PROPIONIC ACIDEMIA FOUNDATION

SPRING 2023

SEARCHING FOR A CURE HOPE FOR OUR CHILDREN

PA/MMA Family Education Conference Summary

On March 4th, the Propionic Acidemia Foundation partnered with Lurie's Children's Hospital for a combined PA/MMA family conference. We were able to meet in their conference center. Families from the Chicago area, as well as, families from Wisconsin, Indiana, Missouri, California, and Michigan were in attendance. Thankfully, the snow that was forecasted did not arrive with the attendees. During meals and in between presentations families were able to visit with one another. There was a wealth of information shared among families.

Drs. Prada and Baker gave an overview of Propionic Acidemia and Methylmalonic Acidemia. Madi Hankins, a genetic counselor, gave a presentation Risk Assessment and Family Planning. She explained the probability of having a child with PA/MMA, different options for testing in utero to determine if a fetus has PA, assisted reproduction options, and adoption.

Over lunch, Carly Abate, a Child Life Specialist, led a breakout session on Caring for the Caregiver. Within small groups, attendees discussed self-care and tips & tricks on dealing with PA/MMA. Some of the self-care that individuals mentioned as helping them cope with stress were: riding a motorcycle, knitting, running, mindfulness, and yoga.

Carolyn Serbinski, a genetic counselor gave an overview about Registries and Clinical Trials. Ann Kozek, a dietician, gave a presentation on Nutrition in PA/MMA.

Brittany Smith, PAF's Treasurer spoke about emergency preparedness and introduced PAF's updated Care Notebook and new Emergency Preparedness Handbook for Those with Propionic Acidemia/Methylmalonic Acidemia.

Brenden Pragasam, brother to Aidan with PA, was able to give everyone an overview of the small feeding pump prototype that he is developing.

We are grateful for the support of CoA, Moderna, Hemoshear, and Nutricia for sponsoring the conference. We were fortunate to have Garrett Austin take photos at the event. The Penny's Purpose provided handmade blankets to those in attendance. Zoia Pharma provided low protein foods that attendees were able to take home with them. Cambrooke provided low protein chips and pasta.

PA Registry

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

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

Request for Research Proposals Due Oct 1

INSIDE

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.

JUANI'S STORY

Juan Ignacio (Juani) was born on 08/15/2011 at the Naval Hospital of Buenos Aires, Argentina, after a normal pregnancy and with two healthy older sisters, Delfina and Manuela. He was a long-awaited and sought-after baby… after two girls, the boy arrived! On the second day of life he fell asleep and there was no way to wake him up to feed.

They took him to neonatology and the next thing we knew, he was in a coma. They had never seen a similar case and first thought of a hospital infection and started giving him antibiotics. But his condition did not change. After a few days of great anguish and uncertainty and through an external consultant doctor that we were able to contact, the first signs of his illness arrived. He had 2117 blood ammonium. Finally,

after about seven days in a coma and receiving treatment with a sodium benzoate solution, he woke up, thus began our story with the PA.

The first years were very hard. We went in and out of the hospital, a little out of precaution and a little out of caution from the doctors who were also learning about this new case… everyone is different! After a very serious pneumonia that had him 45 hospitalized days, he began to feed through a nasogastric tube; His doctors feared that when he used a bottle and in his condition that he had some hypotonia, he would have swallowing problems. Two years later they placed the gastrostomy button and with that the respiratory infections decreased.

Our entire routine and our lives changed. The time between medical check-ups was spaced out more, since we had all learned to recognize and differentiate symptoms and habits, and more time could be used in therapy to improve his hypotonia. and their cognitive disorders. His whole development was very slow and with each hospitalization he seemed to lose acquired skills.

At the age of three and a half he began to walk and the first signs of autism and traces also appeared in his neurological system. But also new discoveries and challenges such as starting a regular kindergarten at age 4, with teachers who understood his problem and taught his classmates to understand and accompany him. He also continued with his therapies and new customs and routines began to appear, such as sitting at a table and using his senses more to try textures and with it new sensations. Later he started his education at a special school, which he continues to go to today and is known as the "hacker", since he knows how to use electronic devices to watch his favorite cartoons on YouTube.

Juani is a very affectionate boy. He does not speak but makes himself understood. He loves the water and Mickey Mouse. With his sisters and his father we form a team that takes care and accompanies him. And there are also his grandparents, uncles and friends who are a fundamental network of support.

