The HCU Herald

Featuring...

HCU Hero
Ari from NY

February 2025

All things Homocystinuria: patient stories, resources, research, events and more!

HCU HERO:
ARI FROM NEW YORK

I'd like to introduce one of the bravest and strongest young ladies I have ever known, my daughter, Ariella. Ari was born in January 1997. She entered this world from an uncomplicated pregnancy and a normal birth. My husband and I went home from the hospital with a beautiful, robust, healthy baby girl. Our hearts were bursting with pride and love. Upon reflection, I wish I had the knowledge then that I now possess; the knowledge that I was forced to acquire about Homocystinuria, to ensure the health and well-being of my sweet girl.

Ariella holds the diagnosis of Classical Homocystinuria. Unfortunately, she was not diagnosed until the age of twelve. Yes, a newborn screening was performed shortly after birth, but that simple little heel prick did not reveal any abnormalities. For whatever reason it may be, that missed diagnosis at birth made a tremendous impact on the direction of Ari's life, as well as the entire family. Anyone that holds the same diagnosis understands the daily challenges: diet, formula, medication, and supplements, and that's just the shortened list. Though, that missed diagnosis at birth continues to provide a framework of existence for Ari even now as she maneuvers through her adult life.

So, how did we arrive at such a rare diagnosis, and why so late? I can share with you that Ari had a fairly normal history as a baby. She reached all her milestones of rolling over, sitting, crawling, walking and talking within normal expectations. Her appetite was fine, and she was thriving, reaching into the higher percentiles for height and weight as she grew. Though, as time went on, we started to notice some questionable patterns.

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There were several indicators that something was not quite right with Ariella. One of the first things we started to notice were spontaneous fits Ari began to demonstrate as a toddler. Fits that were not easily soothed. Ari would cry and squirm, and we could do little to stop it. The fits would happen mostly later in the day, which I attributed to fatigue. Looking back, I am sure these fits were due to discomfort. Of course we visited the pediatrician, but no medical explanation at that time could explain why these fits were occurring.

As Ari entered preschool, it became apparent that her language development was beginning to slow. Ari was now having difficulty with verbal expression. She often chose not to speak in order to avoid the frustration of finding the right words. This pattern with language delays continued on into her primary years in public school. At this point, Ari was showing difficulties with receptive language skills, making reading and comprehension difficult. Of course, she fell well below grade level performance more and more as each year passed. Her expressive abilities continued to suffer as well, which manifested in weak speaking and writing skills. At this point I had to seek educational support for Ari officially through the special education services offered through the school system. Since Ari required such high support in school, she was placed in a special education programs starting in grade two, and continuing through her graduation from high school.

Ari began to wear eyeglasses as early as eight years old. It wasn't a problem at first, but at every annual eye doctor visit, her vision was reported to

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be quickly deteriorating. As parents, of course we were concerned. The eye doctor was equally concerned with Ari's vision and therefore was meticulous in monitoring her. It took years, but as Ari reached age twelve, I learned about lens subluxation. The eye doctor explained how the lenses in both of Ari's eyes were detaching and slightly dropping and this was the cause of the quick changes in Ari's vision. But why? How could this be happening? We were now even closer to diagnosis. Ari's eye doctor is really the initiating factor that led to her HCU diagnosis. I am tremendously thankful and ever grateful that this eye doctor was able to lead us to help for Ariella. The eye doctor suggested we seek the guidance of a geneticist, and that is what we did.

We live on eastern Long Island in New York. So, the choice of pediatric geneticists was limited to one. This doctor worked out of Stony Brook Children's Hospital and was very quick to give us an appointment. We first visited this doctor in April 2009, and this is the doctor that continues to treat Ari today. Ariella presented with mild scoliosis (starting at age 11), a history of special education, and dislocated lens. Upon examination, it was noted Ari had long limbs, fingers and toes. At this point, we were told that it was probable Ariella would be diagnosed with Marfan's Syndrome, a different genetic disorder with similar presenting symptoms. Though, after all blood test results were examined, we received the alarming news that our daughter was born with a rare genetic disorder called Homocystinuria. At diagnosis Ari's levels were extremely elevated. Her Homocystiene level was noted at 377. It was imperative that we return to the doctor to begin treatment immediately as she was at risk for thrombosis.

