



MSUD NEWSLETTER

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METABOLIC FORMULA SHORTAGE UPDATE

By Karen Dolins

Hopefully by the time you are reading this Abbott will have resumed shipments from its Sturgis, Michigan plant. It's been a long, painful road.

On February 17th, 2022, Abbott Nutrition issued a voluntary recall of infant formula due to reports of *Campylobacter* contamination in its Similac, Alimentum, and EleCare powdered infant formulas. At the same time, the FDA closed the manufacturing plant in Sturgis, MI where these products are made. Unfortunately, although no bacteria had been found in metabolic formulas, these were affected by the shutdown as they are made at the same plant. A decision was made to place a hold on previously manufactured formula held in storage. Suddenly and without warning, Abbott formulas including MSUD formulas, Ketonex I and Ketonex II were unavailable to those who depended on them.

The impact of the closure of the Abbott Nutrition plant attracted a good deal of media attention. Photos of empty shelves where baby formula is normally stocked and quotes from distressed parents of infants who use those formulas were broadcast. The impact on those of us who can't get their formula from the grocery store was less publicized. A coalition of patient advocacy groups for Inborn Errors of Metabolism worked hard to make sure our voices were heard. On March 13th we met virtually with metabolic dietitians to address the issue and on March 15th we launched the website

Metabolic Formula continued on page 3

WHAT IS THE MOST IMPORTANT THING YOU CAN DO TODAY TO HELP IMPROVE THE LIVES OF THOSE WITH MSUD?

PARTICIPATE IN THE MSUD REGISTRY WITH CORDS (COORDINATION OF RARE DISEASES AT SANFORD)

WHAT IS IT?

Our patient registry collects information about people affected by MSUD.

WHY DO WE NEED IT?

A registry allows clinicians and scientists to learn about how MSUD affects those with this condition and their families. They use this information to plan research, develop therapies, and hunt for a cure.

WHO SHOULD COMPLETE THE REGISTRY?

- ☐ Individuals with MSUD or a family member regardless of MSUD type.
- ☐ Individuals with MSUD who have received a liver transplant.
- ☐ Family members of a deceased person with MSUD.
- ☐ Anyone with MSUD from any country in the world.

WHAT IF I DON'T SPEAK ENGLISH?

Our registry questionnaires are available in Spanish.

HOW DO I REGISTER?

The registry is available through our website: www.msud-support.org or <https://research.sanfordhealth.org/rare-disease-registry>. Need a hard copy or Spanish questionnaire? Call CoRDS at 877-658-9192 or email them at CORDS@sanfordhealth.org.

HOW LONG WILL IT TAKE TO COMPLETE?

Completing the questionnaires will take approximately 30-40 minutes. It does not need to be completed all at once.

ALREADY REGISTERED?

Thank you! Please review your responses to provide updates and make sure you answered all questions.

QUESTIONS? Contact Karen Dolins at karen.dolins@gmail.com or 914-391-2982.

See summary of our findings on page 17

Inside This Issue:



The information contained herein does not necessarily represent the opinions of the MSUD Board, Medical or Nutritional Advisors, or all of our members. Before applying any of the information contained in this newsletter, you must consult a MSUD specialist.

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FROM THE EDITOR'S COMPUTER

By Susan Needleman



Hard to believe another newsletter is already coming out. As I read the articles that were submitted for this issue, I was happy to find out that Abbott is once again manufacturing metabolic formulas and that by the time you receive this will hopefully be shipping them out!!!!

This has been a long wait as many of us have felt the effects that the hold on this formula has had on our community. Even if you were not on one of Abbott's formulas, you most likely had your formula go on backorder for a time, as other companies could not keep up with the influx of customers who had to find alternatives to Abbott products during this time. What a mess it has been! We endured and persevered and better times are hopefully here!

The Editors Department is entering a new chapter, too. Since our last issue, our Co-Editor Amber Raye, has stepped down. While we are sorry to see her go and wish her the best of luck in her future endeavors, we are also happy to welcome on board Nikolai Rudd as Assistant Editor, while I have changed from Co-Editor to Editor. Thank you for helping out Nikolai, happy to have you! ■

ASSISTANT EDITOR'S NOOK

By Nikolai Rudd



Hello to all in the MSUD community. My name is Nikolai Rudd, and this is my first newsletter as Assistant Editor with Editor Susan Needleman. I am 48 years old and was born with Classic MSUD, but had a "Domino Liver Transplant" in 2006. It has been a little more than 16 years since my liver transplant and my ability to digest protein for the first time. Some of you

might recognize me from the article I wrote in the Spring 2022 MSUD Newsletter issue, "Keeping Hopeful Through Darkness and Isolation" on page 12-13.

The last couple years have been a tumultuous time for us in the U.S., as well as the world in general. We've all had to deal with COVID-19 and the civil unrest across our country, and the continued fight for equality. And among all the chaos, there was an accident that caused an unintentional jamming of the Suez Canal, which led to shortages of many products.

While I didn't have to contend with Abbott's formula shortage personally, I didn't escape the problems of getting

FROM THE PRESIDENT'S DESK

By Sandy Bulcher



I hope that you all are having a happy, healthy year thus far.

August was a busy month for the MSUD Family Support Group Board of Directors. We held our annual in-person meeting in Lancaster, PA in conjunction with the MSUD Translational Science

Summit planned by our Research Lead Karen Dolins in partnership with Dr. Kevin Strauss and Karlla Brigatti of the Clinic for Special Children. (See Karen Dolin's article for more information about that meeting). During our board meeting, we reviewed our budget and finances to remain fiscally responsible. We also reaffirmed our research priorities, which help guide our resources and activities. These include:

- 1) Development of a strong patient registry
- 2) Development of a home leucine monitor
- 3) Supporting research to develop gene therapy for MSUD
- 4) Understanding the neurocognitive impact of MSUD

The board has been active throughout the year. We held our first online interactive Q & A session in the spring. We also held another campaign to increase the participation in our

President's Desk continued on page 3

my transplant medications that occurred because of a severe back-order of medications and drugs, caused by blockage of the Suez Canal, jammed with freighters. Even our own sea ports were so backlogged that freight ships couldn't get in or unloaded, nor could their cargo be delivered. This was due to shortages of dockhands, a system that needs updating, and a shortage of truck drivers to transport the goods to their destinations. I've been nerve-wracked trying to get my immune-suppressive medication, my extended-release pain medication, Mycophenolic Acid (which is almost as important as my immune-suppressive medication), and my Ursodiol medication.

Even this summer, I had to deal with my immune-suppression medication and my extended-release medication being called into (not only the wrong pharmacy but a pharmacy in a different state altogether). Luckily, I was able to get things straightened, and only had a few sleepless nights of discomfort.

I hope that all our issues with what keeps us alive or from fighting ourselves (like my immune system might do with my liver ... without the immunosuppressive medication), will not detract us from living a fruitful life. Here's to a good end to 2022 and a smoother year going forward from there! ■

Metabolic Formula continued from page 1

"metabolicformula.org" to keep our communities informed and to gather stories from patients and families which we shared with the media. We reached out to NORD (National Organization for Rare Diseases) and the FDA (Food and Drug Administration) and were interviewed by the media about our plight.

On April 28th, approximately 10 weeks after closure of the manufacturing plant, Abbott launched its urgent release program which allowed formulas that had previously been manufactured and stored to be released to patients through their dietitians. Abbott maintains that they have enough formula in storage to meet the needs of patients until regular shipments resume.

