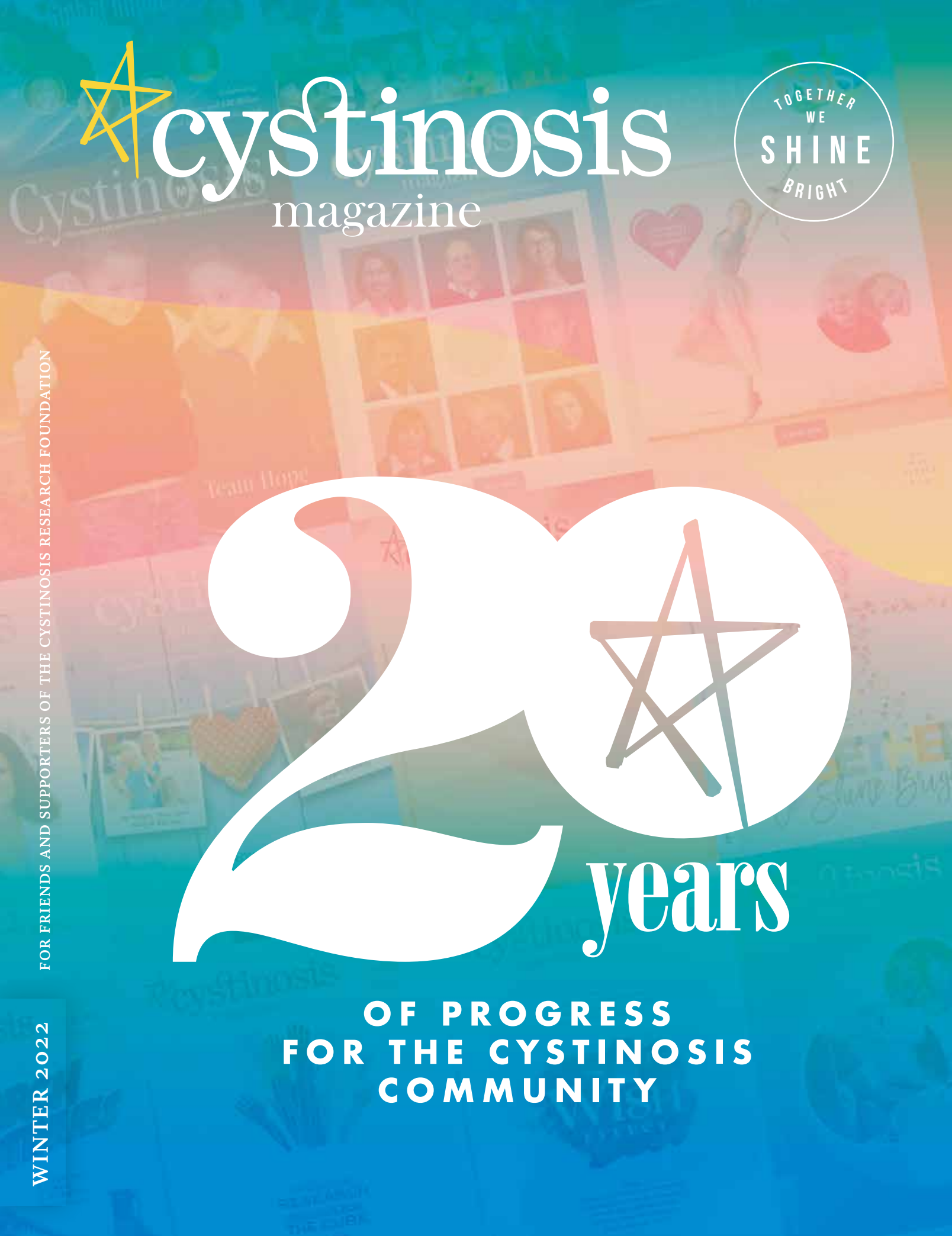
cystinosis magazine

TOGETHER WE SHINE BRIGHT



20 years

OF PROGRESS FOR THE CYSTINOSIS COMMUNITY

FOR FRIENDS AND SUPPORTERS OF THE CYSTINOSIS RESEARCH FOUNDATION

WINTER 2022

cystinosis RESEARCH FOUNDATION | TOGETHER WE SHINE BRIGHT

2003

- Natalie Stack 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 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.

WINTER 2022

20 years

OF **CYSTINOSIS COMMUNITY**
AND **RESEARCH ADVANCEMENT.**

A LIFETIME OF ACCOMPLISHMENTS.

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

To receive our e-newsletter, *Star Facts*, send your email address to *zsolsby@cystinosisresearch.org.*

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cystinosis RESEARCH FOUNDATION

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CHARITY NAVIGATOR ★★★★ Four Star Charity

Platinum Transparency 2022 Candid.

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 $65 million for cystinosis research in an effort to find a cure.

cystinosis RESEARCH FOUNDATION

WELCOME

RESEARCH NEWS

ANNOUNCEMENTS

FAMILY STORIES

CYSTINOSIS MAGAZINE IS A PUBLICATION OF THE CYSTINOSIS RESEARCH FOUNDATION

WINTER 2022

DEAR FAMILY AND FRIENDS,

This issue of Cystinosis Magazine celebrates the start of CRF's 20-year anniversary!

In 2003, Jeff and I held our first fundraiser. We did not know what to expect as we launched CRF but we quickly found out that finding a cure for cystinosis was a cause that our family, friends and other families touched by cystinosis, embraced. Today, we have left an indelible mark in the community.

CRF's commitment to research created the global research community that exists today. We have reached milestones, we have numerous accomplishments to celebrate, we have changed lives, but our work is not over, there is more to learn and more discoveries to make.

The story began in 2003 when our 11-year-old daughter, Natalie, made a wish for her twelfth birthday. It was a profound wish that has unfolded into a global movement. Her wish, scribbled on a napkin changed all of our lives. Those few words "have my disease go away forever" were a wake-up call for us to do something now; there was no time to waste. We never could have imagined how her wish transformed our family and the cystinosis community. From those humble beginnings, we have experienced a life of gratitude, community, and purpose.

As we approach the holiday season, we are filled with a deep sense of appreciation and thanks. As a result of your ongoing support, we are funding cutting-edge research at leading institutions around the world. CRF-funded researchers are forging ahead with bold ideas for innovative treatments and are always in pursuit of the ultimate goal – a cure for cystinosis.

THE REALITIES OF CYSTINOSIS

We know that CRF research has had a significant impact on how we live with cystinosis and how we see the future of the disease but, our reality is that cystinosis remains a progressive and life-threatening disease. Cystinosis destroys every organ in the body including the kidneys, eyes, liver, muscles and brain. As a patient's health deteriorates, kidney transplants become the norm in the teen years. As our children reach adulthood, their symptoms increase and complications from cystinosis become more evident. In adulthood, complications include muscle wasting and myopathy and for some, blindness. We remain hopeful that the stem cell and gene therapy trial is a cure but more time is needed to determine its long-term efficacy. In the meantime, we must continue to search for better treatments to prolong and improve the lives of those living with cystinosis.

The sad truth is that on a far too regular basis, we mourn the loss of people in our community. Within the last year we have lost several adults with cystinosis. Two adults, Tanner Edwards and Jessica Jondle (page 24), were beloved and active in the cystinosis community, including being part of CRF. We celebrate their lives and we remember them for the love and joy they brought to their families and to our community. When someone in our close-knit community dies, it is a loss we all feel on a very personal level. The premature deaths of those we love in our community is a reminder that life is fragile, that time is fleeting and that we have more work to do.

2023 – LOOKING AHEAD WITH EXCITEMENT!

We are already gearing up for a year of celebration in 2023. It will be a year of reflecting on Cystinosis Research Foundation's 20 years of remarkable accomplishments.

Celebrate Natalie's Wish — the Entire Month of April

Celebrate CRF's 20th Anniversary with us in April 2023! Although we will not have an in-person Natalie's Wish fundraising event, we invite you to join us during the month of April 2023 to renew our mutual commitment to the children and adults with cystinosis by raising funds for cystinosis research. We have made significant research advances and we must continue to broaden our research work.

It was 20 years ago, that CRF launched its research program and funded its first study. Since that time, CRF has created a thriving research community dedicated to developing new treatments and finding a cure for cystinosis. To date, CRF has issued 220 research grants, eight extension grants and nine equipment grants in 12 countries leading to significant advances in the treatment of cystinosis and new discoveries about cystinosis and its complications. Most significant, however, is that CRF's commitment to research has led to two FDA approvals, several clinical trials, and a plethora of discoveries about cystinosis and its complications. We are blazing a path to the cure!

Numerous CRF researchers have received 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 103 articles in prestigious scientific 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.

We ask you to join us in April to celebrate 20 years of our accomplishments. We have united and rallied the cystinosis family community and together with you, our family and friends, we have changed the course of cystinosis and given hope to all those with cystinosis. We will have more information about our campaign early next year. See page 14 for more, and mark your calendar!

The Day of Hope Family Conference — A Family Reunion

Our family conference is back in full swing and we anticipate a sold-out family conference in 2023! Not only will we be at a new venue, the VEA Newport Beach, but we will also have some new session topics and an agenda that will touch on all aspects of life with cystinosis.

The Day of Hope family conference allows us to showcase several CRF-funded researchers as well as the most prominent cystinosis clinicians. The conference will blend research, medical information with family and patient stories. Presentations will include areas of research and treatment that are most important to cystinosis families including kidney disease, neurological issues, bone and muscle disease, ocular cystinosis, potential new treatments, current clinical trials and an update on the stem cell and gene therapy trial. The presentations will be fascinating, enlightening and informative.

The best part of the conference will be seeing everyone together – families and researchers – to celebrate our community and to recommit to our goal of working together to find better treatments and a cure for cystinosis.

See page 46 for details about the 2023 conference.

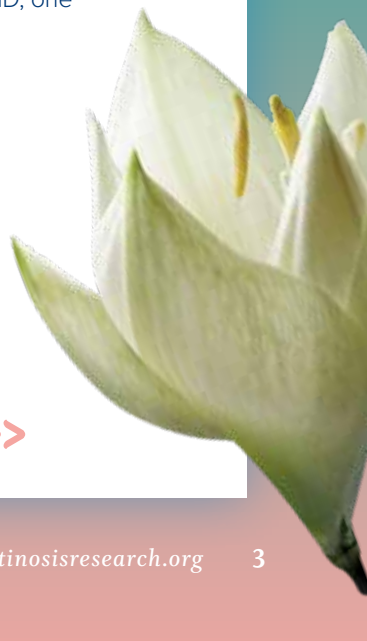
RESEARCH IS OUR FOCUS

Seven Research Grants Awarded in July - $1,287,127

CRF is the leading fund provider of cystinosis research grants in the world, and we have built a global research community that includes hundreds of researchers in countries around the globe.

The success of our research program is because of the leadership and commitment of the CRF Scientific Review Board (SRB) which reviews and critiques the merits of every research application we receive during our spring and fall call for new applications. It is with gratitude that we thank the nine members of the SRB for their expertise and leadership that has resulted in the creation of a flourishing research community dedicated to our children and adults with cystinosis (see page 56 for a list of the SRB members). We have a special interview with Julie Ingelfinger, MD, one of our SRB members on page 52.

In addition to advances in the field of cystinosis, the research we fund has an impact on other more prevalent diseases and disorders. Discoveries made by CRF funded researchers are being applied to Friedreich's Ataxia, Danon disease, corneal diseases, kidney diseases and genetic and systemic diseases similar to cystinosis. It is important to know that cystinosis research benefits people in other disease communities.



We are pleased to announce that so far in 2022, we awarded seven new grants, totaling $1,287,127. The grants were awarded to researchers in Germany, Italy, New Zealand, Switzerland and the United States. We hope you will be as interested as we are to learn more about the exciting research we fund. We will announce another round of grants in December 2022. Please read about the Spring grants on page 63.

THE UCSD STEM CELL AND GENE THERAPY CLINICAL TRIAL

We are very excited to report that the sixth patient was transplanted on October 24, 2022. That patient is the final patient of this phase 1/2 of the FDA approved clinical trial. In December 2018, the FDA approved the clinical trial for six patients. The first patient was transplanted October 7, 2019 and we are pleased to report that all of the patients are doing well and remain off oral cysteamine treatment. This is an exciting and hopeful time for the cystinosis community.

CRF has proudly supported and funded Stéphanie Cherqui, PhD, at UC San Diego for her groundbreaking stem cell and gene therapy work since 2007. CRF has awarded over $6.1 million in grants for her research. The effect of our investment resulted in over $22.7 million in additional grants to Dr. Cherqui from other funding agencies including CIRM and the NIH. With your help, CRF has been the driving force for all cystinosis research and advances in treatment.

We are so grateful to the six patients who pioneered this treatment especially Jordan Janz, Jacob Seachord, Tyler Joynt and, Natalie Stack who have openly and honestly shared their stories with us. All six patient volunteers have helped advance research and they have given us hope that one day this treatment will be available to all children and adults with cystinosis. We are optimistic that this treatment will stop the progression of cystinosis or be a cure. We thank Dr. Cherqui for her dedication and commitment to our community. The next phase of the clinical trial is being planned by Avrobio. We anticipate they will commence phase 3 of the trial in 2023.

UPDATE ON NATALIE

We are awaiting Natalie's post-transplant six-month exam results and are hopeful her engraftment was a success and that she remains off cysteamine treatment. She seems to be doing well, she feels good, she is back to work full time, her hair is growing back (yay!) and life is good for her. Her puppy, Wesley, is growing by leaps and bounds and is keeping her busy. The latest family news is that Natalie recently became engaged to her boyfriend, now fiancé, Danny Morgan. We are excited for Natalie and Danny as they plan their lives together. They are a beautiful couple whose love for each other is apparent. Although they will be moving to Chicago, and we will miss seeing them regularly, they are ready to start their own lives. We will celebrate them next year when they get married!

WE ARE FOREVER GRATEFUL

We know you will thoroughly enjoy reading about all of the patients and families who have shared their amazing and inspiring stories with us in this magazine. Our community is incredible — their openness and honesty when they share their daily lives with us is often humbling and always inspirational. Each story unites us and reminds us how connected we are and how fortunate we are to have each other.

We have faced the challenges of cystinosis together, we have overcome obstacles and we have found a path to better treatments and what we believe to be a cure. We remain resolute in our obligation to help every child and adult with cystinosis. Our faith is strong and our determination is steadfast.

For 20 years we have been working towards the cure and better treatments and look what we have accomplished together! How many people can actually say that they were part of a group of people who found a new FDA approved treatment and whose work led to an FDA clinical trial to find a cure for a rare disease? Well, we have done that together and we have given hope to our community.

The stem cell and gene therapy trial has been a patient-by-patient journey and we know that while the next group of patients wait for the next phase of the trial to begin, we must work to improve the daily lives of all those with cystinosis. Our battle continues; our quest for the cure is not over.

You began this journey with us and you have remained by our side, lifting us up when there have been set backs and sharing the joy when we celebrate our accomplishments. Jeff and I could not do this without you.

Thank you for never giving up, for always supporting our efforts by your friendship and financial commitment to CRF. We are blessed by your love for Natalie and all of our children and adults with cystinosis. You have given the word "hope" new meaning and we are forever grateful.

With heartfelt thanks and gratitude,

Nancy & Jeff

A Note from Natalie Stack

This year I recently became engaged to my wonderful fiancé, Danny, and we are moving to Chicago at the end of the year. I am looking forward to this new journey in another city and beyond excited to start my life with my soon-to-be husband. I have started looking for a new job in Chicago and I would like to continue to work with youth in foster care.

Though I have an exciting future ahead of me, my life still heavily revolves around my medical care. I continue to feel good after my stem cell transplant in March 2022. I just had my six-month post-transplant testing at UCSD. The testing included a multitude of tests including strenuous eye exams, mole mapping, a rectal biopsy, grip strength test, neurological functioning tests, a 24-hour urine collection and of course multiple blood draws.