"We were told that it was probable Ariella would be diagnosed with Marfan's Syndrome, a different genetic disorder with similar presenting symptoms. Though, after all blood test results were examined, we received the alarming news that our daughter was born with a rare genetic disorder called Homocystinuria."

Needless to say, our household became a chaotic environment and all established routines were now gone.

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At this time, Ari was the second of three children, and all attention was focused on her. As hard as we tried to divide our attention between all three children, it always seemed like Ari needed us most. Treatment began: a combination of diet adjustment, medication (Cystadane), supplements, and formula were the beginning steps. Multiple ongoing doctor visits to the geneticist, dietician, hematologist, orthopedist, physical therapist, retinal specialist, and even a rheumatologist. Most things feel into place, but the most difficult piece to this treatment plan was the formula. Finding the right match seemed to be an endless task. Powders or liquids? We found ourselves mixing flavorings into the formula with juices, water, or drinks to find what would be most acceptable for our 12-year-old that already had a preferred established palate. With time, we discovered what worked the best for us.

Outside of the logistics of treatment, we had an equally important task of addressing the emotional side of diagnosis with Ariella. Imagine, at twelve years of age you are now told that you cannot consume most of your favorite foods: icecream, milk, cheese, pizza, cookies, and cakes, to name just a few. This was difficult for Ari. Initially, anger was often displayed. As a parent, I struggled with the guilt of withholding such enjoyable foods in place of protecting my child's health. Though, as time went by, we were able to find substitutions, and even new choices, to take the place of the foods Ari was used to eating.

As months passed and the treatment plan for Ariella became more natural, we were able to focus on other things. Ari had two eye surgeries to remove the dislocated lenses. She also had extensive physical therapy appointments for the scoliosis. We discovered foods and recipes that worked in Ari's diet. Consequently, Ari developed some autoimmune issues as well, Lupus being of priority.

Today Ari is a functioning young lady. She administers all her own medications and formula. She manages her own food and diet. Routine doctor's visits are necessary to monitor her levels. With great pride, Ari is very successful with holding her homocysteine level between 5-10. All-in-all, the shock of diagnosis has been

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replaced with confidence that we have the tools to maintain Ari's health. We cannot reverse the damage as a result of late diagnosis, but we can forge forward making decisions and choices that improve the quality of life for Ariella.

Ari's desire is to not be considered different from her peers, and this is how we raised her. She wants to be treated equally and fairly, and not with pity. HCU has left its mark on Ariella in several ways, though she continues to defy its presence. Even with Ari's limited cognitive ability, she earned her high school diploma. Ari works part-time and is highly respected by her colleagues. Ari has worked hard to acquire her driver's license. She enjoys shopping, playing video games, surfing the internet, visiting with family, and caring for her pet geckos.

More than 15 years have elapsed since Ariella's initial diagnosis. Those years have been filled with a lot of experimenting, learning, and challenges, setbacks, as well as successes. Though, I will never forget the immense fear of being told my child has a rare genetic disorder. It was often that I felt alone and had no one to turn to that could understand the plight of such a diagnosis. It is important to note that staying strong is important so that you can be the best advocate for your child. Along this journey, too often I was confronted with the ignorance of others in understanding Ari's diagnosis. Countless times it was necessary to explain and educate others about HCU, and repeat. Educating myself and having patience was the key to educating others.

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Witnessing my daughter evolve from an angry and confused child upon diagnosis, to a responsible, young adult that understands the consequences of her genetic disorder has been beyond rewarding. I marvel at her ability to persist with the strict requirements and demands of her diet, formula, and medications. Ari's fear of what could happen if she strays from her routines prevents her from doing so, but feeling good keeps her going. So, Ariella, my daughter, is an HCU Hero. She is brave and strong in spite of the challenges she has met, and she is prepared to tackle any obstacles she might come upon in the future. Come what may, I will be of support to her as best I can.

Click here to read Ari's and other patient stories on our webiste!

FOOTBALL SQUARES FUNDRAISER

FEBRUARY 9 6:30 PM ET

$10 PER SQUARE 4 CHANCES TO WIN!

