Happy Summer!

For the past 12 years, the OAA has hosted a Family Conference every other year, partnering with the FOD Family Support group. As we announced at the 2018 conference, we will take a break from this conference in 2020. As a substitute, we will be hosting a one-day OAA Family Workshop on Saturday April 25, 2020 in Austin Texas. This venue was selected because it coincides with the SMID (Society of Inherited Metabolic Disorders) Conference. Many of our medical professionals will be attending SMID and will join us for the Workshop. Erin MacLean (mom to Andrew, MMA Mut 0) will be our workshop chairperson/organizer. Please reach out to me or Erin if you can help us with planning.

In other news, thanks to Laine (mom to Lydia, 3MCC) and Katie (mom to Ali Rae, GA1) who represented OAA at the recent Abbott Nutrition Metabolic Conference in Atlanta, GA in June. Many of our dietitians attend this conference and these ladies shared information with them about the OAA. Also in June, NORD hosted a Family Conference in Houston, TX attended by a group of OAA parents who did a wonderful job promoting the OAA. If you would like to represent us at a local event, please let me know.

All my best – Kathy

Pictured: Shannon, Lillian, and son, Connor (PA), Misty and daughter Sienna (MMA Cbl C).
## Medical Advisors

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<th>Dr. Olaf Bodamer FACMG</th>
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**GET PAID for your opinion & benefit OAA at the same time.**

Patients (14 and older) and Caregivers (family, friends) of any disability, disorder, syndrome, disease or condition are provided an opportunity to voice their opinions through surveys and interviews to improve medical products and services.

Join the community on-line and **earn a Dunkin Donuts, Starbucks or CVS gift card.** We receive $5 for each qualified sign up. Refer others and we will benefit each time. Your information is confidential, and your email/name is never shared. You may be invited to participate in surveys from time to time, where you will earn cash.

Use this link and join today!
[rarepatientvoice.com/for-patients/patient-and-caregiver-sign-up/]
After an easy birth our little Lydia was born on a Monday in late September. The doctors said she was healthy, and we started trying to breastfeed right away. She just wasn’t interested. The nurses said this was common, and many babies are more interested in sleeping after their busy day of being born. We thought nothing of it and spent the next few hours showing off our little to her new family.

When it came time to try feeding her again, Lydia was still very sleepy. The nurses decided to undress her and rub a cold cloth on her back to get her to wake up. As we were trying to get her to latch, Lydia kept falling back to sleep. Again the nurses said not to be concerned because many moms have trouble getting their babies to breastfeed. Somewhere in the middle of that night I got frustrated and asked for a bottle and formula for Lydia. I was a new mom, and I feared what might happen if she never ate. I wanted to breastfeed our little girl, and the fact that I couldn’t was deflating. Even then we still had a hard time keeping her awake long enough to eat.

In the morning, we saw the pediatrician who told us that sometimes babies sleep a lot in the first few days. She would eventually wake up and be hungry. She would eventually start crying, and then we would long for these quiet sleepy days.

That week we went back to the pediatrician for Lydia’s newborn screening. She had lost more than 10% of her birthweight. The pediatrician said that most babies lose weight after birth, but this is a little more than normal. The doctor told us to try feeding her more often, gave us some vitamins for Lydia, and told us to come back in three days to see if she had put on weight. We went home thinking we had a plan that would work.

Around 3:30 that afternoon we got a call from a doctor we had never met about Lydia’s newborn screening. I knew she had been tested in the hospital, but I really didn’t know much about the screening, or what would make it come back abnormal. But something was wrong, and the doctor wanted us to go immediately back to the hospital for more testing.

We brought our tiny little baby back in for the required labs, and they found her blood glucose was at 30. That’s low. Very, very low. They told us to stop feeding her and put her on an IV. This was the first time a nurse looked nervous. They rushed us from the lab to the ER and had an ambulance drive us to LeBonheur, our local children’s hospital. That was a very scary ride.

Once we arrived at LeBonheur, we stayed in the ER until the genetics doctor could come explain to us what was happening. Two ER doctors told us that they were not able to explain because what she had was too complicated, very scary. Dr. Ward arrived and started explaining organic acidemia. She knew Lydia had one of the disorders in that category, but it would take more testing to find out which one.

After talking to her and Lydia’s blood glucose stabilized, they moved us to a room. There was a tiny little bed for Lydia and a couch for us. The nurses came in every three hours for blood work. I was hysterical from having just had a baby and having no sleep and now living in a hospital. It took 5 days to get the test results back. We were waiting to find out which specific organic acidemia she had. At ten days old Lydia was diagnosed with 3-MCC (3-Methylcrotonyl-CoA Carboxylase Deficiency).

