SEARCHING FOR A CURE HOPE FOR OUR CHILDREN

Propionic Acidemia Foundation

VOLUME 1, ISSUE 20 SPRING 2016

Society for Inherited Metabolic Disorders (SIMD) Ponte Vedra Beach, Florida

Jill Chertow Franks, PAF President, and Brittany Smith, PAF Board Member and Treasurer, were able to attend the SIMD 39th Annual Meeting April 3rd to April 6th. PAF shared an exhibitor's booth with the National Urea Cycle Disorders Foundation, who we have partnered with in the past. We were able to meet with researchers, medical providers, other rare disease groups, and some members of our medical advisory board. There were several presentations and posters regarding new insights into Propionic Acidemia.

Dr. Loren Pena of Duke University submitted a poster, "Assessment of Metabolic Markers in Propionic Acidemia" that was approved by SIMD and a brief summary is in *Molecular Genetics and Metabolism,* Volume 117, Issue 3, March 2016. Dr. Pena had received funding for this project from PAF and has collaborated with our foundation on other projects as well. We are grateful for those families who participated in Dr. Pena's study.

Congratulations to Sean Hofherr, Ph.D., of Georgetown University and Children's National Health Systems on presenting the 6th Robert Guthrie Memorial Lecture. The Propionic Acidemia Foundation funded Dr. Hofherr while at Baylor College of Medicine working on his Ph.D on projects studying the effects of Propionic Acidemia on mice, which is important basic research in knowing more about the disorder and has led to further studies on PA.

There were several posters and presentations on PA. There were topics on preserving liver cells from a liver that had been removed at transplant, the drug trial of carglumic acid (Carbaglu) in PA and MMA, and liver transplantation.

Help move research forward for propionic acidemia.

Participate in the **Propionic Acidemia International Registry**. As of March1st, there are 42 participants.

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

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.

PROP NUTRITION GUIDELINES NOMINAL GROUP MEETING

Are we there yet?! The Journey of the development of Propionic Acidemia Nutrition Guidelines

It seems appropriate that the Propionic Acidemia (PROP) Nutrition Guidelines Nominal Group meeting in Atlanta, GA was held on a leap year, the weekend before 2016 Rare Disease Day. We have indeed leaped forward towards our goal of developing the PROP nutrition management guideline based on the feedback gained from the attendees .

The goal of the Southeast Newborn Screening and Genetics Collaborative - Genetic Metabolic Dietitians International (GMDI) Nutrition Guidelines Project is: *To develop nutrition guidelines for the management of genetic metabolic disorders for which there is little published scientific evidence.* Evidence based medical practices should come from scientific findings gathered from randomized control trials (RCT) to guide clinical practice and treatments. RCTs require large numbers of participants to develop statistically significant conclusions, which is challenging to do with rare conditions such as PROP. Hence, most PROP publications are observational studies consisting of single cases or case series. In order to determine best Medical Nutrition Therapy for PROP, a group of experienced metabolic dietitians followed an evidence and consensus based methodology. The workgroup developed a multi-step process for guideline development known as the Delphi-Nominal Group-Delphi-Field Testing (DNDF) methodology1, that includes a review of scientific and grey (unpublished) literature, a Delphi survey of practice, a nominal group meeting to clarify discrepancies, a formulation of recommendations and a second Delphi round to assess the degree of consensus with the proposed recommendations. External review and field testing are also built into the process.