In an unfortunate twist of fate, other formula companies were experiencing supply chain issues just as they were experiencing an increase in demand from those who had been advised by their dietitians to switch to these products. This led to additional shortages and anxiety for our families. The FDA worked with these companies to facilitate the import of ingredients and products. The situation has eased, and we can all breathe easier.

The Abbott plant in Sturgis, MI opened on June 4th, but was closed again after massive flooding on June 15th. They reopened on July 1 and manufacturing of metabolic formula resumed on August 1st. We were advised by Abbott that these products would be shipped in October, but at the end of the month were advised of another two month delay. It will take an additional 4 weeks for formula to be available from suppliers.

We have been in regular communication with Abbott, the FDA, and metabolic dietitians throughout this difficult period. We hope that lessons learned from this experience will compel the FDA and formula companies to take steps to ensure that our communities are never placed in this horrific situation again. But more is needed. Many families do not have access to reasonably priced metabolic formula and foods due to variability in insurance coverage. We see more clearly than ever how critical it is that the Medical Nutrition Equity Act (MNEA) is passed. If you haven't already done so, please urge your representatives to support this legislation. More about this legislation can be found in the "Advocacy Update" on page 4.

Many individuals from the MSUD community and others worked hard over this period to make our voices heard. My special thanks to Sarah Chamberlin, Executive Director of PKU News, for her tireless efforts on behalf of all of us. If you're facing shortages or can't get what you need, email info@metabolicformula.org and we'll do our best to help. ■

Presiden's Desk continued from page 2

CoRDS registry. And earlier this summer, we participated in the Million Dollar Bike Ride to further our fundraising efforts for MSUD research.

These activities and many others require a significant amount of time and commitment. The board is made up of all volunteers. It has been increasingly difficult for a small number of us to move the organization forward and meet our goals. We discussed this issue at our board meeting and voted to hire an Executive Director to run the day-to-day activities of the organization. We will begin the search for an executive director this winter. See ad below.

I have been asked when and where the next symposium will be held. At this time, we do not have that information and hope to make a decision regarding the next symposium in early 2023.

A donation slip is included in this mailing. Your financial support makes it possible for us to continue our work. Please consider donating by mailing a check or online via our website www.msud-support.org

If your contact information has changed, please include that information in the slip and return it so that our database is as accurate as possible. You can also email your contact information to davebulcher@gmail.com.

Incidentally, our current database includes the following:

- 315 US families
- 83 international families
- 30 countries outside of the U.S.
- 456 individuals with MSUD
- 100 of those have had liver transplants

We know that there are U.S. and international families with MSUD that we have not been able to connect with and hope to do so in the future. It's important that we connect with families to provide support and education and to gather more information about the needs of those with MSUD which drives research.

As always, feel free to reach out to me anytime at sandybulcher@gmail.com or 740-972-5619 ■

EXECUTIVE DIRECTOR

The MSUD Family Support Group, currently an all-volunteer organization, is seeking a full time executive director to manage day to day activities. This exciting new opportunity is a paid position.

The ideal candidate will have experience working for a non profit organization in the rare disease community.

If you or someone you know is interested, please contact MSUD Family Support Group Board President Sandy Bulcher, sandybulcher@gmail.com, 740-972-5619

Visit MSUD website for details including a job description.

ADVOCACY UPDATE

By Jordann Coleman

The Abbott formula shortage put an additional emphasis on the needs of the metabolic community. Many voices in the metabolic community shared how the formula shortage was affecting their health & wellbeing. This attention opened the door for the community's voice to be heard as part of the White House Conference on Hunger, Hunger Nutrition and Health, which took place on September 28, 2022. In addition, it brought renewed attention to the Medical Nutrition Equity Act (S.2013/H.R.3783). The Medical Nutrition Equity Act would ensure public and private insurance coverage for medically necessary foods and formulas when prescribed by a physician.

This bill is of vital importance to the MSUD community. Currently there are 22 co-sponsors in the Senate and 96 co-sponsors in the House. The more co-sponsors this bill has, the better chances this bill will have of passing.

Do you know what 90% of these co-sponsors have in common? They have heard from multiple constituents that this bill is important to them and/or heard from the same constituents multiple times. It shows that being a squeaky wheel makes a difference!

We need your support to move this bill forward.

We need more MSUD stories to show how necessary the bill is to our community. Go to www.medicalnutritionequityfor.us to share why having coverage for medical nutrition is important to you and your family. You can also go to <https://nutritionequity.org/contact-congress/> to send an auto-generated email to your members of Congress asking them to become an original co-sponsor of the bill. Social Media is a great (and public!) way to ask for your Representatives and Senators' support (or thank them if they're already a co-sponsor).

Please share with your friends, family & social networks and ask them to contact their Congressional members. Together we can make coverage for medical nutrition a reality.

Lastly, the Newborn Screening Saves Lives Reauthorization Act passed the House last summer. It is currently in the hands of the Senate. The Act reauthorizes existing federal programs that assist states in improving and expanding programs, support parent and provider education, ensure laboratory quality and effective surveillance, and facilitate adding of conditions to the Recommended Uniform Screening Panel (RUSP). It is important that you also contact your Senators to ask them to support this bill. ■



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DETECTION OF MAPLE SYRUP URINE DISEASE IN BABIES

By Harvey L. Levy, MD

Maple syrup urine disease (MSUD) is a biochemical genetic (metabolic) disorder that can cause very severe problems usually appearing within the first days after birth. Treatment that begins as soon as possible after birth can reduce these problems or even prevent them. But treatment cannot begin until the baby is diagnosed with MSUD so the outcome of the child will greatly depend upon how soon after birth the diagnosis is made.

Dr. Robert Guthrie of Buffalo who developed newborn screening for phenylketonuria (PKU) recognized the need to include diseases like MSUD soon after he and his collaborators (like Dr. Robert MacCready of Massachusetts) showed how early diagnosis was important in PKU. He knew that MSUD could be added to newborn screening because he showed that the same blood specimen collected from the heel of the baby for PKU testing could be used to show a high leucine level if the baby had MSUD. Therefore, MSUD newborn screening was added only a few years after newborn screening began. Today, every baby born in the United States is fortunately tested for MSUD within the first few days after birth and if he or she has MSUD is started on treatment immediately. I am sure that many of you reading this newsletter have a child with MSUD who was detected by newborn screening or know of a child in your family or have MSUD yourself.

One point must be added about newborn screening for MSUD. It is possible that a baby, thought to have MSUD, might really have another disorder known as hydroxyprolinemia. This is very important to know because most, or all newborn screening programs, are aware of this possible confusion. Hydroxyprolinemia is a benign disorder, (i.e., does not cause any problems and does not need to be treated), but in newborn screening hydroxyprolinemia looks like MSUD because hydroxyproline and leucine look the same in the screening test. Some newborn screening programs may be able to determine the difference by a second test and not report the baby as having MSUD. But other programs may not be able to make this distinction, so the correct diagnosis may have to await the result of the metabolic evaluation of the baby at the clinic.

