# The HCU Herald

## *In This Issue*



Connecting for a cure. There have been great things happening for the HCU Community and HCUNA. We strive to keep you informed and connected.

HCU Network America

# *News Announcement !*

**HCU Network America now officially includes Cobalamin Defects!**

In 2016 when HCU Network America was formed, our intention was to be a source of support to those with classical homocystinuria (cystathionine beta-synthase), cobalamin defects, severe methylene tetrahydrofolate reductase (MTHFR), and other remethylation defects. We knew that this would take some time to develop a team of board members, medical advisors and volunteers who would be able to advocate, create and develop tools and provide guidance for these diverse groups that all fall under the Homocystinuria umbrella.

It is now 2019 and we are excited and proud to announce HCU Network America officially has a cobalamin steering committee! During the next couple of months, we will be introducing you to our new medical advisors and steering committee members. In light of this celebration, we are also featuring additional patient stories.

**What are the cobalamin defects?**

Vitamin B12 or cobalamin (Cbl) is needed for multiple jobs our bodies do. In the case of homocysteine, it is needed to convert this compound to the safer amino acid. Some people have trouble with processing this vitamin due to abnormalities in their genes and their symptoms and biochemical markers like homocysteine will depend on what step that gene encodes. The names of the disorders and genes can be confusing since we call them Cobalamin C deficiency, Cobalamin D deficiency, Cobalamin F deficiency, Cobalamin G deficiency, Cobalamin X deficiency, etc. Some of these gene changes affect processing of vitamin B12 (cobalamin) so that more than one enzyme is disrupted so one not only has elevations in homocysteine (making this a homocystinuria) but also elevations in a compound called methylmalonic acid (e.g. Cobalamin C and Cobalamin D1) and are called Homocystinurias with methylmalonic acidemias (MMAs). Individuals can have growth problems, eye problems, learning problems, heart differences and sometimes blood problems. Although blood clots can occur, they are less common in these disorders. Sometimes these disorders present in the newborn screen, but sometimes they are missed.

Other genetic changes on cobalamin processing lead to predominately elevations in homocysteine (since problem near same place as MTHFR) such as Cobalamin G (also known as methionine synthase) and Cobalamin E or Cobalamin D2. Blood clots commonly present in these individuals, but they can also have learning differences, seizures and muscle problems.

There are several other cobalamin disorders which are not specifically covered above, but have similar presentations and therapies.

# *Meet our new Medical Advisor*

**Dr. Kristina Cusmano-Ozog, MD**
*Medical Advisor of HCUNA*

## *About Dr. Cusmano-Ozog, MD*

*Dr. Kristina Cusmano-Ozog, MD holds a BS in Biochemistry from the University of Miami (Florida) and earned her MD at the University of South Florida, where she also completed training in pediatrics. She trained in Medical Genetics and Clinical Biochemical Genetics at Stanford University and obtained additional training in Clinical Molecular Genetics through the National Institutes of Health. For the last eight years, she has practiced as a Medical Geneticist at Children's National Medical Center and was also the Director of the Molecular Diagnostics and Biochemical Genetics Laboratories. She is relocating this summer to Stanford University School of Medicine. Her research and clinical work focus on diagnosing and treating individuals with inherited metabolic disorders.*

# *Meet Our Steering Committee Members*

## Misty

Misty lives in Dallas, Texas with her husband Gil, and their daughter Sienna. Sienna is 20 years old and has CblC. Misty likes to read, watch movies and spend time with her family.

## Tracy

Tracy lives in northern Minneapolis suburbs of Minnesota with her husband, AJ, and their daughter Lydia (17 months). She entered the HCU world when Lydia was diagnosed with CblF following an abnormal newborn screening in December 2017. Outside of being a mom and rare disease advocate, Tracy enjoys photography, iced coffee, and warm weather.

## Gig & Amette

Gig (George) and Annette Settle live in the Harrisburg suburbs of Pennsylvania with their son Adam (19) who was diagnosed with CblC deficiency under the then new newborn screening. They believe Adam was the third child diagnosed prior to the onset of serious medical complications. Adam is the youngest of 8 of Gig and Annette's children. Adam's story is being told in a book for children; No Day Wasted: The Adam Settle Story. The expected publishing date is November 2019. The Settle family enjoys mission work in developing countries.