For PROP Nutrition Guideline, our workgroup of 65 individuals have been involved in some aspect of the development of the PROP guideline, including 13 experienced GMDI metabolic dietitians, have been trained in evidence analysis and DNDF methodology. We evaluated ------ 1156 articles, of which 225 published articles and 25 grey articles (book chapters, etc.) met the criteria for inclusion.. The articles were rated for quality and summarized; the areas of certainty for PROP MNT and uncertainty requiring more clarification were identified. The nominal group meeting included the following metabolic experts; 2 physicians, 4 dietitians, 1 physician researcher, and 2 parent group representatives to participate in discussion and review of preliminary PROP nutrition recommendations. Topics addressed included acute and chronic management, energy and protein requirements, nutritional supplements and interventions to optimize outcomes in various circumstances such as pregnancy and transplantation, laboratory values to monitor, and much more. Our next step is to implement another Delphi survey to further validate the nutrition recommendations. The final step will be to summarize and write the PROP Nutrition Management Guideline that will be made publically available and submitted to a metabolic journal for publication by December 2016. We will periodically update them as new evidence to support best clinical practices are discovered. In the future a PROP tool kit will be developed for practical implementation of the PROP Nutrition Management Guideline, including educational resources. This project is supported by a Maternal and Child Health Bureau HRSA grant #2-U22 MC010979. We greatly appreciate the contributions and support of the clinicians and the patient community to help us achieve this goal of improving MNT for people living with propionic acidemia, their families and caregivers.

Principle Investigators: Rani Singh, PhD, RD and Fran Rohr, MS, RD
OA Workgroup Co-Chairs: Elaina Jurecki, MS, RD and Keiko Ueda, MPH, RD

OA Workgroup members: Dianne Frazier PhD, MPH, RD, Christie Hussa, RD, MBA, Julie McClure, MPH, RD, Laura Nagy, MSc, RD, Lisa Obernolte, MS, RD, Matthew Rasberry, RD, LD, CNSC, Bridget Reineking, MS, RD, CD, Ann Marie Roberts, RD, CSP, CNSD, Amie Thompson, RD, LD, Steven Yannicelli, PhD, RD

References

1. Singh RH, Rohr F, Splett PL. 'Bridging evidence and consensus methodology for inherited metabolic disorders: creating nutrition guidelines'. J Eval Clin Pract 2013 Aug; 19(4): 584-90. http://www.ncbi.nlm.nih.gov/pubmed/22168925

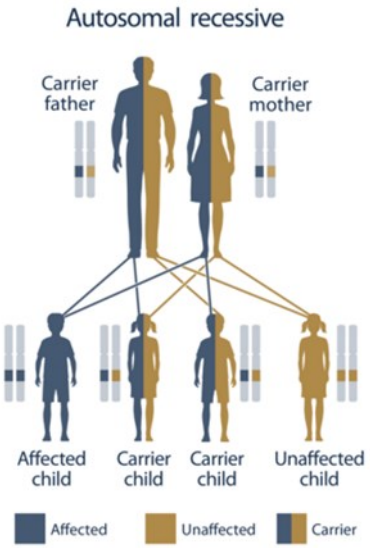
Jill Chertow Franks, President of PAF, participated in the nominal group meeting.

PA GENETICS, PART 1

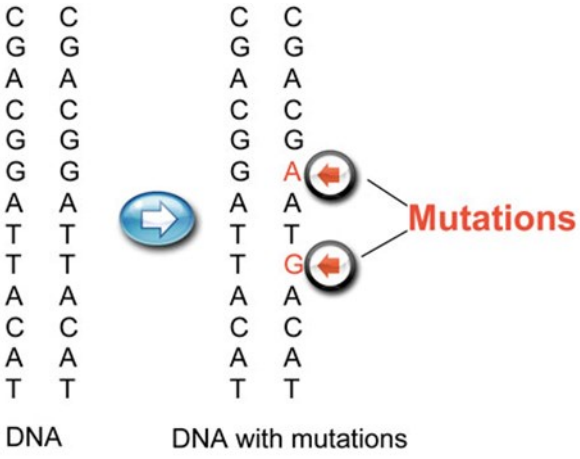
Propionic Acidemia (PA) is a condition caused by changes in the genes that make the propionyl-coenzyme A (CoA) carboxylase enzyme. **Genes** are made of **DNA** which is our hereditary material. Genes have the instructions that tell our bodies how to grow and function. Each gene provides specific instructions for various biological processes in the body.