There is one very important exception to the diagnosis of MSUD by routine newborn screening. That exception is in the Mennonite community. The frequency of MSUD is much higher among Mennonites than in non-Mennonite babies. Moreover, all Mennonite babies with MSUD have two copies of a unique abnormal MSUD gene. Dr. Kevin Strauss, Medical Director of the Clinic for Special Children, has informed me that Mennonite couples of reproductive age are tested to

determine if both carry (i.e., have a copy) of this genetic abnormality, and, if they do, the umbilical cord of the baby is tested for the genetic abnormality. For each pregnancy there is a 25% chance that the baby will have MSUD. So by testing the blood from the umbilical cord, the baby with MSUD can be diagnosed and treated on the first day of life, sooner than would be possible by newborn screening.

When I first entered the field of metabolism (now often referred to as biochemical genetics) very few children with MSUD were detected by newborn screening so almost all came to attention at two or three weeks of age or later because of severe problems that usually required intensive care and very complicated treatment. Many of these babies did not survive and those who did almost always had very severe brain damage due to the late treatment. Now newborn screening has allowed earlier diagnosis and treatment and, in the Mennonite community, much earlier detection and treatment so babies with MSUD today survive and have far less problems or even no obvious problems. However, there remain many challenges in MSUD that all of you recognize. Hopefully, wonderful and very talented physician scientists such as Dr. Strauss and Dr. Holmes Morton, founder of the Clinic for Special Children, will (through their continuing research) provide answers that will better the lives of all with MSUD. ■



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NPS-00013 August 2022

MSUD FILTER PAPER MONITORING FOR NUTRITIONAL MANAGEMENT AND IMPROVING OUTCOMES

Hosana Nagasaka, MPH, RD Post Master's Clinical & Research Fellow

Rani Singh, PhD, RD Professor

Emory University, Department of Human Genetics

Elevations in specific blood markers increase the risk of poor outcomes in patients living with Maple Syrup Urine Disease (MSUD). Those markers include alloisoleucine, branched-chain amino acids (BCAAs), and branched-chain alpha-ketoacids, which increase the risk of neuropsychiatric complications in MSUD. The risk for neurotoxicity is particularly high in the first few months of life. The cornerstone of MSUD treatment is nutritional intervention. Typically, nutritional management consists of restricting foods that contain leucine, providing medical food that is BCAA free, and supplementing the diet with the amino acids isoleucine and valine. This approach should be combined with frequent monitoring of blood BCAA levels.¹

There are several factors that influence BCAA concentration in the blood, making it critical for patients to have access to a BCAA monitoring method that is feasible. The National Institutes of Health (NIH) recommends weekly or twice weekly testing for infants, and weekly to monthly testing in children and adults. Genetic Metabolic Dietitians International (GMDI) recommends collecting BCAA every 12 hours, or as indicated by the patient's metabolic care team, during times of acute illness to reduce the risk of complications. In many (but not all) cases, illness can be managed in the outpatient setting when combined with a predetermined "sick-day" medical formula recipe and increased BCAA monitoring.

There are currently two methods used to monitor the BCAAs leucine, isoleucine, and valine. The first method uses plasma drawn at a local lab or clinic. The second can be done at home and uses dried blood spots (DBS) collected on filter paper which is then sent to the lab for analysis. The patient pokes a finger with a small lancet, and puts drops of blood on the filter paper. Frequent monitoring allows a metabolic dietitian to make frequent formula and diet adjustments and may improve both short- and long-term patient outcomes. Filter paper testing eliminates the need to travel to a lab or hospital. Results are typically available within 2-3 days of reaching the processing lab (averaging 2-3 days) and is a less-

invasive method of sample collection as it doesn't require a blood draw. However, there are limitations, including the testing burden placed on the family or caretaker and the logistics burden placed on institutions that must send out filter paper.

Filter paper testing is not available at all institutions, but patients, families, caretakers, and providers are encouraged to ask if MSUD filter paper monitoring is a possibility at their clinic or hospital. At Emory Genetics Clinic, the Mayo Clinic Laboratories processes filter papers for infants, children, and adults with MSUD. Other institutions may be able to coordinate with their local and/or state laboratories to provide MSUD filter paper monitoring services. Home monitoring using dried blood spots offers an easier approach for patients to monitor their blood biomarkers. Frequent monitoring of biomarkers with diet records can inform the treatment and has the potential to improve patient adherence and outcomes.

Sources

1. Strauss KA, Puffenberger EG, Carson VJ. Maple Syrup Urine Disease. 2006 Jan 30 [Updated 2020 Apr 23]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1319/>
2. Nutrition Management Guidelines for MSUD. (2021). Retrieved 5 August 2022, from <https://managementguidelines.net/guidelines.php/129/tbls/0/0/MSUD%20Nutrition%20Guidelines/Version%201.58/List%20of%20Tables> our Scientific Advisory Board and with approval of the Board of Directors. A list of past, current, and future research projects can be found on our website, msud-support.org. ■

FAMILY NEWS

MIRACLES

By Sage Wang, 16 years old, Classic MSUD



When I was young, I never understood the significance of doctors. Whenever I visited the clinic for a blood check-up at Mount Sinai Hospital, I was never concerned whether my blood levels rose or stayed normal. After all, all I cared about was mingling with doctors and playing games while I waited for my parents to finish discussing important topics with the rest of the staff in the clinic. Even in 5th grade when my levels went higher than ever, I was all cheery and bright as if it were a normal day.

Now that I'm 16 years old, I've achieved a lot throughout my life so far. I've gotten good grades, volunteered in a workspace to deliver items to the homeless, been selected for the choir in my county, and tried various hobbies like acting and singing. That said, I also experienced my first panic attack when I felt I didn't have control over my body and all I could think about was, "how sick am I going to get." I lost weight and I couldn't think straight and was tired and dull during the whole scenario. All I did was stay in my bed while feeling anxious and sick. I felt useless and worn out.. "What's going to happen to me..?" constantly repeated in my mind.

My parents took me to multiple doctors including at Mount Sinai and other practices. Fortunately, they confirmed that my unusual behavior wasn't that serious and was just related to high levels of protein. What made the appointment even better was that they recommended that I have more calories

for my weight and more formula to reduce my levels. That tip alone made me feel relieved. While I was returning home from Mount Sinai, I recalled all of the achievements I accomplished and realized that the only reason why I accomplished those things in my life was because my doctors provided advice to my parents so I could live with MSUD. They provided tips on what foods to eat or not eat to reduce leucine levels. They also told me to take in more formulas when my levels were high. My body was able to function properly with MSUD thanks to their helpful tips.

I know it's a basic step with someone with MSUD but that experience had a big impact for me. I wished I said the word "thank you" to the remaining doctors that had already left the clinic a long time ago. Doctor Diaz and Doctor Angela, if you are reading this, thank you for all of the care you gave me. I never forgot your faces and my sweet memories with you. This whole experience made me realize that we must all recognize our doctors' efforts in saving our lives. It is all thanks to their dedication to treating us and providing up-to-date information and recommendations to alter our formula and how much we can eat. Understanding MSUD has a huge effect on us since this disease is not widely known.

With technologies rapidly advancing to diagnose MSUD efficiently and tastier formulas being produced over time, we can see a bright future ahead of us where we can thrive with our disorder! In the future, I hope to have more metabolic staff members, governments, scientists, journalists, and others become aware of our health conditions and spread this message globally.

