metabolize these acids, her ammonia levels rose drastically.

My husband explained his findings to the head of the PICU and they agreed to do whatever it takes to help Emily survive. After returning to the hospital on Saturday morning the doctors and nurses were elated to report Emily's improved condition. She was pulling at the tubes, waking up, and her ammonia levels were beginning to stabilize. Emily fought fiercely they said. We found a glimmer of hope.

Today, our daughter Emily is 24 years old. Over the years we have encountered miraculous highs and terrifying lows. I've learned that the most rewarding aspects of life are often the most challenging.

Her care system has grown to include 24/7 nursing, Dr. Melissa Wasserstein, a metabolic specialist, and two loving siblings: Nicolas and Abigail. It is with this support and her fierce strength that Emily continues to live a remarkable life.

While each day may not be guaranteed or free of difficult choices, the decision to keep fighting is the easy promise we swear to keep.

BEING PREPARED

With more severe weather events and a second formula company expecting disruptions it is even more important to prepare for an emergency and supply disruption.

Have a supply of essential medications, formula, and feeding supplies on-hand.

- Discuss with clinic staff your desire to have a 2 week supply of medications and formula, including ingredients for your "sick" formula.
- Build your supply of medication and formula by refilling a little bit early every month. Many insurers will allow you to order monthly prescriptions every 23-28 days, by doing so you can build up an emergency supply.
- Maintain a 2 week supply of non-perishable, tolerated low-protein foods.
- Store 3-14 gallons of water. It is recommended that you store 1 gallon of water per person per day. However, you will need to consider any potential illnesses that may cause fluid loss, extra fluid needs with tube flushing, etc., and additional water for hand hygiene.
- Consider sending extra supplies to school with any needed doctor's orders in case of severe weather, lock down, or other emergency event.

Food safety

In the event of power loss, a refrigerator maintains its temperature for up to 4 hours. To keep formula and other liquids cold to assist in maintaining body temperature in the heat, keep a supply of water in the freezer to be moved to an insulated cooler in case of a power failure to keep formula from spoiling. Some coolers can maintain food safe temperature for several days.

Lighting safety

Do not not plan for candles for light in an emergency. LED lanterns or flashlights are a much safer option than an open flame, especially with children or a person with developmental disabilities. An LED headlamp style flashlight is useful to make formula and prepare food.

UNDERSTANDING CARDIAC ALTERATIONS IN PROPIONIC ACIDEMIA

PIs: Eva Richard, Universidad Autónoma de Madrid and
Eva Delpón, Medicina Plaza de Ramón y Cajal S/N Ciudad Universitaria

Eva Richard Group **Eva Delpón Group**

Propionic acidemia (PA) is a rare genetic disorder that leads to serious heart problems among other complications. With the support of the Propionic Acidemia Foundation (PAF), our research team has investigated the underlying mechanisms of PA associated heart alterations using advanced stem cell technology. PA disrupts the body's ability to process certain amino acids and fats, resulting in toxic buildup that can damage organs, including the heart. Traditional animal models, such as mice, do not perfectly mimic human heart conditions, limiting our ability to study PA. To overcome this, we use human induced pluripotent stem cells (iPSCs), which can be differentiated to any cell type, including heart cells. This allows us to generate human heart cell models to study PA more accurately. We reprogrammed skin cells from a PCCA patient into iPSCs and then differentiated them into cardiomyocytes (iPSC-CMs). This method provides us with patient-specific heart cells to investigate how PA deficiency affects this organ.