Though the tests are exhausting, I know that the data from the tests will help advance the trial and help us learn more about the success of the stem cell and gene therapy treatment. I am nervous but hopeful that the results from my recent exams are positive.

Since the stem cell transplant, I have had a couple bumps along the way. Unfortunately, I got COVID-19 about three months posttransplant. I had symptoms for 10 days, took Paxlovid and then got Paxlovid rebound. I had chills, cough, fever, loss of taste and smell, running nose, and sneezing for a total of 21 days. Having COVID-19 was miserable, but I was able to recover at home and avoided the hospital.

I had chemotherapy as part of the stem cell protocol and the chemo drugs wiped out all of my prior vaccines, so I have no protection against mumps, measles, chickenpox, and especially COVID-19. I need to be revaccinated for every childhood disease. My white blood cell count has remained very low and it has been very frustrating not knowing if COVID-19 is the reason why my blood count has not returned to normal. My hope is that my immune system will recover so that my levels return to normal. I am nervous but hopeful that the results are positive so that I do not have to worry about being so hyper vigilant about my health and surroundings.

I continue to be hopeful about the results of the clinical trial. Even though participating in the trial was a lot of stress on my body and the recovery period is longterm, the possibility that the treatment could save my life makes it all worthwhile.

I want to thank all of you whose determination to raise money to support research to find better treatments and a cure for this disease made the stem cell trial possible. You have been with us every step of the way with your love and commitment to find the cure. My parents, especially my mother, have continued to be my strongest advocates and support team. I am grateful to my parents, the entire cystinosis community, and all of the families and friends who made this trial possible.

Thank you for never giving up on my wish - to have my disease go away forever.

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. Build-up 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 2,000 worldwide.

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

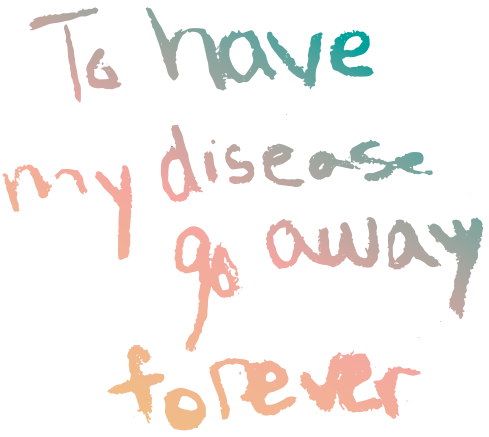
Federal funding for research on cystinosis and other rare diseases is virtually non-existent and most pharmaceutical companies remain uninterested because financial rewards are too small. Yet, while there are only a small number of patients who suffer from any given "orphan" disease, knowledge gained 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 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 220 grants in 12 countries.

CRF has raised more than $65 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

CHARITY NAVIGATOR ★★★★ Four Star Charity

Platinum Transparency 2022 Candid.

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

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.

Since 2003, CRF has:

Funded **220** Multi-Year Grants

in **12** Countries

Published **103** Articles in Prestigious Journals by CRF Researchers

1 FDA Approved Drug and **1** FDA Approved Clinical Trial

Raised More Than **$65 Million** for Cystinosis Research

To date in 2022, CRF has:

Awarded **7** New Research Grants

Totaling More Than **$1.2 Million** in **5** Countries

GERMANY
ITALY
NEW ZEALAND
SWITZERLAND
UNITED STATES

Published **6** Articles in Prestigious Journals by CRF Researchers

100% of Your Donations Directly Support Cystinosis Research

CRF was established in 2003 and since that time we have made astounding progress. We find ourselves reflecting on the early days of the foundation and we are amazed at how far we have come in just 20 years. When we look at where we are today, we are more hopeful than ever that we will fulfill Natalie's wish to "have my disease go away forever."

In 2006 Natalie was part of the study Dr. Dohil conducted for the enteric coated cysteamine that lead to Procysbi®.

It's not just this rare disease —
It's our lives that are healing...

From Hope To Healing

2003

- Cystinosis Research Foundation Formed
- First CRF Fundraiser "Faces of Cystinosis" Raised $100,000
- First CRF Research Grants Totaling $338,542 Issued to Jerry Schneider, MD, and Ranjan Dohil, MD, for Delayed-Release Medication

2004

- Natalie's Wish Newsletter Published
- Natalie's Wish Celebration Raised $245,000
- CRF Funded More Than $736,000 in New Grants

2005

- CRF Website Launched: *natalieswish.org*
- CRF Raised $1,140,000
- CRF Funded 5 Research Grants Totaling $832,986

2006

- CRF Raised $1.6 Million
- CRF Funded 12 Research Grants
- CRF Establishes First Research Fellowship Program
- First Grant Issued To Stéphanie Cherqui, PhD – Stem Cell Therapy

2007

- CRF Science Report Published
- Inaugural Fore A Cure Golf Tournament
- CRF Funded 13 Research Grants Totaling $2,615,592

cystinosis RESEARCH FOUNDATION | TOGETHER WE SHINE BRIGHT

20 years OF PROGRESS FOR THE CYSTINOSIS COMMUNITY

2008

- First CRF International Research Symposium
- CRF Raised $2,784,613

2009

- CRF Funded 19 Research Grants Totaling $3.31 Million

2010

- Second CRF International Research Symposium
- First CRF Day of Hope Family Conference

- Launch of First Patient Registry - CCIR (Cure Cystinosis International Registry)

CURE CYSTINOSIS INTERNATIONAL REGISTRY

2011

- CRF Presented at ALANEPe (Latin American Society of Pediatric Nephrology) in Sao Paulo, Brazil
- First Cystinosis Magazine Published


CRF Families Supporting Natalie's Wish

2012

- Third CRF International Research Symposium
- UCLA Allogeneic Stem Cell Treatment Approved by UCLA IRB

Parental Quest Bears Fruit in a Kidney Disease Treatment

2013

- April 30 – FDA Approval of Delayed-Release Medication Procysbi®

2016

- Natalie's Wish Featured Rachel Platten and Her "Fight Song"
- Fifth CRF International Research Symposium
- CRF Funded 17 Research Grants Totaling $2.79 Million
- CRF and Canadian Families Unite to Fund Cystinosis Research

2014

- Fourth CRF International Research Symposium
- CRF Funded 12 Research Grants Totaling $2,068,247

2015

- Stem Cell and Gene Therapy Consortium formed by Stéphanie Cherqui, PhD
- CRF Funded 9 Research Grants Totaling $1,581,820

2017

CIRM
CALIFORNIA STEM CELL AGENCY

- Stéphanie Cherqui, PhD Receives California Institute of Regenerative Medicine (CIRM) Award of $5.2 Million
- CRF Funded 13 Research Grants Totaling $2.4 Million

20 years

OF PROGRESS FOR THE CYSTINOSIS COMMUNITY

2019

- October 7, Jordan Janz, First Patient, Transplanted in Stem Cell Gene Therapy Trial
- CRF receives the Global Genes Rare Champion of Hope Award – Research and Treatment

2020

- June 29, Second Patient Transplanted and November 16, Jacob Seachord, Third Patient, was Transplanted in Stem Cell Gene Therapy Trial
- Seventh CRF International Research Symposium
- CRF Receives GuideStar Platinum Seal of Transparency

2021

- November 15, Tyler Joynt, Fourth Patient, Transplanted in Stem Cell Gene Therapy Trial
- Updated CCIR Registry Launched

2018

- CRF Receives Charity Navigator 4-star Rating
- Sixth CRF International Research Symposium
- FDA Approves Stéphanie Cherqui, PhD's Autologous Stem Cell Gene Therapy Clinical Trial at UCSD

2022

- March 29, Natalie Stack, Fifth Patient, Transplanted in Stem Cell Gene Therapy Trial
- CRF Presents at IPNA pre-Congress Cystinosis Session in Calgary, Alberta, Canada and Hosts First Family Conference.
- October 24, Sixth Patient Transplanted in Stem Cell and Gene Therapy Trial
- CRF Continues Receiving GuideStar/ Candid Platinum Transparency Honor

2023

Together, we continue to forge the path to a cure!

cystinosis RESEARCH FOUNDATION | TOGETHER WE SHINE BRIGHT

Cure Cystinosis International Registry

Our Link Between Patients and Researchers

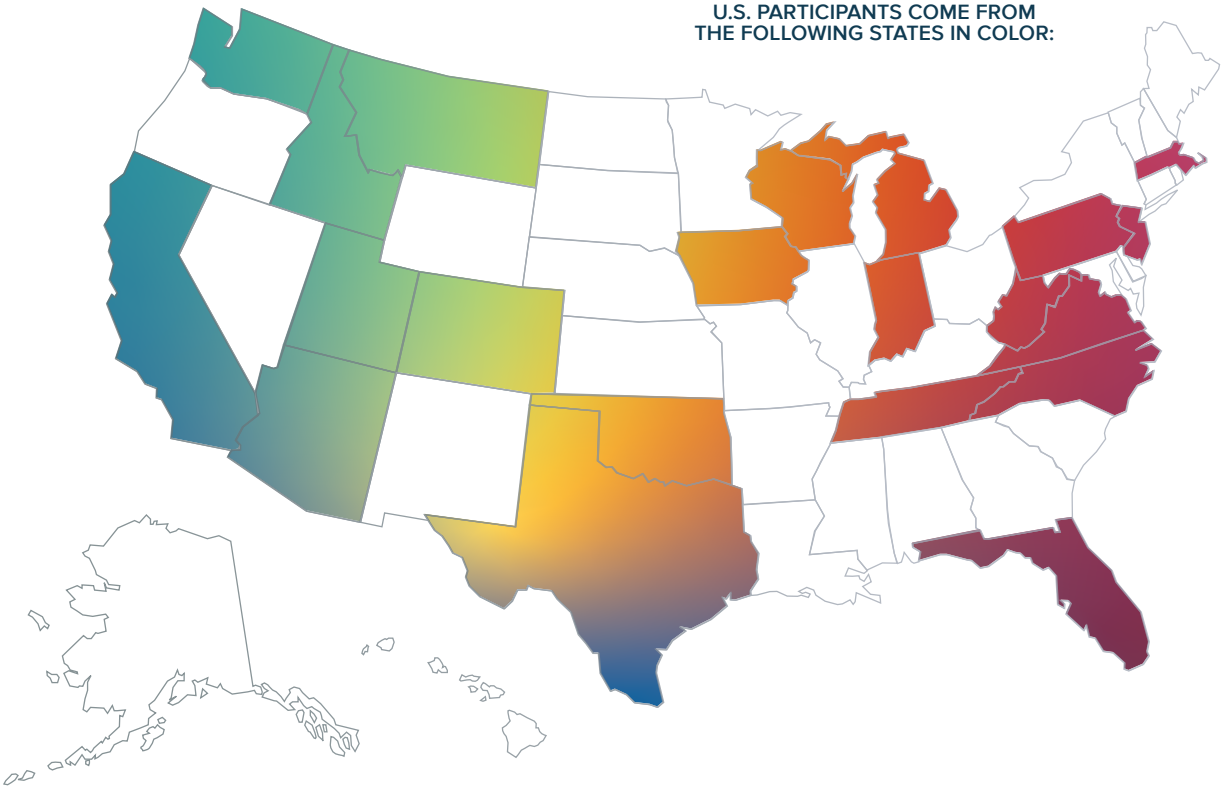
By Clay Emerson, PhD, PE, CFM

CCIR Committee Member and Brooke Emerson's dad

Hammonton, New Jersey, USA

The new Cure Cystinosis International Registry (CCIR) was launched in the Spring of 2021. In just the first year and a half, patients from more than a dozen countries have participated in the registry. Participants in the registry also include patients representing 21 states across the United States.

With 156 registered patients and counting, the registry provides a critical link between patients and researchers. Due to the ultra-rare nature of the disease, as well as the myriad complications the disease presents, progress towards improved treatment and an ultimate cure for cystinosis can only be possible with the valuable input from our limited patient community.



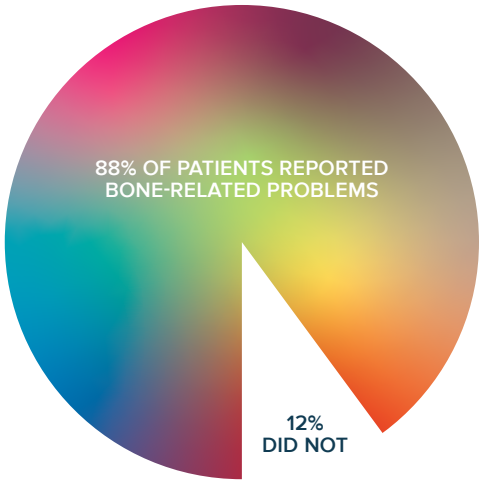
Cure Cystinosis
International Registry

Musculoskeletal Complications

Cystinosis impacts every cell in the body and is therefore a multisystemic disease. Cystinosis also impacts the musculoskeletal system in many different ways. Due to early kidney damage caused by cystinosis, infants and very young children with cystinosis often develop a bone condition known as rickets, where the bones are weak and soft resulting in bowed legs and other bone deformities. This condition is usually remedied following diagnosis with additional supplements of vitamin D, calcium and phosphorus. However, cystinosis also presents other life-long challenges to the skeletal system that are yet to be fully understood. Recent research has shown that some of these bone issues are not resolved by the cysteamine treatment alone. Fortunately, some of these issues are currently being investigated by CRF funded researchers.

Early reports from the CCIR illustrate that bone-related issues are extremely common in the cystinosis patient community. The data shows that 88% of responding patients reported bone-related problems including rickets, bone pain, fractures and many other complications. Among the patients who reported bone-related problems, 11% required surgical intervention.

BONE-RELATED PROBLEMS INCLUDE RICKETS, BONE PAIN, FRACTURES AND MANY OTHER COMPLICATIONS.



Less than two years since its launch, the new cystinosis patient registry is already helping to inform researchers and accelerate the development of better treatments and ultimately a cure for cystinosis. The value of the registry will only truly be realized with patient participation. We strongly encourage patients or caregivers to participate in the registry and help identify the needs of patients with cystinosis and accelerate research. The questionnaire takes about 40 minutes to complete, and registration is simple. Please visit the CRF website to sign up today!

THE VALUE OF THE REGISTRY WILL ONLY TRULY BE REALIZED WITH PATIENT PARTICIPATION

www.cystinosisresearch.org/cure-cystinosis-international-registry

Mark Your Calendars!
Celebrate 20 Years of Natalie's Wish

Month of Funding for a Cure

April 2023

Help us celebrate 20 years of funding groundbreaking research! Although we will not have an in-person event, the entire month of April will be an opportunity for you to renew your commitment to raising funds for life-saving cystinosis research. Over the past 20 years, we have rallied a powerful community of cystinosis friends, families, fundraisers and researchers around one mission: to change the course of cystinosis. And while we have made significant strides, we have more work to do.

Join us next April for our month-long fundraiser to celebrate two decades of impact. Your dedication to Natalie's wish — "to have my disease go away forever" — has united us in our fight against cystinosis, bringing us closer than ever to a cure!

Watch the mail for this opportunity to fund the cure!

Natalie's Wish '23

CELEBRATING TWENTY YEARS of HOPE

Family Stories

20 years

EVERY BREATH I TAKE

By Todd Braye
BLACKIE, ALBERTA, CANADA

This is April, the best caregiver a cystinotic in his sixth decade could ever ask for.

The bomb exploded on the morning of June 6, 2019. Just three days before, Bev and I marked our 24th wedding anniversary, but this day would very quickly make the celebration a distant memory. I remember waking up to the sound of air blowing out of my CPAP mask and pain under the left side of my rib cage. Hunched over my bedside with Bev beside me, an hour of coughing up mucus followed, ending with a surprisingly painless expulsion of what I now believe to be a ruptured pulmonary bulla.