But for those who read this, not everything is "hospital", "diagnoses", and "blood work", there is also the fun part! Juanito also swam on the beaches of Argentina, Brazil, Ecuador (turtles included!) and in South Florida (USA), he met Mickey Mouse and his friends in person, he got on several Disney and Universal games (including one of Jurassic Park, with the fall in a waterfall that mom did not like very much!), walked through Washington and New York, in short…. an adventurer! To those who have just started this race… Courage! Now there are more advances and more knowledge of the disease. My humble advice: try to put together a good medical team. Always have the emergency protocol. Do not waste time in guards or hospitals that do not know about the subject. In many cases parents know more than some doctors. Nobody knows our children better: never stay with a doubt or if you see something that "doesn't go"; or you don't like, TALK ABOUT IT! In these things it is better to apologize than ask for permission. Let's continue supporting the causes of rare diseases, over all doctors and researchers, disseminating them in society. Hopefully the cure for PA will soon appear. and there will be no need to see more sick or hospitalized children. Hope is the last thing you lose!

What's Up With Aiden? An Update

Hemoshear Clinical Trial "HERO" Lurie Children's Hospital

Aiden is nearing completion of Part A of the clinical trial. (whoo hoo!!!)

This first part is focused on safety, but the kicker to be able to move to part B, is that they need at least 12 participants enrolled, which they don't have yet. There are a total of 3 parts. I know it isn't feasible for all our kiddos to take part, but if you can, please check it out and consider enrolling. This will allow those who are currently enrolled to move forward to part B and onto completion to see if the drug will prove as a beneficial treatment.

We live in Ohio and travel to Chicago once a month for visits. I can't say enough about Lurie Children's & the positive experiences we have had with Dr. Prada, Carolyn, and the whole research team. They are compassionate, fun, trustworthy and have a sincere desire to see optimal results from the study! If you have any questions, please email cserbinski@luriechildrens.org. I know Dr. Prada and Carolyn would be happy to discuss the details of the trial.

We are thankful to God, Hemoshear, and to Lurie Children's Research team for making this clinical trial possible.

We hope & pray that the study will yield better treatment to all of those affected with PA.

Fun Facts About Aiden

- 5 yo and has a twin sister, Ava
- loves his family
- primarily gtube fed
- loves taking his levocarnitine by mouth receives bolus feeds three times through out the day, 6 hours continuous feeds through the night.
- receives ST and OT weekly
- currently working on being potty trained!

Favorite activities & foods

- playing in the sand
- mowing the lawn
- veggie straws with guacamole

Main struggle from P.A.

- constipation - giving 4 oz of prune juice/ day is helping tremendously

Publication Note: The PAF Newsletter *is published twice a year. Readers may subscribe by writing to PAF, registering online or calling 877-720-2192. Letters and article submissions are welcome for consideration and may be sent to paf@pafoundation.com or mailed to Propionic Acidemia Foundation, P.O. Box 151, Deerfield, IL 60015-4421. If you would like to be removed from our mailing list or receive the newsletter via email, please contact us.*

PAF AWARDS $50,000 CONTINUATION GRANT

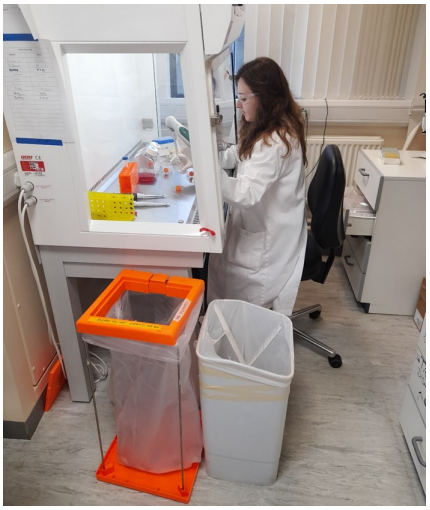
NEW PARADIGM IN ALLEVIATING THE CARDIAC CONSEQUENCES OF PROPIONIC ACIDEMIA: DIVERTING EXCESS PROPIONATE TOWARDS THE HEART'S BETA-ALANINE STORE

Pawel Swietach
Professor of Physiology
Department of Physiology, Anatomy & Genetics
University of Oxford

What can PA mice tell us about new ways of attenuating propionate toxicity in the heart?

