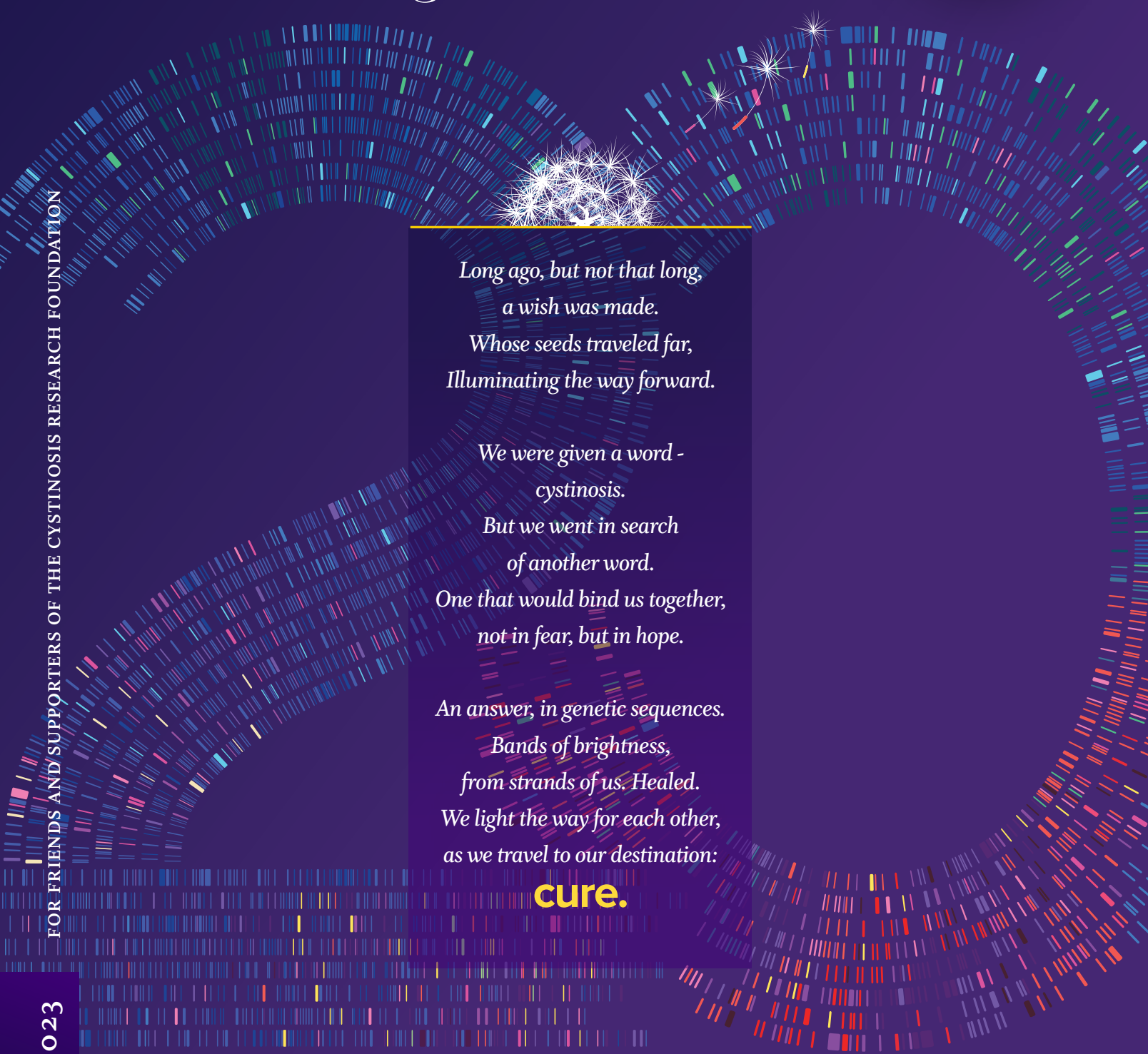
cystinosis magazine

OUR HISTORY IS A VICTORY IN THE MAKING



Long ago, but not that long,
a wish was made.
Whose seeds traveled far,
Illuminating the way forward.

We were given a word -
cystinosis.
But we went in search
of another word.
One that would bind us together,
not in fear, but in hope.

An answer, in genetic sequences.
Bands of brightness,
from strands of us. Healed.
We light the way for each other,
as we travel to our destination:

cure.

FOR FRIENDS AND SUPPORTERS OF THE CYSTINOSIS RESEARCH FOUNDATION

FALL 2023

CYSTINOSIS RESEARCH FOUNDATION THROUGH THE YEARS

2003

- Natalie Stack Morgan made a wish on the eve of her 12th birthday, "to have my disease go away forever."
- The Cystinosis Research Foundation was established with the sole purpose of raising funds to find better treatments and a cure for cystinosis.

2008

- First CRF International Research Symposium

2013

- FDA approval in 2013 for a delayed-release form of cysteamine. CRF funded every early clinical study that led to the discovery of the delayed-release form of the medication now known as Procysbi®.
- First patient pilot study for an allogeneic stem cell study at UCLA.

2018

- FDA approval on December 19, 2018 for first autologous stem cell and gene therapy clinical trial to test a new treatment for cystinosis.

2019

- First patient in stem cell and gene therapy clinical trial transplanted on October 7, 2019.

2020

- Second patient in stem cell and gene therapy clinical trial transplanted on June 29, 2020.
- Third patient in stem cell and gene therapy clinical trial transplanted on November 16, 2020.

2021

- Fourth patient in stem cell and gene therapy clinical trial transplanted on November 15, 2021.
- CRF partnered with Sanford CoRDS to create the new Cure Cystinosis International Registry *(CCIR),* the only international cystinosis patient registry in the world.

2022

- Fifth patient in stem cell and gene therapy clinical trial transplanted on March 29, 2022.
- Sixth patient in stem cell and gene therapy clinical trial transplanted on October 24, 2022.
- CRF Presents at IPNA pre-Congress Cystinosis Session in Calgary, Alberta, Canada, and hosts the first Family Conference.

2023

- CRF hosts the 8th Annual Cystinosis International Research Symposium in Irvine, CA, fostering continued innovation by connecting CRF researchers from around the world.
- Novartis purchases the cystinosis gene therapy program from Avrobio, guaranteeing the final phase of the stem cell transplant trial will soon become a reality.

FALL 2023

The Cystinosis Research Foundation has been building up to this moment for 20 years. With the persistence of CRF-funded research and a steadfast group of families, we are finding ways to restore the CTNS gene sequence in people affected by cystinosis.

Collectively, we are these strips of light coming together to change how we live with cystinosis. Our scientific pursuit and our strength to find courage are equally unwavering.

CONTACT US:
Please send suggestions and comments regarding *Cystinosis Magazine* to *nstack@cystinosisresearch.org.*

To subscribe to our 2024 online *Cystinosis Magazine* visit *www.cystinosisresearch.org/cystinosis-magazine-sign-up* or email *info@cystinosisresearch.org.*

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cystinosis RESEARCH FOUNDATION

Cystinosis Research Foundation
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Irvine, California 92612

949 223 7610

The mission of the Cystinosis Research Foundation is to find better treatments and a cure for cystinosis by supporting bench, clinical and translational research. Since 2003, CRF has raised over $68 million for cystinosis research in an effort to find a cure.

cystinosis RESEARCH FOUNDATION

WELCOME

ANNOUNCEMENTS

FAMILY STORIES

RESEARCH NEWS

CYSTINOSIS MAGAZINE IS A PUBLICATION OF THE CYSTINOSIS RESEARCH FOUNDATION

The Cystinosis Research Foundation is a nonprofit, tax-exempt entity pursuant to Section 501(c)3. Federal Tax ID #32-0067668.
100 percent of your donations go to support cystinosis research. All gifts are tax deductible as allowable by law.
The entire cost to produce and mail the magazine are underwritten by an anonymous donor.

Just as ripples spread out when a single pebble is dropped into water, the actions of individuals can have far-reaching effects.
DALAI LAMA

NOVEMBER 2023

Dear Family and Friends,

We are concluding our 20-year anniversary with fanfare and good news! It has been another year of funding promising research studies and reaching new milestones — all of which are cause for celebration!

Not a day goes by that we do not think about you – our family and friends – who are the reason CRF has been so successful. It is your commitment to our children and adults with cystinosis that has allowed us to reach milestones once unimaginable. Your unwavering support of CRF and our research program throughout the years has created one of the greatest success stories in the history of rare disease research.

The Cystinosis Research Foundation was launched the day Natalie Stack Morgan wrote her birthday wish on a napkin – "to have my disease go away forever." Natalie's wish was the first pebble that created the ripple that has connected and unified the cystinosis community in their common purpose: to find a cure for cystinosis. Her simple but profound wish has reached thousands of people who have become part of the CRF community. Our lives have been immeasurably enriched by your love, support and commitment to our community.

In stark contrast from when CRF was founded in 2003, the life of a patient and family with cystinosis was different from today. Then, 20 years ago, there were only a handful of researchers in the world. You helped change all of that. Your support has allowed us to fund multi-year studies that have, in turn, allowed researchers to commit to a career in the field of cystinosis. Of course, to support research, we had to raise the funds to award research grants. With your help, we have raised over $68 million for cystinosis research. CRF is leading the charge to new treatments and a cure for cystinosis. We have funded 228 research studies in 12 countries.

The CRF community has single-handedly created a dynamic, collaborative global research community. You have been by our side ensuring our success and trusting that we will find better treatments and a cure for cystinosis. Those two lofty goals have become a reality. CRF's commitment to research has led to two FDA approvals, multiple clinical trials, and numerous new discoveries about the pathogenesis of cystinosis.

CRF was started by our family, but early on we were joined by other families, and today we are clearly not alone. We are surrounded by this extraordinary community of families and friends around the world who have one purpose – to support those they know and love with cystinosis. We have soared to new heights; we have given hope to families and patients. Our community knows no bounds; the goodness that you have exhibited is another ripple in the cystinosis world, touching lives and ensuring hope is never far from our minds and hearts. We are forever grateful for your support. We have experienced a life of gratitude, community and purpose because of you.

This issue of *Cystinosis Magazine* promises to warm your heart with new and updated family and patient stories. I am always impressed and moved by the beautiful and inspiring stories we receive from our community. We also are featuring in-depth interviews with three CRF researchers. We have a special interview with Corinne Antignac, MD, PhD, the current chair of the CRF Scientific Review Board and whose research lab in Paris discovered the cystinosis gene among other significant discoveries. We have a feature article with Stéphanie Cherqui, PhD, who discovered the stem cell and gene therapy treatment for cystinosis and is forging potential new treatments for other diseases. We also have an interview with Jennifer Hollywood, PhD, whose promising work might lead to a better treatment for cystinosis. Please read their interviews and learn more about their work starting on page 24.

CYSTINOSIS – A DISEASE THAT AFFECTS EVERY CELL

Cystinosis is a rare, progressive genetic disease that affects every cell in the body. It is characterized by the accumulation of an amino acid, cystine, in all tissues and organs of the body including the kidneys, eyes, liver, muscle and brain. As the disease progresses, so do the complications from cystinosis. The first organs affected are the kidneys and eyes. Most people with cystinosis need a kidney transplant in their teen years. In the second decade of life, bone abnormalities and ocular cystinosis become a challenge for many people with cystinosis. Cystinosis is managed by taking an average of 9-12 different medications every day just to stay alive; there are no days off. The side effects from the medications are horrific and make it difficult for patients to comply. CRF is giving hope to our children and adults with cystinosis by funding research in every area of the body that is affected by this disease.

CRF 8TH INTERNATIONAL RESEARCH SYMPOSIUM

One of the greatest honors for us is to be in a room filled with CRF-funded researchers who are discussing and sharing their research progress on cystinosis. It is a dream come true! That is what it was like at the 8th International Cystinosis Research Symposium. The symposium was organized by three co-chairs: Corinne Antignac, MD, PhD; Julie Ingelfinger, MD; and Stéphanie Cherqui, PhD.

The conference was attended by CRF-funded researchers from seven countries who gave presentations about their work and progress. The high level of science was impressive and stimulating. Every presentation made represented an area of study that was essential to understanding cystinosis. Presentations were made about basic research, using new medications as possible therapies, early clinical trial data and updates on the stem cell trial. The years of CRF funding were all in one room – from bench to bedside; many of the early studies have been or will be soon translated to clinical trials. It was astonishing to see the progress since the last symposium in 2020.

The two-day symposium allowed CRF researchers to present their research studies and progress, explore new ideas, and form collaborations to advance and accelerate new research ideas. We were honored to have Liang Feng, PhD, from Stanford University, give the keynote address, "The Structure, Mechanism, and Dynamics of Cystinosin" based on his recent, highly acclaimed work published in *Cell*.

We are grateful to the CRF-funded researchers for their dedication to finding better treatments and a cure for cystinosis.

RESEARCH NEWS

CRF FUNDS $959,550 IN NEW RESEARCH GRANTS

One reason our community has so much hope is that CRF has created a synergistic, international research community that is working around the clock to find better treatments and a cure for cystinosis. CRF's policy of reviewing research applications twice a year ensures that there are no gaps in the research cycle and that donations are being put to work throughout the year.

CRF is proud to share that the 2023 Spring CRF grant award recipients were collectively awarded $959,550 for their research studies. The five research studies focus on understanding more about the pathogenesis of cystinosis as well as possible new treatments for cystinosis. These newly-funded studies will add to the breadth of knowledge about cystinosis that will assuredly open doors for other researchers to better understand cystinosis. Please read the lay abstracts for the new studies on pages 40-43.

THE DRIVING FORCE - CRF SCIENTIFIC RESEARCH BOARD

The outstanding research we fund only happens because of the CRF Scientific Review Board (SRB). We are grateful to the nine CRF SRB members for their leadership and guidance. The SRB has been led by Corinne Antignac, MD, PhD, for the past 12 years. Dr. Antignac has announced her resignation from the SRB beginning next year. We will miss her contributions and knowledge; she has done an extraordinary job leading the CRF research program and it has been under her leadership that we funded two research projects that have led to FDA approval. We have a special interview with Dr. Antignac as we wish her well and thank her for her commitment to CRF and to the global research community.

With gratitude, we thank the entire CRF SRB for their dedication to CRF. Together, they have created a vibrant research community. Join us in thanking the SRB members: Corinne Antignac, MD, PhD; Sergio Catz, PhD; Stéphanie Cherqui, PhD; Francesco Emma, MD; Laurence Greenbaum, MD, PhD; Paul Grimm, MD; Julie Ingelfinger, MD; Stephen Jenkins, MD; and Aude Servais, MD, PhD.

LOOKING FORWARD TO 2024

DAY OF HOPE 2024

We are excited to announce that after 13 years in Newport Beach, California, we are moving south to San Diego, California! The family conference will be held at the Catamaran Resort Hotel just steps from beautiful Mission Bay, beginning Thursday, April 4, through Saturday, April 6, 2024.

We have an amazing group of CRF board members who are co-chairing the 2024 conference. They are: Jill Emerson, Clay Emerson, Stephen Jenkins, Kristen Murray and Brian Sturgis. They have planned and organized an exciting conference that will blend learning more about CRF-funded research with plenty of time for families and those with cystinosis to connect and spend time together to celebrate our community and to acknowledge the challenges we face. The Co-Chairs look forward to warmly welcoming you to CRF's 2024 Day of Hope Family Conference.

NATALIE'S WISH

We will dedicate the month of April 2024 to raising awareness about cystinosis and raise funds to support new cutting-edge research grants that will bring new hope to the cystinosis community. Much work remains in our effort to bring new and improved treatments for cystinosis to the patients. We strive to support research that seeks new therapies and will bring new understanding to areas of cystinosis research that are understudied.

CRF's strategy of funding studies at their inception, giving researchers the opportunity to successfully test their theories, has helped CRF researchers and scientists seek grants from other funding sources, thereby leveraging CRF's initial grant awards. Our strategic approach to research and our emphasis on collaboration has accelerated research and has expanded the field of cystinosis. CRF-funded researchers have published 108 articles in prestigious research and medical journals. Our success is a direct result of your support and partnership with us to fund research that will lead to a cure.

>>>>

CRF RESEARCH LEADS TO NEW DISCOVERIES IN OTHER DISEASES INCLUDING ALZHEIMER'S

We set out to find better treatments and a cure for cystinosis and while making discoveries and finding new treatments for cystinosis; in the process, we have also positively impacted other disease communities. Discoveries made by CRF-funded researchers are being applied to other disease groups including Friedreich's Ataxia, Danon disease, corneal diseases, kidney diseases, and genetic and systemic diseases like cystinosis.

In a recent breakthrough study published in Cells Report, Stéphanie Cherqui, PhD, professor at UC San Diego School of Medicine, demonstrated that transplanting hematopoietic stem and progenitor cells was effective in rescuing multiple signs and symptoms of Alzheimer's in a mouse model of the disease. Dr. Cherqui revealed that, "Our work shows that hematopoietic stem and progenitor cell transplantation has the potential to prevent complications from Alzheimer's and could be a promising therapeutic avenue for this disease." This new discovery is a result of her work on cystinosis – we are changing lives and giving hope to people beyond the cystinosis community.

STEM CELL AND GENE THERAPY CLINICAL TRIAL UPDATE

IN THEIR OWN WORDS - THE FIVE CYSTINOSIS VOLUNTEERS SHARE THEIR STORIES

As reported last year, all six patients who participated in the FDA-approved stem cell and gene therapy clinical trial were transplanted last year. For the next several years, as part of the FDA protocol, those patients will be followed by Dr. Stéphanie Cherqui and her team at UC San Diego.

In 2007 when CRF issued their first grant to Dr. Cherqui, we had no idea where the research would lead. There were so many uncertainties, risks, and unknowns, but with Dr. Cherqui at the helm, we persevered, survived the setbacks, celebrated the successes and reached that stunning milestone - a clinical trial to test a new treatment that could be the cure for cystinosis.

It was CRF's seed money and subsequent grants totaling over $6.1 million that launched this life-changing project that we hope will be a cure. CRF has been the driving force for all cystinosis research and advances in treatment.

We are so thankful to the five patients who participated in the trial and who risked their lives for the broader cystinosis community. We are honored to share their personal stories about the clinical trial – the good, the difficult and their feelings about their lives today. We have learned so much from them and we will continue to learn more as they remain committed to the clinical study.

A heartfelt thanks to Jordan Janz, Jacob Seachord, Tyler Joynt, Natalie Stack Morgan and Kurt Gillenberg, who have been so open and transparent about their journeys. Their stories will move you because of their honesty and will warm your heart because of their gratitude. Please read their stories beginning on page 14.

The next phase of the clinical trial will be run by Novartis, who bought the cystinosis gene therapy program from Avrobio. We will continue to monitor the program and will advocate on behalf of the cystinosis community that the next phase begins as soon as possible and that the treatment becomes available to all those with cystinosis throughout the world.

HERE COMES THE BRIDE – NATALIE IS MARRIED!

Like others with cystinosis, everyday life for Natalie does not involve any days off – even after a stem cell treatment. Although Natalie had the stem cell transplant in 2022, she got COVID-19 early in the transplant process during a critical time for engraftment, and that disruption caused her cystine levels to rise enough so that she is now on a very low dose of cysteamine. Not the news we wanted to hear or what we expected. Nevertheless, it is Natalie's reality, and one that she has accepted with her usual grace and determination. Although her medical care looms, she has more important things to think about – her recent wedding and starting her life with Danny. We joyfully celebrated Natalie and Danny's wedding with family and close friends on October 21, 2023.

Weddings are a special time for families. The symbolism of your child leaving their family and starting a new life with their partner is an emotional moment. Jeff and I were flooded with so many memories of Natalie growing up, from her early baby days through college and grad school to meeting Danny and falling in love. What was also part of so many of our memories was life with cystinosis. There was never a time that we could forget about cystinosis, but we learned to live with it and to not let it dominate Natalie's life or ours. We discovered early on that through such sadness of the diagnosis and prognosis, we could find joy — yes, joy — from our grief of an unexpected life. We met all of you, you became part of our family. You have cried with us, you have celebrated with us, you have lifted us up, and by your support, you have encouraged us to keep going and never give up.

Our gratitude for your love, support, kindness and commitment to all our children and adults with cystinosis is endless. With your support we have funded studies that have led to two FDA approvals, numerous clinical trials, and significant discoveries about cystinosis — all of that has put us one step closer to the cure. It has taken a village to accomplish the milestones CRF has reached, and what a village we have – every single one of you is part of our village!

Thank you for being part of the Stack family, the CRF family and our cystinosis community. We are forever grateful to you for supporting Natalie, and our beloved community.

With heartfelt thanks and gratitude,

Nancy & Jeff

A Note from Natalie Stack Morgan

I am happy to share that I recently got married to my wonderful husband, Danny, on October 21, 2023. It was a magical day and we were surrounded by our close friends and family. We still live in Chicago and we are getting ready for the cold winter days! Our dog, Wesley, loves the weather there and has made lots of friends in our neighborhood. We are enjoying our time in Chicago but hope to come back to California in the future to settle down and start a family of our own.

I still work at Brightpoint (formerly Children's Home and Aid) where I work with the Illinois Department of Children and Families as a child welfare social worker. I work with children and families to assist them in reunifying as a family. It is hard work and emotionally exhausting, but I am learning and growing in my career every day.

I had the stem cell and gene therapy transplant a year and a half ago. I continue to do my clinical trial testing every six months and it is grueling to say the least. The exams include blood draws, painful eye exams, mole mapping, skin confocal test, a rectal biopsy, skin biopsy, grip strength test, neurological functioning tests, bone density test, pulmonary function test, and a 24-hour urine collection. Though demanding on my body, I know that the results are an important way to measure the success of the transplant and engraftment.

My results have not been as good as I had hoped they would be by now, but I know that the transplant is working; my body is just taking a bit longer to heal given that I had COVID-19 shortly after my transplant in 2022. It is emotionally exhausting to think about, but it is important for me to look at the silver lining of it all- I was able to go through with the clinical trial because I was healthy enough to endure the trial. I know that I am paving the way for better treatments for others. The continued testing and knowledge from Dr. Cherqui's team assures me that the engraftment is working, just taking longer. I am hopeful that my body will continue to respond to the new stem cells and that my results will improve.

As I get older, I know that my body is deteriorating, but with the stem cell transplant, I hope it is slowing the process. What I know is that with research and support from our community, I will live a longer life than what was expected years ago.