Breathing became difficult. With help from my caregiver, Bev rushed me to the emergency room. X-rays confirmed a full lung collapse. As I lay in Trauma Room #1, the doctor explained my situation and gave us the options. They could keep me comfortable until the inevitable – death was imminent. Or they could reinflate my lung with a chest tube and save my life. The next sequence of events is hazy, but I recall how time seemed to stop even though the urgency and immense gravity of the moment crushed us. Given space to collect ourselves, I had a choice to make. I was not ready to leave my wife. But the thought of plastic piercing my flesh was beyond overwhelming. My mortality has always been real. My death was always an event Bev prepared for. But now? Widowhood would surely be the result of death by a thousand cuts, not one slash. Not today!

The pain was excruciating, the procedure barbaric, but my lung reinflated. Relief soon yielded to unconsciousness as the hydromorphone took its welcomed effect. While asleep, phone calls were made, and tears shed. Later that day, I was stretchered out to an ambulance. As the paramedics loaded me onto the 'bus,' Bev and I locked eyes. "I loved you the best way I knew how," I said, not knowing if I would ever see her again. It was the scariest moment of my 52 years. The ambulance sped away, enroute to Calgary's *Foothills Medical Centre* for what would be a five-week stay, two of which were post-op. Out of necessity, staff learned about my needs as a cystinosis patient; Bev was a great teacher. But it was easily the most challenging time of our life together. A bomb exploded in our laps, and it broke us.

So, what happened? This is my theory: cystinosis > ***muscle wasting*** > dysphagia (swallowing dysfunction) > aspiration > lung infection > pulmonary bulla > bulla rupture > pneumothorax. Here's the kicker: Medically speaking, muscle wasting now governs me. Cystinosis has robbed me of countless simple joys (like walking and talking) and now this merciless disease has my lungs in its crosshairs. Reduced respiratory effort does not, in and of itself, cause pneumothorax. However, my pulmonary event dramatically reminds me of the brevity and fragility of life; breathing does in fact require effort, especially for a cystinotic in my 6th decade. Consequently, as an aging adult, every time my chest rises and falls, I am confronted with this inescapable reality: cystinosis sucks!

Thankfully, disease does not have the final word in my life. I need to remind myself of this every day. Though death is at work in me, and though I am wasting away, I must refuse to be driven to despair. For as the Apostle Paul wrote to the suffering saints of ancient Corinth, describing their condition as a 'light ***momentary*** affliction' (2 Cor. 5:17), I must fight to fix my gaze heavenward, keeping my perspective eternal. By God's grace, this is a battle I endeavour to win with every breath I take.

FERA LANKEN

Waterworks:
The first 18 months of cystinosis

By Vanessa Bonneau and Sylvan Lanken, Fera's parents
MONTREAL, QUEBEC, CANADA

Our daughter Fera was born at the start of the pandemic. She was on the small side but seemed to be a healthy baby. We became parents that first spring and summer of the pandemic.

When it came time to start solid food, she would eat some things, sometimes, but in hindsight, she never really got into it. While she wasn't a big eater, we discovered that she loved (needed) water.

She became increasingly cranky around the eight to nine-month mark, as well as constipated. While she had previously been sleeping through the night, sometimes now she would wake up, wanting not breastmilk, but water. She peed through her reusable diapers at a puzzling rate.

We were increasingly worried. Eventually, through a couple of visits to clinics, we realized Fera was losing weight. We had suspected it. When a doctor saw her first blood test results, he told us to go straight to emergency. He said he suspected it was something to do with her kidneys, but that whatever it was, it would be manageable. That word – manageable – still haunts us. We didn't know regular people like us managed a condition as complex as cystinosis.

Fera was 10 months old when we were admitted to the Montreal Children's Hospital, which is a teaching hospital. We met an incredible number of doctors, residents and students. "Failure to thrive," we heard the medical staff repeating in the hallways.

And so it began: blood tests, sleepless nights, waiting to speak with doctors, checking vital signs, the beeping, the fluorescent lights.

They diagnosed Fanconi syndrome pretty quickly, and just three horrible days and nights after admission, an ophthalmologist found crystals in Fera's eyes.

It took another two weeks for the doctors to stabilize Fera and figure out what supplements she needed. She wasn't really eating or gaining weight, so finally, with our blessing, they put in a nasogastric tube and started supplementing Fera's diet with formula.

We were sent home with a neat and tidy drug schedule. It didn't work. Fera vomited often and still wouldn't really eat. We gradually began spacing out her medicines so that we were crouched behind her where the NG-tube was taped to her upper back, giving her a medication pretty much every half hour during the day.

Months went by, and still she vomited. We stopped going to work. Fera was too car sick for us to really go anywhere with her. We mostly got around by bike.

Since her diagnosis in February 2021, Fera has been hospitalised six times, spent countless hours at the day hospital and has had more than 80 blood tests. Medical issues have included a persistent low hemoglobin, a scare with indomethacin, so many viruses and surgery to get her G tube put in. In height and weight, she hovers between the first and third percentile, although we've recently started growth hormone, with the hope of changing that ranking. When she's sick with whatever latest virus she catches, she has a lot of trouble tolerating her cysteamine.

Still, there has been a gradual improvement overall. She is eating more. She has started daycare. She throws up less. We are back at work. We've begun to condense her meds as her tolerance increases.

This past April, we attended the CRF conference in California after never having met anyone with the condition besides Fera.

For the most part, we think Fera is living a pretty good life. At her most recent check-up, her nephrologist said that she was thriving.

We're terrified of the future. At the same time, we don't accept Fera's condition. Fortunately, neither does the CRF or any of the other families we've met.

Still, we don't want Fera to live her life waiting for a cure. We love her as she is. But we'll be in the wings, doing our best to keep her healthy, waiting for better treatments, and yes, some kind of cure.

"...we'll be in the wings, doing our best to keep her healthy, waiting for better treatments, and yes, some kind of cure."

EMERSON FAMILY 2022 UPDATE

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

TIME FLIES

We can't believe that 2022 is almost over! It seems like just yesterday we were dropping Brooke off for her first day of Pre-K, and now she is in 3rd grade.

Brooke still loves school and becomes more mature and independent each day. Once again, she has an amazing IEP team and wonderful teachers, and as she progresses in school, she needs fewer modifications and less assistance. While Brooke once had a paraprofessional to make sure she got to the nurse each day for medicine and to monitor her water and food intake, she insisted that for 3rd grade, she didn't need any assistance. This year, she is managing all of those things on her own, and we couldn't be more proud of her determination to take control of her situation. She is doing a great job.

Brooke has struggled with some health-related anxiety the last couple of years, so health class was always a challenge. But she is determined to conquer her fears and is dealing with health class in her own way. Is she still nervous about some of the content? Absolutely. But she has found ways to cope that make her feel more comfortable and is no longer hesitant to attend health class. Every day, we are amazed by her resilience.

This past September, Clay and I took our first overnight trip together away from Brooke to attend the 2022 International Pediatric Nephrology Association's conference in Calgary, Alberta, Canada. It was an extremely quick trip so we could get home for Brooke's first days of 3rd grade, but we are so glad that we did it! We not only got to speak to professionals and other cystinosis families about Brooke's and our journey, but we also connected with our CRF family, doctors and researchers at a dinner event after the conference. It was an amazing experience, and we are so grateful for the opportunity to attend. And Brooke had a fantastic time at home with her MomMom and PopPop; she didn't miss us a bit!


My Cat, Nicky!

As we wrap up 2022 and prepare for 2023, we are hopeful that things continue to progress positively for Brooke academically and medically. In 2023 and beyond, we look forward to the potential for a pediatric stem cell transplant trial and positive news in research areas such as Solidrops and cysteamine alternatives. We also look forward to seeing our cystinosis community at the 2023 Day of Hope conference; it is sure to be a wonderful event and it will be so nice to have the opportunity to be together again!

Update from Brooke, In Her Own Words

Hi! I am in 3rd grade and my favorite subjects are math and science, and I love Spanish class too! I am so proud of myself because I am brave this year and am not scared of health class anymore.

When I grow up, I want to be a paleontologist and a veterinarian. That way, I can bring my cat Nicky to work with me. I hope one day to have another cat and a dog. I also just started sewing lessons on the weekends and have already made some amazing things.

I have gotten really good at my growth hormone shots, I don't even flinch anymore and it doesn't hurt a single bit. My least favorite medicine is eye drops, definitely eye drops. I just want to get better at them; I don't know why but I just think it's extra hard to do them.

I am so excited to travel to California in 2023!

JULIETTE FOLLAIN

Never Settle for Too Little!

We have been on a learning journey since Juliette was diagnosed almost two years ago. And if this journey taught us one thing, it's to never settle for too little! We discovered an inspiring community of pioneers: dedicated doctors and researchers, fearless patients embarking into new trials, devoted caregivers, fantastic patient associations and much more. Our families were also an unfailing support despite the shock of the diagnosis. All of them have a common denominator: they won't settle for too little.

But neither will our kids!

Juliette is now 3 years old, blossoming as a young little girl, catching up on the growth chart beyond expectations with a giant appetite for life (and for food)! She has been teaching us a lot as well. Ice cream or French fries are her bartering currencies for anything, and you can't win the negotiations as she will never settle for too little. This is undoubtedly her greatest strength; it will certainly be pivotal in the years to come.

The paralyzing anxiety that we sometimes feel as parents is ours, not theirs. Juliette is reasonable, sensible, but always optimistic and ready to have fun. She does not see the challenges the same way we do since it's her norm, and hence has developed an impressive resilience to what we call hardship. That makes us immensely proud.

For us, the first challenge was to avoid the G-tube for Juliette. We don't really know why we had such an uncompromising reaction. Probably because it was, for us, a strong external marker of the disease. Not that we ever hid it, but this was our big "no-no" when we realized that most kids with cystinosis had one. That was perhaps when we started to trade ice cream. We laid out some basic ground rules, like no meds hidden in food, no fight to get her to finish a plate of something she doesn't like or, conversely, no restriction on seconds – she could choose in the fridge what she wants, etc. – and we stuck to those. It was not always easy, and the breakfast menu at home is still something you won't find anywhere else, but we are proud we got there, and we're hopeful she'll never need a G-tube. We did not settle.

The next challenge was to get the best treatments for Juliette. There are so many different levels of care depending on where you live, the doctors that look after you, your insurance, etc. In the UK, Procysbi® is not routinely available for cystinosis patients, although it is now available in Wales thanks to the incredible work of the patient association. We fought hard to get it for Juliette, and we did. Slowly but surely, we also built a network of the top cystinosis doctors around us, which makes a huge difference. We have a fantastic nephrologist, a fantastic pediatrician and now a fantastic ophthalmologist. We did not settle.

Life with cystinosis can be hard, but we should all look back and be proud of what we have achieved so far, individually and as a community. It gives us energy to move forward and tackle the next challenges. Certainly, this is a lesson of teamwork and mutual support, as no one can accomplish this alone.

The route to the cure is not over; there will be highs and lows, there will be many more challenges to take on, but we will never settle for anything less than extraordinary. Thank you, CRF, for paving the way to extraordinary!

Juliette has developed an impressive resilience to what we call hardship.

By Guillaume Follain and Constance Herreman, Juliette's parents
LONDON, ENGLAND

IN LOVING MEMORY OF

Jessica Britt Jondle

"Cherish What Was Given And Fight On"

On Friday, May 27, 2022, Jessica Rachel (Britt) Jondle, loving wife and mother, passed away at the age of 40. Jessica was born July 14, 1981, in San Francisco, CA, to Ernest and Gayle Britt. She received a Bachelor of Arts from the University of California, Berkeley, in 2004. She was a teacher, an author, an editor, and a friend, fundraiser and social influencer in the cystinosis community. On July 1, 2007, she married the love of her life, Wayne David Jondle. Two years ago, they moved to Boise, Idaho, where they were raising 3-year-old Evangeline and 1-year-old Nathan, who brought Jessica great joy.

Jessica met every difficulty with determination and welcomed new challenges. Upon reaching the top of Mt. Kilimanjaro, she was told there was a little higher spot along the ridge. Fighting altitude sickness, Jessica persuaded the guide to take her to that spot. She climbed Mt. Whitney numerous times and was disappointed this year when she couldn't get a permit to do Half Dome. Jessica loved being on a mountain or trail.

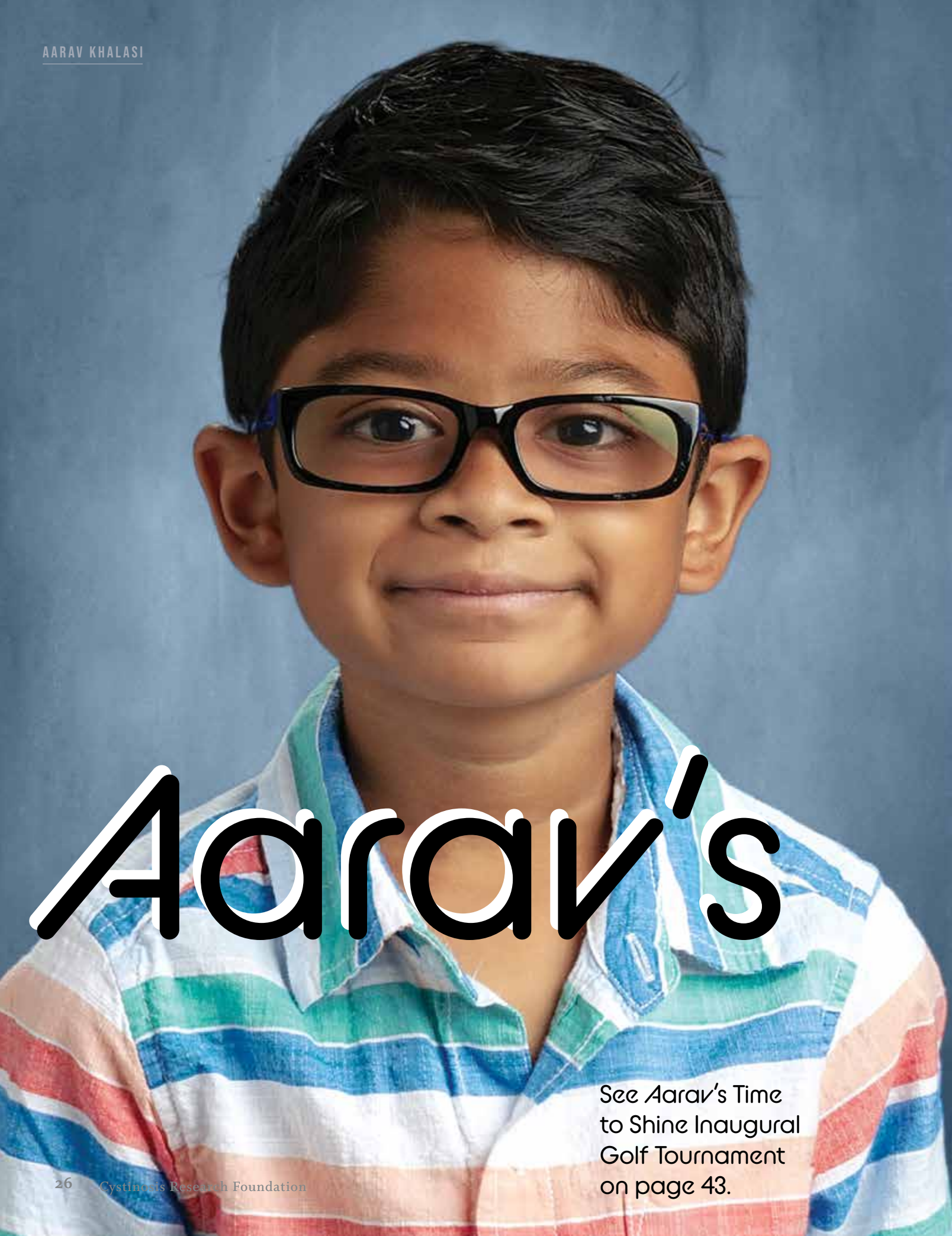
"She may be small but she is fierce." Jessica is remembered for her passion for living a full life and for bringing hope to those in the cystinosis community. She viewed cystinosis graciously as a challenge rather than a limitation. Jessica loved and followed Jesus Christ and we believe that she has been given a new body and new life with her savior in heaven. Those of us still on Earth greatly grieve the loss of Jessica and yet we are comforted that through her writing she still speaks. In her book, "Roller Skating with Rickets", released on March 14, 2012, she says, "Life is full of joy from hardship. Life is full of paradoxes." She tells of her life journey through personal vignettes that detail her transformative experiences. Her writing gives a window into her heart of gratitude for the Lord who was there with her through it all. Psalm 116:15 says, "Precious in the sight of the Lord is the death of His godly ones."