Currently, I belong to a group program where all the topics about MSUD can be discussed and I could never have been happier knowing that I'm not the only one with the disease. The more effort we put in and work together to inform individuals about MSUD, the more we can build an exceptional community to share our stories, experiences, and helpful tips to live healthy and happy lives! ■

TRAVELING WITH MSUD

By Amanda Andraos, Age 35, Classic MSUD

Traveling with MSUD can be difficult. How do I travel with formula? What can I eat along the way and at my destination? To help find solutions to these and other important MSUD related travel questions, the editors of this newsletter, Susan Needleman and Nikolai Rudd, interviewed Amanda Andraos, an adult with MSUD, and a frequent traveler.



Amanda (in red) with her family

Where do you travel?

I travel anywhere I would like to travel. Most recently, I traveled internationally to the Dominican Republic and Sweden. Domestically, I flew to Cleveland, Ohio.

How do you get through Airport Security with your formula?

I pack all my formula for the trip in my carry-on and take it with me on the plane. I get stopped each time at security because they see a can of formula and they test it, which takes a little bit of time. I also make sure there is enough time for any hiccups between flights.

How do you fly with formula?

I pack what I can in my carry-on depending on the length of the trip. If the trip I'm going to be on is longer than 15 days, I would pack some formula cans in my checked bags because you can only get so many in the carry-on. However if my husband or family members are traveling with me they help with formula, storing some in their carry-on bags as well.

How do you connect flights with your formula? Do you have trouble figuring out when to drink your formula when your travels take you to a different time zone?"

I make sure I go ahead and take what I can before I leave to ensure I have gotten in what I can before the first flight, depending on where I was going. If it's the US, I can figure it out via my phone. For international flights, in my experience, they take off at night, usually from the East Coast. So I would have already taken my morning and afternoon formulas and somewhere towards the middle of the flight overseas, I'd take the last one for the day. I always have the world clock on my phone set up to display the time at home and where

I am, so I can make sure I don't miss a dosage. I can always ask the flight attendant of the time onboard as well if I am in between time zones.

What is the longest period of time that you have traveled for?

The longest trip was a month and a half. The longest plane ride was to Dubai and the United Arab Emirates (over 12 hours).

Did your formula or levels ever force you to cut your trip short?

The only time this was an issue was in December 2021. I was supposed to go to Sweden on the 23rd, and ended up getting fluids due to a severe sinus infection that occurred right before my flight. I wasn't able to go to the doctor in due time so my leucine was elevated and I ended up at the hospital for fluids. After I received the necessary fluids, I was still able to go enjoy my trip with no issues.

Have you ever gotten sick while away?

Yes. Specifically, I got sick from food poisoning. I was vomiting excessively and became dehydrated which landed me in a nearby hospital receiving fluids until they were complete. After having received the fluids I was told to continue drinking liquids at home and a low protein diet till I got my strength back and recovered.

What do you do for low protein food while you are away? Do you travel with them?

When I was younger there weren't many options for low-protein foods as there are now. In many places, my mom would pack bread mix and pancake mix, as well as pasta. As an adult, I don't pack any foods as many countries now have gluten free items, which are often low in protein. All countries serve some form of salads and potatoes. As for homemade meals, or being invited to a friends or families for a meal, I'd tell them ahead of time about the foods I can't have so they don't feel as if I'm being rude by not eating. They, in turn, prepare foods that I am able to enjoy with them.

Have you ever been forced to not follow your diet because there wasn't any other food to eat?

I follow my diet because of the consequences it causes if I don't. I'd be miserable on a trip, and would need to be in bed if I went off diet. I know what I'm allowed to have, how much, and balance it out fairly well (depending where I travel). I have realized that increasing my fluid intake in countries that are hot does help keep levels balanced and prevents dehydration from the heat.

Have you ever been hospitalized while away?

Yes, due to food poisoning. I was admitted to the hospital for fluids.

If you were admitted to a hospital, did they talk with your MSUD doctor?

Yes. Prior to leaving, I tell my MSUD doctor where I am going in case anything happens, and they are notified by the hospital if I am admitted. When I do end up at a foreign hospital, I call my regular MSUD doctors directly, and my normal MSUD doctors give orders to the doctors I am with. In my experience, doctors unfamiliar with MSUD have no problem reading the Emergency Protocol Letter I carry, and following my regular MSUD physicians' orders. This results in it going smoothly.

Did you have any MSUD protocol for emergencies translated into the language of the countries you visited?

No

How do you know what hospitals you can go to while away?

Sometimes my metabolic geneticist team will advise me to go to a particular one that treats MSUD. If I need to go, especially if they have a connection to a doctor at my destination. For instance, when I went to a Sweden, one of the geneticists recommended a specific hospital. In other countries that were underdeveloped I went to whichever hospital I was near, and their doctor(s) would speak to the physician here in the U.S. I give them the Emergency Protocol Letter, which explains MSUD and how to treat it, so they understand it.

Did MSUD ever prevent you from enjoying your trip?

No. Even when I am sick, I am down, but other than that when my leucine levels are good, and my diet is well maintained. So there are no real hiccups.

Do you travel by yourself?

I travel alone and I also travel with family depending on the trip. If my husband or some family are going with me they are able to carry some formula on board in their carry-on, which helps a lot specifically for longer trips. However, if I go alone, I fill my carry-on with formula and also fill my checked bag (for longer trips); because with the airlines comes the risk of bags getting lost. Regardless, if I go alone or with someone, I always pack extra because you never know what happens at the airport, in transit, or in the country you're heading to.

To put this in perspective, when I went to Cleveland in June 2022, I packed 2 cans of formula. One was closed completely but the other was opened as I had started using it. I went to the TSA and of course got stopped and they checked it. I put my bag back together not thinking too much of it and went on about my flight (it was just a long weekend). When I got to my hotel and opened my bag I saw that the TSA agent didn't close the formula can completely...so there was formula all in my carry on bag everywhere. I didn't panic because I had what's left of the can and the other closed cans.

Is there any other advice you would like to give other MSUD travelers?

Calculating ahead of time how many times or how long each can of formula can last is very helpful when traveling as well- I take my formula 3 times a day, so before I travel I make sure to mark the lid with a check mark each time I drink so I know how long each can lasts. ■



Amanda and her husband Carlos



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Dear Friends of Vitaflo™,

Vitaflo continues to monitor the status of the ongoing metabolic formula supply interruption in the US, and we are aware of the recent announcement of numerous PKU products impacted by ingredient supply shortages.

We want to give you an update on supply status of Vitaflo formulas and what we are doing to support the community during this time.

The **Vitaflo** team is prepared to serve those in the metabolic community who need to find other suitable formula options:

- **We continue to offer the full array of Vitaflo formulas.** Currently, **Vitaflo** is not facing or anticipating ingredient supply challenges. We have reviewed our product stock levels and have increased them.
- We are working closely with our supply chain to meet the increased demand for formula in the US for individuals with PKU and the larger Inherited Metabolic Disease community.
- We are sampling all **Vitaflo** products except for PKU trio Unflavored which will be available early October.
- In response to the recent PKU product supply shortage, we have created a list of **Vitaflo** alternative formulas for individuals with PKU. This list will be provided to metabolic dietitians who can help you decide which formula options are right for you.

To contact **Vitaflo** customer service Monday-Friday, 9 am to 5 pm ET, please call or email at:

- Tel: [1-888-848-2356](tel:1-888-848-2356)
- Email: customerservice@vitaflousa.com

To learn more about our range of products, please visit: VitafloUSA.com

You may also go directly to our online sample request form by clicking [here](#). Be sure to check with your healthcare provider before making any changes to your diet.