I want to thank the CRF community for their determination and dedication to raising money so that we could support research to find better treatments and a cure for cystinosis. Your support made the stem cell trial a reality. The fight is not over, but I know that our supporters and community will continue to make my wish a reality.

I am so fortunate to be where I am today in my life and it is because of the cystinosis community who has given me a second chance in life. I am beyond grateful to each and every one of you who not only helped save my life but many other lives as well and will help save the lives of those who will be affected by this disease in the future. Thank you for never giving up and for making my wish — to have my disease go away forever — more certain than ever.

Love,
Natalie

What is cystinosis?

Cystinosis is a rare, inherited, metabolic disease that is characterized by the abnormal accumulation of the amino acid cystine in every cell in the body. Buildup of cystine in the cells eventually destroys all major organs of the body, including the kidneys, liver, eyes, muscles, bone marrow, thyroid and brain. Medication is available to control some of the symptoms of this terrible disease, but cystinosis remains incurable. Cystinosis affects approximately 600 people, mostly children, in North America, and about 2,500 people worldwide.

It is one of the 7,000 rare, or "orphan" diseases in the United States that collectively impacts approximately 30 million Americans.

Federal funding for research on cystinosis and other rare diseases is virtually non-existent and most pharmaceutical companies remain uninterested because financial rewards are too small. Yet, while there are only a small number of patients who suffer from any given "orphan" disease, knowledge gained by studying one disease often leads to advancements in other rare diseases and more prevalent and well-known disorders.

Our story

In 2003, Natalie Stack Morgan made a wish on the eve of her 12th birthday, "to have my disease go away forever." That same year, the Cystinosis Research Foundation (CRF) was established with the sole purpose of raising funds to find better treatments and a cure for cystinosis.

Today, CRF is the largest fund provider of grants for cystinosis research in the world, issuing 228 grants in 12 countries.

CRF has raised more than $68 million, with 100% of your donations going to support cystinosis research. CRF's efforts have changed the course of cystinosis and given new energy to its investigators and scientists. CRF's commitment to research has given hope and promise to the global community of cystinosis patients and their families.

cystinosis RESEARCH FOUNDATION | TOGETHER WE SHINE BRIGHT

20 years

CHARITY NAVIGATOR ★★★★ Four Star Charity

Platinum Transparency 2022 Candid.

CRF GLOBAL OUTREACH – 12 COUNTRIES

AUSTRALIA	IRELAND
BELGIUM	ITALY
CANADA	NETHERLANDS
FRANCE	NEW ZEALAND
GERMANY	SWITZERLAND
INDIA	UNITED STATES

100% OF YOUR DONATIONS DIRECTLY **SUPPORT CYSTINOSIS** RESEARCH

We celebrate our CRF community and are grateful every day for your support.

Since 2003, CRF has:

RECEIVED **1 FDA-Approved Drug, and 1 FDA-Approved Clinical Trial**

FUNDED **228** **Multi-Year Grants** in 12 Countries

PUBLISHED **108** **Articles** in Prestigious Journals by CRF Researchers

RAISED MORE THAN **$68 Million** for Cystinosis Research

To date in 2023 CRF

AWARDED **5** **New Research Grants in 4 Countries** *(Canada, Italy, Switzerland and the United States)*

Totaling More Than $959,550 and

PUBLISHED **4** **Articles in Prestigious Journals by CRF Researchers**

CRF's highly strategic approach to funding has resulted in two FDA approvals and several human clinical trials. The research dollars we have invested have been leveraged by over $28 million in grants from other funding agencies. Not only does CRF research help our community, but our discoveries are applied to more prevalent diseases and disorders. CRF-funded research has the potential to help millions of others.

We want to thank our families, friends and donors who have remained steadfast in their commitment to finding better treatments and a cure. Thank you to the cystinosis researchers and scientists who are working around the clock on behalf of our children and adults with cystinosis.

You have changed the course of cystinosis...Thank You!

CYSTINOSIS RESEARCH FOUNDATION

DAY OF HOPE

SAN DIEGO, CA

FAMILY CONFERENCE 2024

Registration Is Open

Please join us at the
2024 Day of Hope Family Conference

Thursday, April 4 — Saturday, April 6, 2024

Catamaran Resort Hotel and Spa
San Diego, California.

Gather together with friends, families and researchers. **Gain** insight into the research that is improving the lives of children and adults living with cystinosis. **Celebrate** the strength and hope of the cystinosis community and the amazing progress that we have made.

Key Events

Thursday, April 4th

Conference begins late afternoon with introductions and a welcome dinner.

Friday, April 5th

All-day sessions followed by a special 'dinner under the stars' celebration.

Saturday, April 6th

Morning sessions followed by a culminating luncheon.

Conference presenters will speak on a broad range of topics including stem cell progress, innovative new treatments, and cutting-edge research.

Confirmed speakers include:

Stéphanie Cherqui, PhD
Paul Grimm, MD
Larry Greenbaum, MD, PhD

Complimentary childcare program is available for infants and children up to age 12. A special program is planned for teens!

Join us for a weekend of community, inspiration and hope.

This year's co-chairs,
Clay Emerson, Jill Emerson, Dr. Stephen Jenkins, Kristen Murray, and Brian Sturgis,
look forward to warmly welcoming you to CRF's 2024 Day of Hope Family Conference.

cystinosis RESEARCH FOUNDATION | TOGETHER WE SHINE BRIGHT

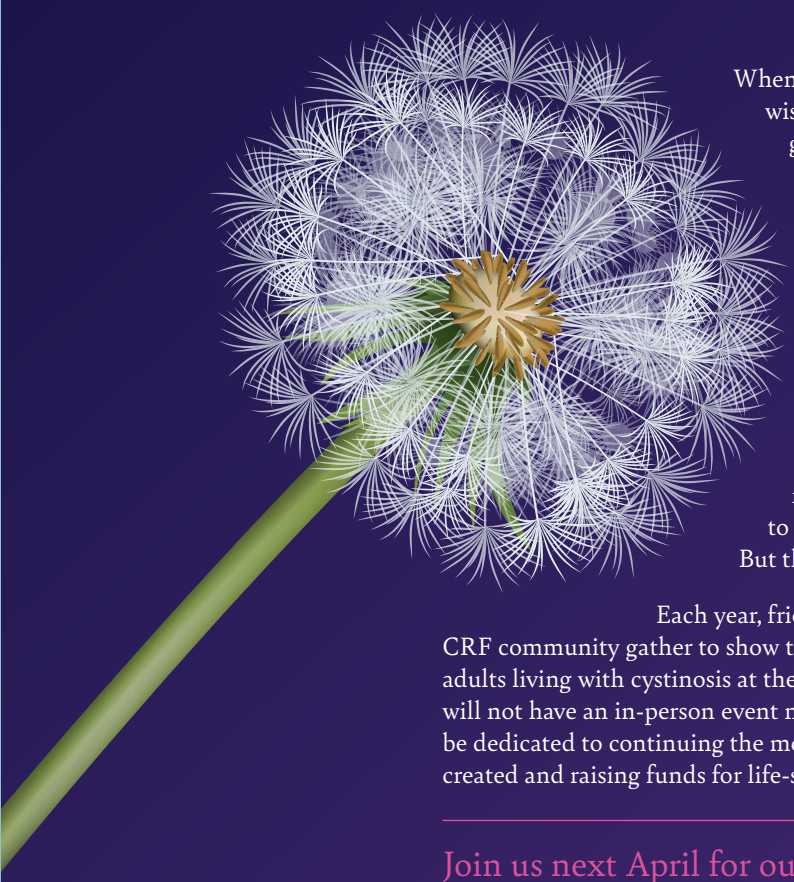
REGISTER TODAY!
www.cystinosisresearch.org/day-of-hope-2024

Questions? Email: ***info@cystinosisresearch.org***

APRIL 2024 MONTH-LONG FUNDRAISER

Natalie's WISH

Much more than a wish. 2024



When Natalie Stack Morgan wished for her "disease to go away forever" on her 12th birthday, few of us could have imagined the innovation, progress and hope her wish would inspire. 20+ years, 228 research studies and two FDA approvals later, Natalie's Wish has transformed into something so much more than a wish – a community, a support system, a research powerhouse and a movement to create a world without cystinosis. But there's so much more to be done.

Each year, friends, families and supporters of the CRF community gather to show their commitment to our children and adults living with cystinosis at the Natalie's Wish fundraiser. Though we will not have an in-person event next year, the entire month of April will be dedicated to continuing the momentum Natalie Stack Morgan's wish created and raising funds for life-saving cystinosis research.

Join us next April for our month-long fundraiser to celebrate over 20 years of impact and ring in a new era of progress for the cystinosis community.

Because at the end of the day, Natalie's Wish is our wish. It fuels our dedication and determination to find better treatments and a cure for cystinosis, and we won't stop until we do.

Watch the mail for this opportunity to fund the cure!

SINCE 2016, CANADIAN FAMILIES HAVE FUNDED $1,284,262 FOR RESEARCH IN PARTNERSHIP WITH CRF

Canadian cystinosis families are committed CRF partners working with CRF to fund research that will lead to better treatments and a cure. Families across Canada continue to organize and plan events to raise money for research. To date in 2023, Canadian families raised $52,808 (CAD) for cystinosis research.

The Cystinosis Awareness and Research Effort (CARE) has partnered with Canada Helps to establish the Canadian Cystinosis Research Foundation. This fund is administered by Aqueduct Foundation and allows for an efficient and effective fundraising process, ensuring that Canadians who donate will receive a charitable tax receipt. Canadians also have the option to donate directly to CRF if they so desire, however, no charitable tax receipt will be issued.

When it comes to finding a cure, there are no country borders!

Working together, our two countries have united efforts to raise awareness about cystinosis, to advocate on behalf of all children and adults with cystinosis and to ensure that we will fund the most qualified researchers in the world.

Since 2016, Canadian families have funded $1,284,262 in grant installments for CRF research studies through the Aqueduct Foundation. CRF is grateful for the support of our Canadian cystinosis families and friends who work tirelessly to find better treatments and a cure for cystinosis.

Canadian families are creative in their organization of fundraising events, supporting CRF research through everything from lemonade stands to bake sales to golf tournaments, building their sense of advocacy and community engagement and having fun along the way.

If you are Canadian and want to donate or raise money for CRF sponsored research, contact one of our CRF Board Members for information.

Barbara Kulyk at *barbiekulyk@hotmail.com* or

Kristen Murray at *murraykristen@hotmail.com.*

Thank you Canada

The following grant payments were funded in 2023 by donations from Canadian Families through Aqueduct Foundation totaling $272,500

Sergio Catz, PhD (Mentor)
Danni Chen, PhD (Fellow)
THE SCRIPPS RESEARCH INSTITUTE
LA JOLLA, CALIFORNIA

"Novel mechanistic and translational studies of inflammation in cystinosis"

$75,000

Sergio Catz, PhD (Mentor)
Aparna Shukla, PhD (Fellow)
THE SCRIPPS RESEARCH INSTITUTE
LA JOLLA, CALIFORNIA

"Translational approaches to repair chaperone mediated autophagy in cystinosis"

$75,000

Liang Feng, PhD
STANFORD UNIVERSITY
PALO ALTO, CALIFORNIA

"Investigating the molecular basis of protein dynamics in cystinosis"

$122,500

Cure Cystinosis International Registry

Our Link Between Patients and Researchers

By Clay Emerson, PhD, PE, CFM

Brooke Emerson's dad, CRF Trustee, and CCIR Committee Member

Hammonton, New Jersey, USA

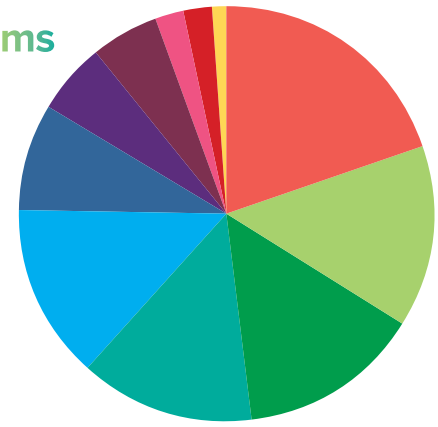
The Cure Cystinosis International Registry (CCIR) was launched in the Spring of 2021. The new registry features revised questions reflecting the ever-evolving treatment of the disease. Patients and caregivers who may have completed the original registry (pre-2021) are encouraged to register for the new registry. To keep the registry data current, all participants are encouraged to update their responses periodically as their treatment and symptoms may change over time.

In less than three years, patients from 15 countries have participated in the registry. The registry also includes patients representing 24 states across the United States. The importance of the registry cannot be overstated, as it provides a critical link between patients and researchers. Due to the ultra-rare nature of the disease and the myriad of complications the disease presents, progress towards improved treatment and an ultimate cure for cystinosis is only possible with the valuable input from our small patient community.

The Trials and Tribulations of Diagnosis

As an ultra-rare disease, cystinosis is exceedingly difficult to diagnose. Although research suggests that cellular-level malfunction and damage likely begins in utero, children born with cystinosis have a normal gestation and birth. Despite the still invisible symptoms of cystinosis, children are typically born healthy and happy. Despite the severity of the disease, early symptoms can be difficult to discern. This is especially true for new parents who do not have the previous experience of nursing and raising an unaffected infant and toddler. As a multisystem disease the initial symptoms vary considerably between patients in both nature and severity. When asked what some of the "first" symptoms of cystinosis were, participants responded with a wide variety of responses, as expected.

First Symptoms



Cure Cystinosis
International Registry

A PEDIATRICIAN WHO HAS ALMOST CERTAINLY NEVER SEEN A PERSON WITH CYSTINOSIS, HAS LIKELY NEVER EVEN HEARD OF THE CONDITION.

Most of these symptoms are things that are often difficult to perceive and more difficult to quantify. Furthermore, many of these symptoms are things that "normal" infants often encounter to some extent. Although the nephrologist soon becomes the quarterback of the cystinosis treatment team, most of the initial symptoms are not cause to seek the advice of a kidney specialist. Instead, poor growth, loss of appetite, vomiting and similar issues bring a parent to a pediatrician — a pediatrician who has almost certainly never seen a person with cystinosis and has likely never even heard of the condition. So begins the downward spiral of routine check-ins, slipping growth percentiles, slowly increasing symptoms and self-doubt — especially among new parents — until finally someone begins to put all the pieces together. Unfortunately, many patients have a similar journey which goes on for months and even years, during which the child is untreated and experiences a cascade of impacts, most notably to the part of the kidney responsible for the reabsorption of water and nutrients which are key to bone growth.

Cystinosis presents numerous hurdles for patients and parents, and at times it seems that none are as daunting as diagnosis. Although early diagnosis and treatment is especially important, cystinosis is unfortunately still not on the list of diseases included on the newborn screening in the United States. Early results of the CCIR have shown that the difficulty in achieving a diagnosis for cystinosis continues to be problematic. Initial diagnosis for patients without an affected family member have only slightly decreased in recent decades, with an average age of diagnosis for births prior to 2010 being 2.5 years compared to 1.7 years of age since 2010.

Symptom	%
Poor Growth	**19.8**
Frequent Urination	14.2
Loss of Appetite	14.2
Vomiting	13.5
Weight Loss	13.5
Problems Walking	8.3
Sensitivity To Light	5.6
Muscle Weakness	5.2
Severe Thirst	2.4
Unusual Urine Odor	2.1
Other	1.0

In just nearly three years since its launch, the new cystinosis patient registry is already helping to inform researchers and accelerate the development of better treatments and a cure for cystinosis. However, the value of the registry will only truly be realized with community-wide participation. We strongly encourage patients or caregivers to pitch in, sign up, and be part of our mission to identify the unmet needs of patients and accelerate research. The questionnaire takes about 40 minutes to complete, and registration is simple. Please visit the CRF website to sign up today!

WE STRONGLY ENCOURAGE PATIENTS OR CAREGIVERS TO PARTICIPATE IN THE REGISTRY

WWW.CYSTINOSISRESEARCH.ORG/CURE-CYSTINOSIS-INTERNATIONAL-REGISTRY

UPDATE

ON THE

STEM CELL AND GENE THERAPY CLINICAL TRIAL

We peek into the lives of the Stem Cell and Gene Therapy Clinical Trial participants and see how the treatment success has shaped their outlook on life and their physical being. The impact of this CRF-funded research is dramatically changing individual lives and our cystinosis community!

OUR CLINICAL TRIAL PARTICIPANTS TELL US ABOUT THEIR EXPERIENCE SO FAR

1. HOW DID YOU DECIDE THAT PARTICIPATING IN THE TRIAL WAS THE RIGHT DECISION FOR YOU? WHAT MOTIVATED YOU TO ENROLL IN THE TRIAL?

JORDAN JANZ: I decided to participate in the trial because I wasn't sure where my life was going to end up in the future. I was afraid that I wasn't going to make it past 30 and I was getting more sick every day. So, it was either I don't try to better my life and my health continues declining, or I do try to better my life, and if it doesn't work then I go back on my medication knowing I tried to better myself.

JACOB SEACHORD: I decided that participating in the trial was the right choice for me after discussing with my parents the pros and cons. The cons were that it was practically untested, during the COVID-19 outbreak, and because of that, I wasn't allowed any visitors during any of my testing or my entire stay in the hospital (that was a big one for my mom). The pros were, "What if it worked?" That's it. That completely outweighed the cons by a mile!

TYLER JOYNT: Originally, I hesitated due to family commitments and uncertainties about recovery. However, I eventually realized that the trial's timing was ideal. I've always been eager to join trials, and since we were already in San Diego, it made sense.

NATALIE STACK MORGAN: The fact that a stem cell transplant was even an option for such a rare disease was astounding and a once-in-a-lifetime opportunity. Given my age, then a 31-year-old, I felt it was the right thing to do given my continuous decline in health — I was not going to improve, only decline in the years to come.

KURT GILLENBERG: When reading about the trial in the CRF magazine back in 2019, I was very interested in being a part of the study. After hearing more about the process during CRF Day of Hope in April 2022, I knew this was something I had to do, and I had the strength to do it. In the last almost five years since my second kidney transplant, I have been working hard to build my body back to fighting form. I made changes to my diet and started working out five days a week for at least an hour with each training session. Within that time, I went from 110 pounds to 130 pounds, gaining about 20 pounds of muscle. When I told my parents I volunteered for the trial, I told them that this is the reason I had been building myself back up for these last few years. I truly believe that God put this opportunity in my path to not only help myself but to bring hope to all other cystinosis patients including future generations. Making medical history is cool too.

STEM CELL AND GENE THERAPY CLINICAL TRIAL

TRANSPLANT DATES

Jordan Janz
October 7, 2019

Jacob Seachord
November 16, 2020

Tyler Joynt
November 15, 2021

Natalie Stack Morgan
March 29, 2022

Kurt Gillenberg
October 24, 2022

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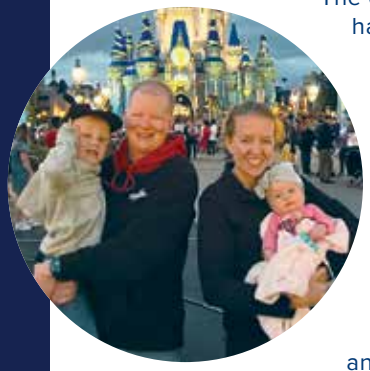
2. CAN YOU SHARE WHAT THE OVERALL EXPERIENCE WAS LIKE PRIOR TO TRANSPLANT AND THEN AFTER TRANSPLANT? WHAT WAS THE HARDEST PART? WHAT WAS THE "EASY" OR "THE BEST" PART OF YOUR EXPERIENCE?

JORDAN JANZ: Prior to the transplant I was very scared. I didn't know what would happen or what was going to happen. I was going to have to live in another country for four months not having any friends there to talk to or some of my family. I remember touring the hospital that I was going to be staying in during the transplant. At the same time, I remember seeing my friends tour colleges that they planned to enroll in that year, and for me that was very hard. After the transplant I enrolled in school for butchery and charcuterie management. I felt like I had a life and a chance to go to college. The hardest part of the transplant for me was the chemo side effects. I didn't expect them to be so harsh and I don't think anyone could have prepared me for that. The best part of my experience was living in such a nice place like San Diego and meeting all the nice people there. There are still people that I keep in touch with there that I will always remember and be grateful for.

JACOB SEACHORD: Prior to transplant, there was a ton of testing that had to happen. Some of the tests were difficult and some were a little painful. The team made sure that I had help throughout the testing process so that it was as smooth as possible. Afterwards, I still had a lot of testing, but I knew what to expect which made it much easier.

I think the toughest part of the whole experience was the multiple biopsies that I had to do. The easiest part was when the new stem cells were being inserted into me because all I had to do was just lay there. After the transplant, while I was still in the hospital, I was tired but I made sure that I went on long walks down the hallways every day to help with recovery.



TYLER JOYNT: Before the transplant, there were standard workups and tests. Physically, mouth sores were challenging and painful, affecting eating and swallowing. Emotionally, being away from family was tough. However, having my wife visit semi-regularly helped. Overall, it was a positive experience where the good outweighed the bad significantly.

NATALIE STACK MORGAN: Prior to the transplant, there was a lot of emotion and anxiety about whether or not it would work — and to this day, I still do not know. My actual stay at the hospital was honestly quite boring for several weeks, but the transplant itself was emotional and the couple weeks before my discharge date were very difficult.

The transplant itself consisted of one day where the nurse injected my "new" stem cells back into my body through an IV that had been placed in my arm before my hospital admission. It was an emotional day for me as well as my family because it was the day that my life would potentially change forever — it was a huge milestone and my new birthday.

My mom and dad worked so hard to find a cure for me for more than half my life and in that moment, it was very emotional to witness what they had accomplished for me and others living with cystinosis. March 29, 2022 is not only my "new" birthday, but it is also the day after my mom's birthday which makes it even more meaningful to me.

Once the stem cells were injected back into my body, it was a waiting game. I felt completely fine for a couple weeks and was nervous maybe something went wrong. The side effects were the worst part of the hospital stay. I had nausea, vomiting, painful mouth sores, hair loss, fever and fatigue. I was very weak and lost a lot of weight because I could not swallow anything due to the multiple sores in my mouth and throat.

Other than the chemotherapy side effects, one of the most difficult parts for me personally has been coming to terms with the fact that I am no longer fertile. Going through the stem cell transplant was a major life decision and though I am happy I chose to do it; I have sacrificed a lot. I struggle with the fact that I cannot have children of my own naturally anymore, but it is my new normal — it is hard to digest.