Since then she has been relatively healthy. Lydia has only been hospitalized three more times due to stomach bugs. She is on a restricted diet and still drinks her I-Valerex 2 everyday, but she loves her food and does really well with her diet. She’s a wonderfully normal little girl who loves to swim and boss the dog around. What started as a very scary time now seems like a life we can manage with the help and support of trusted healthcare professionals. We are looking forward to a very bright future!
**Consents: Why do I care?**

KIMBERLY A CHAPMAN MD PHD » CHILDREN’S NATIONAL RARE DISEASE INSTITUTE, WASHINGTON DC

So, you are thinking in enrolling yourself or your care into a research study? Thank you for considering to help us understand your family’s disorder and search for treatments.

As we discussed last time, research is a process to understand the world in which we live. The most simplistic divisions include very basic research (i.e. the search to understand fundamental processes) and clinical research (most simplistically divided to observational and clinical trials). We have discussed observational clinical trials like registries and natural histories and interventional studies. Here we are focusing on consent.

So, let us talk about consents and here we are focusing on research consent. However, it is important to remember that you also sign consents every time you agree to be treated at the doctor and for any surgical-like procedures. Some of the same issues are applicable to research consents as to “permission to treat” consents. For example, if you need to have your appendix out, you sign a consent for the surgeon to take your appendix out which should list the risks of the surgery (like bleeding, infection, allergic reactions to medications, and yes even death) and the benefits of surgery (having a bad appendix out prevents its rupture, etc.). In the same way, when you participate in research, you also required to sign a consent to participate which reviews the risks and benefits of the study. Unlike a “permission to treat” consent which you are unlikely to refuse, you have the right to not participate in any research study and should not feel obligated in any way. We as researchers are very happy when you participate since it helps us learn more about your disorder, but never feel as though you are obligated to participate because it is your doctor who is asking. If you feel you have to participate because you feel it is right for you, your care or your family, then feel free to participate.

Research consents usually include 1) what is the intervention, procedure, or study, 2) what are the risks in participating and how are the risks mitigated, 3) what are the benefits of participating, and 4) your/your care’s signature and the date signed. You should be allowed to study the consent and ask any questions you wish about the study. Most consents list how to withdraw your consent and who do you contact if you think you have been harmed. They also review the responsibilities of the researchers and the participant.

To help with designing the consents and to determine if the risk and benefits are as balanced as possible, researchers have to present their research plans for interventional clinical trials (and any clinical trial for that matter) to their institutional review board (IRB for short) or ethics board (usually name in Europe). The IRB or ethics board makes a decision with the goal to keep the subject safe and consents are approved by the IRB/ethics board. IRB/ethic boards often have lay members from the community as evaluators of the proposals in addition to researchers unrelated to the research, physicians, research design experts, statisticians and legal experts. Many universities and medical centers have their own IRBs and often are looking for lay members to help, but it can be a big-time commitment, if you happen to be interested.

The goals of consents are to protect you as the participant (and to some extent the investigator and their institution) and to make sure you understand the risks (and benefits) of a particular research study. To “sign” a consent, an individual must be of legal age (in the US usually 18 years), be able to understand the consent, be able to understand the risks and benefits and able to agree the consent. In most cases, children ages 12-17 years should agree to the study as well, this is called “assent” and in many cases they also “sign” the assent. It is “sign” since some are physically unable to actually “sign” (for example a movement disorder making it impossible to physically sign), they may make a mark or have someone else put their signature with some other protections in place. Let us say that your care cannot understand all the implications of a particular study, is over 18 years, and you have their power of attorney for medical decisions, then you as their guardian signs the consent. If they can understand some and are capable of agreeing, we get their assent. Thank you again for considering research.

**About Dr. Kimberly A Chapman, MD, PhD**

Dr. Chapman is an associate professor at Children’s National Rare Disease Institute in Washington, DC where she takes care of patients, runs clinical trials (predominately registries and natural histories, but also some interventional trials) and has a basic science laboratory which studies the interaction of the propionate pathway and Kreb’s cycle. She enjoys swimming and knitting in her free time. Dr. Chapman is happy to answer any of your questions about the topics in the research corner. These discussions are meant to be helpful and reflect her opinion and experiences.
Living with a Cobalamin Cofactor Metabolism Defect

Living with a Cobalamin Cofactor Metabolism Defect is a booklet written for individuals with cobalamin (cbl) disorders, their families, and others who would like to learn more about the disorders. This 20-page booklet provides a general overview of cobalamin defects, how they can affect the body, and how they can be managed.

Cobalamin disorders are rare, genetic disorders in which the body is unable to process cobalamin, also known as vitamin B12. There are many types of cobalamin disorders. Each type is named with a different letter of the alphabet. Cobalamin disorders can cause homocystinuria, methylmalonic acidemia (MMA), or both, depending on which gene is affected.

Homocystinuria occurs when there is a buildup of the amino acid homocysteine in the blood and urine. High levels of homocysteine can be harmful to the body. MMA occurs when there is a buildup of a substance called methylmalonic acid in the body. High levels of methylmalonic acid also can be harmful to the body.

The booklet covers combined disorders that cause both homocystinuria and MMA. These disorders are cblC defect, cblD defect, cblF defect, cblJ defect, and cblX defect. The booklet also covers single disorders that cause only homocystinuria. These disorders are cblD defect variant 1, cblE defect, and cblG defect.