## Brittany

Brittany Parke lives in the Denver suburbs of Colorado with her husband, Robert and three children, Alexis (13), Riley (3) and Grayson (7 wks). While their family is just beginning the journey with Grayson who was diagnosed with Cbl G, they have been involved in the rare diseases community since the birth and death of their son Drew in 2011. Brittany loves to read, run and spend time outside with her family.

## Dana

Dana lives in the Kansas City suburbs of Kansas with her husband, Darren, and their two children, Ethan (16) and Carson (11). She loves being a mom, teaching dance, and spending quality time with her family. While this journey has been difficult, she reminds herself to live, laugh & love every day.

# *Go the Extra Mile for HCU*

## *Virtual Race Recap*

Thank you to the 15 racers and countless people who donated to make our first virtual race a great success! The first week started off very strong! The Rare Runner, Kristin Rap, took the lead logging 28.2 mile of the 160 miles logged overall. In addition to the strong lead by racers, Janna Thomas and Jackie Piccini had an amazing start to the races fundraising effort with the two of them alone raising $2,066!

As week two started, the momentum picked up and racers logged 256.2 miles! As the competition began to increase, we start to see racers cross the finish line. In week two, we saw Kristin Rapp take 1st place, Janna Thomas in 2nd, Laura Pisani take 3rd, while another 4 racers crossed closely behind them. As week two came to a close Janna and Jackie stayed neck in neck in their fundraising efforts both bringing in over $400 each.


The second leg of the race things started to slow down, racers only logged 148.2 miles and our 8th place finisher crossed the finish line. Those watching the race online became slightly skeptical if everyone was going to finish with so many miles left completing.

With only a few days left to go, our racers picked up their pace. Racers logged over 170 more miles allowing 9th, through 13th place to be taken. While these racers were just finishing their first time through the course, racers Marian Cummings, Laura Pisani, Kristin Rapp and Joann Ball were completing the course for the second time! With time ticking donations continued to come in making for a final total of approximately $4,500! This truly was an amazing event. Thank you to all our amazing racers and donors for making this an exceptional first event of its kind!

# Vitaflo

*Advertisements are not an endorsement for products advertised.


# HCU Heroes

## *Grayson*

*From Colorado*

Our son Grayson was born in March 2019 and was diagnosed on day one of life with Cobalamin G and began treatment immediately. His early diagnosis was due to our prior knowledge that our family was a carrier for a Cobalamin disorder. Our first son, Drew, was also born (2011) with Cobalamin G, however we did not know of his diagnosis until 2 months of age and damage caused to his brain resulted in his death. It was not picked up on his new born screen. Only until recently were we able to do rapid genome testing through our metabolic clinic to find the mutations responsible for the defect.

*Grayson is the son of steering committee member Brittany.

## *Carson*

*From Kansas*

Carson was born on July 2007 at St. Luke's Hospital in Kansas City, MO. He almost immediately began telling us something was wrong, despite the fact that nothing unusual was identified on his newborn screen. He was having difficulty feeding, had significant congestion, and noisy breathing. We took him to the hospital, where he was admitted, treated, and released numerous times with having severe acid reflux and bronchiolitis. Over the next few weeks his condition worsened, and he was starting to show signs of failure to thrive, began losing weight, and missing developmental milestones...such as tracking and smiling. At that point we knew something else was wrong, so we took him back to the hospital on September 10. That's when the real tests began.



# *September 2007*

Carson spent several weeks in the hospital being put through about every test you can imagine. A genetics consult revealed that Carson had microcephaly, decreased white matter per MRI, feeding problems, and respiratory distress. In addition, laboratory studies revealed that Carson had an extremely rare genetic disorder called Homocystinuria. We learned that there are many variations of Homocystinuria, and initial findings suggested that Carson's version was an MTHFR deficiency. This can be (although not always) associated with mental retardation, microcephaly, gait disturbances, seizures, vascular occlusions, and limb weakness. We began treatment immediately, which included a long list of daily and weekly medications, along with numerous physical, occupational, and eventually vision and speech therapies.