$100 PAYOUTS 1ST-3RD QUARTER
$200 PAYOUT AT END OF THE GAME

TO PARTICIPATE:

1) VENMO: @TOM-HAWKINS-1
*LAST 4 DIGITS OF PHONE #: 1300

2) EMAIL TOM AFTER TO RECEIVE ACCESS TO BOARD!
TMMYHWK09@GMAIL.COM

ALL FUNDS RAISED SUPPORT HCU NETWORK AMERICA'S EDUCATION & OUTREACH PROGRAMS!

RESEARCH GRANT AWARDED

MEDIA RELEASE

For release: January 15, 2025

HCU Network America announces the recipient of its fifth research grant, awarded to the University of Fribourg in Switzerland. The funding will support the development of new therapies to treat classical homocystinuria. The research, led by Dr. Tomas Majtan, aims to develop a cell-based assay to assess CBS protein stability as a screen for pharmacological chaperones. Dr. Majtan is a senior researcher in the Department of Pharmacology at the University of Fribourg in Switzerland.

HCU Network America thanks the community of supporters whose contributions made this grant possible:

The Hummel Family

Margie McGlynn via
the Hempling Foundation for HCU Research
In memory of her sisters Judy & Susie

Team Dayton

Read about the research on the next page

RESEARCH GRANT AWARDED

Mechanism of action and impact of thiol homeostasis on efficacy of an enzyme replacement therapy for classical homocystinuria

Philipp TM, Bottiglieri T, Clapper W, Liu K, Rodems S, Szabo C and Majtan T

Redox Biology 77, 103383, 2024 (DOI: 10.1016/j.redox.2024.103383)

Classical homocystinuria (HCU) is a rare genetic disorder caused by a deficiency in the enzyme cystathionine beta-synthase (CBS). This enzyme is crucial for breaking down homocysteine (Hcy). Insufficient degradation of Hcy by CBS leads to its accumulation in the tissue and blood, causing various health issues, such as eye problems, skeletal abnormalities, blood clots, and cognitive impairment. HCU is typically treated by a restrictive diet low in methionine (an amino acid that converts to Hcy) and high doses of vitamin B6. However, these treatments are not always effective and especially the restrictive diet negatively affects the quality of life of HCU patients. We have developed and characterized a new potential treatment for HCU: a CBS-based enzyme replacement therapy (ERT) called pegtibatinase to compensate for the lack of CBS activity in patients suffering from HCU and to remove toxic buildup of Hcy in blood. This therapy has shown great promise in lowering Hcy levels in mouse models of HCU and it is now tested in HCU patients in clinical trials carried out by Travere Therapeutics.

Our latest study investigated how CBS (and consequently pegtibatinase as well) works in degrading Hcy and explored ways to increase its effectiveness. One key focus is on the role of accessibility of Hcy as it readily binds to itself and proteins in the blood and hence becomes unavailable for CBS (and potentially to pegtibatinase). We found that only free, reduced, protein-unbound Hcy can be broken down by CBS. Cells and tissues naturally export Hcy in its reduced form, which can then be efficiently degraded by pegtibatinase in the bloodstream. However, conditions in the bloodstream make the bulk of this exported Hcy oxidized by forming Hcy-Hcy aggregates or binding to plasma proteins. We also found that biological reductants, such as N-acetylcysteine, MESNA, and cysteamine, can liberate Hcy from its oxidized forms thus increasing its availability for degradation by CBS. Our experiments using a mouse model of HCU showed that co-treatment with these biological reductants significantly improved the efficacy of CBS-based ERT further lowering Hcy levels compared to those mice treated with ERT alone.

The study provides valuable insights into the mechanism of action of CBS-based ERT and highlights the potential of using biological reductants to enhance its effectiveness. This research represents a significant step forward in developing more effective treatments for classical HCU.

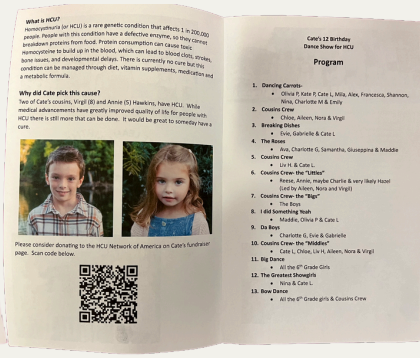
FEATURED FUNDRAISER

Virgil (age 8) & **Annie** (age 5), are siblings who live with **Classical HCU**. Virgil was diagnosed through Newborn Screening, as was his little sister Annie a few years later.