The booklet does not cover single disorders that cause only MMA: cblA defect, cblB defect, and cblD defect variant 2.

Living with a Cobalamin Cofactor Metabolism Defect provides an explanation of the different types of disorders as well as information about inheritance, diagnosis, symptoms, and management.

The booklet was developed by Recordati Rare Diseases Inc. in consultation with the late Dr. James Weisfeld-Adams, a geneticist whose research contributed to the understanding of inherited cobalamin disorders.

Living with a Cobalamin Cofactor Metabolism Defect is available in both English and Spanish. To download a free copy of the booklet, go to: http://bit.ly/2KWrrKs

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You asked for it, and we listened. We’re excited to introduce our fresh, new scents: Juniper Berry, Silver Spruce, and Jasmine Rose.

With the same naturally-derived ingredients and odor controlling power you’ve come to love with our original Lavender Sage scent and unscented variety, these three new members of the Lumē family are sure to surprise and delight your senses.

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Check it out at https://lumedeodorant.com

NEW SCENTS

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Just like it says, plus a crisp citrus note of bergamot

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A fresh fancy floral blend of essential oils and naturally derived elements
The Nutrition Guideline Committee is happy to announce that the Organic Acidemia Workgroup has published the “Propionic Acidemia (PROP) Nutrition Guidelines” in the February, 2019 issue of Molecular Genetics and Metabolism. The article is available and can be downloaded at no cost at doi.org/10.1016/j.ymgme.2019.02.007

Publication of the PROP/PA Nutrition Guidelines in Molecular Genetics and Metabolism brings the latest evidence- and consensus-based nutrition management recommendations to the attention of clinicians, researchers, policy makers, insurers, and patients.

The new Nutrition Management Guidelines for PROP/PA provide:

New directions including:

• A greater emphasis on nutritional needs such as nutrient intake, nutritional interventions, supplementation, etc.
• Less emphasis on medical management which has been covered in previous publications;
• Additional topics such as monitoring to ensure nutritional adequacy, nutritional issues with pregnancy and lactation, nutritional management for secondary complications such as pancreatitis, and finally a section addressing liver transplantation and the nutritional management before, during, and after the procedure.

Two consumer-oriented pieces, Frequently Asked Questions and a Consumer Summary, provide patients and families with information to use when interacting with their providers. The summary highlights key recommendations and suggests questions that patients and families may want to discuss with the metabolic team.

• When patients and health care providers (HCPs) have the same information, they can work together as a team to identify the treatment that is best for the patient’s situation.
• You can access these pieces at the Genetic Metabolic Dietitians International (GMDI) or Southeast Genetics Network websites located at southeastgeneticsnetwork.org/ngp and www.GMDI.org

The new guidelines should lead to greater consistency of care across centers.

• There are several important resources included in the guidelines including recommended nutrient intakes, monitoring schedules, and nutritional interventions tables.
• A web site that provides all the resources and references used to develop the guidelines is available so that health care clinicians and others can readily obtain the background information related to the guidelines at the websites listed above.
• The guidelines development method utilized evidence from published research, practice-based medical literature and expert consensus processes.

The new recommendations were developed following a rigorous, and systematic process based on published standards for guideline development and modified to incorporate consensus methodology. This process took just over 2 years to complete and included:

• 13 experienced metabolic dietitians who conducted an extensive review of 250 scientific and grey (unpublished) publications.
• Two Delphi surveys of practice to obtain input from an additional 54 experienced HCPs,
• A nominal group meeting, which included 7 HCPs and 2 parent group representatives, to clarify discrepancies and determine consensus regarding the proposed recommendations.
• External review and field testing.
• Inclusion of all reference materials and each step of the guideline development process stored on a secured web-based platform which are accessible on the websites listed above.

We greatly appreciate the contributions and support of the clinicians and the patient community, who continue to help us work toward the goal of improving medical nutritional therapy for people living with propionic acidemia and their families and caregivers.
Next steps:

• Nutrition Guideline Committee will continue to periodically update these guidelines as new evidence to support best clinical practices are discovered.

In addition, a PROP tool kit is being developed to facilitate the implementation of the PROP Nutrition Guidelines, including educational resources.

These nutritional guidelines are part of a multi-year project designed to optimize the nutritional management of individuals with inborn errors of metabolism. The guidelines establish nutritional recommendations based on the best available evidence, contribute to reduced uncertainty and variability of practice and identify needs for future research. Nutritional management guidelines have already been published for other metabolic disorders including phenylketonuria (Singh R et al., Updated, web-based nutrition management guideline for PKU: an evidence and consensus-based approach. (2016) Mol Genet Metab, 118(2); 72-83) and maple syrup urine disease (Frazier D et al., Nutrition management guideline for maple syrup urine disease: an evidence- and consensus-based approach. (2014) Mol Genet Metab, 112(3); 210-217), and in the very near future for fatty acid oxidation disorders.