Yours in good health,

The Vitaflo Team

MSUD VIRTUAL MEET-UPS

By Susan Needleman

There are a lot of people in this world, but few who have MSUD or even know what it is. With all that is needed to care for MSUD, and all that is going on in the world now, it is more important than ever to have people in our lives who “get it”. That is why, during the height of COVID, I started MSUD Virtual Meet-Ups (which really has turned into a support group of friends). During these meetings we talk about MSUD and non-MSUD topics while we laugh, cry, or just listen.

There are two meetings a month, one for teens and adults living with MSUD and one for those who care for someone with MSUD. If you would like to attend please email me at susanneedleman.msud@gmail.com.

MSUD

Virtual Meet-Ups

Monthly Saturday Nights

8PM EST

RSVP:
susanneedleman.msud@gmail.com



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THE MSUD FAMILY SUPPORT GROUP RIDES AGAIN IN THE MILLION DOLLAR BIKE RIDE

By Butch Foster and Ed Fischler

The MSUD Family Support Group again participated in the Penn Medicine / Orphan Disease Center's Million Dollar Bike Ride (MDBR). The Penn Medicine Orphan Disease Center (ODC) was established to promote the development of therapies across a broad range of orphan diseases (diseases affecting fewer than 200,000 individuals nationwide). The ODC sponsors and promotes the annual MDBR to help organizations raise funds for pilot research grants for the rare disease represented by each participating team.

This year the bike ride returned to the streets of Philadelphia. Several hundred riders, representing nearly three dozen disease teams, participated in the event. Collectively, over \$2.6 million was raised to support rare disease research. Taryn Kessel traveled to Philadelphia from Chicago to represent our team while others rode in their neighborhoods.

Fifteen families responded to the need for riders and campaigners for the 2022 MSUD team. These included the families of Andrea Brien; Sandy and Dave Bulcher; Jordann and Andre Coleman; Karen and Jerry Dolins, Edward and Lynn Fischler; Herbert and Diane Foster; William Goodwin; Stephen Healy; Doug and Taryn Kessel; Susan and Adrian Mays; Susan Needleman; Cristy Steinberg, Wayne and Chad Farquharson; and Scientific Advisory Board member Dr. Richard "Max" Wynn. Let's again thank the whole team who helped to raise funds for MSUD research.

Research to find better treatments and a cure for diseases like MSUD is a journey. We all want to improve the lives of families affected by MSUD. These families have done some of the heavy lifting that will be necessary to fund the research necessary to achieve these goals. This year, donations for over \$70,000 were contributed to the MDBR campaign towards MSUD research. The University of Pennsylvania/Orphan Disease Center will match our amount with an additional \$30,000, making the total amount raised over \$100,000!

This was the fifth year of our participation in the MDBR. Since our participation began in 2018 we have been able to fund five research projects focused on MSUD. This year we will add to that total. The MSUD Family Support Group Board of Directors has directed the organizers at UPenn to seek proposals to fund two MSUD research projects: One project seeking better treatments for MSUD and one project directed towards the goal of finding a cure for MSUD. The ODC will issue a request for project proposals in August. Reviews of the responses should be completed by November and the selection of the winning proposal(s) will occur in December. ■

12 www.msud-support.org

THE POWER OF PATIENTS AS TEACHERS:

VMP GENETICS' PATIENT-TEACHER REGISTRY

What is the purpose of the Patient-Teacher Registry Project?

We educate the medical community about metabolic diseases so more health professionals can play a role in the diagnosis and management of these disorders. We believe that education has a significant part to play in addressing the workforce shortage in Genetics.

We at VMP Genetics are committed to educating in many ways, and we recognize the incredible power of patient storytelling as a compelling way of informing clinicians and students. The impact of the patient experience is more personal and penetrating than anything a lecturer can deliver and can create long-lasting impressions about rare diseases.

How does the teaching occur?

We facilitate opportunities in which patients and family members participate in live, in-person or virtual presentations at medical schools and hospitals.

How do doctors or educators find the speakers?

VMP Genetics has established on its website a registry of patient-teachers, listing only their diagnosis and geographical location (city/town/state/province). No personal information about the speakers is visible to the public on the registry website. Physicians or educators who wish to have a patient-teacher participate in their curriculum can choose a speaker from this Registry.

What is the process for arranging a patient/family member to speak at a medical school or hospital?

A physician/educator selects a patient-teacher, fills out a Speaker Request Form, and submits it to VMP Genetics. VMP Genetics then confirms the identity and credibility of the request and educator (e.g., status as a faculty member at a medical school). After confirmation, VMP Genetics notifies the patient-teacher about the details of the request and provides her/him with the educator's contact information. The patient-teacher either accepts the request and reaches out to the educator or lets VMP Genetics know s/he is unavailable (and VMP Genetics then notifies the requesting educator).

What happens at a live presentation?

Educators and patient-speakers discuss together in advance the format and content of the presentation. Often the class will have learned about the disease beforehand so the patient-teacher's presentation is more meaningful. Patient-speakers may talk about a variety of topics, including the diagnostic journey, living with the disease, engaging the health care system, impact of the condition at school or at the workplace, what providers did right or what they could have done better, and/or other significant issues. A patient presentation may run anywhere between 20 and 40 minutes, and the format of the presentation (e.g., informal and off-the-cuff, a slide presentation, or a bit of both) is left up to the speaker. The session usually ends with a question-and-answer period and closing remarks. There may be a request to film the presentation for the benefit of others who cannot attend the live session (speakers can decide whether or not they are comfortable with this plan; it is not a requirement).

Are patient-speakers/family members paid to speak?

There is usually no payment involved with volunteering as a patient-teacher for a medical school or a medical center. If an honorarium is provided, it is offered by the school or center directly to the speaker. VMP Genetics is not involved in these arrangements and does not offer payment. Speakers should ask the educator about reimbursement for travel expenses such as gas, parking, or other costs associated with getting to the location, if appropriate.

How is the privacy of patient speakers protected?

The privacy of the patient-teachers is maintained in several ways:

- ☐ The online registry lists only a patient-teacher's diagnosis (the name of the disease) and her/his geographical location (city/town/state/province);
- ☐ VMP Genetics confirms the institutional status of educators/physicians after requests are made and before speakers are contacted;
- ☐ VMP Genetics then provides information about the request to the patient-teachers, not to the requesting physician/educator;
- ☐ Making a connection is the prerogative of the patient-speaker;
- ☐ Speaker information (name, contact information, other personal information) is never released by VMP Genetics to any outside party, organization, or company.

Why is a consent form required?

A consent form helps ensure that patient-teachers and VMP Genetics are both clear about how the program runs, what is

expected of each party, and how privacy is maintained in the project.

Is there a problem if a speaker has never given such a presentation before?

Not at all! For many, this might be the first opportunity to talk to a medical audience! VMP Genetics can provide guidance about how to prepare for such a presentation, what topics might be of interest to the audience, and how to deliver the information effectively so the experience can be a successful and rewarding one.

For more information – see <https://www.vmpgenetics.com/edu-services/patient-teacher>

Please feel free to reach out and ask questions and give comments! And let us know how your teaching experience went!