Thanks to the generous support of the Propionic Acidemia Foundation, our research laboratory in Oxford, UK, has joined the global efforts to find new treatments for propionic acidemia (PA). I am delighted to report that earlier this year, our proposal for a continuation project was funded. On behalf of my group, I want to thank the PAF board and donors for their support. This article provides you with some information about our recent achievements and future plans.

Our group became interested in PA around 2015, when we realized that our expertise in cardiac research could help families affected by PA. As a scientist, I believe that our work is a service to the community, and it is therefore our obligation to reach out to those who may benefit from our scientific knowledge. For many years, we had been studying the effects of acidity on the heart in the broader context of cardiac disease, such as ischemia and hypertrophy. We reasoned that the next steps should consider what happens in the rare forms of acidosis that arise from inherited metabolic disorders. Among the organic acidemias, we felt that we can contribute towards studying PA, because the organic anion that accumulates (propionate) had powerful actions alongside the acidity. We connected with CLIMB, a UK-based association supporting families affected by inborn errors of metabolism, to understand how we can use our expertise to address some of the pressing issues that PA patients face. CLIMB provided seed-funding that started our research and put us in touch with colleagues at Great Ormond Street Hospital where many children affected by rare diseases receive treatment. Funding from CLIMB allowed us to collect pilot data, which formed the basis of a proposal for a doctoral research project. A PhD candidate, KC Park, took on this project, despite all the perceived risks associated with studying rare diseases. KC undertook heroic efforts to characterize the effects of propionate on the heart. The results were promising and we decided to make another strategic investment: bringing a mouse model of PA to Oxford with the help of Michael A. Barry in the US and Lourdes Desviat in Spain. This connection made possible thanks to PAF! Maintaining mice is very expensive but the cost was well justified on the basis of the quality of data collected by KC. The next milestone was our collaboration with Tom Milne who is Professor of Hematology at Oxford and Nick Crump who is now an independent researcher in London. We quickly realized that our skills dovetail and that we can make important discoveries in the PA field. This is how we embarked on a project to study the effects of propionate on the protein-based scaffolds that hold DNA. These structures, called histones, regulate the activity of genes, switching these between an 'on' and 'off' state. We found that mice affected by PA undergo profound changes in genes that are relevant to cardiac contraction. Thus, we showed that a disease of a specific gene (here, coding for propionyl CoA carboxylase) causes a myriad of secondary changes in gene expression: a new paradigm in inherited diseases. The experiments that study DNA scaffolds are complex and expensive, but we were able to pursue them with the help of PAF.



Eva Kocianova preparing samples for analysis.

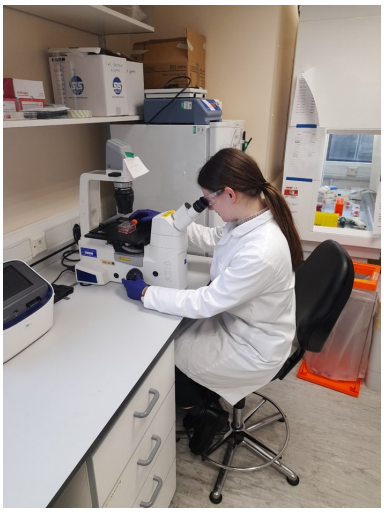
Scientific endeavors are designed to be hypothesis-driven, but many (too many?) discoveries arise by serendipity. This is both a source of frustration, because of the perception that good things happen by chance, and excitement, because when discoveries happen, they bring a great deal of joy. KC's meticulous lab work led to a striking discovery that the hearts of male PA mice are less severely affected than those of females. This is surprising because both sexes carry the same genetic defect. We think this is important because it suggests that male mice must have some sort of protective mechanism which is lacking in females. Exploiting this naturally-occurring phenomenon could form the basis of new therapies for people affected by PA. For example, if male PA mice have a means of reducing propionate toxicity, we want to know what this mechanism is, and how we can implement it in PA patients.

Our discovery came about by comparing the gene expression responses to PA in male and female mice using technology

GRANT (CONT.)

called RNAseq. This method counts the number of 'messages' issued by genes that instruct the cell to make proteins. Some of these messages are issued erroneously because they code for proteins that should not be made, or are made in the wrong amount. We observed that aberrant changes in message level were more prevalent in female mice. With Tom and Nick, we connected this to the way in which propionate affects histones chemically. Female mouse hearts affected by PA had higher levels of the reactive form of propionate, called propionyl-CoA. Using a technique called chromatin immunoprecipitation, we found that female mice suffered from more severe chemical modifications to histones, which causes their hearts to engage in the aforementioned gene expression changes. Consistent with these fundamental changes at the molecular level, we found that cardiac contraction was compromised more significantly in female PA mice.