The genes that make the propionyl CoA carboxylase enzyme are called PCCA and PCCB. The enzyme helps break down certain proteins and fats from food to make into chemical energy and other products the body needs. When there is a change in the gene called a **mutation**, the genes cannot perform their normal function. If these genes do not work and the body cannot break down fats and proteins, there is a buildup of organic acids in the body which can cause the symptoms associated with PA such as vomiting, weak muscle tone, and developmental delays.

If someone has a mutation, it is something he or she was born with. These mutations happen randomly and they are not caused by something the person did. We have two copies of each gene. We inherit one copy from each parent. If someone has one gene with a mutation and one gene that works properly, they are called a **carrier**. Carriers do not have symptoms of propionic acidemia because having one working gene copy means the body is still able to break down fats and proteins.



If both parents are carriers of propionic acidemia, there is a 1 in 4 or 25% chance of having a child with propionic acidemia. This is called **autosomal recessive** inheritance. The condition can affect males and females and an individual has to inherit two mutated genes to be affected with PA. Therefore, in order to be affected by PA, the child has to inherit a gene mutation from both parents. If a child inherits one working gene and one mutated gene, they will also be a carrier of PA and will not have symptoms. If a child inherits both normal copies of the gene, they will not be a carrier and not have the condition.



To find out if you are a carrier of PA, you can have **genetic testing**. Our DNA is written in a four-letter code. Genetic testing works by reading through the code like a spellchecker looking for a change, also called a mutation.

Robyn Hylind
Genetic Counseling Student
Northwestern University
Graduate Program in Genetic Counseling

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 1963 McCraren, Highland Park, IL 60035. If you would like to be removed from our mailing list or receive the newsletter via email, please contact us.*

KIRSTYN'S STORY

Hello PA friends! It has been a long while since we have talked to many of you! I am so glad to be back in touch by sharing Kirstyn's updated story! For those of you who don't know us, I will start from the beginning.

Kirstyn Paige Tripp was born on August 17, 2004 and after ten years of infertility and an uneventful pregnancy she had finally arrived. When she was born she started showing signs of Jaundice and our pediatrician decided to perform some blood work. It came back with the results of ABO Incompatibility and she needed to be transported an hour north of our hometown to Shands at the University of Florida for triple photo-therapy. It also happens to be my Alma Mater…so…GO GATORS! (I had to throw that in there!.) Of course we were worried sick about this diagnosis but we had no clue what was on the horizon. While Kirstyn was in the newborn nursery at Shands she repsonded well to the jaundice treatment , but she started having some other issues. At six days old she became almost lethargic and refused to nurse and seemed to even have a hard time opening her eyes. I became upset and asked the nurse to call a doctor to check her over. He became concerned over her labored breathing and decided that she needed to be admitted to the NICU for further evaluation and testing. As the day went on her condition deteriorated and she actually stopped breathing. Thankfully she was in the hospital and received very quick medical care. Her ammonia had risen to over 700 and she was acidotic. She was on dialysis, intubated and the medical staff expressed their concern that she may not live through the night. She was only seven days old. We were absolutely devastated!

A doctor by the name of Dr. Bernstein was on duty in the NICU and he had some limited experience with metabolic diseases. He immediately called in the Genetics team and after a few days we had the confirmed diagnosis of Propionic Acidemia. She spent nine and 1/2 weeks in the NICU and finally got the discharge orders we had been waiting on! Fast forward…….

Kirstyn is an amazing eleven year old that started middle school this past year. People are so right when they tell you not to blink! How did my baby become old enough to start middle school? She has had about fourteen subsequent hospitalizations over the years and thankfully has not had an admittance for about eighteen months now! She is still treated at Shands and has also developed Cardiomyopothy and borderline long QT. Her doctors are amazing and this medical team has stood by our side her entire life! She has a gtube that was inserted at six weeks old and this decision has saved us numerous trips to the hospital. Kirstyn also eats by mouth and on most days consumes 100 percent of her food by mouth. Her tastes change quite often and her favorite foods of one week will not be her favorite foods of the next week. Sigh…… She loves chocolate, french fries, Doritos, Spaghetti, sweet tea and McDonalds pancakes lots of syrup and hash browns. We are on a very friendly first name basis with our local McDonalds staff. :)

Kirstyn actually has a gifted IQ and while she has the ability to excel in school, it does not always turn out that way due to her moderate diagnosis of ADHD. She is able to take a non stimulant medication to treat her ADHD but the doctor will not authorize any stimulant medications due to her heart issues. Some days the behavior is a real struggle , but she never ceases to amaze us with her charm, wit and sense of humor!