In 2012, Jessica published a book, "Roller Skating With Rickets", about her life with cystinosis and her determination to thrive. Here is a loving message to the cystinosis community from her book:

"And finally, for the cystinosis community: You are one of the reasons that I am happy to have the life I do. Could I go back in time and somehow remove the pain caused by cystinosis, I would not do so, for I know that I would be removing the blessings as well. And the blessings, of which you are included, far outweigh the hardship. Through the modern miracle of social networking, I have been connected to people that I have never had the privilege of meeting in person, but even my "virtual" friends have offered me hope and advice, provided me with a forum in which to vent and given me the opportunity to get to know some of the little ones that I count as my heroes. To you I say: ***Cherish what was given and fight on.***"

Jessica is survived by her husband, their two young children, her parents, and her sister.

Jessica is remembered for her passion for living a full life and for bringing hope to those in the cystinosis community.



See *Aarav's* Time to Shine Inaugural Golf Tournament on page 43.

By Minaxi and Mukund Khalasi, Aarav's parents
SACRAMENTO, CALIFORNIA

Journey

Aarav's journey with cystinosis started at his 1-year checkup and we have come a long way since then. It's crazy to think that at the end of the year he will be turning 8! This journey has taught us so much and has truly changed our entire family's perspective on life. When we first received the news, we had a really hard time with all the information that was coming our way. Our new norm was changing, and we had to do our best to keep up with all the symptoms, medications, appointments and labs.

Aarav was diagnosed in early 2016 and a few months later we attended our first CRF Day of Hope conference. We remember feeling overwhelmed and happy all at the same time. At the end of each day of the conference, we felt hopeful. We knew that we had gained a community of people that we could count on and would completely understand what our family was experiencing.

When Aarav started school, we were well prepared because of the support and information gathered from other cystinosis families. We had all the help and hope in the world. He is now a second grader who loves school and comes home to help his kindergarten sisters. He is very passionate about learning. Like many other children, Aarav is also very passionate about sports. He loves football to the point that he is glued to the TV on Sundays. He has taken golf lessons where he has walked all nine holes in the heat, and he continues to ask to be put in more lessons.

Over time, we noticed that Aarav had managed his new routine a lot better than us. From the moment he was diagnosed, if one thing remained the same it was the fact that he was accepting of all of it. He never complained nor did he feel different, and that is something that we hope remains the same. As he ages, we are aware that his health may decline but as a family we truly hope his strength continues to grow. So much has changed and so much will continue to change before he becomes a teenager, but the truth is we are hopeful for what his future has in store for him. As his parents we are incredibly proud of the strength, courage and compassion that he has. We know that moving forward, he will continue to amaze us because in our eyes, Aarav is the strongest person we know.

KALEB'S CELEBRATION

Kaleb Michael Lawshe turned 9 years old this past August and he is the sunshine of our lives. He has big aspirations when he grows up to be a YouTuber/gamer, but says he is OK waiting until he is at least 10 years old (haha!). He loves playing video and board games with his dad, watching his favorite cartoons, playing on his iPad and especially hanging out with his buddy, Grandpa. He loves to go swimming and started swim lessons this past spring. He attends school virtually through his elementary school's Home Bound program. He loves it and his two teachers are wonderful and so patient with him and us.

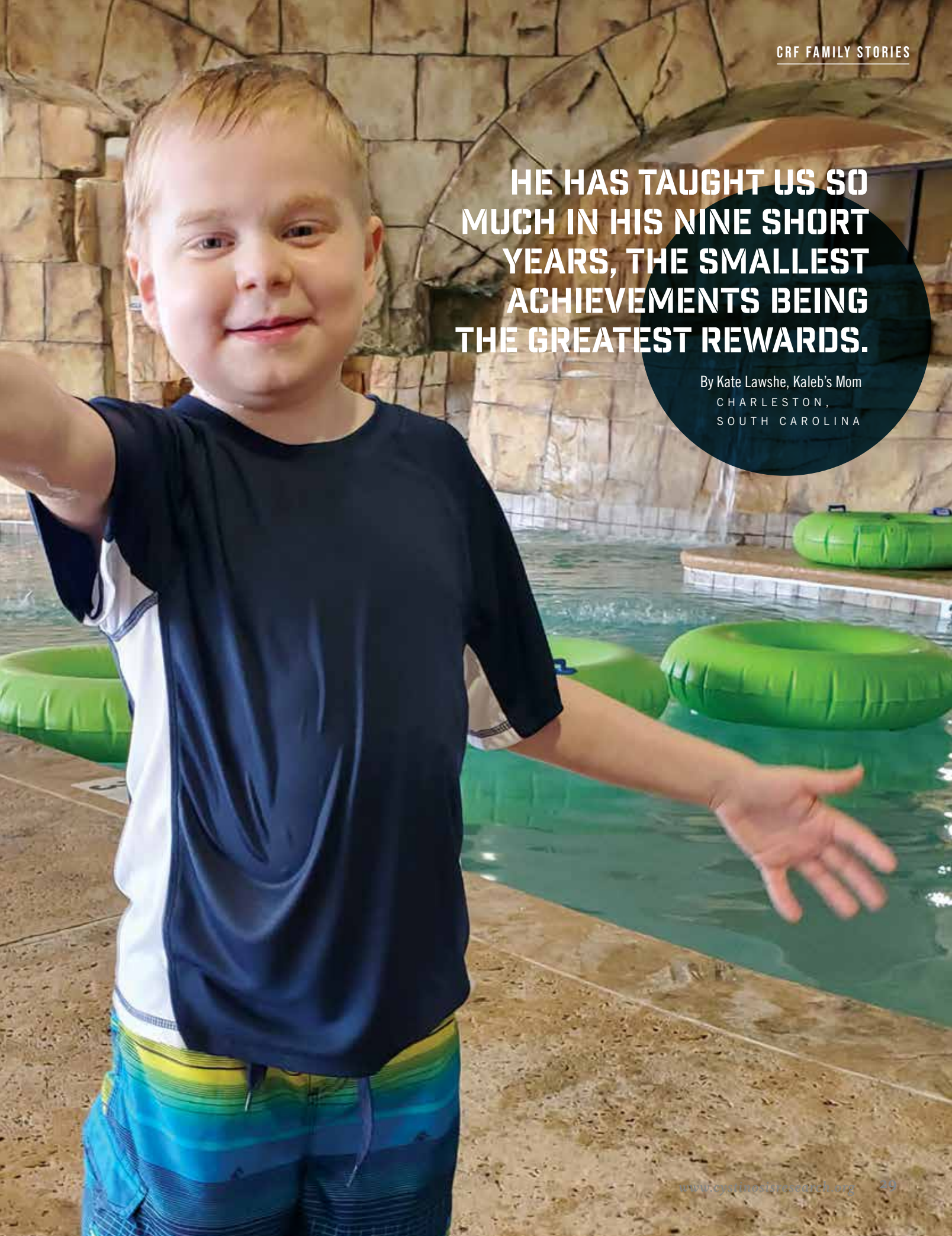
Kaleb was diagnosed with cystinosis at 21 months at the UVA Children's Hospital in May 2015. Six months later, we moved to Charleston, South Carolina, where we continued care through MUSC Children's Hospital. This past year has been even more challenging. Last fall, he was diagnosed with I.B.D. ulcerative colitis. It was like both diseases were battling each other and we just couldn't get him to a good place with his electrolytes and weight. In the past year alone, he had over seven stays at MUSC. After we finally found the right med/supplement mix, he started doing much better and finally gaining weight. But then at the end of July, he had his first ever seizure. We called 911 and back to the hospital he went for extensive testing, where they found he has an optic nerve glioma. On September 13th, he had brain surgery to biopsy it and remove as much of it as they could safely. Thankfully, it went very well and his neurosurgeon was able to remove more than anticipated. Once the biopsy results come in, further treatment will be discussed.

Of course, we have all been a huge ball of nerves. Every time he would hear us talking about it, he would say, "Don't worry, I will be fine." We planned several activities that he wanted to do prior to the surgery: a planned stay at Grandma and Grandpa's house, several trips to a local bowling/arcade center, seeing a couple movies at the theater and going to a hotel with a pool. So, for his 9th birthday celebration we took him to Myrtle Beach and stayed at a resort hotel with a lazy river and pool. He got to go swimming as much as he wanted and loved it.

As we got closer to surgery day, he started asking more questions and talking about "getting this thing out of his head." He wanted to know as much as we were willing to tell him. Does he have a strong personality? Absolutely he does! He doesn't hesitate to correct hospital staff when they mess up his I.V. or attempt to connect with him at a child-like level. That's not Kaleb; he has a strong, honest spirit and wants to enjoy life. Known for his signature "thumbs up," the one thing we have learned from him is his resilience and courage. When we tell him that we are headed back to the hospital, he gets upset at first but then turns it around soon after saying, "It's all right, they will make me better." It is like he ends up comforting us. He has taught us so much in his nine short years, the smallest achievements being the greatest rewards.

The support and prayers we received from everyone has been so appreciated. We see big things for Kaleb one day and can't wait for him to become the person he is meant to be. He truly will be amazing; he already is. After hearing us talk about his future needs, he stopped us again and said, "I'm OK guys, I'm just a different kid, and one day I will figure it out." Yes, you will Kaleb, and we can't wait.

THUMBS UP!



HE HAS TAUGHT US SO MUCH IN HIS NINE SHORT YEARS, THE SMALLEST ACHIEVEMENTS BEING THE GREATEST REWARDS.

By Kate Lawshe, Kaleb's Mom
CHARLESTON, SOUTH CAROLINA

JENNA PARTINGTON *College*

Saint Francis Catholic High School College Application Essay September 22, 2022

When we were 16 months old, my twin brother and I were diagnosed with a genetic disease called cystinosis. A couple months after I was born, I had fallen really sick. I was in and out of the doctor's office, attending many appointments, with the doctors finally diagnosing me with "failure to thrive." I caught a common virus that resulted in severe dehydration and was put into a pediatric intensive care unit. My doctors described me as an "electrolytic marvel" and kept me in the hospital for 13 days, running new tests and trying unproven treatments. Once the cystinosis diagnosis was made, my family began forging ahead in our unique way. Today, I continue to forge ahead. Going to college will be something that doctors tending to me 17 years ago would have considered impossible.

GOING TO COLLEGE WILL BE SOMETHING THAT DOCTORS TENDING TO ME 17 YEARS AGO WOULD HAVE CONSIDERED IMPOSSIBLE.

Throughout elementary school, I faced challenges as a result of my disease. My brother and I would put out as much water as we were taking in, resulting in leaving the classroom to use the bathroom to pee or sometimes even vomit. I had sleepless nights, my parents helping to change my soaked bedding and refilling water bottles that were kept by my bed. I have had six leg surgeries in my life. I had rickets due to cystinosis, and my knees went inward, giving me a limp and bone pain. The surgeries involved having the doctor saw through my femur and tibia bones and adding a "shim" to straighten things out. Today, my legs are straight and have scars that make me proud. I also took many trips to Stanford Hospital for drug trials I participated in. These things, along with feeling ill more often than not, made it difficult to keep up in school.

As high school started, I was scared. I would be attending an all-girls school and away from my brother for the first time. I was scared of trying to make new friends who didn't know about cystinosis and what it entails. I have to take a medication called Procysbi® that causes a strong sulfur smell as it is metabolized. The best way to deal with this is to address the cause by talking about it with people, which opens up all kinds of discussion. Going through high school is difficult enough; add cystinosis to that, and it's really challenging. A teacher once said I have "holes" in my education, which has been shaped by my days feeling unwell, spent at home or spent in the hospital. I think my high school transcript and my GPA illustrates these "holes," which I hope to fill as I continue my education.

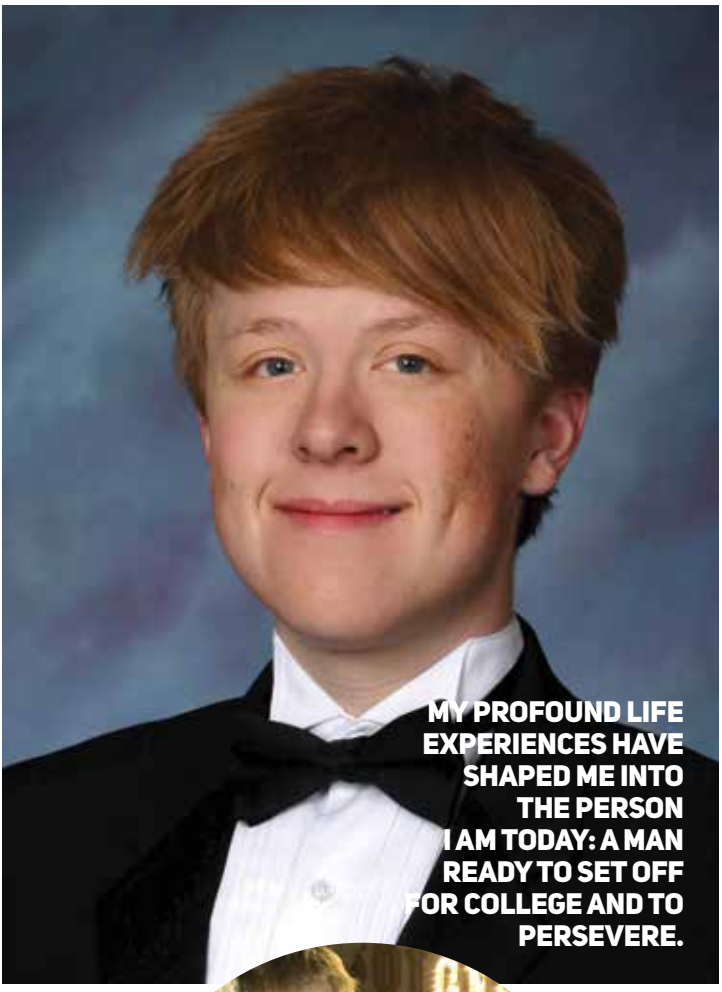
College will come with a lot of responsibility. Something that my parents and brother and I have been talking about for years will be remembering to take my 56 pills per day, as directed and on time. I have gotten better at taking my pills without being reminded. I have set timers and carried them in my pocket, but it sometimes slips my mind. I honestly feel better physically without medications churning in my stomach, but the price to pay for missed meds in the long run is bone damage and further damage to the organs of my body from cystinosis, and even death.

Having a chronic disease has taught me that I am unique and strong, even on days when I am feeling insecure. I have "holes" in my education, but those holes could be filled to overflowing with the life experience I have had and the obstacles I have overcome. I am strong for what I have been through. Cystinosis has been and will continue to be a burden, but it has also been a blessing in disguise, making me tough and full of perseverance, ready to forge ahead.

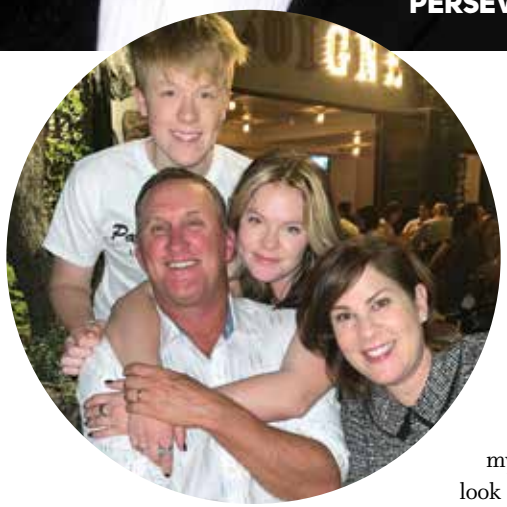
By Jenna Partington

Read about the CAPITAL CUP on page 44.