We wanted to understand how male PA mice achieve their protective effect. To address this, we processed our samples for analysis by our colleague at Oxford, James Mccullagh. James provides access to a method, called metabolomics, which measures every major metabolite in the heart, and allows us to seek patterns. This is normally very expensive to run, and we are grateful to his team to giving us time on his set-up. James' data confirmed that female mice had more profound shifts in metabolites canonically associated with PA. The same data revealed something puzzling: that a specific class of substance appears more abundant in males than in females. We were surprised because those substances have so far been considered rather inert. However, further measurements showed that these male-associated substances are far from being inert by-standers: they may explain why male mice have a degree of protection from PA. These substances are, in fact, a reservoir of amino acids that can absorb excess propionate. This means that propionate levels can be buffered by this protective "sponge" and lessen the disease burden.



Bobby White inspecting cells under a microscope.

So far, we presented the work in meetings in Berlin and Budapest. KC even won a prize for his scientific talk! We are now preparing a manuscript for publication in a scientific journal. Our next step is to study this pathway in further detail, first in mice, and then in PA

patients. This is how we will use PAF funding. Our plan for the coming year is to characterize this buffer system, and seek ways of forcing it to operate at an enhanced rate, so that propionate is mopped up before it can cause damage. This is a first but necessary step to convince the scientific community that our hypothesis is valid and that further efforts to seek treatments based on the "propionate sponge" idea are justified. The reason we are optimistic about this, is because the propionate buffer could be activated by changes in diet, rather than gene therapy. This is important because not all PA patients qualify for gene therapy, even in clinical trials. Treatments based on diet often have an expedited route to approval by authorities.

Last year, we were delighted to start a project with an Oxford -based company called EVOX Therapeutics who develop ways of delivering drugs to cells using small particles, called exosomes, that are naturally produced by the body. We pitched our ideas about PA, and the company was happy to collaborate. This was a breakthrough for us, because support from industry is essential in order to progress our research to the market. Thankfully the wonderful team at EVOX has been incredibly supportive of our ideas. In the near future, we hope to deliver good news on better ways of delivering drugs directly to where they are needed in PA patients.

Whilst the notion of research as a service is part of the fabric that makes me a scientist, I am also realistic about the challenges that we face to make research work. Science is a team sport that relies on retaining the brightest people. Scientists devote many hours in the lab, facing the prospects of many failed experiments flanked by moments of euphoria when things work as expected (or even better … when something surprising happens). Today, many of our brightest scientists cannot continue their ambitions because of the lack of funding. Your contributions make a difference. Even if a project does not deliver what it promises on paper, it still has enabled the highest level of training for scientists who will continue pursuing timely problems that affect our health and wellbeing. Rare diseases are, unfortunately, low on the priority list of already stretched national and international funding agencies. Organizations like PAF play an essential role in providing funding opportunities that would otherwise not be there. We hope that by flagging new ways of thinking about PA, we can attract more attention from major funders to the area of organic acidemias.

Thanks to the valiant efforts made by PAF families, board members, volunteers, and donors, this research has been possible. Thank you for your support, and stayed tuned. Please feel free to contact us for more information.

PA HEART TO HEART CONFERENCE

Hosted by PAF & Sue and Steve Weaver

PROPIONIC ACIDEMIA FOUNDATION

REGISTER TODAY!

Evergreen Park in Kidron, OH
4434 Kidron Rd.
Dalton, OH 44618

July 21-22, 2023

- **Educational speeches**
- **Free CPR/AED Training**
- **Fellowship**
- **Large playground for the children**
- **Free Echos and EKGs - must be pre-scheduled limited availability**

You will learn about:

- Propionic Acidemia
- Treatment
- Research
- Clinical Trials
- CPR & AED Training
- Long QTC
- Arrythmias
- Cardiomyopathy

877-720-2192
paf@pafoundation.com
pafoundation.com

HERO Clinical Trial Recruiting Participants

The **HERO** (**He**lp **R**educe **O**rganic Acids) clinical study, sponsored by HemoShear Therapeutics, is recruiting participants at 12 leading research hospitals across the United States.