This project received funding from the Southeast Newborn Screening and Genetics Collaborative (by a Maternal and Child Health Bureau HRSA grant #2-U22 MC010979), and additional support from Genetic Metabolic Dietitians International (GMDI) to achieve the goal of developing nutritional guidelines for metabolic disorders where there is little published scientific evidence.

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

Guidelines” Are Now Published!

Dr. Jan Kraus passed away, Thursday, July 3rd after a courageous battle with cancer. Jan was a Professor in Pediatric-Clinical Genetics and Metabolism at the University of Colorado. Jan, considered by many as the “Father of Homocystinuria” dedicated his life’s work to the understanding and treatment of Homocystinuria (HCU) and Propionic Acidemia (PA). Since the 1960’s, Jan has authored and co-authored over 160 publications regarding HCU and PA. Jan’s career highlights include building a database of all the genetic mutations associated with PA & Homocystinuria, as well as being the inventor for the OT-58 product (a pegylated version of the CBS enzyme) that is in human trials for Classical Homocystinuria patients.

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OAANews.org

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Before our twins arrived we had just realised our dream of moving onto an acreage property on the outskirts of Sydney, we upsized our car and were ready to expand our family. We were completely and utterly ecstatic when I fell pregnant and even more so, when we received the news that we were expecting twins!!!

Our eldest daughter Amelia who was 3 ½ at the time was so proud to be their big sister and she was given the honour of naming them, Isaac and Charlize. They looked so perfect, everyone loved them instantly and our family felt complete.

Our twins arrived at almost 38 weeks gestation via planned c-section, I got to have a quick look at our beautiful twins before they were quickly whisked away to the special care nursery to be treated for hypoglycaemia and hypothermia where they remained for the next 24 hours. During their first few days of life I always wondered why Isaac looked more awake than Charlize and fed more often than Charlize. I was a little worried that Charlize didn’t look quite as interested in feeding and didn’t feed for as long. The nurses shrugged off my thoughts as just a difference in personalities.

Our twins were discharged from hospital on day 4, with instructions to feed Charlize more frequently as she had lost weight, 8 grams less than the allowable limit but they let us go anyway. However, things quickly changed the following night, Isaac woke up like clockwork for his feed, but Charlize did not. I picked up Charlize, she was completely cold and grey and she wouldn’t wake up or move.

I was terrified. We rushed her to our local hospital but no one at our local hospital knew what was wrong with her and worse still, her twin brother Isaac was getting sick in the same way. The doctors had no answers until they received Isaac & Charlize’s Newborn Screening results a few days later. They both tested positive to a Metabolic Disease called Propionic Acidemia. With these results, Isaac & Charlize were immediately transferred to The Children’s Hospital at Westmead for urgent specialist treatment. We were shocked when we were brought into their room to find our tiny babies were connected to so many lines and machines and there were so many people working on them. The Senior Staff Metabolic Specialist looked very concerned. He told us that he needed to take us ‘somewhere quiet to talk’.

Our hearts just sank, knowing that this situation was very serious.

I had Googled the condition and I begged him to tell us that everything I read was not true. I begged him, to tell me that this disease is curable or at the very least treatable. It was just so heartbreaking to hear him say... ‘There Is No Cure’.

The doctor told us how sick they both were, he asked us if we would like to christen them that night as it was possible that Charlize, especially was so sick that she may not make it through to the morning. During this meeting we were told there were less than a dozen children living with this disease in Australia.

I remember being so upset and even angry as reality soon sank in, that there was no cure or treatment that will fix their problem. I was angry that all medicine could offer was to treat their symptoms as they came and they would have to fight to be here every day and perhaps they were just born at the wrong time in medical history.

During their time in hospital we were coached on how to manage our twins with their disorder. They both required a very low protein diet, special formulas and medicines for life. They required feeding every 3 hours day and night as we could not allow their body’s to fast. Running out of energy would send them into a metabolic crisis which could damage all their organs and could lead to coma and death. Although Charlize was the sickest at birth, it was Isaac who required the most hospital admissions. We averaged 1-2 hospital admissions every month, with each admission their appetite would diminish and take a few weeks to regain.

By 12 months of age, they began to refuse all of their food and special formula and eventually relied on a Nasal Gastric Feeding tube for all of their nutrition. The workload was immense. When they were unwell they had to be fed their unwell formula every 2 hours day and night. It took 30 minutes to feed each one and required over 30 bottles to be prepared and cleaned per day. There was just no time for sleep.

Despite following all our instructions, when Isaac was only 9 months old, he suddenly received damage to his brain. Lesions were found on his Basal Ganglia in his brain (the area which controls movement). Isaac lost most of his muscle tone and
became floppy and un-coordinated. He lost a lot of his skills, was no longer learning any new skills and he could not gain any weight even with a high calorie formula.

A liver transplant was then advised as a last resort treatment option. Large amounts of the missing enzyme that causes Propionic Acidemia is located in the liver, so a liver transplant from a new donor liver will help them to have a more normal life and was their best chance survival.