Bound PATRICK PARTINGTON



MY PROFOUND LIFE EXPERIENCES HAVE SHAPED ME INTO THE PERSON I AM TODAY: A MAN READY TO SET OFF FOR COLLEGE AND TO PERSEVERE.



When we were born, my twin sister, Jenna, and I seemed to be perfectly normal, healthy babies. Over the course of our first year of life, both my sister and I got sick. Really, really sick. We were severely dehydrated and could not stop our rapid intake of water. Our pediatrician diagnosed us with "failure to thrive." My sister got a common virus and became so sick she could barely move. She spent 13 days in the pediatric intensive care unit while I was sick at home. The most highly trained doctors did not know what was going on with Jenna and me; we were referred to as "electrolytic marvels." Jenna was finally diagnosed with cystinosis, a genetic disease that affects every cell and system of the body and for which there is no cure, and my diagnosis was confirmed as well. We were put on medication — a lot of it — which made our health somewhat stable. Our parents joined a family support community, and a nonprofit foundation to discover a cure was formed in our names, but this in no way set me up for a normal childhood.

Elementary school introduced challenges for me. In first grade, my angel of a teacher's aide, Mrs. Guillen, watched for my signal that I needed to go to the bathroom to throw up. This was not an "every once in a while" occurrence. My medicine, prescribed to keep me well, made me sick. Nearly every day of that year with Mrs. Guillen, I would throw up while she waited for me to exit the bathroom. She gave me a piece of candy each time. Social challenges started to appear as well; other students would say things such as, "Your breath smells!" or "Is it contagious?" My cystinosis medicine, Procysbi®, smells like sulfur or rotten eggs as it's metabolized, thus the bad breath. My disease is genetic, not contagious.

Middle school and early high school saw me as a very heavy-set kid. The answer to "failure to thrive" is a high calorie diet and I got used to it. I was overeating and under exercising as I recovered from multiple leg surgeries at Shriners Hospital. The many challenges of cystinosis made it difficult to do physical activity, and I was obese. By the end of sophomore year, I was about 215 pounds. During winter break of 2021, I realized I needed a change. I went fully vegetarian and incorporated regular exercises, including swimming into my days. Swimming turned into daily cardiovascular exercise and weightlifting. I would not refer to myself as a "gym rat," but I see my experience as showing perseverance and having mental strength to keep on going. I have gone from 215 to 160 pounds. There is a lot in life that I can't control, but I like tending to the things that I can. High school has provided social growth and I've started to tell my close friends about my disease. I have good friends who really support me. They see my medicine and marvel at the amount I am required to take: 56 pills of various medications every day. I tell them, "You just get used to it." High school has also seen me dealing with late work and stress caused by sick days. I had four surgeries in three years and have some gaps in my education because of time away from the classroom. I have become great at communicating with my teachers, advocating for myself and learning what I can do to keep up.

My sickness has impacted my education, but just as I've learned to take better care of myself physically, I've risen to the challenge and become a better student. I enjoy learning and look forward to continuing my education and making a difference in the world. My profound life experiences have shaped me into the person I am today: a man ready to set off for college and to persevere.

By Patrick Partington

Rowan's Story

By Makayla and Troy Ritchie, Rowan's parents
BREMERTON, WASHINGTON

The Challenges of Diagnosis

As my eyes welled up with tears, I asked the doctor, "Did I do something wrong?" The orthopedic doctor replied, "Well, that's what we're going to find out." Our son, Rowan, has rickets. As the doctor bluntly showed me the X-rays of his legs, I thought that we must have done something to cause this. Before we left the appointment, we did some labs to confirm the diagnosis and went on our way. We had no idea what was coming the next day.

The next evening rolled around and my husband and I received a phone call from the orthopedist. We were told, "Your son has x-linked hypophosphatemic rickets. It is incurable and he will need to have supplements for the rest of his life." We sat there stunned, but we asked questions, to which his response was, "You should probably Google it."

Needless to say, we got a second opinion and immediately switched Rowan's care. We eventually found the perfect endocrinologist who advocated for Rowan and for us. But every appointment we left feeling more confused; they were at a loss about the cause of our son not absorbing and losing electrolytes. When we looked at Rowan, he seemed to be your average 2-year-old. He is spunky, energetic, loves dinosaurs, macaroni and cheese and using the word "no" – he just has bowed legs. But what his little body was fighting inside, as seen in the results of his labs, was another story.

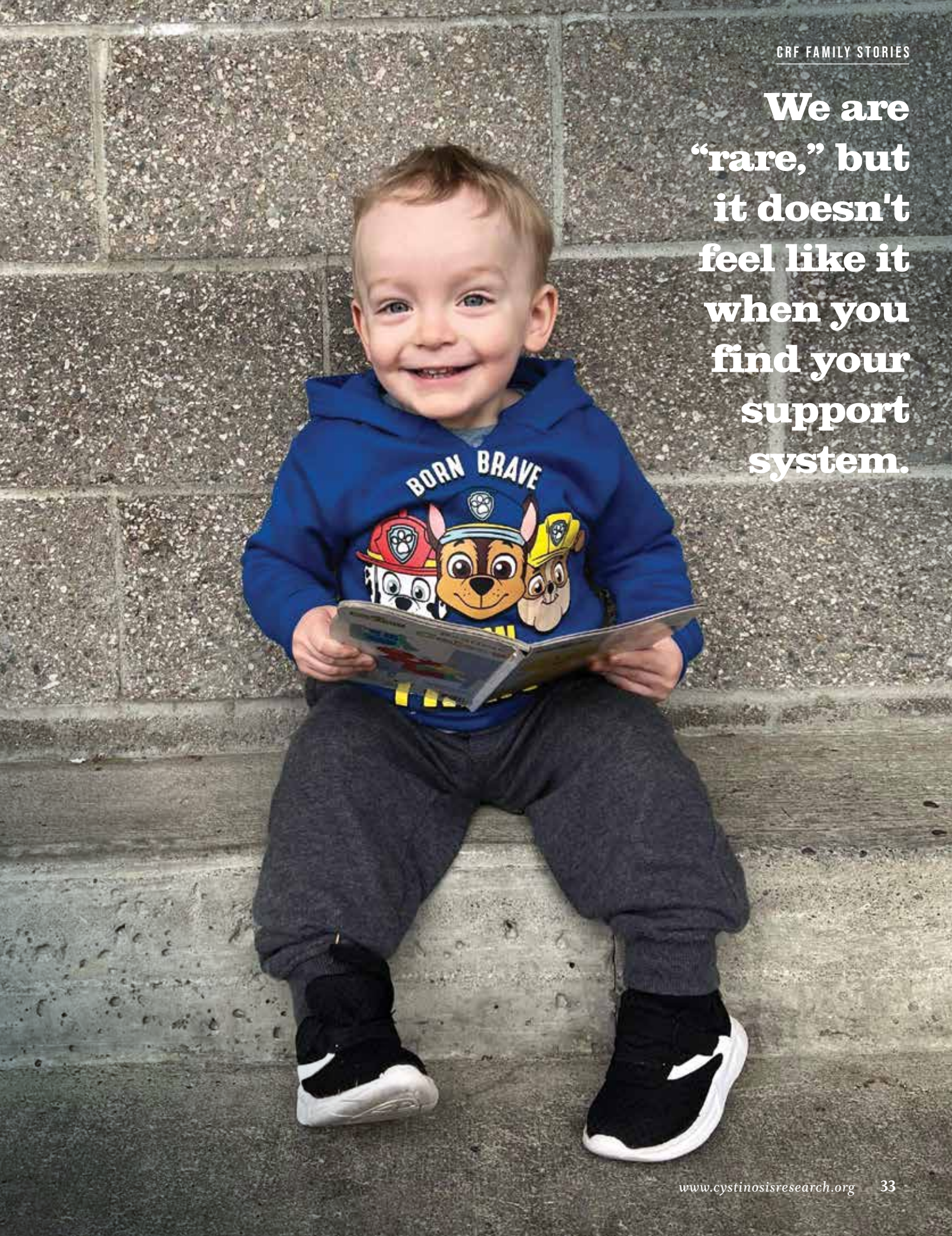
We were eventually sent to a nephrologist at Seattle Children's Hospital, which we knew meant his health issues were bigger than we had imagined. After months of different presumed diagnoses, cystine and genetic testing, we had a confirmation of diagnosis in May 2022. We were told our son has nephropathic cystinosis and Fanconi syndrome. Although scary, in a way it felt like a relief to finally have an answer.

"It felt like a relief to finally have an answer."

Since the diagnosis, our life has felt like it has been turned upside down. We have been grieving his diagnosis, the constant pokes, the urinalyses, the X-rays and the traveling to all of the appointments, not to mention the state of shock and grief we are processing as parents, acknowledging that parenthood won't ever be how we thought it would be.

But now, I can truthfully say that we are finding our new normal. For anyone just starting out on your cystinosis journey, or your child's, we are "rare," but it doesn't feel like it when you find your support system. With support from doctors, friends, family, social workers and the CRF, we all have a new hope.

We are "rare," but it doesn't feel like it when you find your support system.



HENRY STURGIS
My Tough HERO!

By Phil Currie, Henry's neighbor
SANDPOINT, IDAHO

WHY IS HENRY MY HERO? **HENRY IS THE TOUGHEST GUY I HAVE EVER KNOWN.**

Being a neighbor of Henry Sturgis, I have watched Henry's growth for the past 16 years. He was born July 19, 2006. At 16 months he was diagnosed with the immense obstacle of cystinosis. Henry's parents, Brian and Tricia, made a commitment towards strict medical compliance, and Henry continues that compliance today.

This story is not about cystinosis. It is about Henry. From the very beginning, I noticed Henry had something special about him. Yes, as a small child, he suffered from the effects of the massive amount of drugs required for compliance. He had all the symptoms a child suffers from having cystinosis. But Henry toughed it through with a positive outlook. I observed Henry as a young child determined to make the best of his life. He was a fun kid. Henry would play with his friends, and they all had their superhero outfits. Henry's favorite was Spider-Man, but sometimes he would appear as Iron Man. His cousin, Royce, would show up as The Hulk. The neighborhood needed a villain, and I began to verbally challenge them to battles whenever they were wearing their outfits. They named me "Bad Guy." They would conspire and plan ways to find me and attack. They knew I could be found in my garage on weekends. They would sneak up with their lightsabers or whatever weapon they had and try to surprise me. Once, I fended them off with my electric garden blower. On another occasion, they attacked me with water guns. I retreated to my front porch and grabbed the garden hose. And even though I had the upper hand and got them drenched, they kept up the lopsided battle. Henry was always determined to win. We all found the battles to be lively fun.

A highlight for me was being invited to be on the board of 24 Hours for Hank, our local cystinosis foundation. Because living with and caring for cystinosis is a 24-hour ordeal, we raise money by putting participants through 24-hour long endurance cycling, hiking and skiing events. We began fundraising for cystinosis in 2008. I am proud to say that our Sandpoint, Idaho foundation has raised over $1.7 million for CRF.

Henry always was determined to participate in the events. As a child, he rode his bike with training wheels during our bike race. This past year he skied the giant slalom course. During one of our sold-out awards banquets, Henry took the podium and presented a PowerPoint presentation about cystinosis. He showed amazing poise for a young lad only 12 years old.

Why is Henry my hero? Henry is the toughest guy I have ever known. I have never heard him complain about his disease. He does not even talk about it. A year ago, he suffered a severe hand and wrist injury. His recovery has required countless trips to Seattle for multiple surgeries, skin grafts and insertion of pins and plates, coupled with continuous physical therapy. Still, no complaints. He told me it is just something to get past.

As I said before, Henry is special, and we can expect a wonderful productive future for this young lad with his determined attitude. We are so grateful to CRF and the greater cystinosis family to have found a cure that will enable Henry that future.

BEYOND THE PHOTOGRAPH

By Kristen Murray, Seth's mom
CALGARY, ALBERTA, CANADA

As a wildlife biologist and photographer, my husband Nathan has the gift of portraying the spirit as well as the stunning physical details of his furry and feathered subjects. From the start in his role as dad, Nathan was equally adept at capturing the essence of our twins, Leif and Seth.

We've had great photos to share with family and friends over the years. It's no surprise that people often comment on how wonderful we look, how healthy and strong we seem and how fun and adventurous our lives appear to be.

In these photographs, nine years into our journey with cystinosis, our son Seth is smiling, seemingly thriving, despite his cystinosis diagnosis at 18 months.

Perhaps evident in our photo is the depth of our family connection, the hours that we have hiked, peddled and paddled together and the laughter and love we share. You may feel our fervent desire to embrace each precious moment with our boys, the clock of a rare disease always ticking in the background. Because of this ticking clock, there is so much more to our story than what is visible in a single snapshot in time.

BEYOND THE PHOTO: THE CHALLENGES

Not visible in our family photo is the reality of Seth's round-the-clock regime of pills, foul-tasting medications, stinging eye drops, injections, regular visits to the hospital for blood tests and clinic appointments, X-rays, ECGs, ultrasounds and assorted pokes and prods to monitor the progression of his disease.

The photo doesn't show the growing frustration that Seth feels about frequent absences from school for appointments, departures from class to take meds, concern about his short stature relative to peers and the awareness that he "smells bad". So much lies beneath the surface for Seth: the crystals that sear his eyes, vomiting and painful tummy aches that prevent his restful sleep and embarrassment when he wets his bed at night.

Behind the scenes lurks the trepidation in our hearts as parents, as we face the progression of our son's disease and our fear for his future.

Our family photograph doesn't show the weight in our hearts as we think about the other children and adults who live with cystinosis.

Below the surface is the panic we feel, racing against time, and the stress of being stretched beyond our limits, rarely able to engage as we'd like with family, friends and even self-care.

The impacts of cystinosis on our son Leif are also not noticeable at first glance. What it is like for Leif to be the "other," "unafflicted" child? How difficult would it be to feel special and valued when your brother's complex needs to take precedence so often?

And there is still more below the surface: the strain not just on Leif, but on Nathan and me as a couple. Not noticeable in our photo is the challenge to our relationship as we prioritize Seth's medical needs above all else, with tattered nerves, dwindling patience and so little time for anything other than the immediate demands before us.

BEYOND THE PHOTO: STRENGTH, GRATITUDE AND HOPE

We recognize that we are not alone in facing a very demanding situation. Throughout time, philosophers have asserted that challenges serve to strengthen us, and hardship should be welcomed as an opportunity for growth.

While I know that there can be opportunity to develop strength amid hardship, I can't help but wonder if this attitude is overly simplistic, glossing over the suffering and minimizing the wounds that precede the healed scars.

I would like to think that with more time, more healing, we will feel stronger. But for now, behind the smiles in our photographs, we most often feel weary and worn down, without the energy or perspective to heal or reflect on wounds that are still in the making.

Although we may not always feel strong in our daily lives, I wonder if other aspects of our experience might be evident in our photograph, positives that we strive to cultivate in our journey with cystinosis, namely gratitude and hope. **>>>>**

BEYOND THE PHOTOGRAPH

Our photo might portray the gratitude that Nathan and I feel to have been gifted with the presence of such a bold, strong and adventurous fellow traveller as Seth in our lives. I hope there is a hint of the appreciation we feel for Dr. Julian Midgley and his team at Alberta Children's Hospital who provide meticulous, collaborative and cutting-edge care for Seth. You may also see our gratitude for the Stack family, the CRF, the researchers and the cystinosis community as a whole. Perhaps you can sense how thankful we are for our family and friends, for their day in, day out love, support and companionship on our journey, as well as their generous donations in support of CRF-funded research through Seth's annual Circle of Hope.

