

Propionic Acidemia Foundation

VOLUME 1, ISSUE 26

SPRING 2019

Warrior Wisdom Conference

Our Conference Experience By Angela Waits

In October of 2018 my family attended our 2nd PAF conference, The 2018 PAF Warrior Wisdom Conference at the



Nationwide Hotel and Conference Center in Ohio. I attended with my husband, my daughter Nalani (18 PA) and my son Xavier (5). We rode to Ohio with a dear friend who has PA and also spoke at the conference. On Friday after a 6 hour drive we made it just in time to attend the registration and welcome reception dinner.

Saturday we started out with a panel of adults with PA - Khalilah, Peter and Lucy were so inspiring, I think I cried through all them. They gave me such hope for my daughter and for all of our kids. I wish I could have had that kind of hope in the beginning when it was such a struggle with Nalani.

We had game time with Keiko Ueda, MPH, RD who also spoke later about the PROP Nutritional Guidelines Tool Kit Development. The game was about PA and my son was able to (with some help) answer a couple questions about his sister's disorder and win prizes. He talked about that for weeks afterwards. He was very proud to be involved and when he saw his sister on a poster for PAF, he asked me if she was famous. I told him yes, she is. (continued pg. 4)

WARRIOR WISDOM BY THE NUMBERS

- 100 attendees
- 13 states
- 23 PA affected families
- Many physicians, researchers, and other providers
- Representatives from medical foods companies and industry.

PA Registry

Help move research forward for propionic acidemia. Participate in the Propionic Acidemia International Registry.

As of April 15, there are 104 participants. For more information on joining the registry, or to update your information, go to www.paregistry.org.

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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.

PAF AWARDS GRANT TO DUKE UNIVERSITY

PAF Awards \$48,500 Research Grant Guofang Zhang, PhD, Duke University “Propionyl-CoA and propionylcarnitine mediate cardiac complications in patients with propionic acidemia”

Energy production is the central cardiac metabolism for continuous mechanical work. An average human adult heart consumes ~ 6 kg ATP/day. ATP storage in the heart is only sufficient to sustain the heart beat for a few seconds. A tightly coupled cardiac energy metabolism from various substrates is critical for sufficient ATP production required by normal heart function.

One molecule of palmitic acid (fatty acid) generates much more ATP than one molecule of glucose does after their complete metabolism. Fatty acids contribute ~70-90% cardiac energy production in normal condition. However, heart still maintains high flexibility of fuel switch in response to various available substrates. Acetyl-CoA is the first convergent metabolite derived from the diverse fuel substrates via different pathways and enters tricarboxylic acid cycle (TCAC) for energy production. Therefore, the level of acetyl-CoA or the ratio of acetyl-CoA/CoA tightly controls the metabolic fluxes from two major fuels, i.e., glucose and fatty acid, in the heart. Acetyl-CoA or CoA level is also finely tuned by carnitine acetyltransferase (CrAT) that catalyzes the reversible interconversion between short-chain acyl-CoAs and acylcarnitines. Acetylcarnitine level is ~10-100 fold greater than that of acetyl-CoA in heart and is seen as the buffer

of acetyl-CoA. CrAT is highly expressed in high energy demanding organs including heart and mediates fatty acid and glucose metabolism possibly by dynamically interconverting acetyl-CoA and acetylcarnitine into each other. The deficiency of CrAT has been shown to change cardiac fuel selection.



Propionic acidemia (PA) is often associated with cardiac complications. However, the pathological mechanism remains unknown. We have demonstrated that high exogenous propionate led to the propionyl-CoA accumulation and cardiac fuel switch from fatty acid to glucose in the perfused normal rat hearts (Am. J Physiol. Endocrinol. Metab., 2018, 315:E622-E633). The deficiency of propionyl-CoA carboxylase in PA also induces the accumulation of propionyl-CoA. Next, we will attempt to understand whether and how the elevated propionyl-CoA in the *Pcca*^{-/-} heart (collaboration with Dr. Michael Barry) could interrupt cardiac energy metabolism by investigating the fuel switch flexibility, CrAT mediated metabolism, and buffer capacity of acetylcarnitine using stable isotope-based metabolic flux analysis (J. Biol. Chem., 2015, 290:8121-32). We hope that the outcome of this project will provide meaningful therapeutic recommendation for patients with PA, especially with the cardiac complication.