"We are grateful to the patients and families who are participating in our clinical trial, and happy to share that there are still opportunities to join the study," says Pat Horn, MD, PhD, chief medical officer at HemoShear. "We have many locations across the country, and transportation can be provided to make the study more convenient for families to join."

HERO is actively recruiting children and adults with MMA (mutase deficient) and PA aged 2 and older who have not had a transplant and meet the study criteria. While in the study, participants can continue to take their medications, including carnitine. More information about the HERO study is provided at MMA-PAHero.com or clinicaltrials.gov.

Study Assessing Potential New Treatment

HemoShear is developing investigational drug HST5040 as a potential treatment for MMA and PA. HST5040 is a liquid that is taken at home twice daily by mouth or through a gastric or nasogastric feeding tube. The HERO study is designed to assess how HST5040 acts in the body, if it causes side effects and whether it works to reduce harmful toxins in the body and help people with MMA or PA feel better.

Find a Site Near You

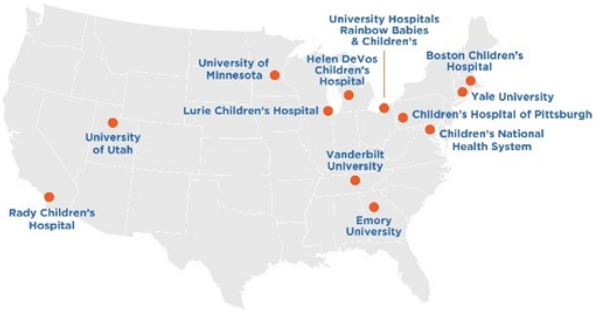
HERO is being conducted at many children's hospitals across the United States - and more sites are being added. Ask your doctor about whether you could be a candidate to participate.

Transportation can be provided to travel to the study sites and stipends are available to cover meals and other study-related expenses. Some visits can also be performed in your home. All study drugs, study visits and assessments will be provided at no cost.

Learn more at MMA-PAHero.com

The safety and effectiveness of HST5040 for the treatment of MMA or PA have not been established.

HELP REDUCE ORGANIC ACIDS
HERO STUDY



PA Heart to Heart Conference Registration Form – July 21-22, 2023
Propionic Acidemia Foundation (PAF) & Sue and Steve Weaver

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 and last)	Relationship (spouse, child, etc.)	Age (if child)	PA? (yes/no)	Diet (low protein, allergies, veg., please specify)

FREE CPR/AED Training (for those over 13):# attending Friday Night Free CPR/AED Training_____ **or**

CPR/AED Refresher Course (over 13) _____ Not interested _____

Dinner Friday - July 21: Adults ____ Children (3-12) ___ Children under 3 _____

Breakfast - July 22: Adults ____ Children (3-12) ___ Children under 3 _____

Lunch - July 22: Adults ____ Children (3-12) ___ Children under 3 _____

Box Dinner to go - July 22: Meat sandwich _____ Vegetable sandwich _____

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 reply by June 15th.**)

I hereby give permission to PAF to use any photographs/videos taken at the 2023 PA Heart to Heart 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 due by July 8, 2023. Please mail completed form to:
Propionic Acidemia Foundation, PO Box 151, Deerfield, IL 60015 or register at pafoundation.com

PAF AWARDS $50,000 CONTINUATION GRANT

PROPIONYL-COA AND PROPIONYLCARNITINE MEDIATE CARDIAC COMPLICATIONS IN PATIENTS WITH PROPIONIC ACIDEMIA

Guo-Fang Zhang, PhD
Duke University, Durham NC, USA

Cardiac disease has a high prevalence among patients with propionic acidemia (PA). The pathological mechanism remains largely unknown, particularly due to the nature of chronic development. It is challenging to predict the cardiac diseases development in PA patients simply by the PCC mutations, propionyl-CoA carboxylase (PCC) enzyme activity or acute metabolic changes in plasma or urine because no strong correlation between cardiac phenotype (severity of disease) and genotype, metabolic decompensations or residual enzyme activity has been observed from the clinical cases.

Fatty acids with various chain-lengths are major fuels for heart. Our previous data demonstrated that propionate rather than amino acids is a major source of cardiac propionyl-CoA. In addition, the deficiency of PCC reduces the hepatic disposal of microbiome-derived propionate and promotes odd-chain fatty acid synthesis, both of which impose metabolic stress on heart. Propionyl-CoA accumulation derived from propionate and odd-chain fatty acids could interrupt cardiac energy metabolism. The low ATP further inhibits propionyl-CoA carboxylation according to our recent ischemia study. The impaired energy metabolism and propionyl-CoA accumulation forms a vicious circle.