We can be reached at - patientteacherregistry@vmpgenetics.com

Thank you

Mark Korson, MD
Director of Physician Support
Director of Education
Biochemistry and Molecular Biology
VMP Genetics

Jacob Athoe, BA
Program Manager

Boston University ■



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CURRENTLY RECRUITING ADULTS FOR STUDY ON NEUROCOGNITIVE OUTCOMES AND QUALITY OF LIFE

By Jessica Gold, MD, PhD

It is an exciting time when people diagnosed with MSUD are living longer with better health. We want to learn to best help adults with MSUD prepare for success. A study sponsored by the Children's Hospital of Philadelphia, entitled "Neurocognitive Outcomes of Adults with MSUD," is looking for people who can help us learn about the experiences of adults with MSUD. The purpose of this research study is to 1) look at thinking skills, behavior skills, life skills, and quality of life in adults with MSUD and 2) examine how medical and personal factors impact these areas.

In this study, you will answer questions on thinking, life skills, behavior skills, and quality of life. All questions will be completed on the internet or over the phone and can be done at your home. You will undergo testing of your thinking and behavior through a series of web-based games that can be accessed on your computer, phone, or tablet. These games will test decision-making, attention, and working memory. You may also have a 1-2 hour telephone conversation about your life so researchers can learn how adults with MSUD think, feel, and live. Together, this evaluation should take 3-4 hours. You will be compensated for your time.

Potential subjects are 21 years and older with a diagnosis of MSUD. People who have received liver transplants are eligible. To learn more about participating in this study, please contact the Co-Investigator, Jessica Gold, MD, PhD directly at goldj@chop.edu or 267-600-4812 ■

MAPLE SYRUP URINE DISEASE DECOMPENSATION MISDIAGNOSED AS A PSYCHOTIC EVENT

Summarized by Karen Dolins

Higashimoto T, Whitehead MT, MacLeod E, Starin D, Regier DS. Mol Genet Metab Rep. 2022 Jun 18;32:100886. doi: 10.1016/j.ymgmr.2022.100886. PMID: 35756860; PMCID: PMC9218201.

ADHD and depression are common in individuals with MSUD. This is the first time an episode has been reported in the scientific literature describing an adult with MSUD who went to the emergency room due to hallucinations brought on by high leucine levels. Due to the COVID-19 pandemic, he was sent to a community hospital rather than the hospital where he is known. He was admitted for psychiatric evaluation and started on medications for agitation. A nurse eventually reached out to Children's National Hospital where he is followed to ask about metabolic formula. At that point his team intervened, and he was successfully treated.

This case shows how metabolic decompensation can present as psychosis in adults with MSUD. It is recommended that adults with MSUD carry identification in the form of a Medic Alert bracelet and/or a wallet card describing their diagnosis and identifying their metabolic physician. Your medical specialist can help you create the most appropriate wording. Medical information can also be stored in a smartphone. This site shows how to do this. <https://www.gottransition.org/resource/?setting-up-medical-id-smartphones>. ■

2022 APHL NEWBORN SCREENING SYMPOSIUM

By Susan Mays

Mom to Indie Age 9, Mild MSUD

This October Indie and Susan Mays were invited to speak at the 2022 APHL (Association of Public Health Laboratories) Newborn Screening Symposium which was held in Tacoma, WA. With over 500 people in attendance, Indie bravely took the stage and shared her experience of living with MSUD. She talked about how she helps monitor her daily protein intake, drinks a medical formula (which she LOVES), and how French fries are her favorite food. Susan was able to share about their family's newborn screening journey, about parenting a child living with MSUD, the importance of connecting with other MSUD families, the MSUD Family Support Group, and to thank the newborn screening community for their commitment to this complex public health program. It was a wonderful experience! ■



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FIRST MSUD SCIENCE SUMMIT

By Karen Dolins, Research Lead



What do we all want? Improved treatments and a cure for MSUD! We took a step towards that goal by convening our first ever Science Summit in Lancaster, PA on August 5th, 2022. The Summit was planned in partnership with the Clinic for Special Children. Dr. Kevin Strauss and genetic counselor Karlla Briganti assisted in the program planning. Attendees included our Scientific Advisory Board and the MSUD Family Support Group Board of Directors. We were thrilled to find ourselves in a room with world-renowned scientists all focused on improving the lives of those with MSUD.

Speakers and topics included:

Dr. Richard "Max" Wynn

University of Texas Southwestern Medical Center

Branched-Chain Ketoacid Dehydrogenase Complex and Kinase Inhibitors

Dr. Kevin Strauss

Clinic for Special Children

A History of Therapeutic Advances in MSUD

Dr. Jessica Gold

Children's Hospital of Philadelphia

Neurocognitive Outcomes and Quality of Life in MSUD

Dr. Rebecca Ahrens-Nicklas

Children's Hospital of Philadelphia

Brain Physiology in MSUD

Karla Brigatti

Clinic for Special Children

Getting Ready for Clinical Trials: Identifying Meaningful Outcomes and Biomarkers

Dr. George Mazariegos and Dr. Kyle Soltys

University of Pittsburgh Medical Center

Liver Transplantation: Outcomes, Challenges, and Limitations

Dr. Jenny Greig

University of Pennsylvania Orphan Disease Center

Gene Therapy in a Mouse Model of MSUD

Dr. James Wilson

University of Pennsylvania Orphan Disease Center

Therapeutic Potential of mRNA in MSUD

Dr. Jiaming Wang and Dr. Dan Wang

University of Massachusetts Chan Medical School

Gene Therapy in a Mouse and Cow Model of MSUD

Dr. Karen Dolins

Teachers College Columbia University
MSUD Family Support Group Research Lead

Moving Forward with MSUD Research

Scientific advisors Dr. Andrea Gropman and Dr. Lindsay Burrage attended remotely, as did a group in England studying gene therapy in MSUD under the leadership of Dr. John Counsel.

Our next task is to synthesize what we learned and to determine next steps. We will keep you posted! ■

Continued from page 1



Preliminary findings of a patient registry for MSUD using CoRDS (Coordination of Rare Diseases at Sanford)

Dolins K¹, Bates K²¹ Teachers College Columbia University, Research Lead MSUD Family Support Group, NY, NY, USA² Sanford Research, Research Design and Biostatistics Core, Sioux Falls, SD, USA

BACKGROUND

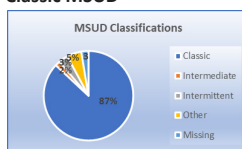
Maple Syrup Urine Disease (MSUD) is an inborn error of metabolism resulting in an impaired ability to metabolize branched-chain amino acids (leucine, isoleucine, and valine) and has a worldwide incidence estimated at 1:190,000. If untreated, MSUD results in severe neurological impairment, coma, and death. Treatment centers around a strict diet and monitoring of blood amino acid levels. Illness can result in severe metabolic decompensation. Understanding the patient experience is essential to inform development of new therapies.

METHODS

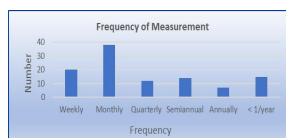
A registry questionnaire was developed by the MSUD Family Support Group and the CoRDS Registry and promoted using direct email, phone calls, and social media. The questionnaire is comprised of 48 questions, 15 of which were analyzed. Prior to analysis of the questionnaire responses, 28 of 143 participants were removed from the data due to no answers recorded, leaving a sample size of n=115. Remaining blank answers were categorized as "Missing". Questions with multiple-selection answers may result in a summation of percentages greater than 100%.