As with all images, including your own family photographs, the truth is to be found in that which is evident and much that lies beyond. And so, I wonder:

- First of all, in looking at a photo or the smiling faces in front of you, it can be easy to assume that all is well. In this busy world of ours, do we take the time to actually ask? And then, are we willing to "show up," to really hear the answers we are given? Rich is the territory for respect, compassion, real friendship and excellent medical care if we strive to understand what things are ***actually*** like for others.
- And secondly, can we be brave enough to share openly about our lives with cystinosis with others who are interested in understanding our unique experience, possibly even finding creative ways to describe our realities?

If we can all acknowledge the full range of our respective experiences and embrace the complexity in the journey, from joy to despair and everything in between, then we have the opportunity, don't we, to live in truth, to develop rich and authentic relationships with one another, to enjoy connections that serve to strengthen us and that help us to live lives full of meaning and hope.

So, I wonder if you would meet us –in the space beyond the photograph.

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!

TOGETHER, WE ARE one

1 PURPOSE.
1 JOURNEY.
1 CURE.

The Suetta Family - Shelly, Derek, Lillyanna, and Emma - Etna, California

6TH ANNUAL LEMONADE FOR A CURE BAKE SALE

The 6th Annual Lemonade for a Cure Bake Sale, held in honor of Emma Suetta, was a huge success thanks to the efforts of the Suetta family! Shelly and her mom Kathleen, along with help from many friends, baked for three days creating over 1,300 cupcakes along with hundreds of other delicious, homemade treats! The day of the sale was threatened by rain, but people still came by to show support for the Suetta family, Lillyanna and Emma, and their friends. The bake sale raised over $5,000 for cystinosis research! News Channel 12 out of Medford, Oregon, covered the event prior to the sale with a news interview and video about Emma. After the broadcast, the Suettas were inundated with new faces, and friends who wanted to support their cause. We are grateful to Shelly, Derek, Lillyanna, Emma, and Kathleen for their baking skills and tireless efforts in supporting cystinosis research for a cure. Thank you, Suetta family!

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

JOLLY FOR JOSIE SUMMER EDITION

On Sunday, June 26, the Kanupke family hosted their first "Jolly for Josie Summer Edition" fundraiser at Rock Island Public House in Blue Island, Illinois. With pizza sales donated by Red's Pizza and kegs of beer donated from multiple sources, the community of friends and family gathered to honor Josie. The donated delectable desserts on display brought in additional revenue to raise more than $6,000 for cystinosis research! We are grateful to the Kanupke family and their amazing community, for the unwavering support for Josie, cystinosis research, and the cystinosis community. Together we are ensuring a brighter future for all those with cystinosis!

The Monaghan Family - Katie, Terry, William and Abbi - St. Catharines, Ontario, Canada

SHOOT FOR CYSTINOSIS FUNDRAISER

The "Shoot for Cystinosis" Event held in honor of Abbi Monaghan began in 2016 to raise money for cystinosis research and bring awareness to the St. Catharines community about this rare genetic disease. The fifth annual event held in July, raised over $27,700, with 100% of the donations going to the Canadian Cystinosis Research Foundation to fund ongoing research for better treatments and a cure. We are grateful to the Monaghan family and their community for helping to improve the lives of those with cystinosis through research, thank you!

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

ROCK AND ROLL FOR A CURE

It was a beautiful day with perfect weather for a rock and roll Sunday Concert held in honor of Lily Beauregard and cystinosis research. The fourth annual fundraiser featured music from RI mainstays D'Vottes, Western Stars, Mark Taber and Sam Taber and Julie Fischer, who all contributed their time and considerable talents. An enthusiastic crowd greeted the bands who played all afternoon while the children were entertained by a balloon artist and face painter. We are grateful to Tom Wallis and his wife Jane, pictured with Lily, who spent countless hours organizing and coordinating the event. Thank you to the musicians, vendors and community who helped to raise $2,000 for cystinosis research!

The Alexander Family - Marcu, Ben, Stella and Hadley - Boise, Idaho

WINE NOT GIVE - FUNDRAISER

Years ago, Marcu and Ben Alexander formed the Hearts for Hadley Foundation in honor of their daughter, Hadley. For the last two years, Split Rail Winery has selected Hearts for Hadley for a Wine Not Give fundraiser. This year the event took place on Monday, June 6, at Split Rail's beautiful new tasting room. The owners graciously donated 20% of the proceeds to Hearts for Hadley which helped raise over $500 for cystinosis research. Thank you, Split Rail Winery, and all those who participated in supporting Hadley and our mission to find better treatments and a cure for cystinosis!

TOGETHER, WE ARE one

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The Fehr Family - Leah, Devin, James and Maya - Warman, Saskatchewan, Canada

HOPE 4 JAMES GOLF TOURNAMENT

The Hope 4 James Golf Tournament was held May 14, at the Legends Golf Course, in honor of James Fehr. Twenty-three teams of four golfers each signed up to participate in the Texas scramble format. The course was set with a few additional challenge games to add to the fun for the golfers, and to raise additional funds for cystinosis research. Everyone stayed following the tournament to enjoy dinner and participate in the silent auction, raffle, and live auction. Live auction donor, Shlimo, contributed a CFL Football Package which a lucky bidder won for an amazing $3,900. Thank you to the Fehr family, the outstanding volunteers, the generous sponsors, and the participants, who contributed so much to help make the tournament a tremendous success raising $28,000 this year! We are grateful to our Canadian friends who support CRF and our mission to fund research for improved treatments and a cure for cystinosis.

The Galloway Family - Christina, Rob, and Collins - Cumming, Georgia

THE GREEN RIBBON CAMPAIGN!

The month of May has become a special time for the Galloway family and the Cumming community. Last year, the family created a Green Ribbon cystinosis awareness campaign in honor of their daughter Collins. They made and sold Green Ribbons to their neighbors and friends in the community and asked everyone to place the ribbons on their mailboxes during the month. The campaign caught on like wildfire which resulted in donations of more than $8,000!! The Ribbon Campaign has been a great way to get people involved and create awareness for cystinosis. With green ribbons everywhere in the neighborhood, it was exciting to see all the people honoring Collins and supporting cystinosis research. Thank you to the friends and neighbors of the Galloway Family, Carol Stevens, Collins' grandmother, and their communities for helping to fund research that will result in a brighter future for Collins and all those with cystinosis!

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The Khalasi Family - Minaxi, Mukund, Aarav, Rani and Isha - Sacramento, California

AARAV'S TIME TO SHINE

On May 14, the Khalasi family hosted Aarav's Time to Shine Inaugural Golf Tournament to raise funds for cystinosis research in honor of their son, Aarav. The community participation and support were overwhelming, with golf registrations selling out weeks before the tournament and more than 20 sponsorships sold for hole sponsors, food, and refreshments. Participants purchased over 1,000 tickets for opportunity drawings, and golfers chipped in to join the games around the course to make Aarav's first golf event extremely successful raising more than $22,000 for research! We are grateful to Minaxi, Mukund, and their community of friends for their commitment to Aarav and cystinosis research. Together we are making a difference in the lives of those with cystinosis. Thank you!

The Krahe Family - Amy, Jeremy, Austin and Jake - Medina, Ohio

THE FIRST "SHOOTING FOR A CURE" EVENT!

Over the years the Krahe family has hosted several fundraisers under the title "A Night of Hopes and Wishes" featuring a gala style event. As it did for many, COVID-19 put a wrinkle in the scheduling of their biennial event! In effort to resume their fundraising efforts, they decided to change things up. Their twin 15-year-old boys, Jake (with cystinosis) and Austin (without), are both involved in competitive shotgun sports; they wanted to introduce their hobby into their event. This year marked their first "Shooting for a Cure" event!

The afternoon featured a 50-target event followed by a picnic style dinner and auction. Participants ranged from experienced shooters to those who have never attempted the sport. Numerous coaches from Jake's shooting team volunteered to help coach newcomers and act as scorekeepers for the afternoon. The event sold out and they had over 100 shooters participate in the event and an additional 100 join them for dinner and the auction. Main event sponsors were incredibly generous along with 19 station sponsorships that helped make the event such a huge success! The Krahe family continues to be astounded by the support and generosity of those in their community who have repeatedly come out to support Jake and their family in their fight for a cure. The Krahe's are thankful to those who participated in the event, sponsored the day, and volunteered their time to support our cause. CRF is grateful to the Krahe Family for their partnership and for their dedication to funding cystinosis research in honor of Jake and all those with cystinosis.

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

LOTS OF LOVE FOR LANDON

The 10th Annual Lots of Love for Landon Charity Golf Tournament was held on Friday, June 3, on a spectacular day for the golfers to enjoy the competition and camaraderie on the course. The tournament raised over $37,377 in honor of Landon and cystinosis research! Thank you to the dedicated volunteers, amazing golfers, generous donors, and crew at Blackhawk Golf Course for creating another successful golf event. Our heartfelt thanks to Lauren and Jimmy Hartz and their family and team for their dedication and commitment to CRF and our mission to find a cure for cystinosis. You have given the cystinosis community hope – thank you!

The Tschannen Family - Barb, Terry and William
- Brookfield, Missouri

5TH ANNUAL WESTON TSCHANNEN MEMORIAL GOLF TOURNAMENT

On May 21st, the Tschannen family hosted the 5th Annual Weston Tschannen Memorial Golf Tournament. The outstanding turnout of golfers, families, and friends made it a perfect day for remembering Weston and celebrating his life. The weather was a challenge, but the rain stopped before the tournament began, so the prayers asking Weston to provide a good day of golf were certainly answered! The tournament raised money for CRF, and other local organizations Weston was passionate about. Thank you to the Tschannen Family, and friends of Weston for donating $5,000 to CRF for cystinosis research in memory of Weston. With your help we will find the cure!

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

SHANNON DEARY-BELL HONORS JENNA AND PATRICK PARTINGTON AT THE CAPITAL CUP

Shannon Deary-Bell, Nor-Cal Beverage Co., President, and CEO, participated in the 2022 Villara Capital Cup for the sixth time. Each year, more than 20 Sacramento area leaders gather and divide into two teams, with each competitor raising funds for a charity of their choosing. Year after year, Shannon vows to raise funds for Jenna and Patrick's Foundation of Hope. Accompanied by her husband, Brad Bell, she raised an incredible $96,410 this year!

Thank you, Shannon, and the wonderful friends in the Sacramento community who have so generously contributed to support Jenna and Patrick's Foundation and their cause to fund cystinosis research for better treatments and a cure!

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.

Saturday, November 12, 2022

COLLINS' CURE CUP TOURNAMENT
IN HONOR OF COLLINS GALLOWAY
Windermere Golf Club, Cumming, Georgia

Sunday, November 20, 2022

PHILADELPHIA MARATHON-TEAM SOFIE FOR CYSTINOSIS
IN HONOR OF SOFIE SOS-FINUCANE
Philadelphia, Pennsylvania
www.teamsofie.org/donate or
Contact Erin Finucane: erinafinucane@gmail.com

Tuesday, November 29, 2022

GIVING TUESDAY – FUND A CURE FOR CYSTINOSIS!
$100,000 GIFT CHALLENGE
Cystinosis Research Foundation
info@cystinosisresearch.org

Tuesday, February 28, 2023

RARE DISEASE DAY
CYSTINOSIS RESEARCH FOUNDATION
www.cystinosisresearch.org

March 2023

EIGHTH ANNUAL FISHING FOR BROOKE'S CURE - HOPE FOR BROOKE
IN HONOR OF BROOKE EMERSON
Fishing Locations North Carolina
Contact Clay Emerson: clay.emerson@gmail.com

Saturday, March 25, 2023

2400 FT OF SCHWEITZER
24 HOURS FOR HANK
IN HONOR OF HENRY STURGIS
Schweitzer Mountain, Sandpoint, Idaho
Contact Brian Sturgis: bsturgis@simulstat.com

Thursday, March 30 – Saturday, April 1, 2023

CRF DAY OF HOPE FAMILY CONFERENCE
VEA Newport Beach Resort
Register Now: www.cystinosisresearch.org/day-of-hope-2023
Contact: info@cystinosisresearch.org

Month of April 2023

NATALIE'S WISH 20TH ANNIVERSARY CELEBRATION — MONTH OF FUNDRAISING FOR A CURE
Cystinosis Research Foundation
Contact Nancy Stack: nstack@cystinosisresearch.org

Friday, June 2, 2023

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

Sunday, June 25, 2023

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

Summer or Fall 2023

HOPES & WISHES
IN HONOR OF JAKE KRAHE
Shooting for a Cure Fundraiser, Medina, Ohio
Contact Jeremy Krahe: jdkrahe25@gmail.com

Thursday, September 7 – Friday, September 8, 2023

CRF INTERNATIONAL CYSTINOSIS RESEARCH SYMPOSIUM (BY INVITATION ONLY)
Mabel and Arnold Beckman Center, Irvine, California
Contact Nancy Stack: nstack@cystinosisresearch.org

Fall 2023

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

Saturday, October 21, 2023

SETH'S CIRCLE OF HOPE
IN HONOR OF SETH DEBRUYN
Calgary, Alberta, Canada
Contact Kristen Murray: murraykristen@hotmail.com

Tuesday, November 28, 2023

GIVING TUESDAY – FUND A CURE FOR CYSTINOSIS!
Cystinosis Research Foundation
info@cystinosisresearch.org

Day of Hope

CRF 2023

CYSTINOSIS RESEARCH FOUNDATION FAMILY CONFERENCE

Thursday, March 30 thru Saturday April 1, 2023

VEA Newport Beach • Oceanfront Resort

900 Newport Center Drive
Newport Beach, CA 92660

We are excited to see you in-person at the 2023 Day of Hope family conference! Join us for three inspiring days spent with fellow members of the cystinosis community as we renew our friendships and strengthen the bonds that created this remarkable CRF family and research community. **When we are together, magic happens!**

The conference will include break-out sessions and presentations by CRF-funded researchers and cystinosis clinicians.

TOPICS WILL INCLUDE:

- Stem cell and gene therapy
- Ocular cystinosis
- Kidney disease and treatment
- Neurological challenges
- Myopathy and muscle wasting

Medical & Scientific Speakers Include:

Sergio Catz, PhD
Stéphanie Cherqui, PhD
Morgan DiLeo, PhD
Francesco Emma, MD
Ana Alves Francisco, PhD
Sophie Molholm, PhD
Benjamin Freedman, PhD
Paul Grimm, MD
Stephen Jenkins, MD
Julian Midgley, MD

For more information about the conference or the Family Assistance Fund, visit: www.cystinosisresearch.org/day-of-hope-2023 or call: (949)223-7610

EIGHTH INTERNATIONAL

CYSTINOSIS RESEARCH SYMPOSIUM

Sponsored by the Cystinosis Research Foundation

SAVE THE DATE

THURSDAY, SEPTEMBER 7, 2023
AND
FRIDAY, SEPTEMBER 8, 2023

Arnold and Mabel Beckman Center of the National Academies of Sciences and Engineering

IRVINE, CALIFORNIA

2023 SYMPOSIUM CO-CHAIRS

Corinne Antignac, MD, PhD

Stéphanie Cherqui, PhD

Julie Ingelfinger, MD

BY INVITATION ONLY

cystinosis RESEARCH FOUNDATION | TOGETHER WE SHINE BRIGHT

For information contact CRF President Nancy Stack
(949) 223-7610 or nstack@cystinosisresearch.org

Day of Hope Goes to Canada

IPNA 2022
7–11 SEPTEMBER, CALGARY

by Stephen Jenkins, MD
CRF Board Member and Sam and Lars' dad

This year the International Pediatric Nephrology Association met in Calgary, Alberta, Canada, and the conference president was one of our beloved cystinosis specialists, Dr. Julian Midgley. Dr. Midgley asked the Cystinosis Research Foundation (CRF) to present a full day session on cystinosis for the attendees on September 7, 2022.

Dr. Julian Midgley
Chair of the Canadian Local Organising Committee - IPNA 2022

Similar to CRF's Day of Hope, many of our Canadian cystinosis families were able to come to the meeting and talk about living with cystinosis, as well as listen to scientists and clinicians talk about the latest in cystinosis research.