Kirstyn is quite the artist and has actually started an art portfolio of her drawings and paintings. She has taken private art lessons and this is her passion. She also practices archery with her dad and enjoys shooting her bow and fishing. She also enjoys antagonizing her younger brother, Cason who is nine years old and unaffected from PA. Last year, we were given the honor of becoming an ambassador for Children's Miracle Network Shands Hospital at UF. She has the incredible opportunity to join kids with other disabilities and I get the honor of sharing her story and bringing awareness to Propionic Acidemia and other metabolic conditions.

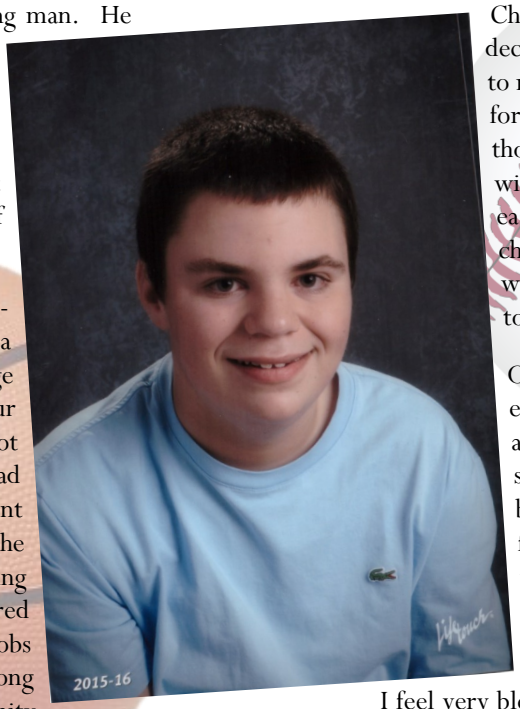
We live about an hour and half away from Disney and have had the fun pleasure of meeting up with some other PA families when they have been on vacation. So, if you are ever in our neck of the woods, please contact us and see if we can meet you too!!

I have made lifelong friends from some of the other PA parents and their experiences have helped us navigate these difficult waters of Propionic Acidemia. As my years of experience continues to grow my hope is that I can hep other parents as well. Much love from the Tripp Family, Ronnie, Marsha, Kirstyn and Cason.

CHASE'S STORY

Hello everyone, the last time we had put out an update on Chase, he was ten years old. He will be turning 18 next month! I can't believe how the time has flown by.

Chase has grown into a handsome young man. He has really lost a lot of baby fat and has gotten leaner and taller. We have had to make adjustments with his formula along the way, but, overall, Chase has been doing really well. He still does not eat anything by mouth except drinks of water.



He currently is a junior at a special education school. He started this school as a sophomore. This was such a great change for him. We tried the program at our local high school, but, it just could not meet all of Chase's needs. Also, it had 2,000 students, whereas Chase's current school has 200 students. The program he is in is wonderful. They are really teaching him life skills, and they have a sheltered workshop on sight. Chase has certain jobs he must do every day. The students, along with the staff go out into the community once a week. He, also, receives speech/language therapy, occupational therapy, and aba therapy.

Chase has not been hospitalized for at least five years. Any sickness he has gotten, we have been able to control at home, including a stomach bug. We have, also, finally have had Chase seizure free for 6 months. He is on three medications for his seizures, and they have really controlled them well.

Chase's physical strength has definitely declined over the years. The doctors want to rule out everything, so a MRI is planned for him soon. He has been fitted for orthotics and this has helped a great deal with his walking. He gets fatigued very easily, and sometimes requires a wheel chair. This is so strange for the boy that when he was younger, you literally had to "chase" him everywhere.