With a third-year grant support from PAF, we will collaborate with Drs Eva Richard Rodríguez and Lourdes R. Desviat from Universidad Autónoma de Madrid on how energy metabolism in PCCA- or PCCB-iPSC-cardiomyocytes derived from human patients is altered by stable isotope analysis, particularly under the stress of propionate and odd-chain fatty acids. Another Aim is to improve cardiac energy
metabolism by targeting propionate and odd-chain fatty acid metabolism.

JOIN US AT FAMILY CAMP HOSTED BY NATIONAL PKU NEWS!

Camp is open to individuals with any inborn error of metabolism, their friends and family. There are 2 ways to participate:

In-person: June 1-4th, 2023 in Antelope, OR at Washington Family Ranch. Four days of community activities, Olympics, breakout sessions, crafts, science talks, delicious low-protein meals, and most of all, FUN!

Virtually: August 12th, 2023 wherever you are in the world!! There will be science, fun, and chances to connect with your IEM community. Registration also includes a camp kit with ingredients to join a a low-protein cooking demo, a teeshirt and a craft kit.

Visit pkunews.org/camp or email NIkki@pkunews.org for more information.

P.S. This year camp will feature a preview of our new app & research platform, flok. If you're interested in learning more about your metabolic health & finding tools to support you, sign up for more info at flok.org.

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.

PAF Spanish chat with Dr. Claudia Soler-Alfonso

November 9th, 2022

Marisa Cotrina, PhD - PAF Board of Directors

Our Spanish chat is more active than ever! The Spanish chat was created to fill up the need to support the Spanish speaking community, which not always has the means to receive and read our newsletters and updates in English. PAF has therefore been organizing a series of Spanish chats to provide support and information to this newly added PA community.

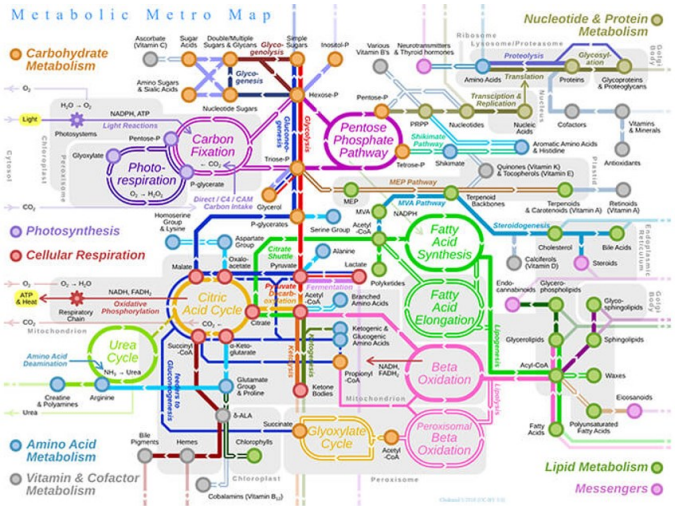
As part of our "Spanish chat series", PAF sponsored a zoom meeting with Dr. Claudia Soler-Alfonso, pediatrician and geneticist at Baylor College of Medicine. Dr. Soler is also an expert in Inborn Errors of Metabolism and takes active care of several PA patients at the Texas Children's Hospital in Houston, Texas, USA.

We had a total of 17 participants attending the chat, representing numerous Spanish-speaking countries, including Argentina, Mexico, Guatemala, Ecuador and Chile, plus some families based in the US. Dr Soler kindly spent almost an entire morning with us to present in Spanish the basics to understand the complexity of PA, current PA treatments, and the new PA therapies under development.

Dr. Soler's presentation covered basic information about what PA is in the context of the thousands of metabolic pathways that exist in our bodies, comparing it to an intricate map of the transportation system of Houston. She talked about how energy is produced from proteins, fats and sugars in our mitochondria (the energy factories of our cells), and what happens when some of these steps malfunction, like in PA. She then talked about all the symptomatology of a child with PA, from acute metabolic crises to the most chronic health challenges and how a diagnostic is made.

Families appreciated very much the explanations of the current clinical management of PA, which ranges from diet control with specialized formulas to the usage of supplements like Carnitine, Flagyl (metronidazole), biotin or carbaglu.