Nancy Stack started off the morning with an overview of the work CRF has done to raise money and become the largest single funder of cystinosis research. Following Nancy's remarks, Dr. Midgley shared reflections on his 30 years as a pediatric nephrologist caring for people with cystinosis in Alberta, Canada. It was inspiring to see a clinician who cares so much for his patients. He has become like a member of the family for many of them.

Dr. Paul Grimm spoke on the perils and pitfalls of managing the renal complications of cystinosis. He shared a lot of practical tips on dealing with Fanconi syndrome and the right way to take your medications. Dr. Justine Bacchetta from Lyon, France spoke about cystinosis care in developed vs. developing countries, as well as her research on metabolic bone disease in cystinosis.

Stem Cell Gene Therapy Trial Participants Jordan Janz and Tyler Joynt

Day of Hope **Goes to Canada**

Dr. Benjamin Freedman shared an update on his research of induced pluripotent stem cells. They have successfully created cystinosis kidney organoids. One day they may be able to insert healthy kidney tissue created from stem cells into diseased kidneys. Dr. Morgan DiLeo gave a virtual update on cysteamine SoliDrops, a potential new treatment for corneal cystinosis. She is finishing up animal studies and planning to go to the FDA soon.

Dr. Stéphanie Cherqui gave an update on the stem cell trial. They have transplanted five adults, all of whom are doing well and remain off cysteamine therapy.

Stéphanie Cherqui, PhD
Professor, Department of Pediatrics Division of Genetics
University of California, San Diego

Clay Emerson, PhD, PE, CFM
CCIR Committee Member and Brooke Emerson's dad

The stem cell transplant appears to be a durable therapy, as the vector copy number is still detectable even two years after transplant. After Dr. Cherqui's talk, we heard from two of the trial participants, Jordan Janz and Tyler Joynt. They shared what it was like to go through the transplant, and how their lives have been since. It was inspiring to hear from such brave people in our cystinosis community!

In addition to hearing from researchers, we had multiple families share their experiences with cystinosis. We heard from Vanessa Bonneau and Sylvan Lanken, Jill and Clay Emerson, Kristen Murray, Crystal and Aliyah Walker, and Susan, Charissa and Courtney Penner. Their stories were very moving and were an important reminder of the powerful connections we share in this small, rare disease community.

Following the session we gathered at the River Café, a rustic restaurant on Prince's Island in the Bow River, for a delicious dinner where families and scientists could mingle and celebrate the important work we are doing. The CRF is so grateful to the many families across Canada who are dedicated to finding a cure and improving the lives of people with cystinosis everywhere. It was a very special day and it made me even more excited for our upcoming Day of Hope in 2023.

NEWLY PUBLISHED STUDIES

FALL 2022

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.

Summaries of articles by Clay Emerson, PhD, PE, CFM

STRUCTURE AND MECHANISM OF HUMAN CYSTINE EXPORTER CYSTINOSIN

published August 20, 2022, in Cell

by ***Liang Feng, PhD, and Xue Guo, PhD***

Stanford University, Stanford, California

CRF awarded the first research grant to Xue Guo, PhD, and Liang Feng, PhD, in 2015 for their study on the "Molecular Mechanism of Cystinosis", since that time, there have been three additional grant awards for a total of $770,000 for their research. This support has resulted in a published paper in Cell*, the most prestigious journal on basic science. The results on the interaction with the mTOR complex confirmed the data published in* JASN *in 2014 by Corrine Antignac, MD, PhD, although questions remain.*

Clay Emerson, PhD, PE, CFM summarized this significant article:

"CRF-funded researcher Xue Guo and co-authors just published a paper in the prestigious journal "Cell". In the paper, the authors focus on deciphering the molecular mechanisms of the protein cystinosin. Cystinosin is the protein that is either defective or absent in people with cystinosis. The protein is essentially the lysosomal gatekeeper for cystine; thereby preventing the accumulation of cystine and the crystals it forms. The paper provides critical fundamental research on the root cause of the disease by examining, on a molecular level, how cystine interacts with the protein to ultimately exit the lysosome. The study used cutting edge technology and provided new insight into the intra-cellular functions of cystinosin and sheds light on potential new treatment mechanisms."

OCULAR BIODISTRIBUTION OF CYSTEAMINE DELIVERED BY A SUSTAINED RELEASE MICROSPHERE/ THERMORESPONSIVE GEL EYEDROP

published July 7, 2022, in the International Journal of Pharmaceutics

by ***Morgan V. DiLeo, PhD, and Ken K. Nischal, MD, FRCO***

University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

The ocular manifestations of cystinosis are especially bothersome. Cystinosis causes cystine crystals to form in the cornea which leads to light sensitivity (photophobia). Photophobia in people with cystinosis can make simply being outside on a sunny day unbearable. Unfortunately, oral cysteamine treatment does not supply cysteamine to the eye's non-vascular cornea. Therefore, current treatment requires the hourly administration of an ophthalmic cysteamine solution. However, in this CRF-funded research effort the authors detail the latest results in the investigation of a new sustained release drug delivery mechanism. In an effort to provide a lengthy and sustained delivery of cysteamine to the eye, the approach uses microspheres of cysteamine suspended in a thermoresponsive gel. The results from this University of Pittsburgh School of Medicine led study indicate that the novel drug delivery mechanism can provide sustained cysteamine to the cornea for a period of 12 hours. This publication represents an important step in providing much-needed advances in the treatment of the ocular complications of cystinosis.

LONGITUDINAL DYSPHAGIA ASSESSMENT IN ADULT PATIENTS WITH NEPHROPATHIC CYSTINOSIS USING THE MODIFIED BARIUM SWALLOW IMPAIRMENT PROFILE

published May 20, 2022, in the Muscle & Nerve *journal*

by ***Reza Seyedsadjadi, MD, and Florian Eichler, MD***

Massachusetts General Hospital, Boston, Massachusetts

Muscle weakness is a significant late complication of cystinosis with many quality-of-life implications. Perhaps one of the most critical is difficulty in swallowing, or dysphagia. CRF-funded researchers from the Massachusetts General Hospital conducted a deep dive into the impaired mechanics of swallowing in a group of volunteer patients. Among other methods, the study included detailed fluoroscopic video analysis of swallowing among the patient volunteers with two separate analyses being completed for each patient one year apart. The study sheds light on the specific mechanisms involved in the difficulties which people with cystinosis experience when swallowing. The study also suggests that dysphagia is often present prior to the onset of advanced muscle weakness. In the future the results of this study may help assist clinicians in better understanding dysphagia and working with patients to maintain or improve swallowing through exercise or other interventions.

Rewards Beyond Measure

RETROSPECTIVE

Twenty years of research impact prove difficult to sum up in words. But for Dr. Julie Ingelfinger, the real joy is seeing the profound hopes of patients fulfilled.

by Dennis Arp

As a physician and scientist, Dr. Julie Ingelfinger prefers to focus on the future rather than dwell in the past. However, recently she allowed herself a few moments of reflection.

She smiled as she considered two decades of progress made possible by the Cystinosis Research Foundation (CRF).

"This 20th anniversary is really an amazing and laudable achievement," said Dr. Ingelfinger, a professor of pediatrics at Harvard Medical School and deputy editor of the New England Journal of Medicine who is also a founding member of the CRF Scientific Review Board.

"What the CRF has brought to the community of those affected by cystinosis is something that, at this point, is not fully appreciated even by those of us involved," she added. "The lessons learned over the past 20 years, and their applicability, provide opportunities for impact that are heartening for us all."

Dr. Ingelfinger saw her first cystinosis patient more than five decades ago, so an abundance of experience informs her powerful commitment to the community. But undergirding it all is a deep wellspring of compassion for cystinosis patients and their families.

"When I was a pediatric nephrology fellow 50 years ago, the first patient I saw with cystinosis had advanced kidney disease and so much proteinuria that he looked as if he had nephrotic syndrome," she recalled. "On top of that, I was told, 'well, there is no cure, so we're just going to treat his symptoms.' "

Inspiring Momentum Starts With Foundational Research

Starting in the 1970s, Dr. Ingelfinger witnessed all that patients and families had to endure – how they navigated incredibly demanding treatments without losing hope, even in the face of grim prognoses.

Those memories make 20 years of research progress that much more satisfying.

"Better preparations of medications, and ease of taking them. Better treatments for some of the problems affecting daily quality of life, such as crystals in the cornea. These and other advances have come because of funding by this family foundation and by the momentum that inspired people to contribute in so many different ways to realizing this great progress," she said.

A vital way that Dr. Ingelfinger contributes to that progress is through her role evaluating funding proposals submitted to her and her colleagues on the CRF Scientific Review Board.

Since its founding in 2003, the board has approved and the CRF has funded hundreds of research projects that together greatly expand the cystinosis knowledgebase as they also improve treatments. That body of foundational and translational research has led to everything from quality-of-life improvements like time-release drugs and eye drops to the development of a life-changing gene therapy pioneered by Dr. Stéphanie Cherqui.

"This 20th anniversary is really an amazing and laudable achievement."

JULIE R. INGELFINGER, MD

Deputy Editor of the New England Journal of Medicine
Professor of Pediatrics

Harvard Medical School, Boston, Massachusetts

It's been quite a journey for the cystinosis community – from dim prospects and inadequate treatments to the threshold of a cure. And to think that it all started with four research proposals for basic and observational investigations – "nothing like the sophisticated, targeted research we're seeing today," Dr. Ingelfinger said.

Still, without those initial research projects funded by the CRF, the breakthroughs that have followed may never have been possible.

"The reality is that the National Institutes of Health, the National Science Foundation and other big research entities tend not to fund research on very rare diseases unless there's a lot of preliminary data that shows its importance," Dr, Ingelfinger said.

"It was essential to have the validation of those early grants funded by the CRF," she added. "They have resulted in NIH funding for a number of the investigators the CRF has supported."

The Chance 'To Be Better Than We Think We Can Be'

"CRF is both condition-based and family-focused, ... on track to find unique ways to cure this disease."

For Dr. Ingelfinger, the rewards of serving on the Scientific Review Board are not always easy to put into words. Ultimately, she settles on a descriptor that some might find surprising.

"It's fun," she said.

Fun?

"I always find enjoyment in things with promise – things that might help us to be better than we think we can be," she said. "So, yes, what could be more fun than that?"

Perhaps the only thing better is looking ahead with optimism.

"I think the CRF is on an excellent path," Dr. Ingelfinger said. "Because it is both condition-based and family-focused, the foundation is on track to find unique ways to cure this disease."

What's more, Dr. Ingelfinger thinks "cross-fertilization" of research might open doors to cures for other conditions as well.

"In medicine and in science, we sometimes end up with silos of information that keep us from broadening our thinking," she said. "There may be lessons in the effective way this organization is run that allow for our experience to be applied to taking on other diseases and meeting other important challenges of our time."

It's certainly an occasion to celebrate when the next 20 years may be the best 20 years.

Stem Cell Gene Therapy Clinical Trial for Cystinosis

Stéphanie Cherqui, PhD

Professor, Department of Pediatrics
University of California, San Diego

After receiving clearance from the Food and Drug Administration in December 2018 and funding from the Cystinosis Research Foundation, the California Institute of Regenerative Medicine, a phase 1/2 clinical trial on stem cell gene therapy for cystinosis started in July 2019 at the University of California San Diego.

The stem cell gene therapy approach was developed through more than a decade of research by Dr. Stéphanie Cherqui, professor of pediatrics at UC San Diego. The approach relies on using autologous bone marrow stem cells, i.e., patients' own stem cells. In this procedure, hematopoietic stem cells (blood cell precursors) are removed from a patient and engineered in a laboratory using gene therapy techniques to introduce the missing cystinosin gene. Then, the cells are returned back to the same patient. These stem cells act as vehicles that carry the corrected gene to every tissue of the body to produce cystinosin protein and to prevent the toxic buildup of cystine in tissues throughout the body.

THE STEM CELL GENE THERAPY APPROACH WAS DEVELOPED THROUGH MORE THAN A DECADE OF RESEARCH

The first patient, Jordan Janz, was enrolled in October 2019 at the age of 20. He was the first volunteer for this new experimental therapeutic approach. Since then, five more patients have been treated with the stem cell therapy, four males and one female. No adverse events related to the drug product have been reported to date. White blood cell cystine was decreased in all treated patients as well as tissue cystine crystals in the skin and rectal mucosa compared to prior to stem cell transplant with patient 1 below 1 nmol half-cystine/mg protein at about three years post stem cell infusion. The six patients are no longer taking oral cysteamine. Patient 2 has restarted eyedrop cysteamine after a year post-infusion.

The sixth patient was treated on October 24, 2022, which now completes this phase 1/2 clinical trial. The next phase of the trial will be conducted by AVROBIO, a biotech company specializing in stem cell gene therapy for metabolic diseases.

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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Sergio D. Catz, PhD
Professor
Department of Molecular Medicine
The Scripps Research Institute
LA JOLLA, CALIFORNIA

Stéphanie Cherqui, PhD
Professor
Department of Pediatrics
Division of Genetics
University of California, San Diego
LA JOLLA, CALIFORNIA

Francesco Emma, MD
Head of Pediatric Nephrology
Director of Nephrology Laboratory
Bambino Gesù Children's Hospital
ROME, ITALY

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Emory School of Medicine
Executive Clinical Director
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Professor of Pediatrics
Pediatric Nephrology
Stanford University School of Medicine
STANFORD, CALIFORNIA

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New England Journal of Medicine
Professor of Pediatrics
Harvard Medical School
BOSTON, MASSACHUSETTS

Stephen L. Jenkins, MD
Assistant Professor, Hospitalist
Department of Internal Medicine
University of Utah Hospital
SALT LAKE CITY, UTAH

Aude Servais, MD, PhD
Senior Nephrologist,
Department of Adult Nephrology
Necker Hospital, Paris Descartes University
PARIS, FRANCE

THANK YOU FOR YOUR DEDICATION TO THE GLOBAL CYSTINOSIS COMMUNITY

CONGRATULATIONS!

CORINNE ANTIGNAC, MD, PHD

ERA AWARD FOR OUTSTANDING BASIC SCIENCE CONTRIBUTIONS TO NEPHROLOGY

Dr. Corinne Antignac, initially trained as a Pediatric Nephrologist, is Professor of Genetics at University Paris Cité, Paris, France, and co-head of the INSERM Laboratory of Hereditary Kidney Diseases at the Imagine Institute, an interdisciplinary research center on rare genetic diseases in the Necker Enfants-Malades University Hospital campus.

Her research focuses on identifying and characterizing genes responsible for inherited renal disorders. Her lab's main results concern the identification and the characterization of genes involved in nephronophthisis, cystinosis and steroid-resistant nephrotic syndrome (SRNS), among which the NPHS2 gene encoding podocin back in 2001. Podocin turned out to be a crucial protein of the podocyte and this discovery was among the pioneer works that point to the podocyte as a major player in the development and maintenance of the glomerular filtration barrier. Prof. Antignac has also been involved in identifying genes and in phenotype/genotype correlation in other hereditary renal disorders, such as Bartter and Alport syndromes and renal tubular dysgenesis.

Dr. Antignac was awarded several French awards (Medical Research Prize from the French Medical Research Foundation, Eloi Collery Prize from the French National Academy of Medicine and the Prize of the French Association of patients with Nephrotic Syndrome) and the Lilian Jean Kaplan International Prize for Advancement in the Understanding of Polycystic Kidney Disease in 2009. She was elected at the French National Academy of Sciences in 2019.

JULIE R. INGELFINGER, MD

2022 BARBARA T. MURPHY AWARD RECIPIENT

Dr. Julie R. Ingelfinger is professor of pediatrics at Harvard Medical School and senior consultant in pediatric nephrology at Mass General for Children at Massachusetts General Hospital.

Her most prominent role is perhaps as deputy editor of The New England Journal of Medicine (NEJM), a position she has held since 2001. She teaches courses at NEJM—the world's highest-impact journal—and mentors authors year round on a one-to-one basis.

