

Propionic Acidemia Foundation

VOLUME 1, ISSUE 9

AUTUMN 2010

Young Family's Benefit for PAF

After seeing what Brett had to go through the first few weeks of life and learning about what PA really is, that was it, although devastated as I am sure most families are, I decided I had two choices, sit back, cry everyday and let it happen, or do something about it and make a difference. The choice was simple, I needed to do something and do something fast, help find a cure for my sweet little boy. So I got in touch with Jill and asked what can I do to help, and she explained what we need and that is funds for research, research and more research. My husband and I want a cure, nothing less! So having attended quite a few beef and beer benefits in my life, I always had a good time and they seemed to be successful, so I mentioned it to my husband and some family members and it was a GO! It was a bit of time, work and effort, but worth every second of it.



Brett with big brother Darren and big sister Morgan

The Beef and Beer Benefit for Propionic Acidemia In Honor of Brett Young was held at St. John's the Baptist Church Hall on June 12th 2010 at 7:00pm til 11:30pm, and I believe it was a success! We built the food cost into the ticket itself, and by asking around, we were able to get the hall free of charge, the DJ free of charge, and got a good bit of gift cards, items for raffle. I was truly amazed at how many people without being asked donated a basket or big item to raffle off. My cousin had mentioned the event to people in her office and next thing you know, people she works with were bringing in items for raffle, making baskets, wow is all I could say, truly amazing, it really restores faith in mankind, especially in this hurting economy!

Although the event itself was a bit busy, it was lots of fun, and it was really nice seeing family and friends that we have not been able to see as well as complete strangers attending for support. We happily raised \$7,800.00 between ticket sales, raffles, 50/50 and people sending money with a friend. Besides the event being a success, it also brought attention to PA itself. We were able to get the local newspaper do an article on us and the event, and we have had a few people call us and donate, strangers no less, but they read the article and it made a difference! Until next time! The Youngs!



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In Memory of Scarlett



April 5, 2006 –
November 21, 2009

In Memory of Tyler



January 22, 1998 –
February 12, 2010

CHAPMAN STUDY UPDATE

Gene expression differs in cell lines from individuals with Propionic Acidemia

Kimberly A. Chapman MD PhD, Children's National Medical Center, Washington, DC

Individuals with Propionic Acidemia (PA) often present with metabolic acidosis and develop a number of secondary complications including problems with their heart, skeletal muscle, and brain. To understand the underlying causes for these findings, **I wanted to know if cells from individuals with PA use the same genes or different genes (gene expression) compared to those without PA.**

Genes (DNA) work by being transcribed into RNAs which is then translated to protein. Proteins are typically enzymes and cellular building blocks. RNA can be measured (gene expression) to examine changes in response to environmental stress in cells from different individuals. Understanding these differences can provide insight into the entire cell's response to the block at propionyl CoA carboxylase (PCC) which causes PA.

In fact, cells from individuals with PA have different gene expression than cells from people without PA. Cells from individuals with PA grown in typical conditions have changes in levels of RNA for about 500 out of nearly 30,000 human genes. These differentially expressed genes are involved in a number of cellular functions, but many are involved in the most fundamental of cellular processes.

If cells from an individual with PA are stressed with low glucose, many genes have changes in expression compared to what is seen when the same cells are grown in typical conditions. **Over 300 of these genes respond differently to low glucose in individuals with PA than in individuals without PA** (controls). These genes fall into multiple categories, including those that regulate energy metabolism. For us, the genes involved in energy metabolism are particularly interesting since individuals with PA often develop cardiomyopathy, metabolic strokes, myopathy, and diabetes; all of which can be presenting signs in patients with primary energy deficiencies.

Examining the results from these studies more closely, cell lines from individuals with PA can be divided into 3 groups. One of these groups had decreased gene expres-

sion in genes that are involved in the tricarboxylic acid cycle (TCA, also known as the Krebs's cycle). One of these groups had no change in gene expression, and the third group had intermediate changes. Moreover, studies in simple animal models in which the propionyl CoA genes are deleted have shown changes in TCA cycle intermediates and similar gene expression patterns to those humans. Because of the essential role of the TCA cycle in maintaining energy levels for a cell and the known role of propionyl CoA carboxylase (PCC) in maintaining intermediates within TCA cycle, this finding provides a target for further study and possibly therapy.