The control of growth, the effects of PA on the heart, the gastrointestinal and immune systems and the kidneys were also central to the discussion. But Dr. Soler did not stop there and also elaborated on the neurological manifestations of PA, the frequency of epilepsy and the alterations in brain structure. How frequently kids with PA are diagnosed in the autism spectrum and the occurrence of psychosis in some patients were some other very interesting topics that Dr. Soler touched upon, without forgetting to discuss the incidence of optic neuropathy, which affects about 11 -25% of our kids.



The last part of the presentation dealt with the new therapies being developed for PA: how mRNA and gene therapy work, and what this means for the newly diagnosed PA kiddos, as well as for older PA patients.

If the first part of the presentation was outstanding, the second part was even better because it gave our Spanish-speaking families the opportunity to ask questions. Our forum was very active, and the participants asked about common PA issues, from skin rashes to formulas, the meaning of high glycine or the treatment of constipation. Families were also very interested in hearing more about liver transplantation, how to obtain Carbaglu or if we need to use probiotics.

For many of the families that struggle to get the PA/MMA specific formulas so widely used in the US, it was particularly important to discuss other dietary alternatives: Can we use maltodextrin? How do we control pancreatitis? What is the best vegetal oil to add to the PA diet? Are laxatives recommended? Should we use CoQ10 for the heart or not?

And what about physical activity: do we need to restrict it, or should it be encouraged?

We were very impressed by Dr. Soler's eagerness to connect with our Spanish-speaking community and by her warm welcome to all our attendees. It was a very exciting and dynamic session, and we are very, very appreciative of Dr. Soler's patience and all the time she devoted, not only to inform us, but also to answer the numerous questions that our families had.

We cannot wait to the next session of the PAF Spanish chat. Stay tuned!

PAF ACTIVITIES & FUNDRAISING SPOTLIGHT

UPCOMING EVENTS

- **May 18-20- Abbott Nutrition Conference**, San Antonio, TX, PAF will be exhibiting
- **July 21-22 - Heart to Heart PA Conference** (see pgs. 6-7)
- **November 5- Team PARunners New York Marathon**

PAST EVENTS

- **March 17-21 PAF Exhibited at SIMD** (see photo)
- **February 28- Rare Disease Day - Panda Express Fundraiser and Rare Gear**
- **December 3, 2022- PA Cardiac Meeting**
- **November 9, 2022 - Zoom Call with Dr. Claudia Soler-Alfonso**
- **November 6, 2022- Team PARunners New York Marathon**

FACEBOOK: Thank you to all of our Facebook Fundraisers and people that donated to their fundraising pages for birthdays, #GivingTuesday or just because: Tara Gerlach's Columbus ½ Marathon, Jill Chertow, Dottie McGee, Mariska Van De Venter, Kathleen Rusch, Claire Howard, Cindy Davis and István Varga

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

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

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

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**: Cora Brenneman, Lucy Harding, Dylan Jaehnke, Laura Lemire, Reily and Judson Lenert, Kate Lowry, Vivienne Lopez, Leah Masten, Trenton McKinley, Gabriel Lopez, Gabrielle Millett, Grant and Sebastian Moss, Brandon Napiwocki, Ben Sweetman, Isabella Velazquez, Chase Workman

- **In Memory Of**: John and Alice Dawe, Kerrie Fessler, Jordan Franks, Vincent Philip Franze, Nicholas Phillips, David Scott, Talli Smith, Angelica Stageman, Kristin Stoebner, Kirstyn Tripp

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.

Thank you for making a difference.

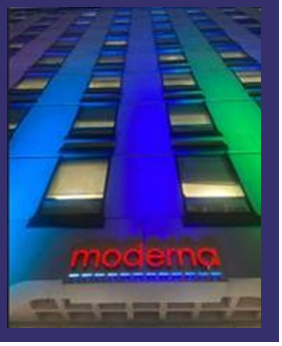
Moderna Honors Rare Disease Day

We hope everyone is having a great start to the year!

We at Moderna care deeply about patients and caregivers and are committed to delivering on the promise of mRNA technology.

Recently, Moderna honored rare disease day in a variety of ways, including lighting up our building Cambridge, MA in support of the rare disease community.

To learn more about our clinical programs in PA and MMA, please visit trials.modernatx.com, clinicaltrials.gov or call the Moderna Clinical Trial Support Center at 1-877-777-7187.