PRELIMINARY RESULTS

A clear majority of respondents (87%) indicate that they have Classic MSUD



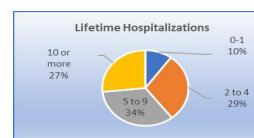
Most MSUD patients measure their blood amino acid levels each week or month.



Almost ¼ of respondents visit a metabolic specialist once or twice a year.



Most MSUD patients have been hospitalized at least 5 time in their lifetime



Dietary Adherence

| Statement | No. |
|---|-----|
| The participant consistently consumes all daily formula and strictly follows their leucine/protein prescription and diet. | 47 |
| The participant sometimes deviates from their daily formula or leucine/protein prescription and diet by minor amounts. | 27 |
| The participant often deviates from their daily formula or leucine/protein prescription and diet by significant amounts. | 1 |
| The participant generally does not follow a daily formula, their leucine/protein prescription or diet | 12 |

CONCLUSIONS

A patient registry is essential to understanding the needs of those living with MSUD and will help inform future research directions. These summary statistics provide preliminary data about the experiences of those with MSUD. Further analysis is hampered by missing data. About 50% of respondents did not respond to key questions related to their ability to function independently in school, work, and life. This emphasizes the need for future data collection initiatives that focus on addressing obstacles to responding to all questions. With a more robust dataset, we will be able to provide a more in-depth analysis aimed at identifying the key needs of individuals and improve their quality of life.

NEW REPORT ON SAFETY OF COVID-19 VACCINES IN CHILDREN WITH INBORN ERRORS OF METABOLISM

In this newly published study, 18 children ages 12-18 with a variety of metabolic diseases including MSUD were followed for one month after receiving COVID-19 vaccines. None of the patients experienced a metabolic decompensation and none required emergency care.

Safety of COVID-19 vaccines in children with inborn errors of metabolism in terms of developing metabolic decompensation. Zubarioglu T, et al Journal of Pediatrics and Child Health. 2022 Sep 29. doi: 10.1111/jpc.16231. Epub ahead of print. PMID: 36173142. ■

CDX-6210: A POTENTIAL ORAL ENZYME THERAPY FOR MSUD

By Subhamoy Das, PhD and Kristen Skvorak, PhD - Translational Scientists at Codexis Inc.

Summary:

Codexis, Inc. is developing an engineered (aka “evolved”) leucine decarboxylase (LDC) enzyme as an oral therapy for MSUD. The concept of this therapy is that when LDC is administered with a meal containing protein it will break down the leucine, reducing the amount absorbed into the blood and prevent it reaching toxic levels. Our patient-centric goal is to lessen the need for low protein and medical foods, which should allow patients to increase consumption of natural protein sources while maintaining healthy levels of amino acids. Consequently, the LDC therapy is expected to improve leucine tolerance, decrease the daily burden of care, and improve quality of life. To achieve these goals, we engineered our LDC variants to be highly stable in the harsh environment of the gastrointestinal (GI) tract and active in the small intestine, the site where dietary protein is broken down and leucine is absorbed. Our lead LDC variant, CDX-6210, shows exceptional GI stability in benchtop experiments and lowers plasma leucine in animal studies when administered with a high protein meal. This program is currently in pre-clinical development; we are diligently working to further assess the safety and efficacy of CDX-6210 towards a potential future clinical program.

About Codexis:

Codexis is a leading enzyme evolution biotech company located in Redwood City, California. At Codexis, we apply our proprietary CodeEvolver® technology platform to engineer enzymes for bio-solutions that benefit human health. We are committed to improving patients’ quality of life and work diligently to develop better biotherapeutics guided by patient input. We support the rare disease community through our commitment to developing transformative therapies for inborn errors of metabolism. Codexis’ current pipeline includes oral enzyme therapies in pre-clinical development for MSUD, HCU, and other metabolic diseases, plus two clinical programs for PKU and exocrine pancreatic insufficiency (both in Phase 1 clinical trials being conducted by our partner, Nestlé Health Science). Codexis also has pre-clinical gene therapy programs for Fabry, Pompe, and other disorders. We correspond directly with patients, clinicians, and advocacy leaders to ensure that our therapies can address patient needs. Our unified vision is what drives Codexis to challenge what is possible.

How Does CDX-6210 Seek to Address the Needs of the MSUD Community?

CDX-6210 is an oral enzyme that is intended to remove dietary leucine in the gut prior to absorption into the blood, thus preventing it from reaching the brain and other tissues. The aspirational goals of this therapy are to 1. help manage leucine levels, 2. reduce reliance on low protein and medical foods, and 3. increase protein tolerance in patients. CDX-6210 works independent of the BCKDH complex deficient in people with MSUD, therefore it is intended to be an option for all MSUD patients, regardless of mutation. Due to the ease of oral administration, we anticipate it to be suitable for patients of all ages.

Scientific Details: CDX-6210 Exhibits Great Promise as a Potential First-In-Class Oral Therapy for MSUD

Once superior GI stability of evolved LDC was shown in benchtop screens, we assessed its ability to reduce blood leucine in animals following a high protein meal. Two species were used, each with important benefits to help better predict the likely impact of our treatment upon patients: the iMSUD mouse model, which accurately mimics the human disease, and healthy non-human primates (NHP), which have a GI-system and metabolism more like humans than the mouse.

For these studies all animals received a high protein whey meal, a natural protein found in milk; treatment groups then received oral LDC. We then measured the leucine concentration in blood plasma up to 24 hours after dosing. In the iMSUD mouse (Panel A), we saw a 59% suppression in plasma leucine area under the curve (AUC) with CDX-6210 treatment after a single dose (administered once). In healthy monkeys, at a dose 4-fold lower than was administered to the mouse, we tested LDC’s ability to impact plasma leucine following a whey meal with either a single dose (Panel B; 37% AUC suppression) or a repeat dose (provided once daily for 3 consecutive days, Panel C). Daily administration over three days indicated a cumulative effect of LDC treatment, with greatest leucine suppression occurring on Day 3 (Panel C). AUC considers the reduction in leucine at all time points throughout the study, and is therefore more relevant than looking at a single point. The leucine suppression observed in these studies is highly significant and represents a clinically relevant outcome.

This work highlights the prospects of a GI-stable leucine-degrading enzyme as a potential therapy for MSUD and may have applications in other inborn errors of branched-chain amino acid metabolism.