## June 2008 through December 2008

Nearly 9 months passed and we continued to treat Carson's genetic condition with the same regimen mentioned above. However, we soon started to notice Carson's eyes shifting and flickering whenever he tried to focus on something. This is called Nystagmus. Most kids have nystagmus when they are babies, but they eventually grow out of it. Carson was not growing out of it. Over the next few months we visited numerous ophthalmologists in Kansas, Missouri, Nebraska, and Boston. They all concluded that Carson has Maculopathy (retinal degeneration). Basically, Carson has scar tissue in the middle of his retinas that, to him, appear like black dots in the middle of his vision that he can't see around. Carson is technically legally blind, although he has enough peripheral vision to be mobile and active. Retinal degeneration can be progressive, so Carson continues to have annual ophthalmology visits at the University of Iowa Vision Clinic to measure how much the degeneration has progressed. Fortunately, at this point, it has not worsened.

# *June 2009*

We had been treating Carson for Homocystinuria due to MTHFR for more than 1 ½ years. But in early 2009 his doctors began seeing some inconsistencies with other MTHFR cases. This led to doubts about the original diagnosis. We discussed
our options and agreed to have some more tests conducted. We had already done everything we could in the United States, so these new tests had to be done internationally.

We initially sent Carson's bloodwork to Germany and Switzerland for tests, both of which came back inconclusive. Then we sent a skin sample to McGill University Health Centre in Canada. We received the results from that test in June 2009. These results suggested that Carson had a different version of Homocystinuria...not MTHFR. McGill concluded that Carson has a Cobalamin G deficiency (CblG).

CblG is even rarer than MTHFR. In fact, according to his doctors at the time, there were only 27 other identified cases of this deficiency in the world (Carson was #28). Common symptoms of CblG include poor feeding, vomiting, failure to thrive, cerebral atrophy, development delay, nystagmus, hypotonia, hypertonia, ataxia, seizures, and blindness. Carson had many of these symptoms at one point in his 2-year life.

The good news was that CblG is treated very similarly to MTHFR, so we only had to make a few dosage changes to some of his existing medications.

## 2010 – Today

We've continued to treat Carson with a daily and weekly regimen of medications and therapies, and he has made tremendous progress. He still has developmental delays,vision impairments, speech issues, and several other concerns, but he's doing much better than we had ever imagined. When Carson was first diagnosed the doctors said there were so few cases that they could not predict what his futurecould be. They said he might grow up with limited function, needing endless care, and never move out of our home. Or even worse, we might lose him before he even has a chance to grow up. Nobody knew, so we've continued torely on Carson to tell us how he is doing...all along giving give him the unconditional love, support, and every resource he needs to thrive.

# *HCU&You:Recipes from the Kitchen*

## *Jackfruit Kabobs*

150 g Canned Whole Jackfruit pieces, well rinsed

1/2 tsp Oil, Olive

1/2 tsp BBQ Seasoning

48 g Onion, Cut into chunks

60 g Peppers, Bell, all colors, raw, cut into chunks

95 g Mushrooms, white or brown (Crimini), medium, whole

90 g Squash, Summer (such as Zucchini), raw, slices

2 tsp Oil, Olive

1/2 tsp Garlic Powder 7

1 tsp Salt, Table

2 fl.oz. Barbecue Sauce

### *Instructions*

1. In a container with a lid, place the jackfruit pieces inside and toss with olive oil and bbq seasoning of your choice. Cover and refrigerate to marinate for 30 minutes.
2. Preheat grill to medium high heat. Toss remaining vegetables with olive oil and seasoning. Remove jackfruit from refrigerator. Push vegetables and jackfruit onto a skewer in any order. Place skewers on the preheated grill, cover, and cook for five minutes. Turn skewers over with tongs and baste with the barbecue sauce. Cook for one minute, turn, then baste the other side. Remove from grill and serve immediately.

**Notes**

*If using wood skewers, soak in water for at least 30 minutes prior to grilling to prevent burning.*

*Makes about 4 skewers.*

*Protein: 2 g per skewer*

## *Roasted Red Pepper, Cammus*

300 g Cauliflower, raw florets

2 tsp Oil, Olive

1/4 tsp Ground Cumin

1/4 tsp Smoked Paprika

1/4 tsp Salt, Table

60 g Roasted Red Peppers

1 1/2 tsp Oil, Olive

1 tsp Lemon Juice

1/4 tsp Garlic Powder

2 TBSP Speculoos Cookie Butter

1/2 tsp Sesame Oil

### *Instructions*

1. Turn oven on to 400 degrees. Line a baking sheet with foil and spray with nonstick spray. Set aside. Cut the florets in half. Toss with olive oil, cumin, and smoked paprika. Place on prepared baking sheet and place in preheated oven. Roast for 10 minutes then turn cauliflower over. Roast for another 10 minutes until the cauliflower can be easily pierced with a knife. Remove from oven and set aside.
2. In the bowl of a food processor with an S blade, add the roasted cauliflower, roasted red peppers, olive oil, lemon juice, and garlic powder. Blend until well combined
3. In a small bowl, add the cookie butter and sesame oil. Gently mix until combined. Add to the “hummus” in the food processor. Pulse until well blended. Add salt and pepper to taste, pulse to combine. Serve topped with a little olive oil, chopped roasted peppers. I added a sprinkle of Tuscan seasoning for added flavor.