Presently, my studies are focusing on whether the cause of these differences in the TCA cycle's enzyme transcription can be identified (as genetic in cause or something inherent with the cell lines but not related to their PCC status). **Moreover, we are studying whether pharmacologic manipulation can improve TCA cycle function in cell lines from individuals with PA, thus providing a possible new therapy.**

Coriell Institute for Medical Research: PA DNA Repository

- 47 subjects in the current catalog
- 65 cell cultures and 38 DNAs shipped
- 4 submissions received in the past year.
- 7 more subjects were added to the catalog and 5 are out for review right now.
- In addition to blood, the repository can accept fibroblast lines made from skin biopsies.
- If you would like to participate, please email paf@pafoundation.com.

WE STILL WANT TO HEAR FROM YOU!

Both the Coriell Repository and the PA Survey project (pg. 3) are still accepting participants and submissions! If you would like to help in this way, please contact the PA Foundation at paf@pafoundation.com.

PA QUESTIONNAIRE RESULTS

The propionic acidemia questionnaire: “Survey of health status and complications among propionic acidemia patients registered with the Propionic Acidemia Foundation” -Loren Pena, MD, PhD, University of Illinois at Chicago

BACKGROUND

- PA is an inborn error of metabolism that involves multiple amino acids and odd-chain fatty acids. *Deficiency in the enzyme propionyl coA carboxylase leads to accumulation of toxic metabolites.*
- Some of the clinical symptoms overlap with common neonatal illnesses.
- Expanded newborn screening has allowed prompt identification and treatment of affected individuals.

RATIONALE

- Although propionic acidemia (PA) was described nearly 50 years ago, we have a limited understanding of the range and frequency of many of the complications related to the disorder. *Examples: cardiomyopathy, arrhythmia, pancreatitis, bone marrow suppression*
- We also have little information on long term outcomes for affected individuals.
- Many complications have been described as isolated case reports, therefore we have no information on how frequently they occur.
- The PAF has a large and varied membership for study, and surveying members can contribute to the current general medical knowledge on PA .

METHODS

- After extensive review of the literature, we wrote a questionnaire that encompassed medical complications described in the literature.
- Questionnaire is available in English and in Spanish on the PAF website (www.pafoundation.com)
- Questionnaire is periodically distributed through email to PAF members that subscribe to the list.
- A special edition of the PAF newsletter with the questionnaire was mailed out during the winter.

RESULTS

- 46 questionnaires have been collected since distribution started ~15 months ago.
- We have had participants from USA and internationally.
- Age range: 3 months to 33 years
- Gender: 16 males, 30 females

CARDIAC COMPLICATIONS

- Two types of cardiac complications have been reported in the literature to date: *Cardiomyopathy and Arrhythmias*
- Among survey participants, 15% (7/46) reported cardiomyopathy. *Age of diagnosis varied, youngest at 2 years of age (range 2-33 years)*
- Arrhythmias were reported in 24% (11/46) *Youngest age at diagnosis: 3 years (range 3-24 years)*

GASTROINTESTINAL COMPLICATIONS

- Pancreatitis has been described in a small number of patients with PA, ages 18 months to 6 years.
- 15% (7/46) patients reported episodes of pancreatitis. *Four of these patients had multiple episodes*

CENTRAL NERVOUS SYSTEM

- A number of complications have been reported in the literature: *Seizures, Metabolic stroke / movement disorder, Brain atrophy, Optic nerve atrophy*
- 37% (17/46) reported seizures
- 9% (4/46) reported having a history of metabolic stroke *Youngest age: 2 weeks (range 2 weeks to 2 years)*
- 9% (4/46) reported optic nerve abnormalities *Youngest patient was diagnosed at 9 months of age (range 9 months-11 years)*

BONE MARROW COMPLICATIONS

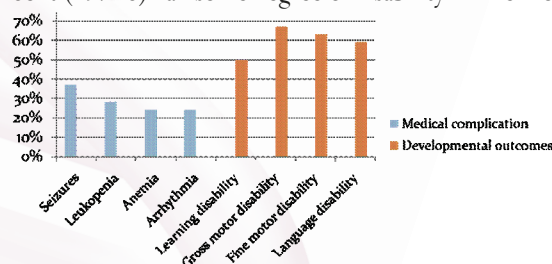
- Toxic metabolites can suppress the bone marrow, leading to decreased production of red & white blood cells & platelets.
- 28% (13/46) of patients reported decreased white blood cell count. *15% (7/46) reported immunodeficiency- (2 were treated with intravenous immunoglobulin (IVIG)*
- 24% (11/46) reported anemia
- 11% (5/46) reported low platelets

MUSCULOSKELETAL COMPLICATIONS

- Diet restriction may also lead to vitamin and mineral deficiencies that are important for skin and bone health.
- 11% (5/46) reported evidence of reduced bone density.
- 27% (12/46) had a history of fractures, usually with trauma.