The Hawkins Family at the 2024 HCU Network America Family Conference in Aurora, CO

Last month, Virgil & Annie's cousin Cate celebrated her 12th birthday by holding a Dance Recital fundraiser in their honor!

The event was called "***Cate's 12th Birthday Dance Show for HCU***". Every girl in her 6th grade glass at St. Mary of Gostyn School was included and all the girls participated and/or donated. Cate held a "practice party" around her birthday in December where the girls came up with a big group dance and split up into small groups for additional dances. The actual show was on Jan 10th.



All of the Hawkins cousins (16 in total... including Virgil and Annie and Cate) also participated by dancing. There were 13 dances in total. All the 6th grade girls and cousins put in a lot of effort making up their dances and practicing. It was truly a kid's production!

Cate asked for Donations to HCU Network America in lieu of birthday gifts. It was a huge success. Cate and her family are very grateful for the generosity of all of the school families (as well as their own family too!)

Cate and her friends & family did an exceptional job, raising over $2,800!

Way to go Cate! Thank you for being an HCU Hero!

UPCOMING EVENTS

RARE DISEASE DAY IS COMING

Mark your calendars...

...for February 28, 2025!

One out of every 10 Americans is living with a rare disease.

Rare Disease Day takes place worldwide, typically on or near the last day of February each year, to raise awareness among policymakers and the public about rare diseases and their impact on patients' lives.

How can I participate on Rare Disease Day?

Share your story: Just by sharing your story with others, you're spreading awareness. Whether it's through social media, at school or at work, or in line at the grocery store, each interaction counts!

Wear your awareness: Wear one of your HCU Network America shirts or sweatshirts on Rare Disease Day! And when folks ask you about it, tell them a little bit about YOUR story living with HCU!

Attend an event: There are a number of in-person or virtual events that you can attend! Below are a few options - click each image to check them out and register!

FDA-NIH **RARE DISEASE DAY**
Feb. 27–28, 2025 | #RDDatFDANIH

NORD® National Organization for Rare Disorders

RARE DISEASE WEEK ON CAPITOL HILL

Registration is open!

Rare Disease Week on Capitol Hill empowers and inspires hundreds of advocates each year. The connections you make during the week will impact rare disease patients for generations to come.

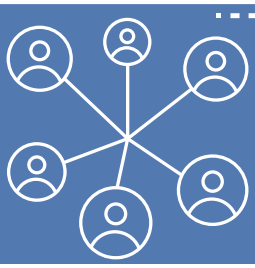
Hosted by the Rare Disease Legislative Advocates (a program of the EveryLife Foundation for Rare Diseases), this multi-day event brings together rare disease advocates from across the country to make their voices heard by their Members of Congress. Participants are educated on policy proposals impacting the rare disease community and provided opportunities to advocate for policy changes directly to their Members of Congress. No matter one's connection to rare disease or their advocacy experience level, all are welcome.

Click here to learn more, and to register to attend!

LET US KNOW!

Planning to attend?

We'd love to connect you with others in our community who will be attending!



Rare Disease Day is coming...

Grab your gear!

https://www.bonfire.com/store/hcu-haberdashery/

Order by February 5 to receive in time for Rare Disease Day!

HC&U Podcast

Meet your hosts!

Welcome to the HC&U Podcast!

We're Ben and Lindsey, your hosts. We are so excited to host this podcast as extra resource for the Homocystinuria community. We hope you like our content!

Read Ben's patient story here.

The latest episodes

Ben welcomes Curtis and Joy to the table!

Curtis is a Clinical Ethicist, with a background in Genetic Counseling. Curtis shares about who should have genetic testing, how to find a legitimate company, how it can help with differential diagnostics, treatment, and research, as well as how access impacts the patient and family.

Joy is the mother of our February HCU Hero, Ari. She shares her diagnostic journey, which includes genetic testing, as well as some updates on how Ari is doing today!

To Listen:

https://hcunetworkamerica.org/hcu-podcast/
or click your favorite option below!