REQUEST FOR PROPOSALS ON PROPIONIC ACIDEMIA

Submission Deadline: October 1, 2019

Award Announcement: January 2020

Funding begins: upon signing of grant agreement

Application: General Information, Research Plan, Budget

Application categories:

- 1) *Research Projects* - Basic and Clinical Research
Awards range from \$5,000-50,000 per year and may last 1 or 2 years upon competitive renewal.

2) *Fellows Program*

This program provides financial support up to \$50,000 per one year for a metabolic/genetic fellow working on a research project in PA. This salary is intended to supplement any existing institutional support for the trainee.

Please visit pafoundation.com for more details or email research@pafoundation.com

The Propionic Acidemia Foundation Newsletter is designed for educational purposes only and is not intended to serve as medical advice. The information provided should not be used for diagnosing or treating a health problem or disease. It is not a substitute for professional care. If you suspect you or your children may have Propionic Acidemia you should consult your health care provider.

The Propionic Acidemia Foundation does not recommend nor endorse any particular products, companies, or manufacturers.

PAF AWARDS GRANT TO UNIVERSIDAD AUTONOMA DE MADRID

**PAF Awards \$33,082.12 Research Grant
Eva Richard, PhD, Universidad Autonoma de Madrid, Spain, "Cardiomyocytes derived from induced pluripotent stem cells as a new model for therapy development in propionic acidemia"**

Understanding the cellular and molecular mechanisms that occur in genetic diseases is essential for the investigation of new strategies for their prevention and treatment. In this context, induced pluripotent stem cells (iPSC) offer unprecedented opportunities for modeling human disease. One of the fundamental powers of iPSC technology lies in the competency of these cells to be directed to become any cell type in the body, thus allowing researchers to examine disease mechanisms and identify and test novel therapeutics in relevant cell types.

The main objective of this project is focused on the generation of human iPSC-derived cardiomyocytes (hiPSC-CMs) from propionic acidemia (PA) patients as a new human cellular model for the disease. In PA, cardiac symptoms, namely cardiac dysfunction and arrhythmias, have been recognized as progressive late-onset complications resulting in one of the major causes of disease mor-

tality. Using hiPSC-CMs we will study cellular processes, such as mitochondrial function and oxidative stress which have been recognized as main contributors for PA pathophysiology. In addition, our aim is to unravel novel altered pathways using high-throughput techniques such as RNAseq and miRNA analysis. We will also examine the potential beneficial effects of an antioxidant and a mitochondrial biogenesis activator in PA cardiomyocytes. The results that derive from this project will be relevant for the disease providing insight into the affected biological processes, and thus providing tools and models for the identification of novel adjuvant treatments for PA.



PA RUNNERS UPDATE: COME RUN WITH US!

Last year, a team of passionate parents and friends of PA hit the pavement to raise funds to support research on PA and raise awareness about rare disease through the Propionic Acidemia Foundation. Our team of runners: Leslie, John, Chef Evie, Jen, Lou, Mark and myself completed more than 15 races ranging from a 5K to a full marathon, from Ohio to Vancouver and raised more than \$5,000 dollars for PAF.



We are very thankful for the incredible support and commitment of all the runners, their friends, families and supporters, who donated their time and resources so wholeheartedly.

Special mention to

Leslie, who completed her first marathon in New York City (go Leslie!) and Aubrey who finished the Vancouver half marathon on the very same Sunday (we missed you in NYC!), John, who came out from surgery to finish a half marathon in Columbus, Ohio less than a month later (amazing!), Chef Evie, who supported the team all the way from NYC to Ohio and completed her fundraising efforts with the Columbus marathon, and Jen, who joined the team in New York City and raised more than \$300 in just 24 hours! (You are a machine!).