The other difficult part about the stem cell transplant thus far is the fact that it has been a waiting game for me. My stem cells have not worked as well as the other patients and my results are not as good as we hoped they would be. I got COVID-19 three months after the transplant which was the absolute worst time to get it because I had no vaccines and my immune system was extremely weak. I believe COVID-19 delayed the stem cell process, but it is still a mystery. It is very hard to comprehend if it "worked" or not. Given that this is a clinical trial, nothing is black and white. I continue to hope and pray that my health gets better and better each day.

KURT GILLENBERG: The process of joining the trial happened very quickly. After the Day of Hope 2022, I sent an email to the coordinator for the study and eagerly waited for a response. I assumed that if they accepted me, it would take at least a couple months to set up all the appointments and testing. Much to my surprise I received a call from the team asking me to be there in just two weeks! Luckily work let me take off the time I needed, and living just a few short hours away from San Diego was helpful too.

The experience prior to the transplant was not easy or very fun to be honest. I feel like they put you through every medical test known to mankind. Some were easy, some were uncomfortable, and some were just plain torture. To be bluntly honest, the process is not for the faint of heart. It is probably the hardest thing I have ever done but I knew going in that it would all be worth it in the end. When I spoke with the other participants in the trial, I believe we all unanimously agreed that the hardest testing was all the different eye exams. As all of you can probably imagine those tests were torture but necessary for the study to see the stem cell effects on the eyes. The best part about the whole experience was, of course, the results. Just one month following the stem cell transplant, my cystine level dropped over 80 percent. The team was ecstatic about the results, my family and I couldn't be happier.

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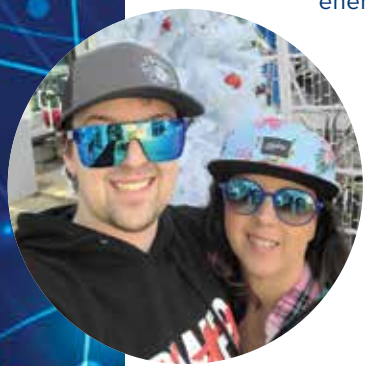
3. HOW WOULD YOU COMPARE YOUR QUALITY OF LIFE OR HEALTH BEFORE THE TRIAL TO TODAY, AFTER THE TRIAL? HOW IS YOUR ENERGY LEVEL? HAVE YOU EXPERIENCED OTHER OUTCOMES – GOOD OR BAD – SINCE THE TRIAL? OR "THE BEST" PART OF YOUR EXPERIENCE?

JORDAN JANZ: My quality of life before the trial compared to after the trial changed incredibly. Before the trial, I was on 55+ pills a day and was nauseous almost all the time. I was tired a lot and was physically drained. After I got the transplant, I felt amazing. I was eating more, my skin tone changed and so did my hair color. My pills went down to 20 pills a day, and I know that still might seem like a lot, but for someone that took 55 pills for most of his life, this was so much nicer and easier. A few months after I got home from having the transplant, my kidney function was on the rapid decline. My kidney function was too far gone to save, so I knew even with the stem cell transplant I was going to need a kidney transplant, but I didn't know when. With my kidney function declining, I started to fall into a downward spiral. I lost 30 lbs. and was so ill I couldn't work. I received my brother's kidney on July 27th, 2022.

I am just over a year of having the kidney transplant and I have gained 35 lbs. I have more muscle and energy than ever and just feel overall amazing.



JACOB SEACHORD: Before the transplant, my quality of life was pretty good, but I always had some side effects of the medication for cystinosis which did impact me. Sometimes the side effects limited what I could do. Plus, the smell of the meds always lingered on my body and in my breath.

Today, my quality of life is fantastic! I don't have to worry about taking my cystinosis medication and worrying about the smells that came with it. My energy levels have definitely increased. I can do more things before getting tired and it seems that I can finally build muscle mass up.

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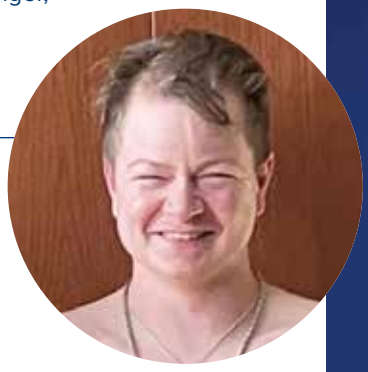
TYLER JOYNT: My quality of life has improved without oral cysteamine, with fewer GI issues and no strict medication schedule. My energy level is good, though managing two young active kids can make it hard to gauge what is causing tiredness when I do experience it.

NATALIE STACK MORGAN: It has been a year and a half since my transplant. My quality of life has improved but my kidney function has rapidly declined. I am currently taking a very small dose of Procysbi® to try to preserve my kidney function. Not taking the amount of Prosycbi® I used to take has been a huge positive for me. I still need about 8-9 hours of sleep each night, but I have much more energy during the day than before my transplant. I also believe that I am getting physically stronger and have more muscle tone. I am still very light sensitive, and my eyes sting more than before, but it is a different feeling. The theory is that the crystals in my eyes are separating and smaller crystals are coming to the surface of my eye causing my eyes to be more sensitive. I am currently taking the eye drops to wash out the crystals as much as possible.

KURT GILLENBERG: As time went on after the trial, every day that went by I felt better and better. Three months post-transplant I was given permission by the team to resume my normal activities and got back to the gym. I could see my progress more than ever before. I felt faster, stronger, and more energized than ever; my stamina had improved greatly. I could not believe the energy I had, and for the first time in my life, I felt hope and promise for my future, that I could live a full and productive life.



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4. ON A DAY-TO-DAY BASIS, DO YOU THINK YOUR QUALITY OF LIFE HAS IMPROVED SINCE THE TRIAL? IF YOU ARE OFF ORAL CYSTEAMINE, HAS THAT IMPACTED YOUR QUALITY OF LIFE?

JORDAN JANZ: Yes, my quality of life has improved. I have been off oral cysteamine for about four years now and my cystine tests are still very low.

JACOB SEACHORD: My quality of life has definitely improved. Like I said, I no longer give off a smell, which has boosted my self-confidence. Plus, I don't have anywhere near the number of medications to take as in the past.

TYLER JOYNT: Yes, being off oral cysteamine has made a significant difference. It's less burdensome, and even if I need to go back on it, it'll be fewer pills.

KURT GILLENBERG: I still, of course, take my kidney transplant meds every day, but those are simple. As all of you know, Procysbi® is not the easiest medication to take. My dose was 14 capsules twice a day and every day; my stomach would be a wreck. Just being off the medication has done wonders for my daily life. I feel so good now looking back I am not sure how I dealt with the pain for all those years. Now I can say yes to the things I was afraid to before since I never knew when those side effects would occur leaving me sidelined.

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5. OTHER PEOPLE WITH CYSTINOSIS ARE EAGER TO PARTICIPATE IN THE NEXT PHASE OF THE TRIAL. WHAT ADVICE WOULD YOU OFFER THEM – DO YOU HAVE ANY "WORDS OF WISDOM" FOR THEM?

JORDAN JANZ: I would say try and keep yourself as healthy as possible. If you can get a stem cell transplant with healthy native kidneys you will do very well.

JACOB SEACHORD: My words of wisdom to someone who is thinking about doing the trial is to BE PATIENT! Everything takes a lot of time. From signing up and getting notified you are a participant, signing all the paperwork, getting things scheduled, many tests, getting results, time in the hospital, waiting for your hair to grow back, etc., everything takes time. The best way to get through it is to just be prepared and be patient. It makes everything go better for everyone involved.

TYLER JOYNT: While impatience is natural, remember this is an early trial with safety as a priority. It's essential to stay informed and patient.

NATALIE STACK MORGAN: My advice to anyone who is thinking about getting the transplant: if you are thinking of doing it, you should go for it! It is definitely a tough journey, but in the end the outcome will likely outweigh the negatives. Cystinosis is a terrible chronic disease that will not get better with time, so being able to stop the progression of the disease is critical for a longer life.

KURT GILLENBERG: My advice to other patients who would like to be part of the trial is honestly prepare yourself mentally and physically. It's not an easy or short process, it's not a pain-free process, and you will be away from friends and family for a while. Keep telling yourself that you're not just going through this for you but for future generations so that one day no one will ever have to suffer from this disease ever again.

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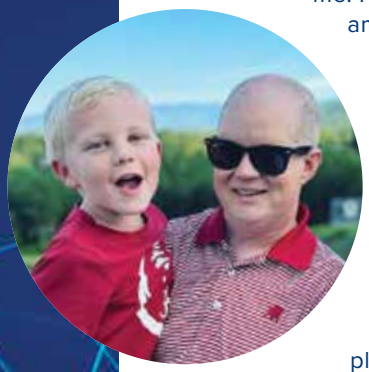
6. DESCRIBE YOUR FUTURE SINCE THE TRANSPLANT – HAS YOUR VISION FOR THE FUTURE CHANGED SINCE THE TREATMENT?

JORDAN JANZ: Since I got the transplant my look on the future has changed. I feel like I need to spend more time with family and put other things first. You only get one life, and now that I got a second chance at life, I feel like I need to make the best of it. My priority used to be work because I was always worried about my future. Now I feel like I need to have a balance and put family and down time first.

JACOB SEACHORD: Since the transplant, I got a new job, which has opened lots of opportunities for me. I get to travel to new places and I will have great opportunities to climb the ladder. In fact, I am leaving for Maine in October for a three-month stay. My future feels very bright with endless opportunities like buying a house and having a family.



TYLER JOYNT: I'm honestly not sure how my vision for the future has changed. I've always tried to have a positive outlook and look forward to what's to come. Since the transplant, we had another baby, and the biggest thing the transplant has done is make me thankful I am healthy enough to help raise both of my children and give them the life they deserve.

NATALIE STACK MORGAN: A little bit. I have always worked full-time and starting a family of my own is still something I will do. Family planning looks a little different now since I am infertile, but a family is a family, biological or not. I also will likely have a kidney transplant in the next couple years due to my decline in kidney function. Though I knew I would eventually have a kidney transplant, it will happen sooner than I thought.

KURT GILLENBERG: I stated before that for the first time in my life, I feel promise and hope for the future. I feel more confidence in myself than ever before. Being a part of this trial has been a privilege that I will not waste. I promise to use this opportunity not just for the betterment of myself but to bring hope to others. I don't know what the future has in store for me, but I know that it's bright.

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7. YOU ARE A TRUE PIONEER IN THE CYSTINOSIS COMMUNITY AND YOU ARE ADMIRED FOR YOUR COURAGE AND FOR FORGING A PATH TO BETTER TREATMENTS AND A CURE FOR THE REST OF THE COMMUNITY. ARE THERE PEOPLE YOU WOULD LIKE TO THANK OR WHO HAVE BEEN AN IMPORTANT PART OF YOUR STEM CELL THERAPY JOURNEY?

JORDAN JANZ: I would like to thank Stéphanie Cherqui and her team for taking such good care of me while I was going through the treatment. I would also like to thank the Stack family for starting this community to raise money for cystinosis research and treating me like family while I was in San Diego. I also want to thank the cystinosis community for sending me letters and gifts. It really helped me get through most days. I appreciate you all so much. I want to thank my family for being so supportive of me while I was going through everything — and they still are. Without all these people in my life, I would not be where I am today. Thank you so very much.

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JACOB SEACHORD: I would like to thank my parents most of all for supporting me every step of the way no matter how hard it was on them. Also, I want to thank Dr. Cherqui and her team for being accommodating and very helpful throughout and after the trial. And lastly, I want to thank the cystinosis community for all the love and support. They say, "It takes a village," and boy, are they right!

TYLER JOYNT: First and foremost, we obviously have to all thank Dr. Cherqui. I've known her for over seven years now, and when I first heard about the possibility of a "cure" it didn't seem real. She has worked incredibly hard on this process, and to have cystinosis be the first disease to get to try this was such a blessing. We are eternally grateful to her. There have been so many other people involved in the process that deserve our thanks and gratitude, but without Dr. Jerry Schnieder's research many years ago to even discover the disease, we would be nowhere.

NATALIE STACK MORGAN: I do not know how to express my gratitude towards everyone who has helped me get to this point in my cystinosis journey. My mom has been the most important person in my life throughout all of this. Without her perseverance and dedication, I would not have had the stem cell transplant at the age of 31. I am forever grateful for her as my mom and as my advocate.

My family and friends were all huge supports to me during this time as well, especially my husband, sister, and my dad. Dr. Cherqui is a true hero to all who went through the transplant, so I am beyond thankful for her and what she has accomplished for our community. Dr. Ball, Dr. Barshop, and all the nurses took really good care of me during the actual transplant. And of course, the cystinosis community — families, adults, donors, doctors — have been a part of this journey since day one, and it is because of our community that we are able to provide the best possible care for patients today. Our community is small, but we certainly know how to make change happen. I felt so loved and supported by everyone during my stem cell transplant. The support was everything to me during such a monumental, yet difficult time in my life. Thank you from the bottom of my heart.

KURT GILLENBERG: I could not have done this trial without the support of my friends and family. They were there every step of the way, and I couldn't have done it without their love and support. I especially want to thank my mom, who was there with me every day during this process, through every procedure, test, appointment — every boring day at the hospital, she was there. I'm pretty sure I would have lost my mind if she hadn't been there. I love you, Mom, with all my heart.

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8. ANY OTHER THOUGHTS ON THE TRIAL – BEFORE, DURING OR AFTER?

JACOB SEACHORD: Before the transplant I was definitely nervous about if it would work and how sick I might get during the treatment.

During the transplant process, I felt sad that I lost my hair, but very hopeful that it would all come back (which it mostly did). I hoped that everything I was going through would be worth it in the end.

After, I am extremely thankful to have been a part of the trial and hope it may help future generations have a bright future without cystinosis. I feel in my bones that my future looks extremely bright!

TYLER JOYNT: Life has transformed, and some days, I forget about the transplant entirely. Which I guess is the ultimate goal — to reduce the burden of cystinosis. I'm excited to see its impact on other diseases, especially orphan ones that pharmaceutical companies take advantage of.

NATALIE STACK MORGAN: I did not realize how much anxiety I would have after the transplant. I guess I just thought either it would work or not work. But I have come to realize that it is not black and white at all. There is so much to measure, analyze, interpret, and each patient is so different. Unfortunately, for me, I am not sure how well the transplant has engrafted at this time. It is an ongoing interpretation with my levels, especially since I had COVID-19 after the transplant. It is working to some extent; my numbers are slowly improving. I am so happy to have been given such a rare opportunity to improve my life. I will never give up hope and know that this was meant to happen for me.

KURT GILLENBERG: During all the testing prior for the stem cell transplant, the team discovered I had some type of growth in the mitral valve of my heart. After further examination and testing, it was determined that I need to have this growth removed. At the time I am writing this I will be having open heart surgery in a week to remove the growth. If I had decided not to do this trial, the growth would have most likely gone undiscovered because I had no cardiac symptoms and something awful could have possibly happened down the road; this is just another example of the trial saving my life.

9. PLEASE TELL US WHAT YOU ARE DOING TODAY – SCHOOL, WORK, FAMILY LIFE, ETC.

JORDAN JANZ: Today I am working at a butcher shop where we make our own Italian meats, cheese, and have fresh food daily. I still try and go to the gym daily after work. I have also taken up playing in poker tournaments. So far, I have been doing pretty good and I found that I am naturally pretty good at it. I would love to play professionally one day.

JACOB SEACHORD: Nowadays I work every day at my job. While I'm home, I ride my bike to and from work every day. Last month, I went on a great vacation to the Oregon sand dunes and had a blast with my family and friends.

Now that everything is done, I joined a dating club so that I can meet single people in person who like to hike, play games, go camping, and experience all other sorts of adventures.

TYLER JOYNT: I still run my motion design business, primarily in sports, and have a wonderful family — a wife of nearly 10 years and two active children. We are starting to prepare to move once again in about 18 months, and hopefully be at our "forever" stop.

NATALIE STACK MORGAN: I currently live in Chicago, Illinois with my husband Danny and our golden retriever. I am a child welfare social worker and work for a private agency that partners with DCFS (Department of Children and Family Services). We celebrated our wedding on October 21st.

KURT GILLENBERG: Currently I have not returned to work yet due to my upcoming heart surgery, but as soon I as I am healed, I will be going back to the grind. During the process of getting ready for the transplant, my sister gave birth to her first child, so it was a pretty crazy but exciting time for my family. His name is Ezra Paul and I am so excited to see him grow up.

One of my plans is to work with my mom on making a presentation about my life living with cystinosis in hopes to present it in front of physicians and medical students to spread awareness about this disease since 99.9% of doctors have never heard of it, maybe even encouraging one of those future doctors to specialize in it. God knows we could use a few more.

STÉPHANIE CHERQUI, PhD (center) AND TEAM

CYSTINOSIS RESEARCH FOUNDATION

SCIENTIFIC REVIEW BOARD

The CRF Scientific Review Board (SRB) is composed of leading cystinosis scientists, researchers, and clinicians from around the world. We are indebted to our Scientific Review Board members for their leadership, guidance and commitment to improving the lives of adults and children with cystinosis. THANK YOU!

CHAIR

Corinne Antignac, MD, PhD
Professor
Laboratory of Hereditary Kidney Diseases
Imagine Institute (Inserm U1163)
PARIS, FRANCE

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cystinosis RESEARCH FOUNDATION | TOGETHER WE SHINE BRIGHT

FALL 2023

RESEARCH UPDATES

20 years TOGETHER

A CAREER-LONG COMMITMENT to INNOVATION and COMMUNITY

Q&A WITH CORINNE ANTIGNAC, MD, PhD

by Dennis Arp

Few people bring as much perspective to their healing work as Corinne Antignac, MD, PhD.

As a pediatric nephrologist who received her MD in 1982, Dr. Antignac started treating children with cystinosis when many didn't live into adulthood. In fact, their pain and their plight helped motivate her to seek better treatments through new training in genetics and a new career as a researcher in hereditary kidney diseases.

Whether in her Paris lab, where Dr. Antignac's pioneering work identified the CTNS "cystinosis" gene, or in a multitude of meeting spaces, where she has fostered groundbreaking collaborations, her influence reverberates across continents and oceans, brightening the outlook of countless patients and loved ones all throughout the cystinosis community.

Now Dr. Antignac is taking a step back from her research and her highly impactful role as chair of the Cystinosis Research Foundation Scientific Review Board.

"Corinne is a universally admired researcher and a cherished friend to both the CRF and the cystinosis community," said Nancy Stack, CRF President and Founding Trustee. "Her contributions will continue to change lives for decades to come."

In this moment of transition, we asked Dr. Antignac to reflect not just on her 12-year stewardship of the Review Board, but more broadly on her three-decade commitment to improving the lives of those with cystinosis.

AS YOU LOOK ACROSS THE YEARS OF CHALLENGES AND PROGRESS WITH CYSTINOSIS TREATMENT AND RESEARCH, WHAT DOES ALL THAT CHANGE LOOK LIKE TO YOU?

I think first we have to consider that in the early 20th century, children with cystinosis were dying before two years old. After that, treatment improved, and children arrived at eight or ten years, when they often died of kidney failure. Then transplantation occurred, and cysteamine made a tremendous difference, but there were all sorts of problems as children lived to become young adults. Now, even before we factor in the possibilities that are opening up through stem cell therapy, patients are living rewarding lives, and all the timelines are getting longer and better. I have seen exponential improvement over the course of my professional life, and CRF support has made so much of that possible.

WHAT ARE THE WAYS YOU KNOW THAT CRF FUNDING AND OVERALL SUPPORT HAVE LED TO MORE SUBSTANTIVE RESEARCH AND ULTIMATELY IMPACT ON LIVES?

I know from both my experience as a pediatric nephrologist and as a researcher that in a lot of places, foundations only fund very short-term research studies. As a member of the CRF Scientific Review Board, what I've heard from CRF is, "We completely trust you." Whether it's basic science or translational research, if the project has a good chance to expand the body of knowledge affecting cystinosis patients, the message is, "We will fund it." This helps make cystinosis known to a larger audience, and this is extraordinary for researchers.

What is the structure of the protein which is mutated in cystinosis? What is the source of the trouble when children with cystinosis have trouble swallowing? Research projects like these and so many others are only possible because of CRF funding. You know, when I first started with the Scientific Review Board, there were very few cystinosis research papers being published. Now last year alone, there were three projects reporting results in very prominent research journals. That progress has been made possible because of the generosity of CRF donors and the work of dedicated researchers.

WHAT WAS THE FEELING LIKE WHEN YOU DISCOVERED THE CTNS GENE IN 1998?

We were very happy to find this gene, of course, because it was so important and because it had been a lot of work. I precisely remember the moment and the place where we were, when analyzing a key sequence of a new gene we had identified, two of my collaborators and myself saw the first point mutation, proving this new gene was really the

CTNS gene. There was a short silence and then a big “hurrah” and cheerful congratulations. This achievement came at a wonderful time, when younger researchers had arrived in our lab, including a 21-year-old very enthusiastic and energetic student named Stéphanie Cherqui, who immediately embarked in the project of identifying the mouse CTNS gene and creating the animal model which has then been so useful for researchers all around the world. Finding the CTNS gene was a moment to celebrate to be sure.

BEYOND YOUR LABORATORY RESEARCH, YOU HAVE PLAYED A VITAL ROLE AS A MENTOR TO THE NEXT GENERATION OF CYSTINOSIS RESEARCHERS. WHAT ABOUT THAT EXPERIENCE AND INFLUENCE IS IMPORTANT TO YOU?

I’m at a period now when I’m thinking of what we’ve accomplished, and I’m so pleased about all the impact of Stéphanie and the others I’ve had come into my lab and then go on to make such a difference through their research. Many of them are women, which I am very proud of. Stéphanie and I have remained close as she has gone on to do groundbreaking work in her own lab in California. One reason I knew that I shouldn’t expect Stéphanie, unfortunately for me, to come back to France is that when you open the fridge in her home, there is a lot of cheese in it, thanks to her husband’s work importing French food products, you know! So, I knew there was no possibility of her coming back to France when she already had so much French food in her home.

WHAT MAKES THIS THE RIGHT TIME TO STEP BACK FROM YOUR RESEARCH AND YOUR SERVICE ON THE CRF SCIENTIFIC REVIEW BOARD?