Our findings indicate that PCCA deficiency leads to a reduction in the firing frequency of spontaneous action potentials in the iPSC-CMs. Action potentials are the electrical signals that heart cells use to communicate and coordinate contraction, so changes in their frequency or form can lead to arrhythmias. Moreover, our studies showed that PCCA deficiency affects the amplitude and duration of these action potentials. Typically, a heart cell will fire an action potential that rapidly rises and falls in voltage. However, in PCCA cells, we observed that after the initial rapid rise, the fall in voltage was delayed, and the overall duration of the action potential was extended. This prolongation of the action potential can be linked to a slowed repolarization phase, which is critical for preparing the cell for its next heartbeat. The slowing of this process can make the heart more susceptible to developing arrhythmic conditions because it disrupts the regular timing of heartbeats. In addition, one of the most striking observations was the presence of delayed afterdepolarizations (DADs) in PCCA iPSC-CMs. DADs are abnormal additional depolarizations that can occur before the cell has fully repolarized. They can lead to extra heartbeats or even sustained abnormal rhythms, which are often observed in various types of cardiomyopathies and can be particularly dangerous, leading to conditions like ventricular tachycardia.

One common problem in PA is the lengthening of the QT interval. This QT interval prolongation can affect up to 70% of PA patients and is the most typical heart-related symptom. When the QT interval is longer than normal, it can lead to irregular heartbeats. These irregular rhythms can sometimes be just extra beats, but they can also be more serious or even life-threatening, causing in rare cases, sudden cardiac death. Our findings suggest that this QT interval prolongation might be linked to increased levels of a specific electric current in heart cells, known as INaL. This increase can worsen the heart's rhythm problems. Furthermore, PCCA deficiency could make the heart less able to conduct electrical signals properly, potentially leading to even more complex and dangerous types of irregular heartbeats. An increase in INaL, along with changes in INCX, disrupts how heart cells manage calcium, which is crucial for their function. Importantly, our results strongly suggest that PA may increase the risk of severe arrhythmias independently of the establishment of progressive late-onset cardiomyopathies (e.g. dilated cardiomyopathy, hypertrophic cardiomyopathy, or left ventricular noncompaction cardiomyopathy) induced by the disease.

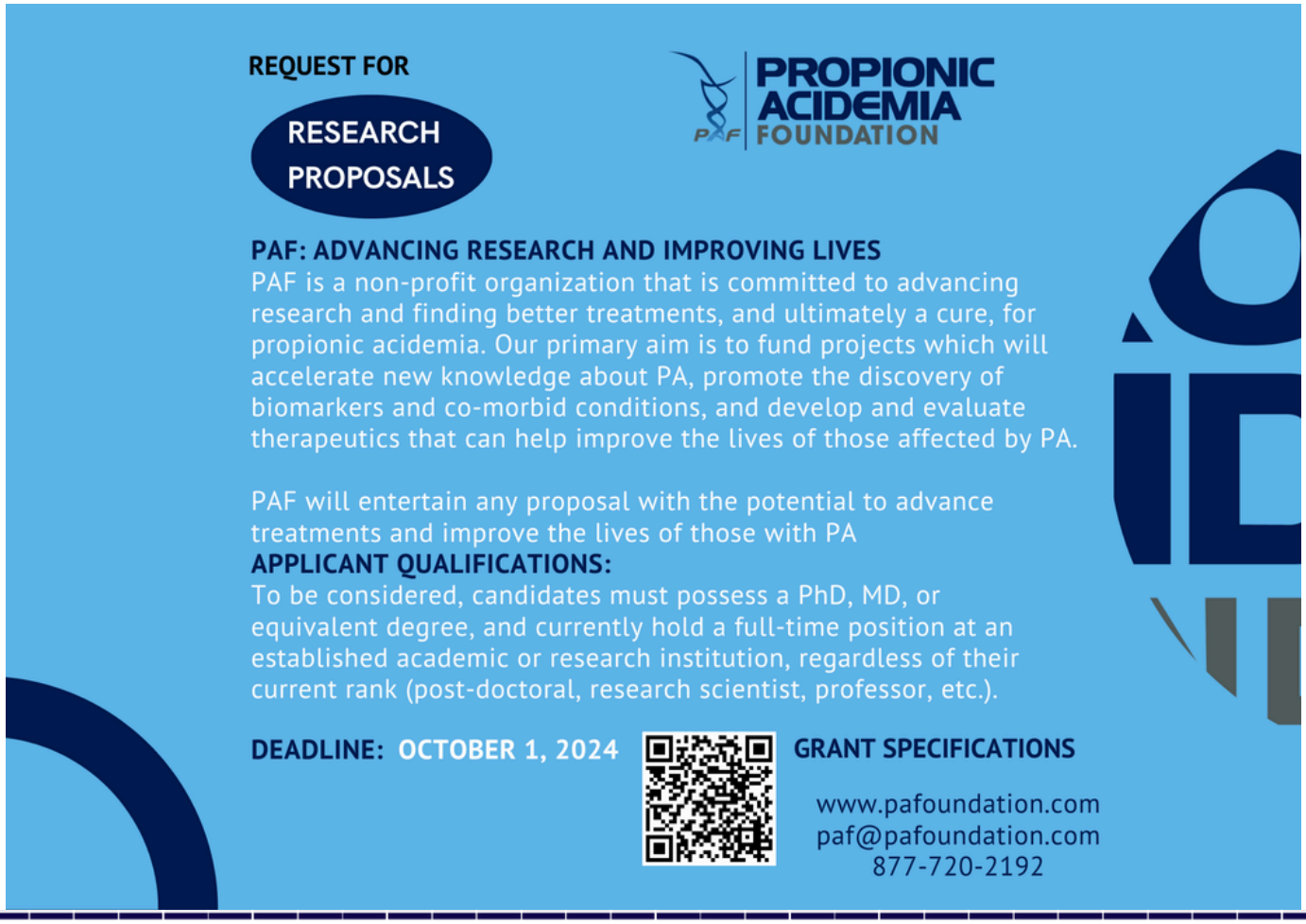
(cont. PAGE 7)