After eight months of waiting, Isaac received his transplant. The next day he woke up, and his liver function was absolutely perfect. He did have many unexpected complications and further surgeries while he was in ICU but once he got to the liver ward, we saw changes in him straight away. He was a brand new boy, he was learning so quickly, he could understand what we were saying, looked less ‘foggy’, started saying some big words like ‘dinosaur’ where weeks prior he could only say ‘mumma’. He developed a healthy appetite and began eating food and even stealing our food that we were eating. Isaac was feeling on top of the world and was loving his new life.

Isaac was discharged after 6 weeks recovering in hospital, just in time for Christmas. We had the best Christmas ever, Isaac had his brand new life ahead of him and we were so excited.

Isaac was home from hospital for less than a month when he developed a temperature. He was rushed to hospital where he deteriorated quickly and went into cardiac arrest. Isaac had an overwhelming mass bacterial infection and went into septic shock.

It was completely unfathomable to be told that our little Zacky, who had the biggest, most beautiful eyes, who would light up a room with his cheeky smile, infectious laugh and enormous sense of humour was not going to survive. Our precious little Isaac passed away in our arms on 23rd January 2017.

As you can imagine, it was such an impossible decision for us to then agree to still subject Charlize to a liver transplant after losing our Isaac. We were devastated that there were just were no other treatment options available for her and she was susceptible to brain damage just like her twin brother.

I wanted to do everything I possibly could, to turn our story around and do whatever I could to help create change for future generations of children born with Propionic Acidemia. I wanted to save Charlize’s liver and push for research here in Australia.

I reached out to centres in America and next door to our hospital, at the Children’s Medical Research Institute. I wanted them to take Charlize’s native liver when she received her transplant, in the hope that it could be used in the future, for gene therapy on Propionic Acidemia.

After reaching out to Professor Ian Alexander at CMRI, he understood my desire and need, to help create change for children born with this disease. He honoured my wish to eternally preserve Charlize’s liver for future research.

After months of waiting for “The Call” that would give Charlize her new liver and life, I was also making my own special calls on the way to hospital, ensuring that everything was in place for Charlize’s native liver to be taken and preserved.

The research was just so important to me.

Unfortunately, Charlize rejected her new liver after just 4 months, she urgently needed a 2nd liver transplant. Charlize received her second liver transplant in March last year, at the time she was in liver failure and her life was saved once again and just in time. Somehow with the grace of God, with her fighting spirit and her twin brother Isaac watching over her…. she made it!

Later last year, I was so overwhelmed, when I was told that CMRI were already working on gene therapy for Propionic Acidemia, using Charlize’s liver cells.

Going into this, I really didn’t expect any research to happen for a very long time with her liver and to hear it was happening right now, was simply incredible.

I now believe, that perhaps Charlize was born at the perfect time!

The perfect time to donate her liver to CMRI for research and the perfect time for CMRI to carry out their research as they work towards a cure.

The journey with Propionic Acidemia and Liver Transplant with our twins has been massive and relentless and absolutely rewarding in so many unexpected ways.

I dedicate myself not only to my family but to raising funds for our Metabolic Team, Liver Team and to The Children’s Medical Research Institute. We celebrate absolutely everything and give thanks for everything we have and for each day we have been given.

Charlize has now been admission free for the past four months which is a record for us. She is eating her full diet and will start pre-school in a few months after winter. She is learning so quickly and is expected to attend a main-stream primary school alongside her older sister Amelia in 2021.

Charlize is one of the faces of this years’ National ‘Jeans for Genes’ campaign, which is run by The Children’s Medical Research Institute. We often see her face as she represents Jeans for Genes and Propionic Acidemia on billboards, television interviews, in most of the national weekly magazines, newspapers and in many other media outlets.

We are so proud of our little Charlize, we just couldn’t love her anymore!!!

She astounds me every day for what she has endured and for the amazing, spirited, articulate (and bossy) little girl she is today.
Well, for my family and many of you here today...here we are again. Twenty plus years have passed since many of us met here to celebrate Stephanie’s life, then also Andy's a short time later. Now we’re here to thank God for Michelle Marie Crook! Mary and I thank you so very much for being here. We thank you for your support of our family during these three plus decades of battle against the genetic disorder called Methymalonic Acidemia.

She battled and lived through it. All through her life. Michelle dealt with wearing braces, for example, to help steady and support her as she grew. She used a walker as a toddler, but as she got just a bit older, she proved she could be mobile without it. It was the beginning of her talking control of her life under her terms. She enjoyed playing in a pool very much. She didn't need braces and the bathing suit hid her G-tube. Hotel pools were a birthday party staple and a must on any family trips. But the reality of her medical condition was always there. An average year may have her in the hospital 10-12 times. This went on year after year, until she became a liver/kidney transplant recipient at 12 years of age.