It’s been a very hard decision because I really love what I do. But things are going very well in cystinosis research, with so many contributing to advances. It’s a good time to give young people more opportunities. I’ve had 12 years on the board, so I was thinking it might be enough, especially as I try to reduce the number of flights between continents. Still, when I left California after the Research Symposium, I was very sad. Jeff and Nancy Stack, CRF and this community mean so much to me.

YOU HAVE SO MANY HONORS, INCLUDING THE LEGION D’HONNEUR, THE HIGHEST DECORATION IN FRANCE – AN AWARD ESTABLISHED BY NAPOLEON BONAPARTE. WHAT BRINGS YOU THE MOST PRIDE WHEN YOU CONSIDER ALL YOUR ACHIEVEMENTS – ESPECIALLY RELATED TO YOUR CONTRIBUTIONS TO THE CYSTINOSIS COMMUNITY?

For me, getting the Légion d’Honneur has always been strange because it seems like something for the army – something for a war hero. Recently I was elected to the French National Academy of Science, and that was for me a very prestigious reward and I have to say that I was very moved by this election.

But more than the awards and honors, I think about all I have gained from being part of the cystinosis community. It has been a privilege to meet so many wonderful people. Everyone has different backgrounds and nationalities, but we have a shared love of science, of research, of patient care. That’s why it’s so important to have all the CRF symposia, and why the Day of Hope makes such a difference. What Nancy and Jeff have built is so meaningful, for the children, the families and for the researchers.

CYSTINOSIS STAR

CORINNE ANTIGNAC, MD, PhD

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FOUNDATION FOR BREAKTHROUGHS

Even as a child, Dr. Stéphanie Cherqui was constructing a future full of life-changing impact. You might say that community-building and discovery are in her genes.

'LES DEVISES SHADOK'

As she navigated the countless challenges of her PhD research on human genetics, Dr. Stéphanie Cherqui drew motivation from a small poster pinned up near her workstation. It features an illustration by French cartoonist Jacques Rouxel, taken from his animated TV series "Les Shadoks." The poster still provides daily inspiration in Dr. Cherqui's office at UC San Diego. The original is in French, but she translated it for us: **"When you keep trying, you end up succeeding. So the more you fail, the more you have chances of succeeding."**

by Dennis Arp

DR. Stéphanie Cherqui is many things to a multitude of people. Wife and mother to an amazing family that sustains her creative energy; architect of breakthroughs to a clinical world craving such pioneers; provider of possibility to a cystinosis community buoyed by real hope that a cure is within reach.

But before she became any of those things, Stéphanie Cherqui was a builder. Her father showed her the way.

Bounding across the hills of Paris and its suburbs, Cherqui trailed with her father as he turned flat construction plans into soaring and spreading structures.

It's a good thing hard hats adjust to child size.

"When I was about 10, my father's company was building a hospital that included a laboratory for research, and I was working with him during the weekends," recalled Dr. Cherqui, professor in the Department of Pediatrics at UC San Diego School of Medicine. "I walked into the labs and, I don't know, I felt something. It's like when you're in a place and you just know that you belong. I met researchers, and I learned what they do. I loved it. I felt very clearly that this is where I belonged."

By middle school, she was studying genetics as the cornerstone of a future career in research. At 16, she earned her first summer internship, to a genetic institute that was mapping the human genome. In college, her bachelor's, master's and PhD work all propelled her passion for genetic discovery.

Brick by brick, she was positioning the pieces to support remarkable impact. Now, we all are witnessing the fulfillment of dreams that Dr. Cherqui's skills and drive have made possible through her research advances.

As the Cystinosis Research Foundation (CRF) celebrates 20 years of turning aspirations into reality, Dr. Cherqui's unparalleled commitment remains at the heart of CRF's overall mission to develop better treatments and achieve a cure.

"At its core, this is an amazing story of hope and resilience – a small rare disease community working together to fund research to help their children," said Nancy Stack, founding trustee and president of the CRF.

CRF SUPPORT NURTURES DR. CHERQUI'S VISION

For Dr. Cherqui's gene therapy and stem cell research, the journey began with CRF funding in 2007, when the foundation was the sole source of support for her work. Over the years, CRF has provided $6.1 million in grants nurturing Dr. Cherqui's research vision.

Through countless challenges, the gene and stem cell project has progressed, hitting multiple milestones along the way, including in 2018, when the FDA approved Phase I/II trials of genetically modified autologous stem cell transplants in six adults with cystinosis.

Over the next four years, those patients were transplanted with the stem cell and gene therapy treatment. Follow-up testing has fueled optimism, revealing overall declines in average white blood cell cystine levels. Five of the patients remain free of the need to take oral cysteamine.

Now Dr. Cherqui's transformative gene therapy is being advanced by the global pharmaceutical company Novartis, which will conduct the next phase of the program.

"Novartis acquiring the cystinosis program is a wonderful validation for the whole hematopoietic gene therapy field and great news for cystinosis patients," said Geoff MacKay, former CEO of AVROBIO, the company with which Dr. Cherqui first partnered on the therapy.

As CRF shared during this year's Day of Hope Family Conference, "We are optimistic that this treatment could cure cystinosis or at least stop the progression of cystinosis, preventing further damage to the body."

Those words mean the world to cystinosis patients and their loved ones.

"We have had two children with cystinosis, and we are absolutely amazed at the progress you have made possible for children with cystinosis," one community member wrote on a CRF Facebook post about Dr. Cherqui's research success. "God bless you and all your team." "You've given so many hope," another added. "Thank you with all my heart!!!" "You are truly an amazing doctor and person," still another enthused. "May you continue to have exciting results."

DISCOVERY EXPANDS TO INCLUDE ALZHEIMER'S AND OTHER DISORDERS

Indeed, positive developments with the gene therapy and stem cell project continue to build out from Dr. Cherqui's lab. In addition to her cystinosis breakthroughs, she has found new potential therapies for other well-known disorders such as Friedreich's Ataxia, Danon disease, and now Alzheimer's disease.

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CYSTINOSIS STAR

STÉPHANIE CHERQUI, PhD

Professor
Department of Pediatrics, Division of Genetics

University of California, San Diego
LA JOLLA, CALIFORNIA

In a recent pioneering study, she showed that transplanting hematopoietic stem and progenitor cells could alleviate the symptoms of Alzheimer's in a mouse model. The transplanted cells improved memory and cognition, but they also reduced neuroinflammation and beta amyloid build-up – two hallmarks of the Alzheimer's.

"We look forward to developing a new therapeutic approach for this devastating disease," Dr. Cherqui said.

There are countless steps on the way to seeing a therapy change patients' lives at the clinical level. That's a big reason why such breakthrough moments create indelible memories.

"When you work on the mouse model and you see it achieve success, it's very exciting – you say, 'Oh, this is amazing!'" Dr. Cherqui said. "But it's still research."

Such a journey requires daily discipline, obsessive attention to detail, especially in reports required by the Food and Drug Administration to prove safety and efficacy. Dr. Cherqui says there are everyday joys in this brick-by-brick assemblage of a case for getting a therapy all the way to patients.

"But it's still not real," she adds.

Her cystinosis therapy only became 100% real in her mind when she stood at the bedside of Jordan Janz as he became Patient 1 at the launch of human trials for the stem cell treatment.

SOMETHING NEW AND WONDERFUL IN THE WORLD

"I will always remember that day and the moment of the stem cell infusion," Dr. Cherqui said, her voice rising to meet the recollection. "It was like the delivery of a baby – something new and wonderful in the world. All the years, all the effort, all the suffering, and now it's going to a patient. As a researcher, it's the kind of moment you live for."

As she thought back to that day in October 2019, Dr. Cherqui took a moment to further collect her thoughts. She became even more wistful.

"The moment was amazingly beautiful, and amazingly trustful. Now it's not a mouse – it's a real patient," she said. "There was some risk, which is why I have so much respect and appreciation for the patients. They had hope but they also had trust that the therapy would add benefits. That's why those moments of infusion are so beautiful."

Still, the excitement of the moment didn't lessen its gravity. Dr. Cherqui felt every ounce of the weight on her shoulders.

"I wasn't sleeping because I was so stressed looking at every single test, every lab result, every aspect of Jordan's progress after the infusion. If something wasn't going exactly the right way, the stress level went up," she said. "Now, more than three years down the line, we see that we are proceeding well with the therapy, but in the beginning, we had hope, but we didn't know for sure. I was happy for any good results, and I'm glad now that we are seeing those results continue."

ILLUMINATING A PATH TO A POSSIBLE CURE

Over the past 16 years of CRF support, scores of other happy moments and significant achievements are etched in Dr. Cherqui's mind. They fuel her commitment to collaboration as well as her passion to continue pursuing discoveries.

She smiles as she recalls the moment in the lab when the mouse model first showed that the gene therapy was viable, illuminating a path to a possible cure.

Dr. Cherqui had transplanted green fluorescent hematopoietic stem cells, and thanks to microscopy and other technology, she could go to a display screen to see if any of the healthy cells had integrated into kidney tissue to help preserve the organ.

At first she didn't believe what she saw.

She knew that healthy cells would appear green on the display, but she saw so much green that she thought she was seeing nothing but background "noise." She was disappointed. Then she went to view the control group, and there was no green on the screen.

"I said, 'Wait a second. Is there so much green because all these cells have traveled to the kidney?'" Dr. Cherqui recalled. "After hours of making sure, I realized it was true. In that moment I knew we were doing something right."

Alone in a lab space lighted only by the screen, "I just wanted to scream to the world that something amazing had happened," she said. "It was just the first step – we didn't know for sure that cystine levels had decreased dramatically. But somehow, I knew."

Even in such moments, while immersed in the solitary everyday tasks that lab work demands, Dr. Cherqui feels connected to those she hopes will benefit from her work.

"There is something that is really amazing about cystinosis families and the overall cystinosis community," she said. "It's good that they put so much pressure on me because I know that it reflects all the hope that they have for my work."

"When they thank me for everything I'm doing for their kids, I say, 'Don't thank me, because we aren't sure this treatment will work.' But they tell me that they are thanking me just for trying, no matter the results. I think that is the most beautiful thing – to separate the effort from the outcomes, which are never guaranteed. That kind of gratitude is really special, and I am very grateful for that."

WHERE "FAMILY" MERGES WITH "COMMUNITY"

From the patients to the parents, research mentors to lab partners, funding providers to support system sustainers, countless people add joy to the journey, Dr. Cherqui said.

She doesn't have to look far to find her biggest boosters. They are inside her own household.

"My family help me keep things in balance, because I could have been into my work too much and completely lost track of myself," she said. "My husband, who is also my high school sweetheart, has been supportive from the start, and my two sons are my best advocates. Even when they were young, they were so invested in cystinosis. They would say, 'Mom, did you find the treatment for cystinosis? Is this the cure?'"

"My family provides the balance that makes me stronger."

To Dr. Cherqui, "family" includes mentors, especially those she calls "my research mother and my research father" – Dr. Corinne Antignac and Dr. Daniel Salomon. It was in the Paris lab of Dr. Antignac that Dr. Cherqui's commitment to gene therapy as a new therapy for cystinosis became the central focus of her research.

"I've been lucky to have two amazing mentors during my career," she said. "Unfortunately, Dr. Salomon passed away, but Corinne and I still talk regularly. She has always supported me and challenged me to do my best work throughout my career."

For her part, Dr. Antignac says she recognized soon after Dr. Cherqui joined her lab that she had found a kindred spirit.

"When you're doing research, you have to feel things in the gut, you have to commit completely in your mind and your soul," she said. "Stéphanie was very enthusiastic from the beginning, very committed to the work. She was confident she could do something important."

With enduring energy and childlike wonder, Dr. Cherqui is still doing important things, thanks in good measure to the transformational support she continues to receive from her extended research family.

In August, a $5 million grant from the Nancy and Geoffrey Stack Foundation helped launch the Gene Therapy Initiative at UC San Diego to research rare diseases like cystinosis. Dr. Cherqui is leading the initiative.

CRF SAW SOMETHING IN THE GENE THERAPY CONCEPT AND IN ME – THEY WERE WILLING TO TAKE A RISK.

It's another example of what can rise from foundational connections and the work of visionary creators committed to digging in and building up.

"I first met Nancy and Jeff before my research had ever been funded, and I really liked them right away," Dr. Cherqui said. "Nancy is so like me – we never take no for an answer, and we will always fight for something we believe in.

"You know, when I first applied for funding for my cystinosis research, it was a very unorthodox idea. I would never have gotten another sponsor with no proof of concept and no preliminary data. But the CRF saw something in the gene therapy concept and in me – they were willing to take a risk. They trusted me. I'm so grateful that all these years later, we still share that level of trust."

PATHWAY FULL OF PROMISE

CRF support helps Dr. Jennifer Hollywood advance a combination therapy that may unlock new treatment possibilities.

by Dennis Arp

DR. Jennifer Hollywood gets it. She understands why cystinosis patients might not be eager to add another pill to a dosing regimen that already can be daunting.

But what if that new pill could further reduce the cystine buildup that damages kidneys? What if the increased organ protection could come without all the bad breath, body odor and stomach upset that cysteamine can bring?

It's clear that such a pill would be an easy one for cystinosis patients to swallow – especially since twice-a-week dosing just might be possible.

Improving the quality of life and longterm health of cystinosis patients motivates Dr. Hollywood as she begins a new phase of her important research project. She's working on a combination therapy that pairs a new version of cysteamine with a drug called Everolimus in hopes that together they will be much more effective than either is alone.

Thanks to funding support from the Cystinosis Research Foundation (CRF), Dr. Hollywood and her lab team have achieved strong results in testing their combo therapy using patients' iPS stem cells and kidney organoids – human kidney tissue derived from stem cells. Now CRF funding is ensuring that the research progresses to preclinical drug testing using a cystinotic rat model that she has also developed.

If all goes well, this phase will further validate the combination treatment and help determine the optimal dosing of the two medications.

"Our research seeks to greatly improve the treatment of cystinosis and lower the unpleasant side effects of cysteamine by advancing a more potent, less unpleasant, combination therapy," said Dr. Hollywood, Postdoctoral Research Fellow in the Department of Molecular Medicine and Pathology at the University of Auckland in New Zealand.

"Combining CF10 [the new form of cysteamine developed by Drs Roz Anderson and Herbie Newell] with Everolimus has the potential to be better tolerated, more potent at reducing cystine levels, more effective at reducing kidney damage so patients delay the need for transplant and provide greater longevity as well as better quality of life than cysteamine does by itself," she added.

Dr. Hollywood's current research links to her foundational work in gene editing to correct genetic diseases. Her focus on cystinosis began in 2014, when a CRF grant helped unite her with Dr. Alan Davidson and his work with iPS stem cells and kidney organoids.

The iPS stem cells Dr. Hollywood works with are not derived from embryos but instead come from adults. She's able to take skin cells and reprogram them in the lab so they revert to stem cells.

"Then we can coax them to become any cell in the body. In this case, we make them become kidney cells," the researcher said.

Creating human kidney organoids for drug trials "has really changed the game," Dr. Hollywood added. "The hope was that it would be an alternative to animal models, and in some aspects this is true, but you also need the whole physiology that you get with animal studies and that is why we developed a rat model of cystinosis too."

This new preclinical trial with cystinotic rats will simultaneously test the effectiveness of CF10 as it also tests the combination therapy of CF10 with Everolimus.

Even on its own, CF10 is a big step forward, Dr. Hollywood said.

"CF10 is a very exciting drug because it's the first one with potential to replace cysteamine as a much better treatment option," she said. "In effect, it's cysteamine, but with additional components so it has fewer side effects."

Still, the more powerful possibilities rest with the combination therapy, because Dr. Hollywood's research has revealed a blockage in the pathway to cell health that goes unaddressed by cysteamine/CF10 alone.

"We know that cysteamine can get rid of the cystine that's so harmful to organs, but we found that it can't get rid of this buildup of toxic debris inside the cell," she said.

That blockage in the so-called autophagy pathway is what prompted Dr. Hollywood to look for alternative

cystinosis treatments. She turned to Everolimus, an mTOR 1 inhibitor drug that has proved effective at inducing autophagy and thereby improving the range of cell function.

A central consideration was that Everolimus is already on the market. “It’s good to have a drug that is already FDA approved and can be repurposed as it makes the route to clinical trials much faster,” she said.

So far, the results with cysteamine and Everolimus together are promising. “We’ve seen greater reduction of cystine levels in blood cells and kidney tissue,” Dr. Hollywood said. “And many of the Fanconi syndrome markers are reduced compared with mono treatments.”

Dosing is still to be determined, but much of that effort is a matter of optimizing beneficial effects of Everolimus while managing its possible side effects, which include the potential for weight loss and immune response suppression, because the drug is also used to prevent organ transplant rejection.

“Our hope is that we can get the dose low enough so that we get the autophagy pathway response without inhibiting the immune response,” Dr. Hollywood said.

Ultimately, getting the dosing right for each patient will take work in the clinic, the doctor added.

“Cancer patients take [Everolimus] every day at 10 milligrams, but you probably wouldn’t want to do that for cystinosis patients. Right now we’re trying a smaller dose daily to see what that looks like,” she said.

The imperative of the moment is “showing that the combination therapy works,” Dr. Hollywood noted. “You can spend years working on the optimal dose.”

It may take several more years to navigate the approval process, but Dr. Hollywood is hopeful that the combination therapy will realize its promise as a life-changer for cystinosis patients.

She knows that there are many hurdles to clear and much more work to do along the way. Still, she’s eager to continue a research journey that CRF support has made possible.

“We want to achieve great things for cystinosis patients because there are things that they need, and obviously a cure is at the top of that pyramid,” Dr. Hollywood said. “But even these small changes to their medicine could be huge in their lives. Those possibilities are what drive our research.”

CYSTINOSIS STAR

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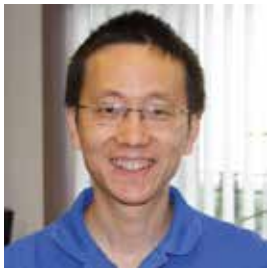
EIGHTH INTERNATIONAL CYSTINOSIS RESEARCH SYMPOSIUM

SPONSORED BY THE CYSTINOSIS RESEARCH FOUNDATION

BY STEPHEN JENKINS, MD

On September 7-8, scientists from around the world met in Irvine, California for the eighth biennial CRF International Cystinosis Research Symposium. The symposium was led by three co-chairs: Corinne Antignac, MD, PhD, Stéphanie Cherqui, PhD, and Julie Ingelfinger, MD. The last symposium was in 2020 at the dawn of the pandemic, so this was the first time we were able to meet in person in three years. It was exciting to see all the progress CRF-funded researchers have made in that time.



The keynote address was by Liang Feng, PhD, who, along with Xue Guo, PhD, published a groundbreaking paper in the prestigious scientific journal Cell *in 2022 on the structure and function of the cystinosin protein. Despite being discovered over 40 years ago, this was the first group of researchers to completely characterize the lysosome transporter protein and elucidate the mechanisms by which it moves cystine from inside the lysosome to the cytosol of the cell. This work is critical to unraveling how the cystinosin protein interacts with other parts of the cell, which could lead to new therapies.*

Several researchers, including Zvonimir Marelja, PhD, and Olivier Devuyst, MD, PhD, presented their findings on how the cystinosin protein is involved in the mTORC1 pathway, which senses nutrient availability in the cell and controls other pathways that cells use to survive periods of starvation, including autophagy. Jennifer Hollywood, PhD, showed that inhibiting MTORC1 with medications like Everolimus in a CTNS knockout rat model may result in improved cystine depletion in combination with cysteamine, probably by activating autophagy. Other researchers, including Ester De Leo, PhD, and Francesco Emma, MD, are investigating the use of flavonoids, which also stimulate autophagy, and found that one compound reduced cystine levels in CTNS knockout mouse kidneys.

Other researchers are focused on the role of inflammation in cystinosis. Sergio Catz, PhD, is investigating the role of neutrophils in the development of organ damage in cystinosis. Neutrophils are normally part of the body's defenses against bacterial infections, but something about cystinosis activates neutrophils and causes them to secrete inflammatory granules that lead to tissue injury. Robert Mak, MD, PhD, and Hal Hoffman, MD, are exploring the role of the NLRP3 inflammasome in muscle and kidney disease and have found that treating CTNS knockout mice with an oral NLRP3 inhibitor (Dapansutrile) improved kidney and muscle function.

Justine Bacchetta, MD, PhD, showed her research on how inflammation affects bone health in cystinosis. She found that interleukin-1β, an inflammatory cytokine, is elevated in bone cells from CTNS knockout mice, and that treatment with an FDA approved medication, Anakinra, reduced inflammation and decreased activation of osteoclasts, the cells that break down bone.

Francesco Bellomo, PhD, gave an update on his study of the ketogenic diet for treatment of cystinosis. CTNS knockout mice fed early with ketogenic diet do not develop Fanconi syndrome, and this finding was replicated in a CTNS knockout rat model. It's not clear why this diet is protective, but studies show it restores

2023 SYMPOSIUM CO-CHAIRS


Corinne Antignac, MD, PhD


Stéphanie Cherqui, PhD


Julie Ingelfinger, MD

normal autophagy, and it may increase production of endogenous cysteamine. More studies are needed to determine whether this could be an effective therapy in humans.

Dr. Stéphanie Cherqui gave an update on the hematopoietic stem cell gene therapy trial. Six adults have now undergone transplantation. The results have been promising, with reductions in white blood cell cystine levels, as well as reduction in cystine crystals in colonic cells. She is investigating this method of gene therapy in other diseases as well and is preparing to start a clinical trial for Friedreich's ataxia. She has also recently published results of successful experiments of knockout mice with hereditary Alzheimer's disease, demonstrating how research funded by CRF is leading to discoveries in other important fields.

Dr. Corinne Antignac, who discovered the gene for cystinosis, presented her research on creating cystinosis kidney organoids from stem cells. It has proven difficult to recreate all the typical features of cystinosis, but the cells do show an increase in cystine levels. Benjamin Freedman, PhD, also shared an update on his kidney organoid research. He has derived induced pluripotent stem cells from the urinary cells of people with cystinosis, reprogrammed them to be kidney cells, and injected these cells into a living mouse kidney. Incredibly, the cells start to incorporate into the mouse kidney, including stimulating new blood vessel development.