UNDERSTANDING CARDIAC... (CONT. PAGE 6)

Collaborative studies with Dr. Guofang Zhang have revealed metabolic alterations in PA hiPSC-CMs, including changes in glucose and fatty acid metabolism and a decrease in TCA cycle intermediates. These metabolic changes are significant as they may underlie some of the cardiac dysfunctions observed in PA. In addition, the generation of knockout (KO) iPSC lines for the PCCA and PCCB genes represents a major advance in our research project. Using CRISPR-Cas9 technology, these genes were edited in a control iPSC line, producing clones with out-of-frame deletions confirmed by next-generation sequencing. The isogenic control, PCCA and PCCB KO iPSC lines are essential for future differentiation studies and for better understanding the cellular pathophysiology of PA.

In summary, this project has made significant progress in understanding how PCCA deficiency affects the heart. Our findings thus far are promising and open new avenues for research and treatment of PA. But, this story is far from over. The journey to find a cure for PA is challenging, but every step forward brings a glimmer of hope. With our dedication and hard work, and with the support from organizations like PAF, we are confident that we will continue to make meaningful advances towards effective treatments for this disease. We are deeply grateful to the Propionic Acidemia Foundation, the families, board members, volunteers, and donors for their support. Your contributions have been instrumental in advancing our research and bringing us closer to better treatments for PA.

REQUEST FOR PROPOSALS



JORDAN'S STORY

We're the Simmons Family from Long Island, NY. Our son Jordan Lee was born on February 24, 2024 at 30 weeks, and although he was in the neonatal intensive care unit, he was doing well overall. On day three of his life his condition deteriorated rapidly and the genetics team at Stony Brook University Medical Center became involved in our care due to elevated ammonia levels.

It was determined by newborn screening and genetic testing that Jordan has Propionic Acidemia. Protein was stopped and his fluids were adjusted accordingly, and we began the long road to see how he would respond to treatment. Jordan's NICU journey was a true roller coaster but after 98 days, we were able to bring our warrior home.

Jordan is the love of our lives and is truly the sweetest boy. It's a joy being his parents and seeing how many obstacles he was able to overcome.

We are excited to advocate for treatments and a cure for PA and truly feel that we were called to be Jordan's parents for a reason. We are thankful for the PA Foundation and look forward to being active participants.

Zoom Chat and Birthday Club

Zoom Chat in Spanish with Carolina Galarreta from NIH and Jennifer Myles

WARRIORS BIRTHDAY CLUB

This year birthday cards will be made by students at Oak Lawn-Hometown Middle School and St. Linus for participating families. We are thankful they have volunteered to do it again this school year. Please sign up a patient or sibling for the Warriors Birthday Club at http://www.pafoundation.com/warriors-birthday-club/.