Stay safe and well,

Moderna

CONGRATULATIONS PARUNNERS 2022

$30,000!!! for PAF

OFFICIAL CHARITY PARTNER

TCS NEW YORK CITY MARATHON

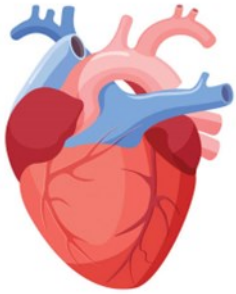
PAF CARDIAC MEETING – DECEMBER 3RD, 2022

Marisa Cotrina, PhD - PAF Board of Directors

On December 3rd, the Propionic Acidemia Foundation had the privilege to bring together an outstanding panel of specialists interested in figuring out the underlying causes of the cardiac symptoms that are so frequently seen in patients with PA.

It was a full 2.5 hours, packed with information: a brief 20-minute presentation of the work of each of the experts, followed by an open discussion with the PAF scientific board and the PAF executive board.

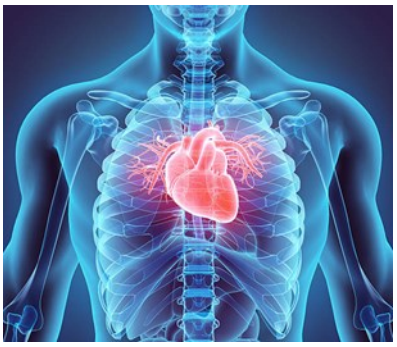
This was a unique opportunity for the PAF Board to listen firsthand from the investigators that have received funding from the Foundation to carry out some of this research and to discuss with other researchers who are also working on understanding the heart problems of PA patients. It was also a unique opportunity to encourage potential collaborations among these very talented investigators.



Some of the talks focused on understanding what metabolites alter energy utilization in the heart of mice that carry mutations that cause PA in patients (Guofang Zhang; Duke University, North Carolina, USA), the changes that propionic acid and other metabolites cause in proteins that control gene expression by binding to them and changing their function (Dr. Pawel Swietach, Univesity of Oxford, UK), and the effect of calcium, which is well known to modulate electrical activity in the heart and other organs (Zhang, Swietach).

A different line of research was presented by Dr. Eva Richard and Dr. Lourdes Ruiz Desviat (Centro Biología Molecular Severo Ochoa, Madrid, Spain). They have directly studied the electrical currents that are present in heart cells derived from patients with PA. These cells are an incredibly useful model to study PA because, as they come from actual patients with the disease, they provide clues that may be directly relevant to what happens in the hearts of patients with PA.

Last, Dr. Devyani Chowdhury (Cardiology Care for Children, Lancaster, Pennsylvania, USA) and Dr. Bart Bijnens (ICREA, Barcelona, Spain) presented their data from echocardiograms obtained in PA patients from the Amish community. In some instances, the images showed a striking change in the shape of the heart that may explain why the ejection function of the PA heart becomes less efficient over time, ultimately resulting in heart failure. By collecting many more images from this patient population, these two researchers may eventually create models of heart function to predict who has the highest risk of developing heart failure.



The take-home message: there is still a lot to be done to understand all the different ways in which the heart function declines in PA patients, but the work that the Foundation has supported is beginning to bear fruit. A lot of intriguing ideas for future research were shared among the investigators, ideas that sparked a very exciting discussion among all the participants.

Two immediate action points from the meeting:
-Dr. Devyani Chowdhury/Dr. Bijnens would be delighted to analyze echocardiograms from PA patients using their unique analytical approach. If you would like to contribute to her project, please, email her at dchowdhury@cardiologylancaster.com or email PAF to coordinate.

-Dr. Eva Richard's group and Dr. Zhang are planning a new collaboration to confirm if the hypothesis about the metabolic origin of abnormal cardiac function (obtained from experiments in the mice with the PA mutation) is also true in the cardiac cells from patients with PA.

Overall, the meeting was a big success, generated new ideas for collaboration, and set the tone for a new series of research meetings sponsored by PAF among the different investigators, with the goal to try to accelerate new findings that could generate therapies that alleviate the cardiac damage in PA.

We want to hear from you!

Have a PA story to tell, event to promote or news?

Fall newsletter submissions due by August 1, 2023.

SEARCHING FOR A CURE
HOPE FOR OUR CHILDREN

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