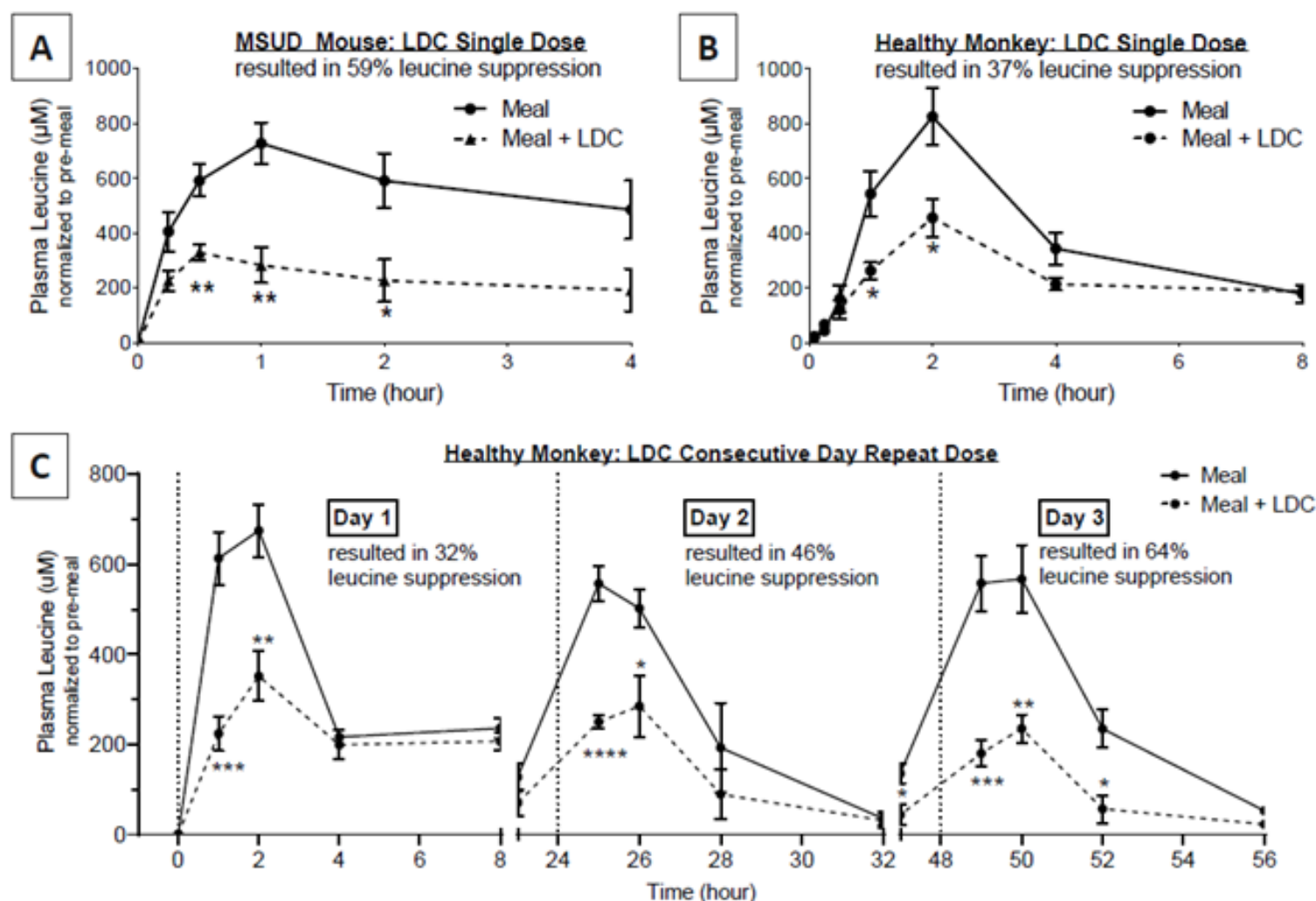


Figure 1. A whey protein meal was provided to all animals in the study, which were either MSUD mice (A) or healthy non-human primates (B & C). Treatment groups then received oral LDC (dashed line) while Control groups received meal only (solid line). Blood plasma leucine was measured at multiple time points post-dose up to 24 hours later. A single dose (A & B) and a 3-day repeat dose (C) of LDC were evaluated for impact on plasma leucine. In the repeat dose study, dosing occurred at Hour 0, 24, and 48 over the 3 days (dotted lines). Statistics: Graphical data is represented as the mean \pm standard error. Statistical significance between experimental groups at specific time points was calculated using multiple t-tests (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$). Area under the curve (AUC) was used to calculate the % leucine suppression observed after LDC treatment.

What is the Status?

This program is currently in pre-clinical development and has not yet entered clinical trials. We are diligently working to further characterize CDX-6210 and assess safety and efficacy in animal studies to help inform the design of our future clinical program.

How Can I Learn More About CDX-6210?

Please follow Codexis on LinkedIn to keep updated or visit www.codexis.com/focus-areas/biotherapeutics. Additionally, we would love to hear from you! Please reach out if you have any questions at kristen.skvorak@codexis.com or subhamoy.das@codexis.com ■

ORGANIZATIONAL AND PROFESSIONAL CONTACTS

This Newsletter does not attempt to provide medical advice for individuals. Consult your specialist before making any changes in treatment.

RESOURCE PERSONS:

Organizational information, printed material or addition to our mailing list:

PRESIDENT

Sandy Bulcher

Delaware, OH
740-972-5619
sandybulcher@gmail.com

Donations:

TREASURER

Dave Bulcher

4656 Winding Oak Dr.
Delaware, OH 43015
740-972-5618
davebulcher@gmail.com

Research Lead:

Karen R. Dolins, Ed.D, R.D.

Scarsdale, New York
914-391-2982
karen.dolins@yahoo.com

Inquiries in Spanish:

Adriana Carbajal (MSUD parent)

Mesa, Arizona
480-278-4713
adrianamc2014@yahoo.com

Vanessa Funes (MSUD adult)

Boston, Massachusetts
508-654-0663
mamilindafunes@live.com

Newsletter Editor:

Susan Needleman

Malden, MA
781-420-2676
msueditor@gmail.com

Editor Assistant:

Nikolai Rudd

North Adams, MA
413-652-2002
msueditor@gmail.com

Advocacy:

ADVOCACY CHAIR

Jordann Coleman

Walnut Creek, CA
925-330-9378
Coleman.jordann@gmail.com

MEDICAL ADVISORS:

Melissa Wasserstein, M.D.

Chief, Division of Pediatric Genetic Medicine
Children's Hospital at Montefiore
Associate Professor
Albert Einstein College of Medicine
Bronx, NY
718-741-2318

Harvey Levy, M.D.

Senior Physician in Medicine and Genetics
Division of Genetics and Genomics
Boston Children's Hospital
Professor of Pediatrics
Harvard Medical School
Boston, MA
617-355-6394

Can Ficicioglu, M.D., Ph.D.

Associate Professor of Pediatrics
Perelman School of Medicine at the
University of Pennsylvania
The Children's Hospital of Philadelphia
Division of Human Genetics/Metabolism
Director, Newborn Screening Program
Director, Lysosomal Storage Disorders Program
Philadelphia, PA
215-590-3376

Jessica Scott Schwoerer, M.D. (she/her)

Associate Professor, Dept of Pediatrics - Genetics
Medical College of Wisconsin / Children's Wisconsin
Metabolic Consultant, Wisconsin Newborn Screening
8701 Watertown Plank Rd. P.O. Box 1997
Milwaukee, WI 53201-1997
(414) 266-3347

Nicholas Ah Mew, M.D.

Director, Inherited Metabolic Disorders Program
111 Michigan Ave, NW
Washington, District of Columbia 20010
202-545-2531

NUTRITIONAL ADVISORS:

Rani Singh, Ph.D., R.D.

Emory University
Division of Medical Genetics
2040 Ridgewood Dr.
Atlanta, GA 30322
404-778-8519
Fax: 404-778-8562
rsingh@genetics.emory.edu

NUTRITIONAL ADVISORS:

Sandy van Calcar, Ph.D., R.D., C.D.

Child Development & Rehabilitation
Oregon Health and Science University
3181 SW Sam Jackson Rd
Portland, OR 97239
503-494-5500
vancalca@ohsu.edu

MSUD FAMILY SUPPORT GROUP BOARD

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