LISTEN ON Spotify | LISTEN ON iHeartRADIO | Listen on Apple Podcasts | Listen on amazon music

HOMOCYSTINURIAS DATA COLLECTION PROGRAM

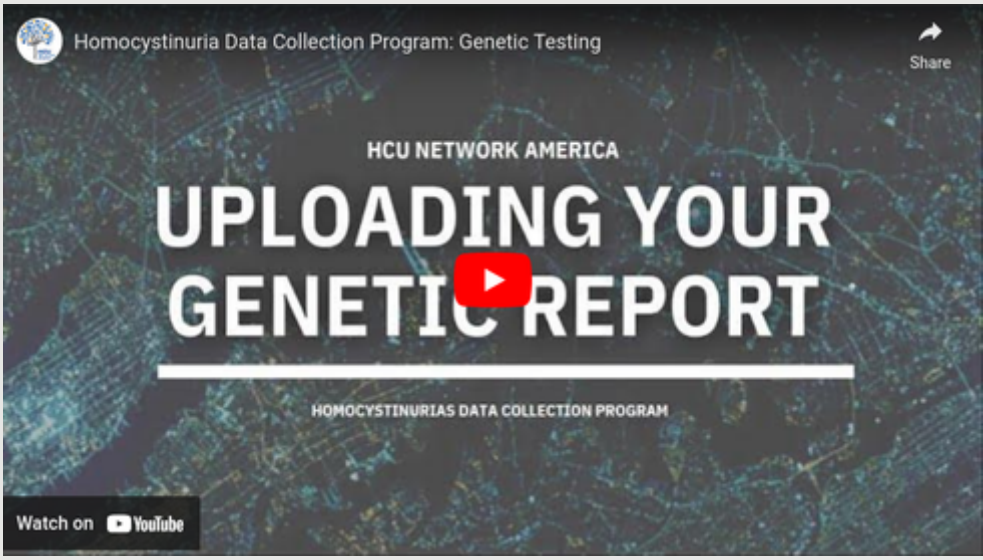
POWERED BY RARE X

UPLOADING YOUR GENETIC REPORT

Did you know a genetics report can help build a better understanding of homocystinuria?

Watch to find out:

- What is genetic testing?
- The components of a genetic report
- How I upload it into Rare-X
- Benefits of a genetic report
- Ways to get tested
- What you should expect



Upload your genetics report:
https://rare-x.org/homocystinuria/

CANPKU+ CANPKU+ HCU

HCU NETWORK AMERICA

HCU Network Australia

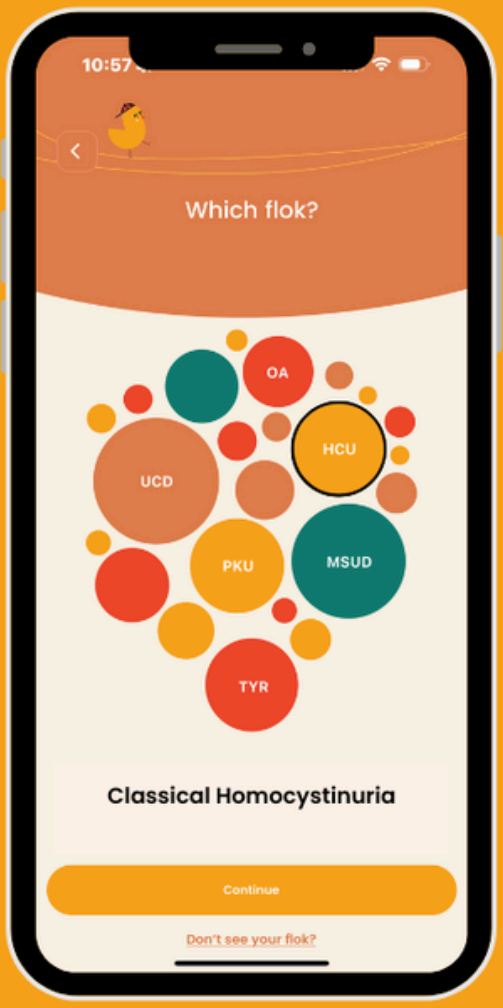
Start using the flok app today!