I was glad to see that multiple scientists are doing research on muscle and bone disease in cystinosis. Andrea Del Fattore, PhD, shared her research on the negative effects of cysteamine on bone, and a novel treatment, Pepstatin A, which normalized bone development in CTNS knockout mice in the absence of cysteamine treatment. Aude Servais, MD, PhD, Pascal Laforêt, MD, PhD, and Hélène Prigent, MD, PhD, are doing a study of neuromuscular complications in adult patients in France. They presented data on 15 adults that they have enrolled so far. Many of them had significant distal muscle weakness. A few had dysphagia and severe restrictive lung disease. Two of the patients with severe symptoms had been off cysteamine therapy for prolonged periods of time.

Reza Seyedsadjadi, MD, shared an update on his study of myopathy in adults in the US, including new analyses of swallowing studies that showed many adults have significant problems in the oral phase of swallowing. This is associated with a reduction in quality-of-life scores. Dr. Seyedsadjadi is working with Feodor Price, PhD, to investigate muscle stem cells (called satellite cells) isolated from three adults with cystinosis. This could provide an in-vitro model for further research on why cystinosis leads to muscle disease. Dieter Haffner, MD, shared his research on a new biomarker, musclin, which is suppressed in CTNS knockout mice with muscle atrophy. If this biomarker is validated in humans, it could serve as a target to demonstrate efficacy of new therapies.

Sophie Molholm, PhD, and John Foxe, PhD, presented their research on cognition, executive function and sensory perception, which they have performed with advanced EEG testing in people with cystinosis, as well as CTNS knockout mice. They found differences in response inhibition, error monitoring and hyperexcitability in the early visual cortex.

It was amazing to see the breadth and quality of the research being done by these scientists. I am so grateful for their hard work, and they all expressed a deep gratitude for the Cystinosis Research Foundation, without which their work would not be possible. Seeing so much collaboration and progress gives me and my family hope for the future. I look forward to reading the next round of research proposals later this year!

THE IMPACT of CRF RESEARCH

20 years

AREAS OF RESEARCH FOCUS & GRANTS AWARDED SINCE 2002

New Drug Discovery Cysteamine, New Medications and Devices

32 GRANTS

Ghanashyam Acharya, PhD
BAYLOR COLLEGE OF MEDICINE, HOUSTON, TEXAS

Francesco Bellomo, PhD
Francesco Emma, MD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Pierre Courtoy, MD, PhD
Christophe Pierreux, PhD
DE DUVE INSTITUTE, LOUVAIN UNIVERSITY MEDICAL SCHOOL, BRUSSELS, BELGIUM

Laura Rita Rega, PhD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Antonella De Matteis, MD
TELETHON INSTITUTE OF GENETICS AND MEDICINE, NAPLES, ITALY

Ranjan Dohil, MD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Francesco Emma, MD
Laura Rita Rega, PhD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Paul Goodyer, MD
MONTRÉAL CHILDREN'S HOSPITAL, MONTRÉAL, QUÉBEC, CANADA

NEW
Paul Goodyer, MD
Elena Torban, PhD
RESEARCH INSTITUTE OF THE MCGILL UNIVERSITY HEALTH CENTRE, MONTRÉAL, QUÉBEC, CANADA

Jennifer Hollywood, PhD
Alan Davidson, PhD
UNIVERSITY OF AUCKLAND, AUCKLAND, NEW ZEALAND

Michael Sekar, PhD
AMMA THERAPEUTICS, INC., HAYWARD, CALIFORNIA

Laura Rita Rega, PhD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Vincent Stanton, Jr., MD
Patrice Rioux, MD, PhD
THIOGENESIS THERAPEUTICS, INC., SAN DIEGO, CALIFORNIA

Cure Cystinosis International Registry (CCIR)

1 GRANT

Ranjan Dohil, MD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Cellular and/or Molecular Studies of the Pathogenesis of Cystinosis

65 GRANTS

Corinne Antignac, MD, PhD
IMAGINE INSTITUTE (INSERM U1163), PARIS, FRANCE

Francesco Bellomo, PhD
Francesco Emma, MD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Sergio Catz, PhD
Raquel Carvalho Gontijo, PhD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

Sergio Catz, PhD
Danni Chen, PhD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

Sergio Catz, PhD
Farhana Rahman, PhD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

Sergio Catz, PhD
Apama Shukla, PhD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

Sergio Catz, PhD
Nadia Zgajnar, PhD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

NEW
Sergio Catz, PhD
Juan Yu, PhD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

NEW
Ester De Leo, PhD
Francesco Emma, MD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Antonella De Matteis, MD
TELETHON INSTITUTE OF GENETICS AND MEDICINE, NAPLES, ITALY

Olivier Devuyst, MD, PhD
Zhiyong Chen, PhD
UNIVERSITY OF ZÜRICH, ZÜRICH, SWITZERLAND

Olivier Devuyst, MD, PhD
Alessandro Luciani, PhD
UNIVERSITY OF ZÜRICH, ZÜRICH, SWITZERLAND

Liang Feng, PhD
STANFORD UNIVERSITY, PALO ALTO, CALIFORNIA

Liang Feng, PhD
Xue Guo, PhD
STANFORD UNIVERSITY, PALO ALTO, CALIFORNIA

Bruno Gasnier, PhD
Yann Terras, MSc
CNRS/UNIVERSITÉ DE PARIS, PARIS, FRANCE

Taosheng Huang, MD, PhD
UNIVERSITY OF CALIFORNIA, IRVINE, IRVINE, CALIFORNIA

Elena Levtchenko, MD, PhD
UNIVERSITY HOSPITAL, LEUVEN, BELGIUM

Ming Li, PhD
Jacob Kitzman, PhD
UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN

Alessandro Luciani, PhD
UNIVERSITY OF ZÜRICH, ZÜRICH, SWITZERLAND

Gennaro Napolitano, PhD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

Norbert Perrimon, PhD
HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS

Giusi Prencipe, PhD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Matias Simons, MD
Zvonimir Marelja, PhD
IMAGINE INSTITUTE, PARIS, FRANCE

Jess Thoene, MD
TULANE UNIVERSITY SCHOOL OF MEDICINE, NEW ORLEANS, LOUISIANA

Bruno Vogt, MD
Daniel Pouly, PhD
UNIVERSITY HOSPITAL OF BERN, BERN, SWITZERLAND

Skin, Muscle and Bone

20 GRANTS

Justine Bacchetta, MD, PhD
Irma Machuca-Gayet, PhD
HOSPICES CIVILS DE LYON UNIVERSITÉ DE LYON, LYON, FRANCE

Robert Ballotti, PhD
Christine Chiaverini, MD, PhD
FACULTÉ DE MÉDECINE, NICE, FRANCE

Andrea Del Fattore, PhD
Giulia Battafarano, PhD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Paul Grimm, MD
STANFORD UNIVERSITY SCHOOL OF MEDICINE, PALO ALTO, CALIFORNIA

Dieter Haffner, MD
Malgorzata Szaroszyk, PhD
HANNOVER MEDICAL SCHOOL, HANNOVER, GERMANY

Mary Leonard, MD, MSCE
STANFORD UNIVERSITY SCHOOL OF MEDICINE, PALO ALTO, CALIFORNIA

Robert Mak, MD, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Richard Reimer, MD
Jacinda Sampson, MD, PhD
Mary Leonard, MD, MSCE
Paul Grimm, MD
Trinh Tina Duong, MPT
Feliks Kogan, PhD
STANFORD UNIVERSITY, PALO ALTO, CALIFORNIA

Reza Seyedsadjadi, MD
Florian Eichler, MD
Lee Rubin, PhD
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS

THE IMPACT of CRF RESEARCH

AREAS OF RESEARCH FOCUS & GRANTS AWARDED SINCE 2002

Cystine Measurement and Cysteamine Toxicity Study

10 GRANTS

Bruce Barshop, MD, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Shawn Davidson, PhD
PRINCETON UNIVERSITY, PRINCETON, NEW JERSEY

Thomas Jeitner, PhD
NEW YORK MEDICAL COLLEGE, VALHALLA, NEW YORK

Elena Levtchenko, MD, PhD
UNIVERSITY HOSPITAL, LEUVEN, BELGIUM

Genetic Analysis of Cystinosis

5 GRANTS

Katy Freed, PhD
TEXAS BIOMEDICAL RESEARCH INSTITUTE, SAN ANTONIO, TEXAS

Sihoun Hahn, MD, PhD
SEATTLE CHILDREN'S HOSPITAL, SEATTLE, WASHINGTON

Elena Levtchenko, MD, PhD
UNIVERSITY HOSPITAL, LEUVEN, BELGIUM

Eric Moses, PhD
TEXAS BIOMEDICAL RESEARCH INSTITUTE, SAN ANTONIO, TEXAS

Minnie Sarwal, MD, PhD
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, SAN FRANCISCO, CALIFORNIA

Stem Cells and Gene Therapy: Bone Marrow Stem Cells, Induced Pluripotent Stem Cells, Gene Therapy and Gene Editing

34 GRANTS

Stéphanie Cherqui, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Alan Davidson, PhD
THE UNIVERSITY OF AUCKLAND, GRAFTON, AUCKLAND, NEW ZEALAND

Bruno Gasnier, PhD
PARIS DESCARTES UNIVERSITY, PARIS, FRANCE

Paul Goodyer, MD
MONTRÉAL CHILDREN'S HOSPITAL, MONTRÉAL, QUÉBEC, CANADA

Patrick Harrison, PhD
UNIVERSITY COLLEGE CORK, CORK, IRELAND

Vasiliki Kalatzis, PhD
INSTITUTE OF MOLECULAR GENETICS OF MONTPELLIER, MONTPELLIER, FRANCE

Winston Kao, PhD
Hassane Amlal, PhD
UNIVERSITY OF CINCINNATI, CINCINNATI, OHIO

Daniel Salomon, MD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

Holger Willenbring, MD
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, SAN FRANCISCO, CALIFORNIA

Eye-Corneal Cystinosis Research

11 GRANTS

Ghanashyam Acharya, PhD
BAYLOR COLLEGE OF MEDICINE, HOUSTON, TEXAS

Stéphanie Cherqui, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Morgan DiLeo, PhD
Xin Fan, PhD
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE, PITTSBURGH, PENNSYLVANIA

Morgan Fedorchak, PhD
Kanwal Nischal, MD, FRCO
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE, PITTSBURGH, PENNSYLVANIA

Jennifer Simpson, MD
UNIVERSITY OF CALIFORNIA, IRVINE, IRVINE, CALIFORNIA

Kang Zhang, MD, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Neurological

17 GRANTS

Angela Ballantyne, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Miriam Britt Sach, MD, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Rita Ceponiene, MD, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Florian Eichler, MD
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS

Pascal Laforêt, MD, PhD
Hélène Prigent, MD, PhD
RAYMOND POINCARÉ UNIVERSITY HOSPITAL, GARCHES, FRANCE

Sophie Molholm, PhD
John Foxe, PhD
ALBERT EINSTEIN COLLEGE OF MEDICINE, BRONX, NEW YORK

Aude Servais, MD, PhD
NECKER HOSPITAL, PARIS, FRANCE

Amy Spilkin, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Doris Trauner, MD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Kidney Research

26 GRANTS

Robert Chevalier, MD
UNIVERSITY OF VIRGINIA, CHARLOTTESVILLE, VIRGINIA

Pierre Courtoy, MD, PhD
Christophe Pierreux, PhD
DE DUVE INSTITUTE, LOUVAIN UNIVERSITY MEDICAL SCHOOL, BRUSSELS, BELGIUM

Olivier Devuyst, MD, PhD
UNIVERSITY OF ZÜRICH, INSTITUTE OF PHYSIOLOGY, ZÜRICH, SWITZERLAND

Olivier Devuyst, MD, PhD
Marine Berquez, PhD
UNIVERSITY OF ZÜRICH, ZÜRICH, SWITZERLAND

NEW
Olivier Devuyst, MD, PhD
Alessandro Luciani, PhD
UNIVERSITY OF ZÜRICH, ZÜRICH, SWITZERLAND

Allison Eddy, MD
BC CHILDREN'S HOSPITAL, VANCOUVER, CANADA

Francesco Emma, MD
Anna Taranta, PhD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Benjamin Freedman, PhD
UNIVERSITY OF WASHINGTON, SEATTLE, WASHINGTON

Elena Levtchenko, MD, PhD
UNIVERSITY HOSPITAL, LEUVEN, BELGIUM

Robert Mak, MD, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Tara McMorrow, MD
UNIVERSITY COLLEGE DUBLIN, BELFIELD, DUBLIN, IRELAND

Philip Newsholme, PhD
CURTIN UNIVERSITY, PERTH, WESTERN AUSTRALIA

Daryl Okamura, MD
SEATTLE CHILDREN'S RESEARCH INSTITUTE, SEATTLE, WASHINGTON

Laura Rita Rega, PhD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Mary Taub, PhD
UNIVERSITY AT BUFFALO, THE STATE UNIVERSITY OF NEW YORK, BUFFALO, NEW YORK

Thyroid

1 GRANT

Pierre Courtoy, MD, PhD
DE DUVE INSTITUTE, LOUVAIN UNIVERSITY MEDICAL SCHOOL, BRUSSELS, BELGIUM

Rat Model for Cystinosis

4 GRANTS

NEW
Francesco Emma, MD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Olivier Devuyst, MD, PhD
UNIVERSITY OF ZÜRICH, ZÜRICH, SWITZERLAND

THE IMPACT *of* CRF RESEARCH

AREAS OF RESEARCH FOCUS & GRANTS AWARDED SINCE 2002

Molecular Study of Cystinosis in the Yeast Model

3 GRANTS

Bruno André, PhD
UNIVERSITÉ LIBRE DE BRUXELLES, GOSSELIES, BELGIUM

Anand Bachhawat, PhD
IISER MOHALI, MANAULI, PUNJAB, INDIA

David Pearce, PhD
UNIVERSITY OF ROCHESTER MEDICAL CENTER, ROCHESTER, NEW YORK

Lab Equipment for Cystinosis

9 GRANTS

Ghanashyam Acharya, PhD
BAYLOR COLLEGE OF MEDICINE, HOUSTON, TEXAS

Corinne Antignac, MD, PhD
IMAGINE INSTITUTE, PARIS, FRANCE

Bruce Barshop, MD, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

Sergio Catz, PhD
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

Stéphanie Cherqui, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO, LA JOLLA, CALIFORNIA

RESEARCH & FELLOWSHIP GRANT AWARDS

CYSTINOSIS RESEARCH FOUNDATION

SPRING **2023** | $959,550

Sergio Catz, PhD (Mentor) and Juan Yu, PhD (Fellow)
The Scripps Research Institute
"Studies of global inflammation in patients with cystinosis"
$150,000 TWO-YEAR FELLOWSHIP

Ester De Leo, PhD and Francesco Emma, MD
Bambino Gesù Children's Hospital
"Efficacy and safety of genistein in Ctns-/- rats"
$209,550 TWO-YEAR STUDY

Olivier Devuyst, MD, PhD and Alessandro Luciani, PhD
University of Zürich
"SGLT2 inhibitors reveal new therapeutic opportunities for cystinosis"
$320,000 TWO-YEAR STUDY

Olivier Devuyst, MD, PhD and Francesco Emma, MD
Bambino Gesù Children's Hospital
Maintenance of CTNS Rat Model
$40,000 TWO-YEAR STUDY

Paul Goodyer, MD and Elena Torban, PhD
Research Institute of the McGill University Health Centre
"mRNA therapy for cystinosis"
$240,000 TWO-YEAR STUDY

SEE LAY ABSTRACTS STARTING ON NEXT PAGE

Studies of global inflammation in patients with cystinosis

Sergio D. Catz, PhD, *Mentor*
Juan Yu, PhD, *Fellow*
THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

OBJECTIVE/RATIONALE:

The immune system protects the organism from infections but can also cause inflammation, which can be defined as the excessive activation of the immune system. If uncontrolled or dysregulated, the inflammatory response can be deleterious causing cellular and tissue damage. In cystinosis, a lysosomal storage disease caused by a genetic defect of the CTNS gene, inflammation is emerging as a causative factor of kidney disease. We previously showed that the cystinotic kidney can release factors that attract inflammatory leukocytes. Uncontrolled white blood cell (leukocyte) activation in cystinosis may lead to tissue damage and cell death. We will study inflammation in cystinosis. Our studies utilize state-of-the-art microscopy approaches to characterize immune white blood cell identity and function in blood from patients with cystinosis.

PROJECT DESCRIPTION:

The objective of this research plan is to utilize state-of-the-art inflammatory mediator (cytokine) analysis and omics analysis of pro-inflammatory plasma proteins and lipids, and to apply modern cell-based analysis to characterize the putative inflammatory phenotype in patients with cystinosis. We will also utilize high-dimensional CyTOF (mass cytometry) and muti-marker flow cytometry to identify white blood cell progenitors and subtypes in blood from cystinosis patients. Pro-inflammatory cell subsets from these patients will be used in functional studies.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

We anticipate finding elevated numbers of pro-inflammatory immune cell-subtypes in circulation, in cystinotic patients, that positively correlate with inflammatory mediators and kidney disease. We also expect that patients with cystinosis will have increased numbers and dysfunctional white blood cells. The identification of inflammatory cells and markers in blood from cystinosis patients is an step forward toward the discovery of new therapies to treat this devastating disease.

ANTICIPATED OUTCOME:

We anticipate that we will discover specific pro-inflammatory markers and white blood cell subtypes to be upregulated in cystinosis. Understanding the different stages of inflammation in cystinosis will help design better therapies to treat this disease.

Efficacy and safety of genistein in Ctns-/- rats

Ester De Leo, PhD, *Principal Investigator*
Francesco Emma, MD, *Co-Principal Investigator*
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

OBJECTIVE/RATIONALE:

Cystinosis is a rare disease that still lacks complete and definitive cure. In previous studies, we have shown using cells derived from patients with cystinosis that genistein decreases cystine content and reverts some altered key cellular functions. Subsequently, we have shown that prolonged genistein administration to female cystinotic mice decreases cystine crystal accumulation in the kidneys and protects their function. In order to proceed to testing genistein in human subjects, we need to confirm these results in another model and perform additional experiments to test the safety of the drug.

PROJECT DESCRIPTION:

The present study represents the last pre-clinical step of our research on genistein. We will use our recently developed Ctns-/- rat model to confirm the beneficial effects of genistein on kidneys. In addition, we will test the effects of genistein on other organs. We will study in particular if genistein reduces the deposition of cystine crystals in the skin because these may represent an important marker of efficacy that can be monitored with noninvasive techniques in patients. Since genistein may have unwanted endocrine effects, in particular on the reproductive system, we will closely monitor the hormonal profiles of treated female and male animals.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Should results obtained in mice be replicate in rats and toxicity tests be satisfactory, they will provide a strong rationale to perform a clinical study in human subjects. Potentially, genistein could be used in the clinical practice in combination with cysteamine to potentiate its cystine-lowering effect by acting on a different mechanism of cystine clearance.

ANTICIPATED OUTCOME:

We expect to confirm in rats the reduction of cystine crystal deposition that we observed in mice, as well as the protective effects of genistein on the kidneys. Duplicating our results in a second animal model is important, since sometimes responses to drugs are specific to a given animal model. We also expect that the safety profile of genistein will be satisfactory, but until the tests planned in this project are performed, a clinical trial in humans cannot be planned.

SGLT2 inhibitors reveal new therapeutic opportunities for cystinosis

Olivier Devuyst, MD, PhD, *Principal Investigator*
Alessandro Luciani, PhD, *Co-Principal Investigator*
UNIVERSITY OF ZÜRICH, ZÜRICH, SWITZERLAND

OBJECTIVE/RATIONALE:

Nephropathic cystinosis causes inherited dysfunction of the kidney proximal tubule (PT), often complicated by chronic kidney disease (CKD) and life-threatening manifestations. The deficiency of CTNS is consistently associated with defective autophagy-lysosome degradation systems and dysfunction of PT cells, as reflected by low-molecular-weight (LMW) proteinuria. There is an urgent need to identify novel transformative therapies for patients with cystinosis, as the use of cysteamine is limited by side effects and lack of efficacy to alleviate PT dysfunction.

PROJECT DESCRIPTION:

Our preclinical studies have indicated that modulation of overactive mTORC1 pathway rescues lysosome storage-related phenotypes and proximal tubulopathy downstream of CTNS loss and cystine storage, offering novel targets for intervention. However, the translatability of mTORC1 inhibitors is hindered by lack of specificity and toxicity, limiting their usefulness. Sodium-glucose cotransporter 2 (SGLT2) inhibitors (SGLT2i), originally designed to treat type 2 diabetes, slow CKD progression in non-diabetic patients. These inhibitors target mechanisms controlling nutrient sensing and mTORC1 signaling pathways in PT cells. We plan to use a combination of preclinical models, cell- and lysosome-based function assays and disease-relevant screening technologies: i) To reveal whether and how SGLT2i counteract the aberrant mTORC1 activation in CTNS-deficient tubular cells; ii) To evaluate the preclinical efficacy of SGLT2i on lysosome storage-related phenotypes and proximal tubulopathy in CTNS-deficient/cystinosis-affected kidneys; iii) if successful in preclinical testing, to design a first-in-human clinical trial protocol to determine whether the SGLT2i dapagliflozin improves proximal tubulopathy in young children with cystinosis.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

SGLT2i appear to pharmacologically reproduce many of the beneficial effects of fasting regimens, making them potentially attractive for long-term treatment of chronic mTORC1-related diseases, including cystinosis. In this project, we wish to unlock new therapeutic possibilities for children with cystinosis by extending the therapeutic potential of SGLT2 inhibitors.

ANTICIPATED OUTCOME:

These studies based on screening and validation workflow in innovative model organisms and relevant cellular systems could enable fast therapeutic translation of SGLT2i from preclinical systems to clinical benefit for children with cystinosis.

CALL FOR FALL 2023 GRANT APPLICATIONS

When Nancy and Jeff Stack established the Cystinosis Research Foundation (CRF) in 2003, they were committed to aggressively funding cystinosis research to ensure the development of new and improved therapies and a cure for cystinosis. But never in their wildest dreams could they have imagined what has been accomplished in 20 short years. Since its inception, CRF has funded 228 multi-year research studies in 12 countries. Our researchers have published 108 articles in prestigious journals as a result of CRF funding. Every dollar donated goes directly to support cystinosis research.

The goal of CRF is to accelerate promising cystinosis research toward clinical trials. To that end, CRF prioritizes research that will lead to better treatments and a cure for cystinosis. CRF issues grants for bench, clinical and translational research, with a strong emphasis on translational and clinical research. CRF is interested in supporting new investigators and encourages them to apply either as research fellows or investigators.