DEVELOPMENTAL OUTCOMES

- 50% (23/46) of responders required an individualized learning plan or special education
- 59% (27/46) had some degree of language disability
- 67% (31/46) had some degree of disability in gross motor
- 63% (29/46) had some degree of disability in fine motor



HOW IS THIS INFORMATION USEFUL

- Data from the PA survey will be useful in formulating health care guidelines for PA.
- Illinois is involved in a registry for patients with inborn errors of metabolism, which will be useful in developing treatment programs and determining long-term outcomes.
- Data from the survey can complement the data from registry.

ACKNOWLEDGEMENTS

- The Propionic Acidemia Foundation Board and membership
- Barbara Burton, MD, Children's Memorial Hospital

PAF EDUCATION CONFERENCE IS A HIT WITH FAMILIES

This past August in Chicago, PAF, along with Children's Memorial Hospital (CMH), hosted the first PAF Education Conference. The purpose was to bring together affected families, while learning about current research, treatments, and nutrition. There were approximately 60 people in attendance, with 14 families affected by PA and 2 families affected by cblC from 10 states: CA, IN, IL, KY, MI, NC, OH, NY, TX, and WI. Even our most experienced families learned something new.

We had four amazing speakers, who were eager to spend the entire day at the conference.

- Barbara K. Burton, MD: *physician of Medical Genetics, Clinical and Biochemical Genetics at CMH and leader in treating patients with rare inborn errors of metabolism.* She presented an overview of organic acidemias and current treatments in a simple, yet comprehensive format.
- Katherine Kim, MS: *genetic counselor at CMH.* She presented the major complications and options for families considering additional children.
- Maryam Naziri, RD, LDN: *metabolic dietitian at CMH.* She discussed the nutritional aspects of treatments, and why many individuals with PA are fed through feeding tubes.
- Dr. Loren Pena, MD, PhD: *physician of Medical and Clinical Genetics at the University of Illinois, College of Medicine.* She presented a summary of results from 46 surveys that had been received to date.



Kate



Dr. Pena, Jill Franks, Dr. Burton



While parents were soaking in knowledge, the children had a blast in the childcare room with arts, crafts, games, and videos.

During lunch, families had a chance to visit with each other, talk to medical professionals, and try low protein foods from our sponsors. Cambrooke Foods, Vitaflo USA, Nutricia North America and PKU of Illinois were on hand to tell families about their products and services. Prevention Genetics also sponsored the event and Applied Nutrition sent samples for families to try out at lunch.

Following the presentations, families had time to ask questions and visit various booths in the area. Several of our families with infants were starting to evaluate feeding tubes for their children and they were able to look at and handle g-buttons and supplies. There was additional time to visit with families and specialists. It was great seeing the interaction between experienced families and our new families.

Preceding the conference, we held an on-line silent auction that raised \$2,370 and had a raffle at the event that raised an additional \$365 for PAF. Everyone went home with giveaways.



Our heartfelt thanks to Children's Memorial Hospital and their staff for all of their help in making this event possible.



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.

IN MEMORY OF SCARLETT CAMILLE

The most wonderful thing in the world happened on April 5th, 2006 ... you were born...
Scarlett Camille.

Since then life was changed forever in a very special way!

There's so many things you brought to my life, endless wonders,
incredible sweetness, such a tiny little miracle child,
unforgettable moments, joy that grew and grew,
more love than you could ever dream possible!

I will never forget your strength and courage,
and I will be forever proud to have had such a
darling daughter.

Although your time here was short, you filled my
heart with a lifetime of memories.

What a treasure, a touch of heaven here on earth.

Mommy's little angel...

Awaiting the touch of a little hand and a smile
from a little face.

Love you Bunny Bunny Bunny*



IN MEMORY OF TYLER

Tyler M. Quinones born 1-22-98, passed on 2-12-10

He was always happy. He might not of talked but he had his own way of showing his love.

He was definitely a mama's boy. Tyler loved going to school and riding
the bus.

When he finally learned to walk, we were all so happy! No one thought he
would ever walk.

We still see signs that Tyler is with us
everyday. We miss him so much.

He changed our lives and he will for-
ever be remembered as `our baby
boy`!!

Mama loves you Tyler XOXO



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. We are deeply appreciative to Publishers Printing Company for donating the printing costs of the newsletter.