Overall, Chase is very happy. He really enjoys his books, his certain music toys, and watching sports on tv. He likes to spend time with his family especially his big brother Kyle when he comes home from college. He enjoys his extracurricular activities of basketball and baseball, he may not always participate, but he really enjoys being a spectator!

I feel very blessed to be Chase's mom. He is such a special kid. I am, also, very grateful for the PA foundation, as well as, the OAA.

LAB UPDATE

Update on "Laboratory parameters reflective of metabolic control in individuals with propionic acidemia" at Duke University Understanding how the results of laboratory tests relate to a person's current health, treatment options, and future health risks can be invaluable. However, this is an area on which little information is available for people with propionic acidemia (PA). To address this question, we have measuring and comparing levels of plasma and urine metabolites in people with PA when they are well and during illness.

Since the research study began in April 2013, we have received samples from 12 participants. We have already seen some promising results that warrant further investigation, and we still have a wealth of data to analyze. We are currently working on the data analysis with the help of a statistician. Until the statistical analysis is complete, we will not be requesting additional samples from anyone enrolled in the study, or enrolling new participants. We look forward to providing an update with our results in the future. We greatly appreciate the support for this study. We would like to thank all of the families

and healthcare providers involved for their help and commitment.

Forquestions about the study, please contact the study coordinator, Jennifer Goldstein, at phone number (919) 684-0626 or email jennifer.goldstein@duke.edu

PAF EVENT & FUNDRAISING SPOTLIGHT

PAST EVENTS & CAMPAIGNS:

- Branch Family Superbowl Party, Indiana, $775
- Ladies Night "Art" Expo, Columbus, OH, $250
- Billy & Lauren Whitten's wedding dollar dance, $202 (that's a lot of dancing!)

ONLINE TOTALS RAISED IN 2015:

- Igive: $278.68
- Goodsearch: $1410 (cumulative as of 9/12/2015)
- AmazonSmile: $64.01

CORPORATE DONATIONS (Including matching and volunteer hours):

Verizon, JPMorgan Chase, Shell Oil Company Foundation, Enterprise Holdings Foundation, Cardinal Health Foundation

Corporate Matching Gifts for cash donations or volunteer time may enable you to double your donation. Check with your HR department to see if they match. It makes a big difference!

PAF is always looking for volunteers. Please check with Human Resources to see if they have a program.

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:** Teegan Keith Sakaguchi, Nila Branch, Brett Young, Zach Matz, Brandon Napiwocki, Hogan Koehl, Trent McKinley, Gabrielle Millett, Jordan Franks, Kristin Boecker, Talli Smith, Maren Stecken, Isabella Velazquez, Benjamin Sweetman, Judson Lenert, Dania Martinez, Edgar Martinez Jr., Nalani Johnson, Chase Workman, Kate Lowry, Lisa Napiwocki's Birthday, :)
- **In Memory Of:** Nicholas Alexander Phillips, Angelica Stageman, Vincent Franze, Sharon Esses, John and Alice Dawe, Bob Buck, Connor McKillop, Donald Sciss, Bailey Sciss

Thank you to all of those who donated in our annual giving campaign at the end of 2015. We raised nearly $15,000! If you have anyone you would like to have us add to our campaign, please e-mail paf@pafoundation.com

VOLUNTEER SPOTLIGHT: YOU MATTER!

Julie Howard is our first Volunteer Spotlight recipient and we would like to thank her for her support, countless hours of time, and energy. Julie is a PA aunt, the PAF Newsletter editor, and a volunteer extraordinaire. In addition to all of the amazing support she has provided to her sister, Jen, and niece, Gwen, that you will read about below, she has put together this newsletter and countless others, run in the Columbus Marathon year after year, helped raise money and awareness for PA, and I am proud to consider her a friend. - Jill Franks

As horrific as PA has been to my daughter, this life altering occurrence has brought so many blessings. I like to say that Gwen's supporting cast is second to none & my sister, Julie Howard, has been a rock star for the team. For me, it has been an extreme time of change since Gwen was born. She was so sick & on life support her first week of life. That suddenly changed everything for me. I had to do something to help her and it had to be something that would give me peace if she passed, in knowing I did everything I could. Sharing this decisions with family & friends, I was overwhelmed by their support. In particular, Julie stepped up to help in any way I asked, & sometimes when I didn't ask .