In September, CRF announced $5 million was available for the Fall 2023 call for research and fellowship applications. The new grant awards will be announced in December.

In Spring 2023, CRF issued five new grants totaling $959,550 that will bring us closer to better treatments and a cure. All research applications received by CRF are evaluated by CRF's Scientific Review Board (SRB), composed of the leading international experts in the field of cystinosis. The SRB provides independent, objective reviews and recommendations for each research proposal submitted based on the NIH scale of standards. Additionally, the SRB follows grant review guidelines established by CRF and advises the foundation on the scientific merits of each proposal. CRF has created a thriving and collaborative international research community. If you are a scientist or researcher and would like to apply for a grant, please visit our website for more details.

Cure Cystinosis
International Registry

In 2021, CRF updated the registry questionnaire to include questions that are relevant to recent scientific advancements, new medications and patient care. CRF partnered with CoRDS *(Coordination of Rare Diseases at Sanford)* to create a new Cure Cystinosis International Registry (CCIR), the only international cystinosis patient registry in the world. The site includes a professional Research Portal so that researchers and scientists who register can access and view de-identified, aggregate cystinosis patient information. The registry will connect all of the stakeholders in the cystinosis community – the scientists, researchers, clinicians, pharmaceutical companies, patients and families – and provide them with resources that have never been available in one place before, all to accelerate patient care.

The value of the registry will only truly be realized with patient participation. We strongly encourage patients or caregivers to enroll in the registry and help identify the needs of patients with cystinosis. This information is essential to advancing cystinosis research.

Visit the CRF website to learn more about CCIR and enroll.

WWW.CYSTINOSISRESEARCH.ORG/CURE-CYSTINOSIS-INTERNATIONAL-REGISTRY

WWW.CYSTINOSISRESEARCH.ORG/APPLY-FOR-RESEARCH-GRANT

CRF is excited about the future of cystinosis research and is grateful to researchers for their interest in the cystinosis community. We look forward to working together to find better treatments and a cure for cystinosis.

RECENTLY PUBLISHED STUDIES

CRF-funded researchers have been instrumental in advancing the field of cystinosis through the publication of articles in prestigious journals. Published articles enable other scientists, pharmaceutical companies, and the cystinosis community to learn more about the pathogenesis of cystinosis, to explore ideas for novel treatments, and to prepare for clinical trials. We congratulate all of the published CRF-funded researchers who have dedicated their careers to the children and adults with cystinosis.

Dr. Doris Trauner

University of California, San Diego Health Sciences,
Rady Children's Hospital

Doris Trauner, MD is a pediatric neurologist, and specialist in neurodevelopmental disabilities at the University of California, San Diego Health Sciences, Rady Children's Hospital, San Diego, California. Her recently published article "**Neuro-Cognitive Complications of Nephropathic Cystinosis"** appeared in the *Journal of Rare Diseases*, in July 2023. Dr. Trauner has been awarded numerous grants from CRF since 2009. Her research paper is a review of the neuro-cognitive complications of nephropathic cystinosis.

Dr. Francesco Emma and Dr. Olivier Devuyst

Bambino Gesù Children's Hospital,
Rome, Italy

The development of a rat model for cystinosis was the result of a CRF-funded grant to Francesco Emma, MD, and Olivier Devuyst, MD, PhD, that was initiated in 2018. Read more about their work in the 2023 published article in *Human Molecular Genetics* titled, **"Multisystem Involvement, Defective Lysosomes and Impaired Autophagy in a Novel Rat Model of Nephropathic Cystinosis."**

The rat model is the preferred model organism in many fields of biology and medicine. There are many advantages to using rats versus mice for research, larger body size, better characterization, and more similar physiology to humans. In particular, the metabolic physiology of rat models is particularly relevant for testing new therapies, and their size allows for frequent sampling to monitor organ function and/or drug toxicity. Thank you, Dr. Emma and Dr. Devuyst, for developing the rat model that will help advance new, potential therapies.

Cell Reports

CYSTINOSIS RESEARCH LEADS TO DISCOVERIES IN ALZHEIMER'S DISEASE:

Groundbreaking Research by

Dr. Stéphanie Cherqui

University of California, San Diego

In 2003, CRF set out to find better treatments and a cure for cystinosis. Now, in a recent breakthrough study, Dr. Stéphanie Cherqui demonstrated that transplantation of hematopoietic stem and progenitor cells could effectively alleviate Alzheimer's symptoms in a mouse model. The transplanted cells not only improved memory and cognition, but also reduced neuroinflammation and β-amyloid buildup – a hallmark of the disease.

Congratulations to Dr. Cherqui and thank you to our donors whose support of cystinosis research is now helping others with more prevalent diseases and disorders. Dr. Cherqui's Alzheimer's research was published in the prestigious *Cell Reports* on August 8, 2023,

"Rescue of Alzheimer's disease phenotype in a mouse model by transplantation of wild-type hematopoietic stem and progenitor cells."

nature communications

Dr. Olivier Devuyst and Dr. Alessandro Luciani

University of Zürich, Switzerland

Read all about the CRF-funded study published in July 2023 in *Nature Communications* titled **"Lysosomal Cystine Export Regulates mTORC1 Signaling to Guide Kidney Epithelial Cell Fate Specialization,"** by Olivier Devuyst, MD, PhD, and Alessandro Luciani, PhD, from the University of Zürich. This article focuses on unraveling the mystery surrounding initial kidney damage caused by cystinosis. Thank you, Dr. Devuyst and Dr. Luciani, for your excellent research and dedication to the cystinosis community.

scientific reports

Dr. Pierre Courtoy

de Duve Institute, Louvain University Medical School , Brussels, Belgium

"Dietary supplementation of cystinotic mice by lysine inhibits the megalin pathway and decreases kidney cystine content."

One of the earliest impacts on an infant with cystinosis is the deleterious effects the disease has on a portion of the kidney known as the proximal tubule. This portion of the kidney provides for the reabsorption of water and many nutrients critical for growth. This specific type of kidney damage is why the first symptoms of the disease are often associated with extreme thirst, poor growth and bone deformities.

In this study, researchers led by Dr. Pierre Courtoy used a mouse model of the disease to investigate the effects of a highly modified diet with increased levels of bibasic amino acids (lysine and arginine). The dietary supplements were designed to specifically target the megalin pathway which has been previously shown to play a key role in cystinosis-driven proximal tubule damage. Results showed that the modified diets were able to alter the megalin pathway and provided critical insight into this critical early manifestation of the disease.

To read and/or download all the articles published in 2023, go to:
WWW.CYSTINOSISRESEARCH.ORG/PUBLISHED-STUDIES

FALL 2023

FAMILY STORIES

20 years TOGETHER

TINA FLERCHINGER

CRF BOARD MEMBER FAMILY

The Reality of our disease

By Tina Flerchinger

CLARKSTON, WASHINGTON

Over the years, life has moved fast and steady. When you are living with a disease, you are often reminded of your challenges; these challenges become your norm. But often you see others and realize it is not normal to take mountains of pills to keep you alive, have multiple kidney transplants, suffer with eye pain, hospital visits, etc. As a child, I always left my parents to do these things for me so that I could have the most normal childhood possible. Now that I am 20, I am faced with the reality of my disease. Having any disease is hard, but not having people who share your struggles is harder. Challenges are a way of life; without them, we would not be grateful. Our challenges bring us closer to God and bring people together. As a community, we have become so strong and hopeful. We support each other, extending into our lives that hope. The cystinosis community truly is a strong threshold in the face of cystinosis. Every year we all meet up at the conference, and we all feel so hopeful and not alone. Hearing other people's struggles with the same disease you have gives you the strength to continue. There are so many inspiring people with cystinosis; all of you are so strong. We uplift each other and support one another. I wanted to say an appreciation of thanks to all those I have met who have cystinosis and those who have known it in their life. Together, we can conquer this disease in hopes that one day it will be in the past.

There are so many inspiring people with cystinosis

Pure Reciprocity

Generational Love Generates Wisdom

By Marcu Alexander, Hadley's mom
BOISE, IDAHO

Our family has been through many highs and lows this year, which have resulted in personal growth for each of us. My mom was diagnosed with cancer in 2022. After a courageous battle, she sadly passed away this May. Our lives are greatly impacted by her loss, but we are all grateful for the time we had with her and will forever treasure the memories. My mom played a huge role in our lives and helped shape who my girls are today.

When Hadley was diagnosed with cystinosis in 2012, my mom was a huge source of support. She helped take care of Stella during hospital stays and doctor appointments. She learned Hadley's new schedule and how to administer all her medications so Ben and I could have date nights or time to recharge. To this day, she still has remnants of Procysbi® beads on the ceiling in her kitchen and guest room from when Hadley had a G-tube. Funny little reminders of how challenging it was to push Procysbi® mixed with applesauce through a small tube. She was always front and center at every Hearts for Hadley fundraising event we threw and wanted nothing more than to witness a cure for her granddaughter and everyone else living with cystinosis. I'm grateful she was alive to see six patients successfully undergo the gene therapy stem cell transplant.

The girls were faced with watching their grandma who was always active and busy with gardening, baking, reading, and quilting transition to not being able to do any of the things she loved anymore. Instead of grandma helping take care of them, the roles reversed, and they helped me take care of her. Through this experience, I have watched my daughters develop a new understanding of what it means to love unconditionally and to live selflessly. Life with cystinosis has already taught us many of these lessons, but as they mature it is more apparent.

I have watched my daughters develop a new understanding of what it means to love unconditionally and to live selflessly.

BROOKE EMERSON

THEN AN

By Jill Emerson, Brooke's mom
HAMMONTON, NEW JERSEY

It's been almost eight years since our daughter's diagnosis, and while the management of cystinosis has become a normal part of our routine and it sometimes feels like cystinosis has been a part of our lives forever, so much has changed in such a short period of time.

When Brooke was first diagnosed, I had to leave my full-time job to care for her needs. It felt like we couldn't juggle it all, and that was the best way to ensure that Brooke had all her needs met, including medication administration, tube feeds to gain weight, etc. And now, cystinosis has just become part of our daily routine, and we all participate in the management of it, including Brooke. We have found a rhythm, and now I am back working full-time, at the job I love and was so sad to have to leave (thank you to my wonderful employer who was so patient and flexible with me!).

When Brooke first started elementary school, it was so scary to entrust virtual strangers – the school nurse and various teachers – with Brooke's care during the school day. In her first years of school starting with Pre-K, she had to go to the nurse daily for medications. And now, Brooke has started 4th grade, and we have been able to switch her medication frequency and timing so that she doesn't even need to see the nurse during the school day. She especially loves the feeling of independence this year.

Soon after diagnosis we went to our first CRF Day of Hope family conference. We listened to Dr. Stéphanie Cherqui's presentation on the results of her research treating cystinosis with stem cells in the mouse model of the disease. Admittedly, at that time it all sounded like a crazy idea, and the thought of it being applied to patients seemed like a dream. And yet, to date six adults have been transplanted in the trial, and we are on the cusp of this treatment being available for everyone. And the wonderful Dr. Cherqui has found ways to apply her cystinosis research to more common diseases including Alzheimer's.

AS WE REFLECT ON "THEN AND NOW," SO MUCH HAS CHANGED IN THESE EIGHT SHORT YEARS.

ND NOW

When we had our first Hope for Brooke fundraiser, we didn't know what to expect, whether we would raise any funds, have another fundraiser in the future, or what our involvement in the cystinosis community would be. And now, we will have our ninth fishing fundraiser in a few months, both my husband Clay and I are members of the CRF Board of Trustees, and we will forever be involved with CRF, and fundraise to ensure that research continues for all cystinosis patients.

When Brooke was younger, we worried about every developmental milestone, every cold, every bad day, wondering if it was an electrolyte imbalance or an all-too-frequent side effect of her medication. The fear that life would be harder for Brooke because cystinosis loomed over everything, and the worry wasn't far from our mind, even on good days, as we waited for the proverbial "other shoe" to drop. And now, we worry a little less, and we celebrate the amazing person Brooke is. She is a vibrant girl who is a wonderful friend, a smart and studious student who tries so hard and loves school, an aspiring artist, a funny chatty character, a swimmer, a voracious reader, and a girl with big dreams to become a veterinarian.

This is to say to recently diagnosed families, it does get easier, and while it might feel like this is going to be what the rest of your child's and your lives are like, things do change, and the ever-present worry does subside. I remember feeling that our lives would always be weighed down by the thought of cystinosis. But now, our perspective has changed, and we've begun to accept how things are, and most importantly, we have hope. As we reflect on "Then and Now," so much has changed in these eight short years. And we believe that in another several years, more research breakthroughs will have been made, better treatments will be available for Brooke and others, and a cure will be an option for so many more.

WE WORRY A LITTLE LESS, AND WE CELEBRATE THE AMAZING PERSON BROOKE IS.

2023

CAMP CYSTINOSIS

ON JULY 20, WE WELCOMED EIGHT CAMPERS TO SALT LAKE CITY FOR THE FIRST **CAMP CYSTINOSIS.**

By Stephen Jenkins, MD, Sam and Lars' dad
SALT LAKE CITY, UTAH

Every year we go to the Day of Hope family conference so we can see our cystinosis friends. Samuel and Lars love to hang out with other kids with cystinosis, especially their best buddy Henry Sturgis. The conference goes by so fast, and when we say goodbye on Saturday night, my kids always say they wish they had more time.

Over the last couple years, we started daydreaming about how great it would be to have a Cystinosis Summer Camp. Many kids with cystinosis don't go to traditional summer camps because of medications, the risk of dehydration, and the nighttime issues with polyuria. What if we had a camp designed specifically for our kids that was designed around their unique challenges, but gave them a chance to spend time together and make stronger connections?

Well, this year we decided to pull the trigger and give it a go! Since this was the first time, we had to keep it small to see if it was even feasible. We asked other families with teenagers at the Day of Hope if they would be interested in sending their kids to Utah for five days. To our delight, several people said yes!

On July 20, we welcomed six teenagers, in addition to our own two sons, to Salt Lake City, Utah, for the first Camp Cystinosis. People traveled from Idaho, Washington and Canada to join us. Tina Flerchinger, age 19 at the time, was one of our designated camp counselors. Instead of a rustic camping experience, we decided to rent a condo up in the scenic mountain town of Midway.

On the second day of camp, we took the kids rafting on the Provo River. We all piled into one 12-person-raft, and the kids took turns rowing while I tried (and failed) to steer our boat away from obstacles. Multiple water fights broke out on the river, including with other peaceful rafters. Fortunately, we all survived the trek and headed

More →

CAMP CYSTINOSIS

back to the condo for lunch and recovery. That night, they got all dressed up for the opening night of the film *Barbie*.

The next day we took the kids to Park City Mountain resort, where we rode the chairlift to the top of the ski hill and rode the Alpine Slide all the way down. They discouraged us from racing, but we couldn't help ourselves. After riding the slide, the girls decided they needed to go shopping at the Park City Outlets. We learned that they shop just as long as any other teenage girls! That night we took a dip in the famous Midway Crater, an underground hot springs inside a volcano-shaped mountain. The pool is 30 feet deep! The kids floated in life jackets and practiced their synchronized swimming.

On day four we took the kids hiking at Silver Lake in Big Cottonwood Canyon. We took a leisurely stroll around the lake and took in the nice mountain air. We spent the rest of the day relaxing, and playing board games and some evening mini-golf.

The next day we sent everyone home. It was bittersweet to say goodbye after having so much fun together. We learned a lot about cystinosis teenagers! For example, they really like hot sauce and making sandwiches at 10:00 p.m. I've never seen teenagers devour a charcuterie plate so fast. They liked staying up till 2:00 a.m. every night. They didn't eat much breakfast, but they took over 50 pills a day without complaining. Two large cases of water bottles from Costco were not nearly enough. And we couldn't have done it without help from Monique Carriere, Brooke's mom. She was a lifesaver!

Camp Cystinosis was pretty exhausting, but the kids had so much fun, I think we're going to have to do it again in the future! If that's something you think your teenager might enjoy, send me a message!

Letter from Gran

Dear Seth,

I remember the day when Gramps and I found out that you and your twin brother were on the way to be part of our lives. We were watching a movie with your Uncle Marc, and when your parents phoned, we jumped up and down and shouted for joy. Can you imagine your grandparents doing that?

I also remember the first time I held you. Because you were a little bit early, we were spending lots of time with you in the hospital, and learned about skin-to-skin time. You probably cringe at the idea of that now, but it was very special for us and helped you overcome some early challenges for your little body. I will never forget how my love for you blossomed during those days. I said to someone that I would jump in front of a train or fight off a grizzly bear to save you, and I meant it!

Another memory, which came with tears, was on the day that your parents called with the not-so-happy news that you had a rare condition called cystinosis. Of course, we read all we could about this genetic glitch and our first reaction was one of sadness for you and your parents and your brother, as we tried to imagine what the impact would be on all your lives.

A decade has passed, you've celebrated your 11th birthday with your brother, Leif, and are now on the cusp of your teen years.

This is an exciting time — with greater knowledge and skills, you are able to be more responsible and independent, making more of your own decisions, big and small. Your parents have done an incredible job of raising you and your brother. From our perspective as grandparents, they have been masterful at providing you with the perfect balance of support and challenge, giving you a warm, loving and safe home base from which to explore the adventures the world holds for you. You have also been very fortunate to benefit from the enfoldment of Cystinosis Research Foundation who do so much to gather and use the resources of family, friends and experts to ensure your future long-term wellbeing.

You are a blessing to those who know you, and will continue to shine a special light wherever you are.

By Sherry Taylor, grandmother to Seth deBruyn

SUMMERLAND, BRITISH COLUMBIA, CANADA

We've watched as you've been faced with trying new things and struggling with your feelings. It's scary and not fun to be not-so-good at something in the beginning, but you have persevered and learned how to ski and backpack, mountain bike and swim, paddle and fish, play soccer and the piano, cook and write and draw — to do so many things that you'll now be able to enjoy for years to come.

You are passing from the somewhat blissful naivety of childhood into another phase where you are becoming more aware of the realities of life in general, and of life with cystinosis in particular. You have always been a real trooper when it came to the unfun aspects of your cystinosis like needles and eye drops. What you are becoming aware of are some of the other aspects of cystinosis that your parents have been dealing with all these years. The other day you asked them about the money that was being spent on your medications, and what that meant for your family. Other questions will occur to you, and you will probably find many answers interesting and inspiring and others more difficult.

L-R: Jim Laviolette, Seth deBruyn, Leif deBruyn, Kristen Murray, Nathan deBruyn, Sherry Taylor

I am writing this letter to you, in a public space, because Gramps and I want you to know that you are part of a large community that believes in you. We believe in the young lad who is so much more than the condition he happens to have, a courageous young lad who has shown over and over again that he can overcome hardships, laugh heartily, bask in loving and being loved and live a wonderful life. You are a blessing to those who know you, and will continue to shine a special light wherever you are.

Love,
Gran

Khalasi Family Update

By Minaxi Khalasi, Aarav's mom
SACRAMENTO, CALIFORNIA

Aarav's cystinosis journey began in 2015 when he was just one year old. In all honesty, so much has changed since his diagnosis. The improvements in our lives or what we identify as our norm have changed significantly. We went from wondering if he would eat to purposely going to his favorite spots to eat.

Thanks to CRF, a medication that received FDA approval in 2013 became a saving grace in his life. In 2019, our community came together to start Aarav's Time to Shine and the support we received was amazing. Our hearts were full, and we will forever be grateful for our community who has always encouraged us.

Every day is different, and Aarav has proven to triumph through times where we as parents found it hard to hide our pain.

This year we held our third event and once again the support we received was incredible. I will not forget the reaction of our guests to seeing a shadow box display showing the medications that Aarav receives daily. The visual representation really helped put his daily life into perspective. As parents, we tend to forget the struggles because labs, medications and doctor appointments are all very normal to us.

This year was the first year Aarav was truly able to understand the concept of Aarav's Time to Shine and the Cystinosis Research Foundation. During this whole process, we were able to raise awareness in our own household. We were amazed to see how fast the kids were growing up and understanding the complexity that cystinosis entails. Isha and Rani are now six years old and have a good idea about Aarav's medication times and his needs. They support him and know the importance of his health.

Over the years our lives have changed significantly and a big part of that has been cystinosis. Another part was Aarav's outlook and positivity. It can truly make one wonder because he never complains about his countless medications, labs and appointments. Like most kids he looks forward to school, friends, and his one and only true passion, which is football. Our family knows that this journey is not going to be an easy one, but with every milestone we hope that Aarav continues to shine with his amazing personality. The positivity that we didn't have when he was diagnosed, we now have, and it is all because of CRF and, of course, Aarav.

Aarav's Time to Shine Grand Gala Planning Committee

A SUCCESSFUL AARAV'S TIME TO SHINE GRAND GALA

Aarav's Time to Shine Foundation, formed by Minaxi and Mukund Khalasi in honor of their son Aarav, hosted their Grand Gala fundraiser on Saturday, September 16, at the White Lotus Banquet Hall in Citrus Heights, California. Over 200 of their friends and family attended the event to help raise funds for cystinosis research. The Khalasi family greeted guests during the cocktail reception, as people joined in playing games to purchase raffle tickets and win prizes. Teresa and Kevin Partington, whose twins have cystinosis, were special guests at the event. Teresa gave a heartwarming talk about what it is like living with cystinosis. Following dinner and the live auction at the end of the evening, **an incredible $87,000 had been raised for cystinosis research!** We are grateful to the Khalasi family, their supportive sponsors and dedicated volunteers, and their generous community for their commitment to Aarav and all those with cystinosis. Thank you!

A True Cause For Celebration

Teresa Partington Gives a Talk at Aarav's Time to Shine Cystinosis Fundraising Event

"Good evening to all of you who are here to celebrate and support Aarav and his beautiful family. My husband and I are parents to Jenna and Patrick, 18-year-old twins who have cystinosis. Having been in the position of hosting an event like this, I can speak to the excitement, stress, time commitments and emotion that Mukund and Minaxi have put into this evening. Everybody loves a party, but it can be difficult to celebrate when the reason you're having a party is that your kid is sick. The balance to this emotion, or the "mojo," if you will, comes from taking in the support shown by family and loved ones. And the more subtle bit of spirit comes from the realization that this is not just about cystinosis, but about Aarav and his family's bravery. A night in support of meaningful charity makes our world feel a bit clearer, a bit better. His courage and fight is our cause for celebration. Aarav, Jenna and Patrick have inspired all of you to be here to help ignite the far reaching spark that they have lit.