Once transplanted, she was able to complete her studies through Rockford Schools, on-time with her class of 2003. Michelle entered the workplace for a couple of years, enjoying the customer contact out at Bostwick Bakery, then to a childcare center SW of town when she moved out to her own apartment. Unfortunately, her medical situation still interfered too much, so she went into volunteering. She enjoyed many years helping Wealthy Elementary, assisting the children in their studies and activities. She also helped care for people at God’s Kitchen. She found that there was a Spectrum Health Hospice office right across the street from her apartment, so she helped with filling and organizing info packets. She always liked to help others.

I’ve got to mention the daredevil in her! She never met a roller coaster she didn’t like. Loved plane rides, too. She and Mary had a couple of Angel Flights small private airplanes going to and from her NIH study annual visit, that had stormy weather. Michelle loved it...Mom, not so much! But those amusement park rides... the scarier the faster, the better! No fear. She felt free. She even got up on a glider ride by herself as well (with pilot, of course) and a ride in a Nascar around Berlin raceway. Mentioning NIH, the National Institutes of Health in Bethesda, Maryland, she was proud to be part of their on-going study to find better treatments and cure to her disorder. Dr. Charles Venditti and his team of many are Saints. Their tireless work and research helped give us those 34+ years with Michelle a cure is close! With that cure in mind, Michelle made the brave decision to donate her body to further their work. Also, the trips to the biennial Organic Acidemia Association conferences were a joy to her. She would spend most weekends meeting others with similar disorders, most all younger than herself, and their families. She and a few others who were a bit older, gave the younger kids and their family hope. Michelle even flew to a couple of those conferences on her own. At those, she was a Rock Star! The kids would say, “you came here by yourself?”
Another constant in her post-transplant world was singing karaoke. Where she got the guts to get up in front of others and sign is beyond me! It was simply and wonderfully something she thoroughly enjoyed! It allowed her to do something anyone could do and be like everyone else there. We are very grateful to her karaoke friends for making her feel welcome and protected.

A very, very important part of Michelle’s life was growing up with her big brother, Jim. She and Jim are just under three years apart, so he learned at an early age that he had a very special sister to love and care for. Which he certainly did! Helping us in so many ways through the years, helped him grow into the strong, caring man we love today. He and his wife Kate now have two boys, Charlie and Ben. Michelle absolutely delighted in playing with them both. She just lit up when she saw them! They brought her so much joy. Michelle’s beautiful smile was always on display when we visited them.

I’ll finish with a bible verse given to Michelle by her nephrologist, her kidney doctor, Dr. James Visser, as they met for the final time. This is from Philippians 4: 4-7.

Rejoice in the Lord always. I will say it again: Rejoice! Let your gentleness be evident to all. The Lord is near. Do not be anxious about anything, but in every situation, by prayer and petition, with thanksgiving, present your requests to God. And the peace of God, which is beyond our understanding, will guard your hearts and our thoughts in Christ Jesus.
MMA Study Visit at the NIH

STEPHANIE & JOSH
PARENTS TO LEO, MMA CBL A

Many parents have contacted me about MMA, but are hesitant to coordinate a visit or contact the researchers at the NIH. I wanted to let you know some things that have been helpful for me and to encourage you to please participate in the NIH research study for your child (* if your child’s health allows). The first most helpful thing I learned is that if your child is under 2 and not able to participate in this study your doctor can contact one of the MMA researchers in the MMA study and the MMA researchers could respond via email to your doctor to make sure your child is being appropriately managed. There is a standard protocol that your child should receive upon diagnosis and it’s not buffet style where certain meds are left out. Because your child has an inborn error of metabolism the way they process their food is incomplete, the medical foods they receive are supposed to help your child receive the nutrition your child needs to complete the energy cycle.

I would like everyone to consider the following when planning a visit to the NIH 1) Getting on their schedule takes time 2) coordinating the records release of the care providers for your child is never easy 3) they can cover some domestic travel costs and you can stay at the Children’s Inn which makes your visit more affordable 4) Remember that the visit will help you better understand what your child is dealing with and manage their needs but this visit will not fix your child’s MMA (at least not yet).

1) We like to get our researchers buy-in before we consider making any larger changes, as they see more MMA kids than anyone else that I know of. I emailed Susan Ferry (susan.ferry@nih.gov) to ask that we be added to their schedule. Our son has dialogic CP with a movement disorder and the NIH has movement disorder clinic which has a 2 year wait. There was a cancellation, so Susan was able to schedule a visit with to co-inside with the Movement Disorder Clinic.

The movement disorder clinic needed a sedated MRI which means that Leo needed to be put under and intubated because it’s safer for them to manage his breathing. Dr Oleg [Shchelochkov, M.D.] came to our appointments so make sure Leo was sedated correctly.

We thought that they were worried about our ability to keep appointments, but the researchers accompany everyone in the MMA appointments we were told.

The MRI showed the damage was not as significant as they thought, and that Leo was making progress. We talked about meds and devices that could be implanted but it was determined that slow and steady progress was better than changing what is working. Again, I was hoping for a magic solution but what is ahead is more therapy and more appointment and more hard work for Leo to gain back the skills he lost prior to crisis at 16 months.