We decided we would raise money for research & hopefully a cure for PA. Julie set up a personal website for Gwen & her friend Allison Ellis, so friends could get updates on the girls, & information on upcoming fundraisers. I recall a conversation we had when we first started this mission, and decided to set our lifetime fundraising goal at $10,000. Amazingly, we've hosted dozens of events & raised many times that amount for the PA Foundation, which would not have happened without her constant support. But that's just the beginning of what she's done. She's listened thousands of my thoughts, dreams, hopes & fears, always being supportive & understanding, even though she couldn't possibly understand. In the early days, when Gwen was sick all the time, she wanted to learn how to take care of her, or offer to watch Gwen's brother Robbie, who was only 2 when Gwen was born. That was remarkable to me because she lives 100 miles from us & has a family of her own. She's volunteered for several years as newsletter editor for the PA Foundation, takes time off work to help organize events, & continues to be an advocate for all who are impacted by PA.

I know it is truly rare to have such an advocate in the world of rare disease, so I appreciate her support more than she will ever know. She's not just doing this for Gwen, but for all PA families. It is my hope each of you reading this article will find comfort in knowing there are amazing people, like Julie, who are helping to fight the battle against PA. Feel free to send her an email of appreciation: jbhoward_99@yahoo.com.

- Jen Mouat

MORE TO KNOW ABOUT PA

VOMIT

An easy way to remember which amino acids and other substances contribute to propionic acid is the acronym VOMIT.

Valine, an essential amino acid
Odd-chained fats
Methionine, an essential amino acid
Isoleucine, an essential amino acid
Threonine, an essential amino acid

An essential amino acid is one in which a person cannot make in their own body and is needed for life, so it needs to be included in the diet. An odd-chained fat can come from plants or animals and contains an odd number of carbon atoms.

PA Word Find

Vomit, **O**dd Chained Fats, **M**ethionine, **I**soleucine and **T**hreonine
Bonus words: Propionic, Acidemia, Protein, Genetics, Scale, Labs, Ammonia, Carnitine

O	G	I	S	0	L	E	U	C	I	N	E	H	O
I	D	R	G	E	N	E	T	I	C	S	P	P	A
C	A	D	S	E	A	R	C	H	I	N	G	R	C
E	M	S	C	A	L	E	F	O	R	A	F	O	I
V	I	R	A	H	C	U	R	E	H	O	P	P	D
O	N	C	F	V	A	L	I	N	E	O	R	I	E
M	O	O	A	P	U	I	R	C	A	H	I	O	M
I	L	G	D	R	R	E	N	N	C	R	E	N	I
T	H	R	E	O	N	I	N	E	I	S	E	I	A
A	R	A	C	T	H	I	C	U	D	R	E	C	S
A	P	P	L	E	A	D	T	U	L	F	L	T	S
L	O	E	W	I	P	R	O	I	T	E	A	I	N
A	M	M	O	N	I	A	F	O	N	O	B	T	D
S	M	E	T	H	I	O	N	I	N	E	S	B	S

Help Us Find the Cure!

*Name*_____
*Address*_____
City, State, Zip _____
*Phone*_____
*E-mail*_____

Please send an acknowledgement to:
*Name*_____
*Address*_____
*City, State, Zip*_____

*Enclosed is my contribution of $*_____ *in honor of/in memory of* _____
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

PROPIONIC ACIDEMIA FOUNDATION

PAF volunteers and board members are needed!

paf@pafoundation.com

Please email paf@pafoundation.com to join a committee.

Join and follow Propionic Acidemia Foundation on Facebook