When asked to give a talk, one leans into a subject at the forefront of their mind.

When our twins were babies and toddlers, I might have talked about vomit and two-hour-long meals, and vomit, and the many ways our family vision had changed. I'd have discussed how Kevin and I forcibly, heartbreakingly, held our kids arms and legs pinned to the floor, many times per day, to give them their life sustaining medication. Those were the hardest years.

When they were in first grade I spoke about living for a short time in Palo Alto while the kids participated in a drug trial at Stanford University's Research Lab, pioneering an improved cystinosis treatment (taken every 12 hours instead of every six) that most patients enjoy the benefits of today.

The grade school and high school years would be about nausea (and a bit less vomiting), mysterious but definite learning differences, low stamina, as well as knocked knees and the surgical repair of them. All of these hallmarks of cystinosis.

Alas, we have arrived in Fall 2023. Jenna and Patrick have persevered and found themselves at college, something that Kevin and I were not always able to visualize for them. What is on my mind now is medicine - ordering meds, receiving meds, prepping meds, shipping meds, and above all, praying that Patrick and Jenna TAKE their meds! Their piles of "horse pills" are easy to skip, relieving to skip and dangerous to skip. Our kids feel better when they miss their meds, as uncomfortable and sometimes embarrassing side effects disappear. But the life of a person with cystinosis is made shorter when meds are missed. Cystinosis is a quiet, invisible threat. The only antidote to its progress is MEDS.

READ ABOUT THE 2023 L5 CAPITAL CUP GOLF TOURNAMENT THAT RAISED $62K ON PAGE 78.

By Teresa Partington, Jenna and Patrick's mom
SACRAMENTO, CALIFORNIA

I will admit I'm not the only person in the room thinking about their kids' medicine.

This is a photo that Aarav's mom, Minaxi, shared with me: One day's medication for Aarav. This is only one day. Aarav is young and at home and his folks are in charge, which encourages great adherence.

Kevin and I have chased, nagged, inquired and double checked our kids' compliance for 18 years, and now it's on them. It is, quite frankly, frightening.

While they adjust to college life, Kevin and I are happy to continue to gather, prepare and ship meds so all Patrick and Jenna need to do is take them.

Jenna and Patrick take all their medications in pill form. I took a photo of a recent "pill box assembly day." After a month's worth of twice-daily doses are parceled out and locked in pill boxes, they are shipped off and we pray that what we've taught the kids' about drug compliance over the years has stuck. Kevin and I are the opposite of our peers who are sending their kids to college, pleading with our kids to take their drugs!


Assembling a months worth of prepared medication for shipping to college students.

Their most miraculous medication, Procysbi®, was approved over a decade ago and contains a time release formulation of cysteamine, the first effective treatment for cystinosis discovered in the 1970s, helping those with the disease live beyond the age of nine. Fun fact: the compound cysteamine was initially tested by the US military as an antidote to radiation from nuclear attack.

Procysbi® works by binding to cysteine, which most humans rid their cells of by way of a protein that carries it away as waste. Cystinosis patients lack this protein, causing cystine to crystallize and kill cells. The dead, crystallized cells stick to tissues and organs of the body, causing blockage, dysfunction and ultimately organ failure. A patient who takes Procysbi® as directed is usually able to bring cell cystine content to normal levels, helping slow progression of the disease, but it is by no means a cure. The side effects can be unbearable. Procysbi® is both a blessing and a curse.

The treatment of damage done is accomplished with other drugs and supplements: gobs of potassium, phosphorus, Calcitriol, Lipitor, Cystaran, Nutropin, Levocarnitine, Amiloride, vitamin B and coenzymeQ10. When it's all said and done, Jenna and Patrick take around 56 pills a day.

The stem cell and gene therapy treatment that is about to enter phase three clinical trials would all but eliminate the need for most of the meds mentioned, as well as the side effects that come with them. Very simply put, the therapy inserts a repaired gene into the cells of a person with cystinosis, introducing the protein that eliminates cystine from their cells. The first six patients in the stem cell and gene therapy trial have all ceased taking Procysbi® which is nothing less than miraculous.

The key to continued research of improved drugs and cutting edge treatments is funding. What you have contributed to this evening will be passed on to the Cystinosis Research Foundation. Since its inception 20 years ago, community events like *Aarav's Time to Shine* have helped raise over 68 million dollars, and funded 228 research studies to date. If approved by the FDA, stem cell and gene therapy may be an option for some, but the way gene therapies will be brought to market, prescribed and covered by insurance remains to be seen. For this reason, the mechanics of cystinosis must be further researched and better understood, paving the way for reliable new therapies that can reach the greatest number of patients.

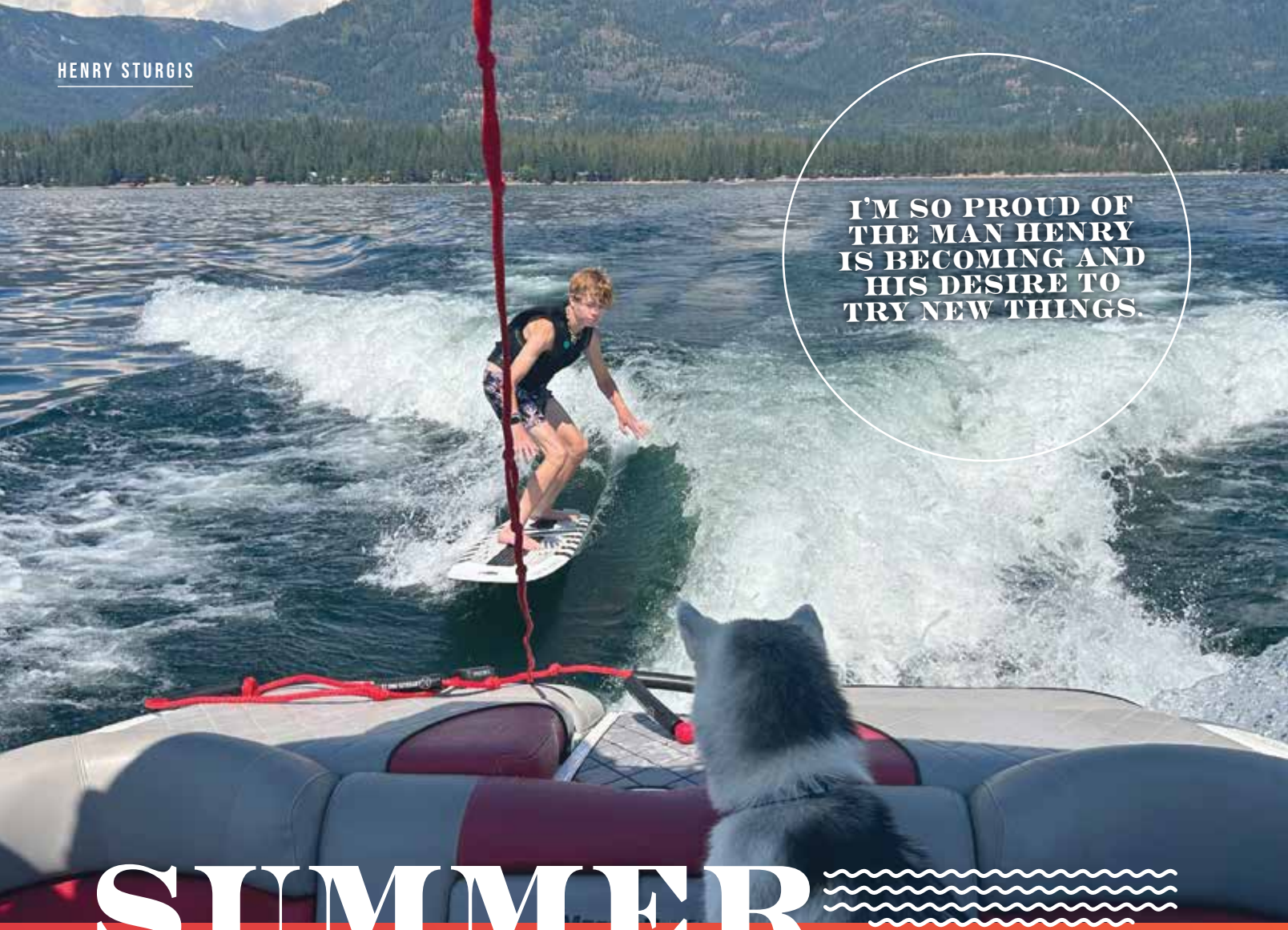
And so, we continue to be tasked with advocating for our children, and asking you to help us fund research. Kevin and I want to see our children enjoy a long life of happiness and good health. We are able to pursue this personal desire knowing we are contributing to progress that will benefit the field of medicine and help many.

Case in point: A study published in the medical journal *Cell Reports* on August 8th of this year highlighted a study by CRF funded researcher Stéphanie Cherqui, who has effectively rescued multiple signs and symptoms of Alzheimer's in a mouse model of the disease. To quote the article, "Mice that received healthy stem cells showed preserved memory and cognition, reduced neuroinflammation and significantly less B-Amyloid build-up, compared to other Alzheimer's mice."

Imagine, if the spark that children like Aarav, Jenna and Patrick have lit, leads to the cure of not just cystinosis, but of Alzheimer's? A disease so prevalent that many of us have been touched by it?

This evening, as you celebrate Aarav's bravery and fight for good health, you are contributing to cutting edge medical progress. You are facing the next generation of medicine, and funding the researchers at the forefront of the effort. These kiddos we love have inspired something beyond what we'd imagined. This is truly cause for celebration.

HENRY STURGIS



I'M SO PROUD OF THE MAN HENRY IS BECOMING AND HIS DESIRE TO TRY NEW THINGS.

SUMMER HIGHLIGHTS

By Brian Sturgis, Henry's dad
SANDPOINT, IDAHO

Henry turned 17 this summer and is now a junior in high school. Time is flying by, but it feels like it was yesterday that we would lay on the floor every six hours trying to get him to drink a bottle filled with juice and Cystagon®. I don't miss putting him through that, but I do miss those times together.

Summer was filled with lots of fun, surfing and boating. If you were to ask Henry what the highlight of the summer was it would be two things: Camp Cystinosis and the Patterson twins visiting Sandpoint.

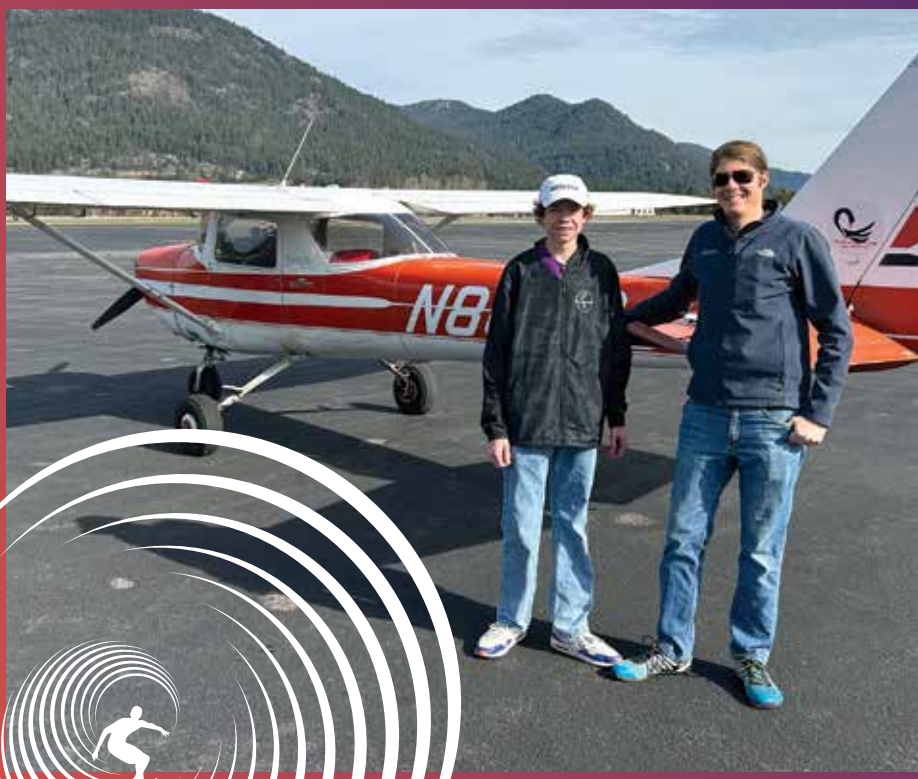
In July, the Jenkins family hosted the first Camp Cystinosis in Utah (see page 52). Henry and Tina Flerchinger were the official/unofficial camp counselors. Henry had been looking forward to this trip for months and it did not disappoint! The Jenkins did an outstanding job of organizing the trip and activities. The kids got to see and do things that most of them never had, including hiking in Utah, hot springs, river rafting, and Alpine sliding in Park City. I can't thank the Jenkins enough for putting the camp together. I think it was a learning experience for them too, as teenagers in a group are completely different animals than younger kids.

Only a few weeks after returning from Camp Cystinosis, Emma and Gracie Patterson (twins with cystinosis) from Federal Way, Washington, came to our house for a week. Henry really enjoyed showing them around Sandpoint and they did everything from hiking at Schweitzer, boating around the lake, and just enjoying time together in town. We finished off the week with a two-night camping trip on an island at Priest Lake.

Over the last year and a half, Henry has taken a big interest in aviation. It started with an aviation club through the high school that meets on Saturdays where they build a plane from the ground up. Once a month, each kid has an opportunity to fly with one of the instructors and get a taste of what being a pilot is like. Henry loved it and is currently obtaining his private pilot license and will be doing his first solo flight soon. This is both exciting and nerve-racking as a parent.

Henry's other focus over the last year and a half has been his health. He has really taken a lead managing his health and with help from a couple of friends they put together a workout program and diet to follow to help build muscle and strength. Henry follows it closely going to the gym at least three days a week if not everyday after school. He is focused on how much he is eating and what he is eating. It's been a big change for our dinner routine as he now eats way more than I do. He also helps with prepping/organizing his meds for the month and has even started to pick them up at the pharmacy.

While I look back at the past 17 years, I'm so proud of the man Henry is becoming and his desire to try new things, whether it be learning to fly, new food and management of his health, new tricks on his surfboard or his work ethic at school.



THIS IS Our Story

By Stacey Maw, Cillian's mom

CAMBRIDGE, ONTARIO, CANADA

Our son Cillian was born your "normal" average kid; average height, average weight, hitting all the proper milestones a "normal" kid his age should. Cillian was always so happy and energetic, which made it hard for us as new parents to say something was off, but something was definitely off. Around 12 months old, Cillian stopped wanting a bottle and reached for water instead, and his weight started to slowly decline. When I shared our concerns with his doctor I was told not to let him drink water, only milk/formula, as water was "empty calories." We did our best to follow this instruction; we were new parents, what did we know? But, as time went on I felt I needed to follow my gut, and pushed for a second opinion, and we were finally referred to a pediatrician. Seeing all the signs of dehydration, even though he was drinking tons of water, bloodwork was ordered straight away.

It was Friday afternoon; I took Cillian for bloodwork, and Saturday morning at 3:00 a.m. we got a call from the hospital, saying, "Bring him into the emergency room straight away." My heart was in my throat. We were in the height of the COVID-19 pandemic, hospitals were full; what could be so wrong with him? With no clear answers as to why, we rushed him to the hospital. Little did we know that the 3:00 a.m. phone call was the beginning of our lives being turned upside-down.

It was 12 hours later and they had diagnosed Cillian with Fanconi syndrome and arranged for his first ambulance ride to a hospital better equipped to handle his care and find the cause for this strange diagnosis. We spent seven days in the hospital; Cillian was hooked up to monitoring machines and an IV, pushing medication in his body and running bloodwork every couple hours. It was a nightmare for us, and Cillian was drained, but somehow, he still managed to smile and wanted to play whenever he could gather up the energy.

We were told cystinosis was a possibility, but highly unlikely as it was such a rare disease. It was a month before tests came back to confirm Cillian was, in fact, that rare. It was a huge adjustment and a learning curve for our entire family; all the medications, the information, our new schedule and way of life. We struggled with the changes, having little support due to the pandemic, but Cillian got us through. His good nature never wavered; he remained his happy, funny, silly self. This made life easier for us, however, it was still hard to think about his future and what life would look like for our family.

HOPE came months after diagnosis; after so many medication changes, appointments and G-tube surgery, we read about Jordan Janz and the work that CRF was doing, and a weight was immediately lifted. There was hope. This was all going to be OK. We would survive this "new normal" and make Cillian's future bright again!

NOW THREE YEARS INTO DIAGNOSIS, CILLIAN IS ABSOLUTELY FLYING! HE HAS STARTED JK AND HAS TURNED INTO QUITE THE LITTLE ARTIST. HE LOVES RIDING HIS BIKE AND PLAYING, TELLING JOKES AND MAKING PEOPLE LAUGH. HE HAS THE BIGGEST HEART AND A SHARP MIND AND I KNOW HE IS GOING TO GO SO FAR IN LIFE!

We cannot thank the CRF enough for what they have done and what they are doing for the cystinosis community. It has already been a journey, and there is a long road ahead, but together we can make a difference.

THANK YOU CRF!

Cillian got us through. His good nature never wavered; he remained his happy, funny, silly self.

READ ABOUT "CAMINO FOR CILLIAN" THE 1000km WALK ACROSS SPAIN THAT RAISED MORE THAN $24K ON PAGE 77.

My Tribe — MY CYSTAHOOD

In the journey of life, we often find ourselves in unique communities, connected by shared experiences and challenges. For those who navigate the path of raising a child or having a loved one with cystinosis, there is a remarkable sisterhood, aka "Cystahood," that offers strength, support and solace.

Cystinosis is not just a medical condition; it's a constant presence in our lives, shaping our daily routines, decisions, and even our dreams. In the face of this relentless adversary, the power of a tribe of women who have walked this path alongside me has been nothing short of a blessing. While there are so many incredible men, including my husband, Don, who travel this journey alongside us, there is something truly magical about the Cystahood.

Our Cystahood is a sanctuary of understanding. It's a place where we don't have to explain the intricacies of the disease or the endless medication schedules. It's where we can speak openly about our fears, frustrations and hopes without fear of judgment. In the Cystahood, every sigh, every tear, and every triumph are met with empathy because we've all been there.

Together, we are unrelenting against the challenges of cystinosis and face each day with unwavering determination to battle alongside our loved ones. We share knowledge and resources while helping each other navigate the many complex healthcare systems we find ourselves in. We share information about the best specialists and rejoice collectively with advances being made through the latest research. When one of us discovers a creative way to manage symptoms, we all benefit.

But our Cystahood is not just about facing challenges — it's also about celebrating the victories, big and small. We cheer each other on when a child reaches a developmental milestone or endures a challenging medical procedure. We rejoice in the strength and resilience of our little heroes.

In our tribe, hope is our constant companion. When one of us feels overwhelmed by the weight of cystinosis, the others lift her up with words of encouragement. We remind each other that even in the darkest moments, there is always a glimmer of hope. Together, we carry the torch of optimism that lights our way forward.

She made broken look beautiful and strong look invincible. She walked with the universe on her shoulders and made it look like a pair of wings.

By Karen McCullagh,
Mom to Andrew (with cystinosis) and Kelsey Cunningham

LEIXLIP, CO. KILDARE, IRELAND

Through the Cystahood, we find solace in the company of those who truly understand the emotional rollercoaster of this journey. We know the guilt that sometimes gnaws at us when we can't protect our children from pain. We understand the sleepless nights filled with worry and the moments of despair that occasionally visit us.

But we also know the unbreakable bond of love that forms between us and our children. We witness their courage in the face of adversity, their resilience in enduring treatments, and their radiant smiles that light up our lives. Our children with cystinosis inspire us every day, teaching us the profound meaning of strength and grace.

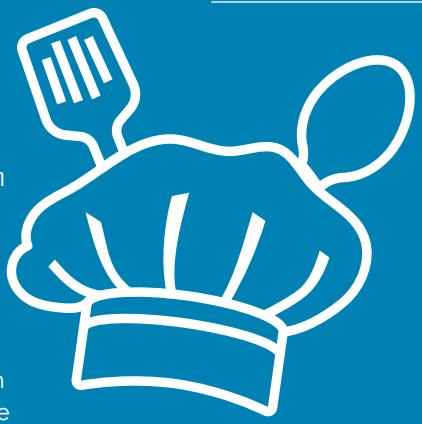
We are not just mothers, grandmothers, sisters, aunts, wives and daughters; we are advocates and change-makers. We bring our own skills and passions to the Cystahood in the fight against cystinosis. We organize support networks, fundraisers and awareness campaigns. We use our expertise and life experiences to advocate for better research, treatments and resources for our children and all those affected by cystinosis.

In our Cystahood, we find friendship and sisterhood that transcends the boundaries of geography. When I moved to Ireland in 2019, I was anxious that I might lose my tribe of women. Instead I found even more amazing women to help share the burden and lighten the load. Regardless of where we live, our connection remains unshaken. We've laughed together, cried together, and celebrated together. We've become a second family, bound by love and united in purpose.

The power and blessing of having a tribe of women who also have a child or loved one with cystinosis — our Cystahood — is a testament to the strength of the human spirit. We face adversity with grace, support each other with unwavering devotion, and find hope in the darkest of moments. Our journey may be challenging, but with the Cystahood by our side, we are never alone. Together, we rise, we thrive, and we continue to inspire each other and the world with our boundless love and resilience. I know that despite all the negatives that cystinosis can be, I am ever grateful for the women who walk this path with me; my tribe — my Cystahood.

WE EXPRESS OUR GRATITUDE, LOVE, AND RESPECT TO EVERYONE THAT HAS BEEN PART OF OUR JOURNEY.

A MIRACULOUS JOURNEY



By Maria Gabriela Davila de Quintana, Luis' mom
BROOKLYN, NEW YORK

It happened more than 11 years ago, but I remember it as though it was yesterday. Fear, guilt, frustration, and especially hopelessness, are some of the feelings I had when I received the diagnosis for my 14-month-old son, Luis — "cystinosis."