**Notes**

*If you have Cambrooke’s Pea-not butter, you can use 2 tablespoons in place of the cookie butter mixture. May lower protein by 0.3g in whole recipe*

*Makes 7.5 servings*

*Serving: 2 Tbsp= 1.1g protein*

### *Asian Slaw*

2 c Cabbage, green, raw, shredded 44mg

1 c Shredded Carrots 40mg

1 TBSP Coconut Aminos 1mg

1 tsp Minced ginger 1mg

1/4 c Rice Vinegar

1/4 tsp Oil, Sesame

2 tsp Dried Green Onions 7mg

4 TBSP Oil, Olive

1/2 tsp Salt, Table

1/8 tsp Pepper, black 1mg

1/4 tsp Sugar, White Granulated

### *Instructions*

1. Place the shredded cabbage and carrots in a medium bowl.

2. In a 2-cup measuring cup add the remaining ingredients and whisk to combine. Pour over the shredded cabbage and carrots. Gently toss to combine. Refrigerate for at least 4 hours to allow flavors to marinate. Serve for your next cook out!
   **Notes**
   *1 oz serving = 0.3g protein*
   *11 servings total*

### *Instructions*

### *Chocolate Mousse*

5 oz (145g) Vegan Marshmallows (0.203g protein)

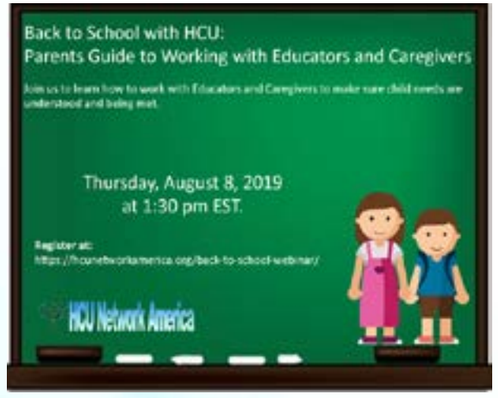
20 pieces (125g) Cambrooke Cha Chas, unwrapped (1.5g protein)

1 ½ cup So Delicious Original Coconut Milk (0.8 g protein)

1. In a small sauce pan add the marshmallows and the coconut milk. Place over medium heat and cook until marshmallows are completely melted and well mix with the milk. Stir frequently to prevent burning.

2. Place the chocolate cha cha's in a 4-cup measuring cup. Pour the melted marshmallow cream over the cha cha's and gently stir until all the chocolates have melted. Make sure it is well mixed. Pour into ramekins, or container of choice. I got three servings at 6.5 oz each with the glasses I used. Refrigerate for at least 1 hour. Garnish with whipped cream and chocolate shavings to serve.
   **Notes**
   *3 servings*
   *6.5 oz/ 180g per serving= 0.83g protein per serving!*

# *Upcoming Events*



Check out the fantastic list of event sponsors for our patient/family meeting. Thank you for supporting the HCU Community!

Make sure to register so you can check out what they have to offer at their booths in person at our conference.

### *Platinum*

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### *Bronze*

Abbott A Promise for Life

### *Supporter Level*

FLAVIS

# *HCU Hero Nominations*

HCU Network America

We are asking for nominations this year by the HCU community to help HCU Network America choose our HCU Hero Award recipient. The award will be presented at our national conference held October

**19-20, 2019 in Indianapolis, IN.**

The criteria for the award is that is goes to individuals at the pinnacle or toward the end of their career, recognizing their excellent body of work over a long time to improve the lives of people with HCU. They should have had a significant positive outcome along the way.

Previous awardees have included:

*2018: Dr. Harvey Levy*

To nominate someone qualified and deserving of the 2019 HCU Hero Award, please send an email to Danae' Bartke, Executive Director, at dbartke@hcunetworkamerica.org with the subject line noting: HCU Hero Award Nomination

Please provide their name, title and a brief summary as to why you feel they are deserving, including work history, volunteerism and other ways they have gone above and beyond for those with HCU.