2) Our records arrived during our visit and throughout during the movement clinic. I wanted a compare contrast which doesn’t always correlate so the imagery history. I started to request the transfer of our information early March for Mid May- and absolutely nothing transferred on the first try. I used the providers forms and the NIH forms it didn’t matter it took at least 3 tries. It is best to talk to a real person in the records dept and have them confirm they received your information and will transfer the information by a specific date.

3) The entire trip felt like a college NIH orientation. You have housing and a schedule and it’s a full day. They do cover some domestic travel costs and there is no cost to stay at the Children’s Inn. The NIH is a secure government facility so they background check you before you can stay at the Children’s Inn. The check your ID, your vehicle, your belonging before you can be allowed on site.

4) We are participating in a research study and your child is rare and important. Nobody has all the answers. The study helps everybody better understand MMA.
and how it manifests in your child. Leo asked me, why am I here? Are they going to fix me? Which is a difficult question that I tried to make the doctors answer because I didn’t have a good answer myself. I told him about how we have to make sure he eats low protein foods so he doesn’t get sick and the doctors wanted to make sure he was doing ok. After that, I would just tell him why we were at each appointment, like they want to look at your heart to make sure it’s doing its job. Our kids aren’t broken, they metabolize food differently. Your child is already their own person and was going to be their own person with or without MMA. Each time, we go to the NIH we are glad we went. We are so relieved to see doctors who understand Leo’s condition and are not afraid of it. We try to let our kids be kids and having a sister has really helped. She already accepts that he does things differently or gets a daily injection because for her it has always been this way.

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GENE THERAPY FUTURE FOR PROPIONIC ACIDEMIA

When Charlize Gravina underwent her life-saving liver transplant, mum Julie made sure the cells went to the Gene Therapy Unit at Children’s Medical Research Institute (CMRI) in Sydney which is led by Professor Ian Alexander.

As a scientist and a clinician, he wants to get to a point where children don’t need to have a transplant and could instead use gene therapy to replace or correct a faulty gene.

“This technology could translate into saving the lives of infants with life-threatening conditions,” Prof Alexander said. “It’s about getting cures into the clinic as soon as we can.

“We’re trying to get to a point where instead of a liver transplant in a very young infant, we can genetically repair the liver without major surgery. It’s a very exciting time to be doing gene therapy.”

Professor Alexander works with Dr Leszek Lisowski who leads the Translational Vectorology Group at Children’s Medical Research Institute. He produces the vectors to make gene therapy possible. Together they would like to establish a facility in Westmead that would manufacture vectors, so patients weren’t waiting years for them to come from overseas.

“CMRI is globally competitive in gene therapy, with a special interest and a strong track record in liver-targeting therapies,” Professor Alexander said. “Currently, our expertise is in gene therapies for the liver, for which we are globally recognised, but we also work on other tissues besides liver. It is not just about the technology, it is about the patients.”

Together Professor Alexander and Dr Lisowski want to see things work faster in Australia.

“Gene therapy has the potential to cure kids right now,” Professor Alexander said. “Gene therapy has the potential to cure kids right now, and we need to be able to conduct trials here in Australia.

“Australia punches well above its weight, given only 3% of global biomedical research happens here. However, most trials are conducted overseas, and our aim is to bring overseas clinical trials to Australia as soon as possible so we don’t have to wait two years for clinical vectors.

We need a facility in this country to be able to compress a 5-7-year journey into a 2-3-year journey for children with devastating diseases.

“Delivering gene therapies from bench to bedside within two years would be extremely exciting.”
Kelly Lindert, MD, is the Head of Metabolic Rare Diseases Clinical Development at Moderna, a biotechnology company in Cambridge, Mass. that is working to develop messenger RNA (mRNA) therapeutics for a variety of areas, including rare metabolic disorders like methylmalonic acidemia (MMA) and propionic acidemia (PA). We sat down with her to talk about Moderna’s work.

What is the approach Moderna is taking toward treating inherited metabolic disorders?

Inherited metabolic disorders occur when a genetic mutation leads to a missing or dysfunctional version of a protein that is important for metabolism. While certain lifestyle changes, like dietary restrictions, may help alleviate the most severe symptoms, there are no treatments for the underlying genetic cause for many of these disorders.

Moderna is working to address this underlying cause by providing new instructions to cells so the body can replace these missing or dysfunctional proteins. These instructions are known as messenger RNA or mRNA. Our cells use mRNA to interpret information passed down through our genes and turns this information into proteins that build or regulate our bodies. Moderna’s approach is to give specially-engineered mRNA to provide new instructions to the protein-making machinery already inside the cell to treat the underlying cause of inherited metabolic disorders and other diseases.

The animal data evaluating our mRNA study drug targeting methylmalonic acidemia (MMA) are compelling. We recently published data evaluating our mRNA study drug in mouse models of methylmalonic acidemia (MMA), which were developed at NIH. In other words, in mice that have a form of MMA, our study drug substantially improved survival and led to sustained growth with long-term dosing and no safety concerns were observed.