And, of course, our most special thanks to our star fundraisers, Leslie Hancock Vess and Aubrey Que Delima.

As for me, I am so very proud of these incredible runners who decided to join the team this year. I hope to share many more miles with all of you. It was a true honor.

Stay tuned for PArunners 2020. If you are interested in joining the team please, contact Marisa Cotrina at teamPAR4@gmail.com or through Facebook messenger.

WISDOM WARRIOR CONFERENCE (CONTINUED)

Dr. Olivia Wenger gave an update from Ohio's Amish Country. Jodie M. Vento MGC, LCGC spoke about protocols for liver transplants with propionic acidemia. Elaina Jurecki, MS, RD spoke about nutritional intake recommendations for propionic acidemia based on the SERN-GMDI Management Guidelines. Elaina talked about the balancing of our kids diets like walking on a tightrope, and that is exactly how I feel every day.



There were several breaks for visiting exhibitors, getting information and tasting low protein samples. (One of the exhibitors even had Halloween goodie bags with low pro chocolate and playdough). One parent sold T-shirts and pet calendars to raise money for PAF at the conference. Time was scheduled to get questions answered by our fantastic speakers. We completed the day with dinner and more conversation.

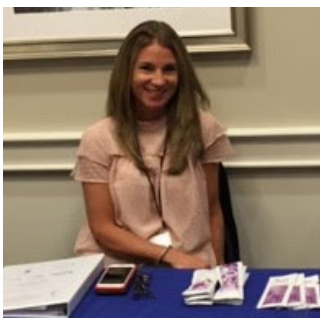
On Sunday we had our dedicated PAF runners that ran in the Nationwide Columbus Marathon and 1/2 Marathon in the cold winter weather to raise awareness and money for our cause.

We had such a great experience. I loved meeting the families I have followed for years on Facebook and through family stories as well as the awesome clinicians who came. I met Dr. Z, who had so much compassion for people with rare diseases, that it gave me hope for the new generation of doctors that will be treating our kids. I met a wonderful girl who showed me her YouTube channel where she posts funny videos and her cousin that my daughter had a blast with. I met a chef who teaches one of our kiddos how to cook healthy food!

Dr. Oleg Schchechlov and Dr. Irini Manoli, our heroes from NIH came to speak and hang out with the families. Dr. Oleg updated everyone on the "Natural History, Physiology, Microbiome and Biochemistry Studies of Propionic Acidemia" and Dr. Manoli discussed the rationale behind the changes in the nutritional management of PA/MMA. I was excited for them to see my daughter and to be able to thank them in person, after the changes to her formula were made and her ammonia has been down.

Nalani attended some of the events and also, loved being in the playroom. It was so beautiful to see all those PA kids in one room. Thank you to the Ohio families that took care of our kiddos during the events you guys were so wonderful!

We attended our first PA conference when Nalani was 16, I regret not doing this earlier. It is an invaluable opportunity as a caregiver to learn, and to feel at home with a group of people who can relate to your story because it is also their story.



IN MEMORY OF TALLI SMITH 10/04/01—2/17/19



Talli gracefully and fiercely endured the terrible nastiness of Propionic Acidemia; she departed this life with a sepsis scorecard of Talli 5 and sepsis 1.

She only encountered two bowls of nacho cheese sauce that she did not love; frequently devoured Scooby-Doo fruit snacks, except the orange ones; and was determined to be independent and do things in her

way and order, unless she wanted you to be her servant. She could build a Lego tower of questionable stability far larger than her 4'8" self. Male teens athletes from her Church, were in awe of her endurance and strength in keeping up with them while pushing a handcart for miles in a Mormon Trail reenactment. She hated to miss Church services at the Naperville 3rd ward of The Church of Jesus

Christ of Latter-day Saints, even if she was hospitalized or vomiting and would tell anyone who would listen to "watch Veggie Tales to learn a lesson".