If you signed up last year, you will need to sign up again, so we have current information.

PA RUNNERS 2024

OFFICIAL
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NOVEMBER 3, 2024
The 2024 TCS NEW YORK CITY MARATHON TEAM
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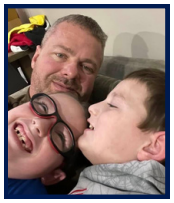
Meet our 6 amazing 2024 NYC Marathon PA runners. Please support our runners.



John Moss, St Louis-Missouri. John has twins Grant and Sebastian affected by PA. John is a tireless supporter of PAF and its mission to fund research for a cure, treatments and keep up the networking for families. This year, John is running half in search of a cure for Grant and all the other kids with PA, and half in memory of Sebastian and all the other kids that have passed from PA.
https://fundraisers.hakuapp.com/fundraisers/bd3c8f7bb76143622777

Sofia Gulati, New York. Sofia Gulati is a raising sophomore at Columbia University. She has been running for 6 years and is super-excited to be running her first marathon on behalf of the Propionic Acidemia Foundation and to raise awareness to support PAF.
https://fundraisers.hakuapp.com/fundraisers/99269a9a750893ed2eda

Daniela Ortega, New York. "I'm Daniela Ortega Toro, a research specialist at RTW Funds. I'm thrilled to embark on my first-ever marathon, especially the iconic NYC Marathon, in support of the Propionic Acidemia Foundation. While running hasn't always been part of my journey, it has become a meaningful way for me to push my limits. I'm deeply honored to run for Gabriel, the son of a coworker, whose resilience in facing Propionic Acidemia is inspiring. Running the NYC Marathon represents a significant personal challenge, and I'm eager to grow through this experience, both for myself and to support this important cause."
https://fundraisers.hakuapp.com/fundraisers/d9d55ea51bd7655c1065

Bella Grayken, New York. "Hi, I'm Bella and I'm very excited to be representing the Propionic Acidemia Foundation in the NYC marathon this November! Although I don't know any personally affected by this condition, the importance of funding research for the development of a treatment is crystal clear to myself and my loved ones. I'm really honored to be supporting this amazing foundation and grateful to those who awakened me to the cause.
https://fundraisers.hakuapp.com/fundraisers/f275f68862963a1ea084

Alexandra Pearson, New York. "I am a native of Houston, Texas but moved to NYC in 2022 and I now work as an RN at NYU Langone. I love the city and love to exercise. I have always love running and have found it to be a crucial outlet for both my physical and mental health throughout my adult life, so I am thrilled to be able to take it to the next level and run my first marathon with PAF!".
https://fundraisers.hakuapp.com/fundraisers/44bdc12771b1794a485f

Paul Speakman, Annapolis, Maryland. Paul is 41 years old and a father of 3. He was inspired to run the NYC Marathon by his father, he remembers watching his dad run in 1989 and it has always been an ambition to compete in the race. This is the third time Paul has trained for a marathon, having completed the London Marathon in 2010. Paul also competed in triathlons and recently completed a 1/2 Ironman in 2022.
https://fundraisers.hakuapp.com/fundraisers/8a8bf40ff6c83cb38b10

PAF ACTIVITIES AND FUNDRAISING SPOTLIGHT

UPCOMING EVENTS:

- Zoom Chat with Families in Spanish - 8/23
- PA: Hope in the Heartland, Shipshewana, IN 10/19
- Tara Gerlach Nationwide Children's Hospital Columbus Marathon - 10/20
- OH Families Fall Fest - 11/2
- The TCS New York City Marathon 2024 - 11/3

PAST EVENTS:

- PAF exhibited and presented at Society for Inherited Metabolic Disorders (SIMD) 4/14/-4/17 and Genetic Metabolic Dietitians International (GMDI) Annual Meetings 4/17-4/20, Charlotte, NC (see below)
- PAF presented at North America Rare Disease Summit (NARDS) from Bamberg Health 7/11 - Chicago, IL (see below)