**Deadline is Sunday, August 31st at 11:59 p.m. CST.**

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## HELP US TEACH PHYSICIANS ABOUT HOMOCYSTINURIA

***FACT!*** Teaching about metabolic diseases in medical school and residency programs is poor.
***FACT!*** Most patients live and die without a diagnosis being made, especially when the disease presents in adulthood.
***FACT!*** Patients cannot access effective therapies unless a proper diagnosis is made.
***FACT!*** The sooner a diagnosis is made and treatment begun, the better the outcome.

## WE NEED YOUR HELP!

We at VMP Genetics believe in the power of "patient-teaching" and are bringing patients and families into lectures and presentations - at conferences and in the classroom around the country. While doctors teach facts, patients tell stories. Story-telling is a more compelling teaching method with better recall over time than didactic lecturing. We also believe that doctors are more likely to make a diagnosis if they have already seen a patient and heard her/his story. Story-telling can be live or taped...

## WE ARE LOOKING FOR...

- ***Patients and/or family members who are interested in telling their stories in local medical classroom settings...*** We are developing a Patient Teacher Registry. If a medical school faculty member is looking to introduce the patient story in a teaching session, the Registry can tell him/her if there are patient-speakers in the area and what diagnoses they have.

- ***Patients and/or family members who are interested in having their stories videotaped...*** As we secure funding, we are interested in recording stories that reflect the broader patient experience. The more variety in the stories, the richer the learning potential.

- ***Videos of patients and families telling their stories...*** A 5-or 10-minute clip can be downloaded into a lecture about that disease or relevant biochemistry to enhance the learning potential of the session.

Please help us in our efforts to raise awareness about Homocystinuria through this innovative educational outreach to the medical community. To Volunteer or participate, or for more information about this project... please contact Jacob Athoe at PatientTeacherRegistry@vmpgenetics.com

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## *OT-58, Enzyme Replacement Therapy  Clinical Trial Recruitment*

Orphan Technologies has initiated a first in human (Phase 1) clinical trial of OT-58, an enzyme replacement therapy that addresses the underlying enzyme defect for patients living with classical homocystinuria. The goal of this trial is to evaluate the safety and efficacy of OT-58 in patients with classical homocystinuria and identify the appropriate dose. Patients between the ages of 12 and 65 years of age with classical homocystinuria may be eligible to join. For additional information on criteria for eligibility, please go to:

https://clinicaltrials.gov/ct2/show/NCT03406611?cond=Homocystinuria&rank=1
There are four sites in the US currently participating in the trial:
- Children's Hospital of Philadelphia – open to patient enrollment
- Boston Children's Hospital – open to patient enrollment
- Indiana University – open to patient enrollment
- Children's Hospital Colorado - open to patient enrollment

Payment for time and travel may be available to patients who participate in this trial.
To inquire about participation into the trial, please email: info@orphantechnologies.com


# *Contact Register*

**What is the contact register?**
The contact register is a secured private survey that allows you to share information on you or your family member with HCU with us. This includes where you are from, your relationship to homocystinuria, the patient's birthdate, gender, their exact diagnosis (e.g. CBS, cobalamin, or MTHFR), how they were diagnosed, and if the patient was diagnosed through newborn screening. This information is kept confidential and will not be shared unless you give us permission to. By registering, you will be also be able to identify other affected patients in your state and request their contact information, and you will be able to access information posted over time that can only be shared with the patient community. (For example, we may have webinars that the expert presenter does not want to be publicly available, but is willing to share with the HCU community.)

**What will this information be used for?**
HCU Network America strives to inform and provide resources for patients and families, create connections, and support advancement of diagnosis and treatment of HCU and related disorders. The information you provide helps us succeed in our mission, plan events, develop resources and educational tools, and ensure everything is being done to support timely and accurate diagnosis from birth. It also allows us to have informed conversations with doctors, pharmaceutical companies, and law makers. Your information helps us understand the landscape better so we can better advocate for you!

**How do I participate?**
The contact register form takes approximately 3-5 minutes to complete. You can find the form either by visiting our website and clicking on the "Contact Register" tab, or you can fill it out by going directly to:

**We'd like to thank the following content contributors:**
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*Fundraising Committee: Go the Extra Mile for HCU, Recap*