PAF FUNDRAISING SPOTLIGHT

Past Events and Campaigns

- 11/09 In Honor of Ryan's Bar Mitzvah, Highland Park, IL - \$600
- 11/09 Veronica Alfano's Boutique - raised \$260, CA
- 12/09 Lights of Love, in honor of Talli, raised \$550, Naperville, IL
- 6/10 Beef & Beer Benefit for PAF, in honor of Brett Young, raised \$7800, Manayunk, PA *(photo: top right and pg. 1)*
- 8/10 PAF Education Conference Silent Auction, raised \$2940, Chicago, IL
- 8/10 PAF Education Conference Raffles, raised \$365, Chicago, IL
- 8/10 Ready, Set, Grow Carwash, \$300, New Albany, OH
- 8/10 Corn Hole Tournament for PA, \$2300, Pomeroy, OH *(photo: bottom middle right)*
- 8/10 Poker Run for PA, raised \$2550, Columbus, OH *(photo: bottom right)*
- 8/10 Axemen Ride-In Bike Show, Car/Truck Show, raised \$518, Dublin, OH *(photo: middle right)*
- **Ongoing:** Cans for a Cure, raised an additional \$2300 for recycling cans and bottles, Sandy McKillop, NY



Upcoming Fundraisers

- 9/3/10 Zumba for PA, Milford, CT
- 9/18/10 5th Annual Tailgate Party & Corn Hole Tournament for PA, Gahanna, OH
- 9/25/10 OSU Tailgate Parties for PA, Columbus, OH
- 10/12/10 TGBK Basketball Shootout in honor of their Bar Mitzvahs - Deerfield, IL



Fundraise online by doing what you already do!

- Feller Business Solutions: Open a business account as a "Friend of PAF" and 25% of the profit from your monthly purchases will be donated on a quarterly basis to PAF! For more information and to receive a free sample gift, catalog and \$25 toward your first order go to www.fellerandsons.com, click "request catalog", indicate you are a "Friend of PAF" or call Wendy Pike 630-766-3700.
- Sell items on Ebay using MissionFish. You pick what percentage goes to PAF.
- "Club Bing", clubbing.com - play games and donate tickets to PAF.
- Search the internet through GoodSearch.com
- Shop through GoodBuy.com
- Search or shop through iGive.com
- Sign up for eScrip at eScrip.com



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Propionic Acidemia Foundation
on Facebook



**We want to hear from you! Have a PA story to tell, event to promote or news?
Spring Newsletter submissions due by Feb. 15!**

ANNUAL REPORT: PAF AUGUST 1, 2009– JULY 31, 2010

FINANCIAL REPORT

Revenue:

Contributions: \$68,518
 Grant Reimbursement: \$2,214
 Interest Income: \$747
 In Kind Donations: \$1,253
Total Revenue: \$72,732



Expenses

Research Grants/Exp.Grants: \$70,183
 Programs & Outreach Total: \$2,161
 Fundraising Total: \$0
 Operational Expenses: \$1,311
Total Expenses: \$73,655
 Cash Assets 8/1/2009 \$82,570
 Cash Assets 7/31/2010 \$81,648

BOARD OF DIRECTORS/OFFICERS

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 Michael Rosenson

Board disclosure: Jill Chertow Franks is the sister-in-law of Michael Rosenson.
 Donations made by board members totaled \$910

PROGRAM ACCOMPLISHMENTS

Research:

- Distributed “Survey of health status and complications among propionic acidemia patients registered with the PAF” conducted by Dr. Loren Pena and Dr. Barbara Burton. Received 46 completed surveys.
- 4 submissions to DNA Repository at Coriell Institute for Medical Research in Camden, NJ

Grant Disbursements:

- \$30,000- Jan P Kraus, Ph.D., University of Colorado at Denver and Health Sciences Center (UCDHSC) Denver, CO: “Crystallization and structure determination of human propionyl-CoA carboxylase”
- \$20,000 - Jan P. Kraus, Ph.D., CDHSC Denver, CO: “Genotype –phenotype correlations in PA”
- \$20,000- Michael A. Barry, Ph.D. Mayo Clinic College of Medicine, MN: “Feasibility of translating gene therapy for propionyl CoA carboxylase (PCCA) deficiency”

OUTREACH:

Newsletter: We published and distributed fall newsletters this year to affected families, clinicians, and donors.

Help Us Find the Cure!

Name _____

Please send an acknowledgement to:

Address _____

Name _____

City, State, Zip _____

Address _____

Phone _____

City, State, Zip _____

E-mail _____

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

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Thank you Publishers Printing
Company for contributing
the printing and mailing of
the PAF Newsletters.

We would like to acknowl-
edge and thank each of you
personally for making a
difference for families affected
by Propionic Acidemia.

Propionic Acidemia Founda-
tion is run 100% by volun-
teers and we couldn't do it
without you.

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.