DEDICATED GIFTS FROM INDIVIDUALS:

- IN HONOR OF: Kate Lowry, Trent McKinley, Dylan Jaehnke
- IN MEMORY OF: Jordan Franks, Brandon Napiwocki, Jean Phillips, Nicholas Phillips

FACEBOOK: Thank you to all of our Facebook Fundraisers and people that donated to their fundraising pages for birthdays, #GivingTuesday or just because: Jenn Simmons, Vivian Sanders, Mimmy Angelique Santiago, Carmela Delli Santi, Nicole Bilski

STOCK DONATIONS: PAF accepts stock donations. Please email paf@pafoundation.com with any questions.

MATCHING DONATIONS & VOLUNTEER HOURS:
This may enable you to double your donation. Check with Human Resources to see if your employer matches. Some companies have a volunteer program and will donate based on your volunteer hours. PAF is always looking for volunteers.

INTERNET:
Thank you for using iGive, Goodsearch, and Bing; selling on Ebay and setting up Facebook Fundraising Pages and designating Propionic Acidemia Foundation as your charity. Every dollar helps.

SIMD/GMDI (left)
"Stronger together: The Case for Supporting Clinic-Patient Organization Collaboration" Sarah Chamberlin, flok, Jill Chertow, Propionic Acidemia Foundation, Karen Dolins, MSUD Family Support Group, Teachers College Columbia University, Danae' Bartke, HCU Network America, Sandy Van Calcar, PhD, RD, Molecular and Medical Genetics, Oregon Health & Science University, Angela P Dempsey, RD, CNSC, The Medical University of South Carolina

Outreach and Collaboration

NARDS (right)
"Thriving Through Diagnostic Uncertainty: Collaborations to overcome isolation and Stress in Rare Disease Journeys" Megan Nolan, CEO, Rare Parenting, Jill Chertow, Propionic Acidemia Foundation, Barbara Van Hare, Rare Cancer Research Foundation Frank Rivera, Stronger than Sarcoidosis,

PAF CONFERENCE REGISTRATION FORM - OCTOBER 19, 2024

HOSTED BY: Propionic Acidemia Foundation (PAF) & The Community Health Clinic

PERSONAL INFORMATION

Name (first and last)_____
Address _____City _____State_____ Zip Code _____
Email Address _____ Phone _____
Do you have PA? Yes____ No ____Other diet requirements ?_____

Check all that apply: __Family __ Presenter __ Exhibitor __ Medical Professional __Volunteer
Information of others attending with you (add additional page, if necessary)

NAME (FIRST & LAST)	RELATIONSHIP (SPOUSE, CHILD, ETC)	AGE (IF CHILD)	PA (YES/NO

Please note any other special needs:_____
_____

Dr. Chowdhury's research including FREE Echos/EKG (for the family-affected, carriers, and non-affected), Please indicate how many people: Adults ____ Children (3-12) ___ Children under 3 ___ Not Interested:___
(**Limited availability - must contact Daniela - Dcavet@cardiologylancaster.com - 717-925-8300**

I hereby give permission to PAF to use any photographs/videos taken at the 2024 PA Family Conference in which I or members of my family may be a part (for use in, but not limited to, newsletters, PAF websites, social media, and reports). Yes___ No___

In consideration of the acceptance of this registration, I/we the undersigned, assume full responsibility for any injury or accident which may occur while I/we am/are attending the conference events. I/we hereby release and hold harmless the PAF, its officers, directors, staff, volunteers, members, representatives, agents or assigns associated with this event from any and all personal injury, loss or damages.

Signature: _____ Date: _____

Registration is due by September 28, 2024. Please mail completed form to: Propionic Acidemia Foundation, PO Box 151, Deerfield, IL 60015 or register at pafoundation.com

Propionic Acidemia Foundation
P.O. Box 151
Deerfield, IL. 60015

SEARCHING FOR A CURE
HOPE FOR OUR CHILDREN

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