Welcome to the next generation of metabolic care for the CLASSICAL HCU COMMUNITY

The flok app is now in Open Beta in the United States.

Download at flok.org/app

flok



Big news!

The flok app is now in Open Beta, available for download to everyone in the U.S.!

Jump in and start exploring - the app helps you manage your diet and build a full picture of your metabolic health - including symptoms & moods, activity, medications, and lab tests.

Scholarship opportunity!

flok The Guthrie-Koch Scholarship

- **Do you have Classical HCU?**
- **Are you a *high-school senior* or *current student* pursuing an undergraduate degree or technical school?**

If you answered 'yes', you are eligible to apply for the Guthrie-Koch Scholarship Program!

The Guthrie-Koch Scholarship Program was founded in 1997 to recognize outstanding young adults with PKU pursuing higher education and provide financial support to these efforts, but has now been expanded to include young adults with Classical HCU and other metabolic disorders!

Click here to learn more and to start your application!

The application deadline is March 15, 2025.

Now Enrolling

Acappella

Sponsor: Travere Therapeutics
Study type: Natural History (no investigational medicine given)
Study duration: About 6.5 years
Goal: To learn more about classical HCU & the course of the disease

TO QUALIFY*	AGE OF PARTICIPANTS	DETAILS
Diagnosis of Homocystinuria due to CBS Deficiency (Classical Homocystinuria)	Currently enrolling 1 to 4 years old	The study will include three key stages (screening, enrollment, and observational follow-up) and will last approximately 6.5 years.

**Your child will need to meet all other study criteria to take part in the ACAPPELLA Study.*

Study Locations
United States: Colorado, Washington DC, Georgia, Pennsylvania
Countries outside of the US: Ireland and Qatar

Approximately 150 people aged between 1 and 65 will participate at sites in the US, Europe and other countries around the world.

150

The ACAPPELLA Study has already enrolled 100 adults and children over 5 years old, and is now looking for children aged 1 to 4 years old to take part.

You may be able to receive payment for time and travel if your child participates in this study.

Talk to your doctor and family members about your child joining the ACAPPELLA study.

Sites are open and currently enrolling participants. For the most current information about the ACAPPELLA Study and to see additional eligibility criteria, please visit:

https://www.clinicaltrials.gov/study/NCT02998710

If you have any questions, please email:

medinfo@travere.com

For more information, please scan the QR code or visit:

www.hcuconnection.com.

MA-PE-24-0008. Version 2.0; en-US; March 2024

TRAVERE THERAPEUTICS

Sign our NBS Screening Petition!

In this petition, we call for state newborn screening labs to **revise screening protocols for Classical Homocystinuria** to *ensure fewer false negative screening results and delayed diagnoses.*

Click here to sign the petition!

Get your kit!

Our FREE Customizable Kits are here!

Request yours today!

At HCU Network America, we believe that one of the most important steps to empowering patients and caregivers is giving them the support and tools needed to succeed! We know that a new diagnosis can be overwhelming and riddled with concerns and questions. To us, one way to combat those feelings, and give you the confidence you need, is by providing you with one-on-one support, educational resources, and practical tools, such as scales, cooler bags, and more! Our request for a kit survey allows you the opportunity to request a one-on-one introductory call (with more opportunities to connect), and then a customized kit to the patient's needs. Don't want a call or a Zoom? That's fine too - we are happy to send you the customized kit.

Request your kit now - **https://www.surveymonkey.com/r/HCUKitSurvey**

**Kits can only be sent to patients in the continental US. However, we are happy to connect virtually and share the educational materials with you via weblinks*!

Stay connected: Join our Contact Register!

What is a contact register?

- a secured private survey that allows you to share information on you or your family member with HCU with us. (general contact info, diagnosis, etc)
- kept confidential and will not be shared unless you permit us

Why join?

- subscribe to our monthly newsletter and other communications
- identify other patients in your state and request their contact information
- access information posted over time that can only be shared with the patient community
- helps us plan events and inform the development of resources and educational tools
- supports our advocacy efforts and enables us to have informed conversations with doctors, pharmaceutical companies, state newborn screening labs, and lawmakers.

I want to participate! What's next?

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:
https://www.surveymonkey.com/r/HCUContact

HOPE CONNECTS US

FOLLOW US