She was highly anticipating her senior year next year at Naperville Central High and she felt she was one of the star athletes of Special Olympics, Team Fire 203 in basketball, bowling, and track. She loved meeting others who have PA; whether it was at a PAF meeting or traveling the country and stopping by to see them at their homes. She had numerous complications from PA including losing most of her vision and had a compromised immune system; however, she kept a positive attitude and dealt with her challenges with resolve.



FUNDRAISER IN HONOR OF KIRSTYN



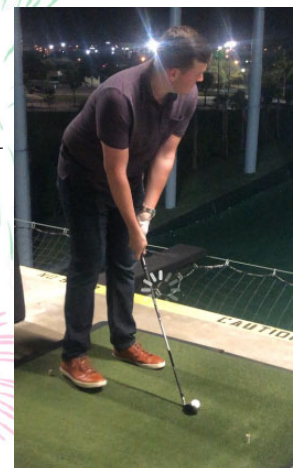
Often times we get so caught up in our daily activities that we forget what a blessing it is to be alive. ONE. We have ONE life to live. ONE chance to lead a spectacular life. Kirstyn Tripp embodied every aspect of this concept, and I am blessed to have gotten to know her and her family during my time at the University of Florida. Despite being born with a life-threatening condition that required weekly hospital visits,

Kirstyn was a sweet, creative girl with a warm smile and even better laugh. She had a HUGE heart. She often looked after younger kids during the events that we hosted for Dance Marathon. She loved french fries and loved Bitmoji (even though she would always make me look like an Alien for some reason). It's hard to imagine that such a sweet girl did not live past her teens, but it is important to focus on the SPECTACULAR life that Kirstyn lived. At just 13 years of age, Kirstyn was able to inspire everyone from her peers to college students to 60-year old adults with the positivity and strength she showed in the face of adversity. An entire community rallied around her family. That's more than most of us can say that we've done in our lives. Kirstyn Tripp will always have a place in my heart, and we should all aim to use our time on Earth to live a SPECTACULAR life

like she was able to in her short time.

With that being said, I reached out to Kirstyn's mother, Marsha, about potentially doing an event with my company in her honor. Marsha indicated that she thought this was a wonderful idea; thus, the CDI Top Golf Fundraiser was born. One of the main pillars of our firm, RSM, is Culture, Diversity, and Inclusion (CDI). The firm creates different communities within it to encourage a culturally diverse and inclusive workplace. One of our Employee Network Groups (ENGs), Abilities, aims to raise awareness for those with psychological, physical, and/or physiological ailments/conditions. The Abilities group partnered with some of our other ENGs, including Pride (LBGT-related network), AACE (African American-related network), HOLA (Hispanic-related network), and Stars & Stripes (Veteran-related network), to put on this event for Kirstyn. In November, over 30 members our firm attended the event, and \$500 was raised for the Propionic Acidemia Foundation in honor of Kirstyn Tripp."

Submitted by Tyler Drescher



PAF EVENT & FUNDRAISING SPOTLIGHT

UPCOMING/ONGOING EVENTS

- **Fall 2019- 14th Annual Tailgate Party & Corn Hole Tourney for PAF**, Gahanna, Ohio, 4:00 p.m. at the Goat in Gahanna. For more information go to gwenforacure.com
- **Oct 20- Team PA Runners, Nationwide Children's Hospital Columbus Marathon**

PAST EVENTS

- **13th Annual Tailgate Party & Corn Hole Tourney for PAF**, Gahanna, Ohio, \$10,921
- **Branch Family Fundraiser**, \$750
- **Top Golf event**, honoring Kirstyn (pg.5)

CORPORATE MATCHING GIFTS AND VOLUNTEER HOURS DONATIONS:

- **Corporate Matching Gifts:** This may enable you to double your donation. Check with Human Resources to see if your employer matches. It makes a big difference.
- **Volunteer Hours:** Some companies have a volunteers program and will donate based on your volunteer hours. PAF is always looking for volunteers. Please check with Human Resources to see if they have a program.

FACEBOOK: Thank you to all of our Facebook Fundraisers and people that donated to their fundraising pages: Kelli Johnston's Birthday, Rowena Smith's Birthday Fundraiser, Lao Marie Robertson-Wilson's Birthday, Sarah Mullins Birthday, John Moss's birthday fundraiser, Frances Torres's birthday fundraiser. Thank you for making a difference!