We believe mRNA therapeutics and vaccines have the potential to work beyond what’s possible with today’s small molecules (or pills), biologics and vaccines. As of May 2019, we have 11 programs in clinical studies across different areas such as infectious diseases, immuno-oncology, rare diseases and cardiovascular diseases, and more than 1,000 clinical trial participants have been dosed with our mRNA technology. Some of these programs are being led by our team and others are being developed in collaboration with Merck and AstraZeneca.

How is mRNA therapy different than other approaches like gene therapy or gene editing?

Helping the body make its own medicine using mRNA sounds like it might be similar to gene therapy or gene editing. While these treatment approaches seek to treat disease through genetic information, they take fundamentally different approaches.

Gene therapy and gene editing alter the original genetic information each cell carries. The goal is to produce a permanent fix to the underlying genetic problem by changing the defective gene.

Moderna is taking a different approach to address the underlying cause of MMA and other diseases. mRNA transfers the instructions stored in DNA to make the proteins required in every living cell. Our approach aims to help the body make its own missing or defective protein (in this case, MUT). Unlike gene editing and gene therapy, mRNA technology does not change the genetic information of the cell, and it’s short-acting. It acts like traditional drugs that can be adjusted over time based on the dose and frequency needed. In simple terms, we are working to provide physicians and patients with a “controllable” way to start and manage their therapy over time.

What are you most excited about in your role?

It’s an exciting time in medical research right now & we’re learning so much about the potential for new approaches to treat the underlying cause of diseases like MMA. The potential to help patients in more meaningful ways motivates me and my colleagues at Moderna every day.

Could Moderna’s mRNA therapy apply to other disease areas?

Absolutely! The amazing thing about an mRNA platform is that it has the potential for broad applicability. Proteins are the basis of so many functions of the body. If we can provide the right mRNA instructions, we can in theory create a large inventory of proteins the body may need to address a variety of diseases.
At Moderna, we’re exploring options to address many disease areas, including developing study drugs to potentially help the body fight cancer, to protect the body against infectious diseases, and, importantly, other rare diseases without treatment options.

**What do you want the patient community to know?**

I want the community to know that everyone in my company is committed to partnering with them and listening to them along the way. We want to learn from patients and their families, and we will continue to share our research and findings so you can learn from our work.

I am also excited to share that we have two studies we are working on presently, and both are actively enrolling patients.

The latest study that we are eager to share is referred to as the “Phase 1/2 study.” It is designed to evaluate our investigational mRNA therapy, known as mRNA-3704, in patients with MMA who have a MUT deficiency. We are particularly looking forward to learning from this study, because this represents our first rare disease study drug to advance into clinical trials. The study is now recruiting patients and you can click here to learn more about it.

The FDA has granted Fast Track Designation to mRNA-3704, which is provided to facilitate development of drugs designed to treat a serious or life-threatening condition and fill an unmet medical need. The program has also received Rare Pediatric Disease Designation by the FDA and Orphan Drug Designation by both the FDA and the European Medicines Agency (EMA).

The other study that is open is the MMA and PA Natural History Study or “MaP” study. This has a similar goal of other studies being conducted by the NIH and OAA: it is designed to learn more about the clinical experiences of patients with organic acidemia but does not involve study drugs. Each of these studies asks different questions about these conditions, and participation is greatly needed across all of them.

We thank the OAA community for sharing their experiences with us in starting this journey, and we look forward to additional communication as we learn from you and from our clinical trials.
Organic Acidemia Association (OAA) provides information and support to parents and professionals dealing with a set of inborn errors of metabolism collectively called organic acidemias. The OAA is a volunteer organization registered with the IRS as a 501(c)(3) non-profit corporation. Donations to the OAA are tax deductible. OAA publishes a newsletter three times a year, hosts a Google Group for information exchange and maintains a website and Facebook page. Services are funded by corporate & individual donations. Annual membership donation of $25 (US) and $35 (international) plus $5 for the family roster is requested, but not required. Our 501(c)(3) non-profit status qualifies OAA for United Way donations through their write-in option. If there is a write-in option, just write “Organic Acidemia Association” in the blank line on your pledge card.

Donations can also be made at OAA’s website through the “PayPal” and the “Network for Good” option.

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Organic Acidemia Association

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Please accept $_____________ as our annual tax deductible donation to the Organic Acidemia Association.

Suggested membership donation is $25 (US) and $35 (international). Extra funds are welcome and can be designated for research, OAA operating expenses, or to help others attend conferences.

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OAA Google Group

OAA’s main mission is to empower families with knowledge about organic acidemias. If you would like to connect with other families who share the same or similar diagnoses, please join our private OAA Group. Visit the OAA News.org web site to sign up.

is on Facebook - donations can be sent through our “Cause” Page, connection with other parents can be found through our private “OAA Group” and private “Fan” Page.