Luis, now 13, was born in Venezuela. He was a sweet, healthy boy until 6-7 months old, when he started with all the typical symptoms: dehydration, vomiting, polyurea, polydipsia, and he stopped gaining weight. We visited several doctors; we had so many doctor appointments, labs, and tests, but Luis was getting worse every day without knowing the cause. He got very sick, to the point that he had to be hospitalized for almost three months, including in the ICU at some point. After so many needles, IVs, labs, doctor visits and tears we received his first diagnosis: Fanconi syndrome. He was discharged with a list of 13 different medications and almost 40 doses per day. Of course, as parents, we were scared and overwhelmed but ready to step up and advocate for our kid.

Unfortunately, the political and socioeconomic situation in Venezuela was already chaotic.

There was a lack of all kinds of different basic needs, like toilet paper, diapers (so imagine a seven-month-old baby that needed more than 10 diapers per day and not being able to find them!), food (including baby formula), and medications (not even basic medications like phosphate, potassium, sodium, etc.). Of course, there wasn't any kind of treatment available for cystinosis, not cysteamine (Cystagon®) or eye drops, not labs, and there were not many doctors with the knowledge to manage this rare and complex illness.

Thankfully we had a great support system back in Venezuela. We had so many family members and friends willing to help us. They would help us find medications and other needs all over the country and send them to us. We also met a marvelous nephrologist with the biggest heart and most compassion, Dr. Alexander Mendez. He was very knowledgeable and caring about cystinosis. He founded the Venezuelan Cystinosis Foundation and helped us get in touch with the international Cystinosis Foundation in Mexico and Brazil. They helped us send Cystagon® to the families in Venezuela on some occasions.

Since the situation in Venezuela was getting worse every day and our son's health was deteriorating, we were determined to find a better solution and treatment for him. We decided that we needed to move away to guarantee his treatment and wellness. We got in touch with a very special friend, Xavier Wehe, who was living in the US — he is our real hero. He helped us get in touch with Cystinosis Research Foundation and the National Institute of Health (NIH) where Luis was accepted as part of the Cystinosis Research Program conducted by Dr. Bill Gahl and Dr. Galina Nesterova. We visited the NIH for the first time when Luis was three years old, and everything has changed since then. It was not easy, but with the help of very special people, Luis was able to finally start receiving the treatment that he needed and deserved.

After so much effort, challenges and fights, we were able to finally move to New York, where we found all the treatment and specialists that Luis needed. Luis is healthy and stable nowadays, enjoying every minute of his life, and we are so grateful to see how much his quality of life has improved.

We have no words to express our gratitude, love, and respect to everyone that has been part of our journey. And we cannot stop thanking God for bringing us here and making this miracle possible.

TODAY, OUR CHAMPION, LUIS, IS GETTING READY TO START EIGHTH GRADE. HE ATTENDS MARK TWAIN FOR THE GIFTED AND TALENTED MIDDLE SCHOOL, STUDYING ART AS HIS TALENT, AND WANTS TO BE A PROFESSIONAL CHEF WHEN HE GROWS UP!

Last spring, we attended the CRF Day of Hope Family Conference in California for the first time, and had the fortune to meet such a wonderful community, full of joy and hope. It felt like a dream come true; we cannot believe the journey we have made. We feel very grateful, and know that we are not alone, that there is hope, that Luis Fabian and all the cystinosis families will have a great future and that the cure is closer every day!

THANK YOU TO THE TRUE TRAILBLAZERS

By Kevin Simpson, Charlie's dad

NEW ORLEANS, LOUISIANA

Our son, Charlie, was diagnosed with cystinosis in June 2019, meaning a CRF "Day of Hope" conference had just concluded two months before. Subsequently, COVID-19 precautions overwhelmed this important and inspiring event, so it was not until 2022 that we were able to gather and meet face-to-face with other families who were going through what we were.

Fortunately, many of you proactively reached out in the early days of diagnosis offering comfort and counsel to two parents who would otherwise have felt even more disoriented and alone on this journey. Like so many others, we had no idea what we were up against. It began with a three-week hospital stay where Charlie almost died, then stabilization, and finally diagnosis of a disease we had never heard of. So, to hear and discuss the myths and realities, shared experiences, and common hope was quite literally life-giving.

Naturally, nearly all of these conversations centered on the day-to-day care of a tiny child with this terrible condition. That was the priority because we didn't know what we didn't know. The other part of the conversation was forward-looking because one of the very first calls came from Nancy Stack, who we can remember saying, "We think this is the cure," in reference to Dr. Cherqui's incredible research. We started this note as an update on Charlie – he's really doing pretty well, with more visible problems common to any 5-year-old than problems with his meds or his illness – but we need to share space to acknowledge some things that make this update possible.

Last year, when we had our first chance to attend the "Day of Hope," we came to appreciate the importance of the past as much as our attention is on the present and future. It became obvious to us that this is not just a story about children, nor is it just a kids' cause. This story was founded and is rooted in the adults who have suffered this terrifying disease not just as toddlers but as teenagers and young adults. And they did that, depending on timing, with far fewer treatments and much less science to guide their care, most with no email or social media to connect and compare notes with other families. How could they carry on for so many years with no view to a cure? As horrible as cystinosis has been for all of our children, it was certainly far worse for those who came before.

What we can say here is that these are the true trailblazers who've undoubtedly explained more to doctors about the effects of this disease than they ever could have read about. They agreed to experiments for treatments, innovated home remedies, and crafted workarounds to the myriad challenges.

To say "thank you" feels small and not nearly enough. To say we are in awe of you is truer. You have persevered to become strong and confident adults, living as parents and professionals and mentors and true role models to a small but powerful community which will never forget you. You've given the gift of a better life with fewer side effects, more time to focus on life's passions, and more time to fix the other challenges.

Charlie's at an age where he's just beginning to understand his condition and all the people it takes to help him. In time, his gratitude will exceed even ours.

ONE OF THE VERY FIRST CALLS CAME FROM NANCY STACK, "WE THINK THIS IS THE CURE," IN REFERENCE TO DR. CHERQUI'S INCREDIBLE RESEARCH.

WE ENJOY WATCHING KEEGAN CHALLENGE HIMSELF IN WAYS WE NEVER COULD HAVE IMAGINED!

ADVENTURES ABOUND!

By Nicole and Brad Manz, Keegan's mom and dad
CHAPEL HILL, NORTH CAROLINA

This fall marks the tenth anniversary of Keegan's diagnosis. Reflecting on those early days, we remember all the sleepless nights, hospitalizations, doctor's appointments, and vomiting. Brad and I were scared and uncertain about what life would look like for Keegan. However, we were determined to build a life for our family that was full of love, support and fun!

Keegan is now ten years old and getting ready to start 4th grade. He loves learning, reading, swimming and playing with friends. Most weekends, you will find him cheering for his big brother on the baseball field! He loves keeping score and calling pitches. Over the last few years, Keegan has developed a love for travel and is always looking to plan his next adventure on an airplane! We are so grateful for his health and enjoy watching him challenge himself in ways we never could have imagined!

UPDATE FROM KEEGAN, 10 YEARS OLD

What is the best part of being 10 years old?

Keegan: **I get to stay up late on weekends.**

What excites you most about 4th grade?

Keegan: **I get to be in a new classroom and play on the Ponderosa (big kids' playground).**

What are some of your favorite things to do?

Keegan: **Watch movies, play on my Nintendo Switch, go to the pool and to the trampoline park.**

Name the 3 favorite places you have traveled.

Keegan: **1. MEXICO: I loved the waterslides, lazy river, playing putt-putt golf and the arcade at the hotel. 2. DOMINICAN REPUBLIC: I loved the big waterslides, lazy river, swimming with the dolphins and the shows at night. I ate pizza by the ocean every day for lunch. 3. SAVANNAH, GEORGIA: I loved taking the trolley all around and going to the train museum. The best part was when we went to Tybee Island. I played with Shane in the sand and on our way home played putt-putt.**

What are you most proud of?

Keegan: **Going underwater at the pool.**

What scares you?

Keegan: **Heights. I don't know why. I am just afraid.**

What piece of advice do you have for kids that have to take a lot of vitamins?

Keegan: **Don't be scared. It's no big deal.**

UPDATE FROM SHANE MANZ, KEEGAN'S BROTHER, 14 YEARS OLD

When Keegan first got sick, I was four years old. It was hard to grasp what was happening when my mom left to stay with Keegan in the hospital for two months. I went and saw them in the hospital with my dad every now and then, but it wasn't the same. When my mom and brother came home, he was hooked up to this machine with all these tubes connected to his nose. It was scary. I thought he was going to die.

Flash forward ten years. I'm fourteen now, and about to start my freshmen year of high school. Growing up with Keegan has been a rollercoaster. Most days seem normal now. We play with our dog, play video games and go to the pool. Keegan loves going to my baseball games and keeping score. However, other days can be scary, and I am reminded of how different Keegan's life is from mine. He takes so many medications, gets blood drawn and sometimes he gets sick. I worry about Keegan getting teased about his smell because of his medication, his learning challenges and what his adult life will be like. Keegan has taught me to accept people for their differences.

I want to thank Nancy for everything she has done for cystinosis. Meeting the other siblings at the CRF Day of Hope conferences was good for me because I found other siblings I could relate to. I learned that no matter how hard life hits you, you always can get up and hit back harder.

TOGETHER, WE ARE one

1 PURPOSE. 1 JOURNEY. 1 CURE.

COMMUNITY NEWS

The following pages celebrate the events dedicated to awareness and a cure by our cystinosis community. Together, we are stronger. Together, we are one!

HELP CRF CONTINUE FUNDING LIFE-SAVING RESEARCH!

Did you know you can help support the Cystinosis Research Foundation's ongoing research efforts by planning your own GoFundMe fundraiser? Planning an event on behalf of someone you love with cystinosis is not only gratifying, but it also gives others a chance to support a cause that is important to you.

A lot has changed since CRF was established in 2003. With your help, CRF has become the driving force for all cystinosis research and advances in treatment. CRF has changed the course of cystinosis research and changed lives, but there is more to learn and more discoveries to be made - we need your help!

To start your own fundraiser through GoFundMe, simply visit WWW.GOFUNDME.COM/START/CHARITY-FUNDRAISING search for Cystinosis Research Foundation and follow the prompts to start your campaign. Every dollar donated goes directly toward supporting cystinosis research!

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The Beauregard Family – Courtney, Kevin and Lily – Swansea, Massachusetts

CONCERT FOR LILY FUNDRAISER

The Fifth Annual Concert in honor of Lily Beauregard and cystinosis research was held Sunday, June 25, and was a wonderful success, raising $2,500 for cystinosis research! More than 140 enthusiastic friends and families enjoyed the live rock 'n' roll performances and the picture-perfect summer weather! The concert featured Rhode Island Hall of Fame musicians the D'Vottes, Mark and Sam Taber, and The Dick Clark's contributing their time and extensive talents.

The event was enjoyable for Lily and her family as they shared the afternoon with friends Nelson Lima and his son Jackson, Laura and Jonathan Shields, and their children, Zeke and Eden, who also have cystinosis. The highlight was watching Lily and her playmates being entertained by the balloon artist, laughing and having fun with the bubble wands, and of course, getting their faces painted.

We are so grateful to Tom Wallis for his countless hours of organizing and coordinating the annual event, and thank you to the musicians, vendors and the community who have helped raise nearly $20,000 since 2018 for cystinosis research!

The Fehr Family – Leah, Devin, James and Maya – Rosthern, Saskatchewan, Canada

HOPE FOR JAMES GOLF TOURNAMENT

The Hope For James Golf Tournament was held this year on Saturday, July 29, at Legends Golf Course in Saskatchewan, Canada. It was a beautiful day with the weather cooperating as nearly 90 golfers teed up to honor James Fehr and support cystinosis research. Each year, family and friends in the community contribute in a big way by playing golf, buying sponsorships, bidding on silent and live auction items, and chipping in for raffle tickets. This year, at the end of the event, more than $18,000 was raised to donate to Canada Helps for the Canadian Cystinosis Research Foundation through the Aqueduct Foundation.

Thank you to the Fehr family and all the participants who contributed to help make the tournament another tremendous success. We are grateful to our Canadian friends who support CRF and our mission to fund research for improved treatments and a cure for cystinosis.

TOGETHER, WE ARE one

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The Galloway Family – Christina, Hunt, Rowyn and Collins – Cumming, Georgia

ANOTHER GREEN RIBBON SUCCESS!

Each year in May, the community of Cumming, Georgia, joins the Galloway Family to support their annual Green Ribbon awareness campaign in honor of their daughter Collins. In 2021, Carol Stevens, Collins' grandmother, launched the Green Ribbon campaign and it has caught on and spread like wildfire throughout their community! The beautiful green ribbons are made and sold to neighbors and friends who proudly display them on their mailboxes. The campaign has been a great way to get people involved and create awareness about cystinosis. It is exciting to see the sea of green ribbons everywhere in the neighborhood! This year the campaign raised more than $6,270 for research! Thank you to the friends and neighbors of the Galloway Family, Carol Stevens, and their generous communities for helping to fund research that will result in a brighter future for children and adults with cystinosis.

The Hartz Family – Lauren, Jimmy, Landon and Jordan – Pittsburgh, Pennsylvania

LOTS OF LOVE FOR LANDON GOLF OUTING

The 11th Annual Lots of Love for Landon Charity Golf Outing was held on June 2 at the Black Hawk Golf Course in honor of Landon Hartz. The sold-out field of golfers enjoyed a perfect day of golf competition and camaraderie. Following the tournament, the enthusiastic crowd shared dinner and the opportunity to bid on a wide array of auction items. The tournament raised over $29,233 in honor of Landon and cystinosis research! Thank you to the dedicated volunteers, amazing golfers, generous donors, and the organizing committee of Jason Hartz, Brad Hamilton, Jason Whitfield, Derek Even, Josh Larrow and Jimmy Hartz, who worked diligently to ensure the tournament's success. Our heartfelt thanks to Lauren and Jimmy, their family, and team for their dedication and commitment to CRF and our mission to find better treatments and a cure for cystinosis.

The Kanupke Family – Katie, Tom, Brendan and Josie – Crown Point, Indiana

JOLLY FOR JOSIE — SUMMER EDITION

On Sunday, June 4th, the Kanupke family hosted their second Jolly for Josie Summer Edition fundraiser at the Rock Island Public House in Blue Island, Illinois. Friends and family gathered on a beautiful afternoon to raise money in honor of their daughter Josie. Activities included a balloon artist and face painter for the children, three tables of delicious desserts for sale, donated kegs, and profits from Red's Pizza, helping raise $5,330 to support CRF and cystinosis research. Thank you to the Kanupke family and their community for their unwavering support of Josie and the cystinosis community. Together we are helping to improve the lives of those with cystinosis through research!

TOGETHER, WE ARE one

1 PURPOSE.
1 JOURNEY.
1 CURE.

The Lawatsch Family – Katie and Kenzie – Marinette, Wisconsin

KENZIE'S RIDE FOR A CURE

The Saturday, July 29, Ride for a Cure began at 8:00 a.m. with beautiful weather and excited riders gathering to honor Kenzie and support cystinosis research. By 10:30 a.m., motorcycle kickstands were up, ready for the road ahead. The scenery along the five-and-a-half-hour journey was breathtaking, and by the time the riders reached the Dome Lanes in Marinette, Wisconsin, old and new friendships were secured. Kenzie was so excited and surprised to see all the motorcycle riders pulling into the parking lot to join the fundraising festivities. We are grateful to the Lawatsch family, their community, and riders for their generosity and support in raising $5,700 for cystinosis research. Thank you!

The McQuillan Family – Stacey Maw, Sean and Cillian
Cambridge, Ontario, Canada

CAMINO FOR CILLIAN, 1000KM WALK ACROSS SPAIN

The McQuillan Family friend, Eamonn Boyle, has committed to walk the Camino Del Norte trail starting in Irun, France on September 25, then following the coast of Spain, covering 1000km to raise money for the Cystinosis Research Foundation, in honor of their son Cillian! Eamonn's goal is to complete the walk in 45 days, reaching his destination in Fisterra, Spain. The family has set up a Facebook Group to help promote the fundraiser and a GoFundMe account linked directly to CRF for donations.

WWW.GOFUNDME.COM/F/CAMINO-FOR-CILLIAN-A-1000KM-FOR-A-CURE

As of the magazine publication date, more than $24,734 has been raised so far! The pages will be updated regularly with Eamonn's progress as he tracks his steps, and posts photos and videos along the way. Let's follow Eamonn's progress and support him along his journey for Cillian and cystinosis research!

TOGETHER, WE ARE one

1 PURPOSE.
1 JOURNEY.
1 CURE.

The Partington Family – Teresa, Kevin, Jenna and Patrick – Sacramento, California

SACRAMENTO L5 CAPITAL CUP GOLF TOURNAMENT

Long-time friend and advocate for the Jenna and Patrick's Foundation of Hope, Shannon Deary-Bell, CEO of Nor-Cal Beverage, once again participated in the 2023 L5 Capital Cup Golf Tournament to support Jenna and Patrick and raise money for cystinosis research. The three-day competition, held September 7 to September 9, challenges 32 of Sacramento's most prominent CEOs against each other in a Ryder Cup format to raise funds for charity. This was the seventh time Shannon has played in honor of Jenna and Patrick, this year raising $62,000! The Partington family and CRF are honored and so grateful to the Sacramento community for their generous support of Shannon and cystinosis research. Together, we are creating a brighter future for everyone with cystinosis. Thank you!

The Suetta Family – Shelly, Derek, Lillyanna and Emma Grace – Etna, California

7TH ANNUAL LILLYANNA'S LEMONADE AND BAKE SALE

The 7th Annual Lillyanna's Lemonade and Bake Sale for a Cure held Saturday, June 3, was started by Lillyanna Suetta to raise money for cystinosis research in honor of her sister, Emma Grace. This year's event was even more successful than all the past fundraisers. Shelly, Nana Kathleen, Lilly and Emma baked for three long days, resulting in 1,300 cupcakes and countless other sweets. Derek squeezed 40 lbs. of lemons to make the fresh lemonade sold at the sale. The weather was perfect for sale day, bringing out swarms of people from the community to support Lillyanna, Emma and their friends! The event proceeds and online donations totaled over $6,270 for cystinosis research. We are grateful to the Suetta Family for their special baking skills and the Etna community for supporting Emma Grace and cystinosis research. Together we are providing hope for a future without cystinosis!

2024 CYSTINOSIS COMMUNITY CALENDAR OF EVENTS

We would like to acknowledge all families for their support of cystinosis research, unfortunately some events may have passed by the time this issue is mailed.

February 28, 2024

RARE DISEASE DAY
CYSTINOSIS RESEARCH FOUNDATION
www.cystinosisresearch.org/donate

March 2024

NINTH ANNUAL
FISHING FOR BROOKE'S CURE
HOPE FOR BROOKE
IN HONOR OF BROOKE EMERSON
Contact Clay Emerson: clay.emerson@gmail.com

April 2024

NATALIE'S WISH CELEBRATION
ONLINE FUNDRAISER
CYSTINOSIS RESEARCH FOUNDATION
Contact Nancy Stack: nstack@cystinosisresearch.org

Thursday, April 4 – Saturday, April 6, 2024

CRF DAY OF HOPE FAMILY CONFERENCE
Catamaran Resort and Hotel, San Diego, California
Contact: info@cystinosisresearch.org

May 2024

GREEN RIBBON CAMPAIGN
IN HONOR OF COLLINS GALLOWAY
Cumming, Georgia
Contact Christina Galloway: hootonc@gmail.com

June 2024

LOTS OF LOVE FOR LANDON
CHARITY GOLF OUTING
IN HONOR OF LANDON HARTZ
Black Hawk Golf Course, Beaver Falls, Pennsylvania
Contact: lotsofloveforlandonCRF@gmail.com

June 2024

LILLYANNA'S LEMONADE FOR A CURE
IN HONOR OF HER SISTER EMMA GRACE
Etna, California
Contact: shellysuetta@hotmail.com

June 2024

FIFTH ANNUAL CONCERT
FUNDRAISER FOR LILY
IN HONOR OF LILY BEAUREGARD
East Warren Rod & Gun Club, Warren, Rhode Island
Contact Tom Wallis: thomaswallis@cox.net

Summer or Fall 2024

SHOOTING FOR A CURE FUNDRAISER
HOPES & WISHES
IN HONOR OF JAKE KRAHE
Medina, Ohio
Contact Jeremy Krahe: jdkrahe25@gmail.com

September 2024

L5 CAPITAL CUP GOLF TOURNAMENT
IN HONOR OF JENNA & PATRICK'S
FOUNDATION OF HOPE
Sacramento, California
Contact Kevin Partington: kevin.partington@cushwake.com
or www.jpfh.org

CYSTINOSIS MAGAZINE IS *going green!*

NEXT ISSUE UPDATE

Starting in Spring 2024, *Cystinosis Magazine* will be making the long-awaited transition from print to digital. With deforestation continuing to destroy ecosystems across the planet, every effort – big and small – can help make a difference.

As a foundation dedicated to making the world a better, healthier place, we are excited to officially bring *Cystinosis Magazine* into the digital space and do our part for the environment. **PLUS,** you'll enjoy the convenience of having our magazine available at your fingertips, whenever and wherever you are!

cystinosis RESEARCH FOUNDATION

Don't miss out on any future editions! Sign up for our mailing list for the digital Cystinosis Magazine *today by scanning this QR code and filling out our contact form!*

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cystinosis RESEARCH FOUNDATION

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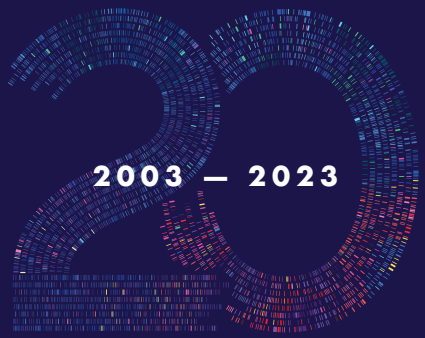
MISSION

The mission of the Cystinosis Research Foundation is to find better treatments and a cure for cystinosis by supporting bench, clinical and translational research. Since 2003, CRF has raised over $68 million with 100% of your donations going to support cystinosis research.

EDUCATION

CRF is dedicated to educating the medical and public communities about cystinosis to ensure early diagnosis and proper treatment.



The sequence of bands above
the CRF gold line is the CTNS gene sequence.

It is this one section that carries
the mutation that creates cystinosis.

The strips of light, combining to create the
“20” represent the collective maps of human
genetics, shining brightly
together.

Our scientific pursuit to restore that one section,
like our courage, is unwavering.

cystinosis RESEARCH FOUNDATION | TOGETHER WE SHINE BRIGHT