#GivingTuesday FUNDRAISING PAGES: Rachel Krajacic Smith, Jennifer Buck Mouat, Toni Ashbaugh McKinley, and Jayme Delgado

MAKE YOUR ONLINE SHOPPING COUNT:

Thank you for using Igive, Goodsearch and AmazonSmile and designating Propionic Acidemia Foundation as your charity and setting up Facebook Fundraising Pages. Every dollar counts.

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

DEDICATED GIFTS FROM INDIVIDUALS:

Among the many contributions received, the following is a list of some that were dedicated to those who have inspired the giver.

- **In Honor Of:** Carson Alfano, Kristin Boecker, Nila Branch, Katilin Burns, Sean and Courtney Callahan, Alexa and Anna Cardone, Jenna Delima, Camille Franze honoring Vincent, Lucy Harding, Dylan Jaehnke, Reuben Kleckley, The Lenerts, Gabriel Lopez, Kate Lowry, Dania & Edgar Jr. Martinez, Zach Matz, Trent McKinley, Michael J. Messersmith, Gwen Mouat, Remek, Mike Messersmith, Honey Stecken, Ben Sweetman, Chase Workman, and Brett Young
- **In Memory Of:** Bob Buck, Lauren Delima, Sharon and Jack Esses, Kerrie Lynn Fessler, Jordan Franks, Vincent Franze, Connor McKillop, Nicholas Alexander Phillips, Charlie Pirozzi, Talli Smith, Angelica Stageman, and Kirstyn Tripp

PAF at SIMD 2019

Jill Chertow and Maria L. Cotrina represented PAF and the PA Community at the Society for Inherited Metabolic Disorders (SIMD) 41st Annual Meeting on April 6-9, 2019 in Bellevue, Washington. (right)

Maria L. Cotrina shared her poster on "High Incidence of Autism/ASD in Propionic Acidemia: Data from the Propionic Acidemia and Urea Cycle Disorders Registries. (bottom right)

Congratulations to Arianna F. Anzmann, MS on receiving the SIMD Founders Award, Best Oral Presentation by a Trainee. (left) Her presentation "Multi-Omics Studies in Patient-Derived and CRISPR-Edited Cellular Models of Methylmalonic Acidemia and Propionic Acidemia Reveal Dysregulation of Serine Metabolism: New Directions for Cellular Pathogenesis in Disorders of Branch Chain Amino Acid Metabolism." was a result of a 2017 PAF awarded grant to Hilary Vernon, MD, PhD, Johns Hopkins University for the project "Targeting Serine and Thiol Metabolism in Propionic Acidemia".





**Propionic Acidemia Foundation
WARRIOR WISDOM CONFERENCE**

October 19-21, 2018



A Heart Felt Thank You to Our Conference Sponsors

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Thank you for all donations and the kind notes we receive throughout the year. Your support overwhelms us and continues to be a source of inspiration. PAF couldn't do what we do without your incredible support.



We want to hear from you! Have a PA story to tell, event to promote or news? Fall newsletter submissions due by August 15, 2019!

Help Us Find the Cure!

Name _____
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Enclosed is my contribution of \$_____ in honor of/ in memory of _____

- By providing your e-mail address you are opting in to receiving e-mails from the Propionic Acidemia Foundation. We will not share your information with those outside of the foundation.
- If you work for a company that has a matching program, please include the matching form.
- Please mail your check made payable to: Propionic Acidemia Foundation 1963 McCraren, Highland Park, IL 60035

Thank you for making a difference.

SEARCHING FOR A CURE
HOPE FOR OUR CHILDREN

Propionic Acidemia Foundation
1963 McCraren Rd.
Highland Park, IL. 60035



Phone: 1-877-720-2192 toll free
Fax: 1-877-720-2192
E-mail: paf@pafoundation.com
Website: www.pafoundation.com

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**PAF volunteers and
board members are
needed!**

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