Dr. Ingelfinger has been studying the intrarenal renin angiotensin aldosterone system for many years. Her other current projects focus on the role of maternal nutrition and maternal diabetes in renal development and perinatal programming. She is also investigating the role of maternal nutrition in renal development and the subsequent development of hypertension and mechanisms of proximal tubule injury.

She authored a text on pediatric hypertension and was an editor of the textbooks "Current Pediatric Therapy" and "Pediatric Hypertension."

Among her many honors, Dr. Ingelfinger received the Dr. Donald N. Medearis Teaching Award from Massachusetts General Hospital, the Henry L. Barnett Award from the American Academy of Pediatrics, the Founders' Award from the American Society of Pediatric Nephrology and the Honors Award from the National Kidney Foundation.

Dr. Ingelfinger received her MD from the Albert Einstein College of Medicine in New York City, followed by an internship in pediatrics at the Bronx Municipal Hospital Center. She completed residencies and fellowships in pediatrics and pediatric nephrology at St. Louis Children's Hospital, followed by further pediatrics training at St. Joseph's Hospital and Medical Center in Phoenix, Arizona.

Dr. Ingelfinger has spent her career at Harvard University, where she was appointed assistant professor in 1982, associate professor in 1988 and professor of pediatrics in 1999. She was chief of pediatric nephrology at Massachusetts General Hospital for eight years.

THE IMPACT of CRF RESEARCH

AREAS OF RESEARCH FOCUS & GRANTS AWARDED SINCE 2002

New Drug Discovery Cysteamine, New Medications and Devices

31 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
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

63 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

NEW
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

NEW
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

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

NEW
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

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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

19 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

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HANNOVER MEDICAL SCHOOL, HANOVER, GERMANY

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Trinh Tina Duong, MPT
Feliks Kogan, PhD
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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, QUEBEC, 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

10 GRANTS

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

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

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
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SAN DIEGO,
LA JOLLA, CALIFORNIA

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UNIVERSITY OF CALIFORNIA,
SAN DIEGO,
LA JOLLA, CALIFORNIA

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

Florian Eichler, MD
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GENERAL HOSPITAL,
BOSTON, MASSACHUSETTS

Pascal Laforêt, MD, PhD
Hélène Prigent, MD, PhD
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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

25 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

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

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

NEW
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

3 GRANTS

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

2022 SPRING CRF RESEARCH GRANT AWARDS

2022 SPRING RESEARCH GRANTS AWARDED **$1,287,127**

Sergio Catz, PhD *(Mentor)* **and**
Danni Chen, PhD *(Fellow)*
The Scripps Research Institute, La Jolla, California

"Novel mechanistic and translational studies of inflammation in cystinosis"

$150,000 TWO-YEAR FELLOWSHIP

Sergio Catz, PhD *(Mentor)* **and**
Aparna Shukla, PhD *(Fellow)*
The Scripps Research Institute, La Jolla, California

"Translational approaches to repair chaperone mediated autophagy in cystinosis"

$150,000 TWO-YEAR FELLOWSHIP

Olivier Devuyst, MD, PhD *(Mentor)* **and**
Marine Berquez, PhD *(Fellow)*
University of Zürich, Switzerland

"Role of nutrient sensing and mTORC1 signaling in cystinosis"

$150,000 TWO-YEAR FELLOWSHIP

Francesco Emma, MD and Anna Taranta, PhD
Bambino Gesù Children's Hospital, Rome, Italy

"Impact of diet composition on renal function and bone disease of Ctns-/- mice"

$287,320 TWO-YEAR STUDY

Liang Feng, PhD
Stanford University, Stanford, California

"Investigating the molecular basis of protein dynamics in cystinosis"

$245,000 TWO-YEAR STUDY

Dieter Haffner, MD *(Mentor)* **and**
Malgorzata Szaroszyk, PhD *(Fellow)*
Hannover Medical School, Germany

"Musclin as a new marker for muscle health in cystinosis"

$74,915 ONE-YEAR FELLOWSHIP

Jennifer Hollywood, PhD and
Alan Davidson, PhD
University of Auckland, New Zealand

Herbie Newell, PhD *(Collaborator)*
University of Sunderland, United Kingdom

"Evaluation of a novel drug combination treatment of CF10 and everolimus for nephropathic cystinosis in a new cystinotic rat model"

$229,892 TWO-YEAR STUDY

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Novel mechanistic and translational studies of inflammation in cystinosis

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

OBJECTIVE/RATIONALE:

One of the main characteristics of cystinosis is the de-differentiation (loss of specific function) of kidney proximal tubule cells (PTC). In recent years, inflammation, a reaction caused by our own immune system, has been implicated in the deterioration of the kidney function in cystinosis. The mechanisms mediating inflammation in cystinosis are not well understood. Preliminary data from our laboratory suggests that the protein inhibitor of differentiation-1 (Id1) is increased in cystinotic kidneys. In this project, we aim to investigate the relationship between inflammation, defective autophagy, defective transcriptional regulation and PTC de-differentiation in cystinosis.

PROJECT DESCRIPTION:

First, we will study the relationship between autophagy and Id1 accumulation in cystinotic cells using state-of-the-art biochemical and microscopy approaches. Second, we will test the hypothesis that Id1 accumulation caused by defective autophagy exacerbates neutrophil (white blood cells)-mediated PTC inflammation, using cystinosis mouse models. Finally, we will study the effect of Id1 inhibition on PTC function.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Establishing the function of the inhibitor of differentiation Id1 in the process of neutrophil-mediated PTC inflammation will help us elucidate the link between defective autophagy, PTC dedifferentiation and inflammation in cystinosis. The results from this study will help design new treatments for cystinosis.

ANTICIPATED OUTCOME:

By completing this project, we will be able to demonstrate how the inhibitor of differentiation-1 (Id1) is regulated by autophagy, and at the same time elucidate how the overexpression of Id1 contributes to the impaired kidney function in cystinosis. We also aim to demonstrate that the inhibition of Id1 will decrease inflammation and improve kidney function in cystinosis.

Translational approaches to repair chaperone mediated autophagy in cystinosis

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

OBJECTIVE/RATIONALE:

Cystinotic cells are affected by impaired function of the degradative and recycling compartment, the lysosome. In particular, a protein that facilitates the transport of macromolecules into the lysosome for degradation is mislocalized in cystinotic cells. This is caused by impaired trafficking of the protein named LAMP2A. LAMP2A mislocalization can be corrected by CTNS gene expression, but not by cysteamine. We showed that the correction of LAMP2A function increases cellular survival to stress and proximal tubule cell function in cystinosis. Our research aims to identify small molecules (potential drugs) to improve LAMP2A localization and to improve cellular homeostasis in cystinosis.

PROJECT DESCRIPTION:

To accelerate the discovery of new therapies for cystinosis, we will study compounds that are either approved by the Food and Drug Administration (FDA) or are in clinical trials. We will apply an integrated approach of computational screening, laboratory testing (in-vitro) in cellular systems and further validation in animal models to find compounds that improve cellular and kidney function in cystinosis. In our preliminary work, we applied computational screening of >13,000 small molecules to activate the process of autophagy and have selected the top 84 compounds for further testing in cystinotic cells.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

In cystinotic cells, the activation of autophagy improves cellular function. Our work seeks to identify already approved FDA drugs with excellent druggability profiles that can improve cellular and kidney function in cystinotic mice, which will be repurposed to treat cystinosis. We believe that our research will speed up the discovery of active molecules for cystinosis management.

ANTICIPATED OUTCOME:

Our work will identify FDA-approved compounds to be repurposed for cystinosis treatment, and initiate pre-clinical studies with one or two selected molecules to accelerate the discovery of new therapeutics to improve kidney function in cystinosis.

Role of nutrient sensing and mTORC1 signaling in cystinosis

Olivier Devuyst, MD, PhD, *Mentor*
Marine Berquez, PhD, *Fellow*
UNIVERSITY OF ZÜRICH, SWITZERLAND

OBJECTIVE/RATIONALE:

Cystinosis is a lysosomal storage disease caused by loss-of-function mutations in the CTNS gene coding for the proton-driven transporter cystinosin (CTNS) that exports cystine out of lysosomes. The loss of CTNS results in the lysosomal cystine storage, causing early manifestations of kidney proximal tubule (PT) dysfunction followed by multi-systemic complications and kidney failure.

Lysosomal alterations in cystinosis lead to defective autophagy-mediated clearance of damaged mitochondria, which triggers a signaling cascade driving cell proliferation and apical dedifferentiation, as evidenced by multiple transport defects. However, the mechanisms linking CTNS loss and the resulting cystine storage to imbalances in metabolism and differentiation remain unknown.

A crucial step in nutrient sensing is the recruitment of an evolutionarily conserved protein kinase named mechanistic target of rapamycin complex 1 (mTORC1) to the surface of lysosomes. In presence of nutrients, such as amino acids, glucose and lipids, the activation of mTORC1 pathway initiates anabolic programs that boost anabolic growth and proliferation while inhibiting autophagy and lysosome biogenesis. The functional interactions between CTNS function, lysosomal cystine levels, mTORC1 signaling and maintenance of differentiation in PT cells remain to be characterized.

PROJECT DESCRIPTION:

In this project, we will take advantage of established disease model organisms and physiologically relevant PT cellular systems, in combination with cutting-edge cell biology tools developed with the support of the CRF, to: (i) investigate whether the loss of CTNS disrupts metabolic homeostasis and differentiation by constitutively activating the mTORC1 signaling at the surface of lysosomes; (ii) dissect how the absence of CTNS and the resulting cystine storage shape the response of mTORC1 signaling in PT cells; (iii) assess the potential effect of targeting mTORC1 pathway by dietary and pharmacological approaches to rescue the lysosome and PT function in cystinosis cells.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

These studies will shed new light on how the lysosome controls homeostasis in the context of normal and diseased PT of the kidney, taken as a paradigm of highly differentiated epithelial cell system. Insights into the cellular coordinators linking lysosomal deficits to epithelial dysfunction may provide new druggable targets relevant for nephropathic cystinosis.

ANTICIPATED OUTCOME:

The combination of a knowledge and target-driven approach with phenotypic screening in disease relevant model organisms and cellular systems will address the translatability gap and accelerate drug discovery and development of transformative therapeutics in cystinosis.

Impact of diet composition on renal function and bone disease of *Ctns-/-* mice

Francesco Emma, MD, *Principal Investigator*
Anna Taranta, PhD, *Co-Principal Investigator*
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

OBJECTIVE/RATIONALE:

The *Ctns-/-* knock-out mouse model has been instrumental in the past years to increase our understanding of cystinosis and to develop new treatments. Recently, we have observed that a simple change in "standard diet" can substantially modify the severity of the disease in mice. This observation led us to hypothesize that differences in kidney and bone results between laboratories may be related to subtle differences in the composition of food that is used by different animal facilities. The purpose of this study is to understand which dietary components influence kidney and bone health to ensure homogeneity of results among different laboratories and to acquire new knowledge on the physiopathology of cystinosis.

PROJECT DESCRIPTION:

In preliminary studies, we have evaluated the effects of four different commercial diets on the renal tubular function of Ctns-/- mice and observed major differences ranging from nearly normal function to severe disease. In this project, we will use an elementary diet and selectively change single components to see which one influences the severity of renal Fanconi syndrome and bone disease. Animals will be fed at libitum and caloric intake will be monitored. We will evaluate biochemical aspects of Fanconi and perform histological analyses after harvesting the kidneys. For the bone experiments, we will selectively modify calcium and/or phosphate and/or vitamin D content in five different diets and will perform hormonal measurements, radiological investigations and histological analyses.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Cystinosis research has benefitted greatly from the availability of animal models. However, the severity of the disease is not homogeneous in different laboratories. To compare results, it is important that the same diet be used by all investigators. In addition, understanding which dietary elements influence the severity of the disease will increase our understanding of cystinosis.

ANTICIPATED OUTCOME:

With this study, we expect to:

- Define which dietary components are essential to develop a severe disease in mice in order to test better potential treatments.
- Understand what dietary components cause damage to tissues; this could pave the way for developing new therapeutic approaches in the future.

Investigating the molecular basis of protein dynamics in cystinosis

Liang Feng, PhD, *Principal Investigator*
STANFORD UNIVERSITY, STANFORD, CALIFORNIA

OBJECTIVE/RATIONALE:

The dysfunction of lysosomal membrane transport underlies cystinosis. The lysosomal membrane transport proteins undergo substantial transitions in their conformation (i.e., are dynamic) to fulfill their functions. Thus, to understand their normal functions in supporting physiology and their malfunctions in diseases, we need to elucidate the molecular basis of the conformational dynamics of these membrane proteins. Such crucial knowledge will provide a framework that facilitates developing new strategies to modulate transport functions for potential therapeutic applications in cystinosis.

PROJECT DESCRIPTION:

To elucidate the molecular basis of the conformational dynamics of lysosomal membrane transport proteins, we will use the target membrane proteins purified away from other macromolecules. We will take biophysical measurements of protein conformational states using strategically located pairs of reporter probes. We aim to identify key factors that regulate the conformational dynamics of the membrane transport proteins and elucidate how conformational dynamics are linked to the pathogenesis of cystinosis. These studies will develop our understanding of how these membrane proteins work at the molecular level and provide significant insights into how to control their activities.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Cystinosis is caused by defective transport across the lysosomal membrane. Understanding fundamental dynamic properties of the lysosomal membrane proteins will produce essential knowledge about how these proteins carry out their normal functions, how their functions can be modulated and what causes their dysfunctions. Together, these studies will provide essential insights into disease-causing mechanisms in cystinosis and provide a new therapeutic strategy to modulate the transport process.

ANTICIPATED OUTCOME:

The proposed research will reveal, at the molecular level, how the protein molecular machines that are relevant to cystinosis work dynamically, how the dynamic properties are linked to cystinosis and how these protein dynamics are regulated. This will deepen our understanding of important cellular processes that are relevant to cystinosis, enrich our knowledge on lysosomal membrane transport and potentially provide a new strategy for designing targeted therapeutic agents to alleviate cystinosis.

Musclin as a new marker for muscle health in cystinosis

Dieter Haffner, MD, *Mentor*
Malgorzata Szaroszyk, PhD, *Fellow*
HANNOVER MEDICAL SCHOOL, HANOVER, GERMANY

OBJECTIVE/RATIONALE:

Muscle and bone impairment is a frequent and unsolved complication in children and adults suffering from cystinosis. Despite vigorous measures for Fanconi syndrome and adequate cystine depleting therapy, cystinosis patients present progressive distal muscular atrophy resulting in significant morbidity and impaired quality of life. Musclin, a skeletal muscle-derived and bone-secreted protein is reduced in atrophic muscle. The involvement of musclin in the pathogenesis of muscle and bone impairment in patients with cystinosis is unknown. In this study, we propose musclin as a novel therapeutic target with potential of improving muscle and bone health of cystinosis patients.

PROJECT DESCRIPTION:

Based on previous data, we postulate that musclin is reduced in cystinosis and associated with impaired muscle and bone health. In this study, we want to measure circulating musclin level with ELISA in a large cohort of children with cystinosis in comparison to healthy children and CKD controls, and correlate musclin level with parameters of muscle and bone health. In addition, we aim to investigate if musclin synthesis is impaired in muscle and bone of Ctns-/- mice, which is an excellent mouse model to study the potentially therapeutic use of measures to normalize musclin and thereby improve muscle and bone health in cystinosis.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

The proposed studies directly address the goal of CRF to find treatments to improve life for cystinosis patients. In this project, we will investigate for the first time the role of musclin in cystinosis and draw attention to a promising new biomarker that will assess muscle health. Musclin could be used as a therapy to counteract muscle wasting and/or improve muscle strength in patients with cystinosis and other CKD entities.

ANTICIPATED OUTCOME:

Muscular disorders like muscle atrophy are significant complications of cystinosis patients, especially in untreated patients and those with poor compliance to cysteamine therapy.

We hypothesize that musclin is reduced in children with cystinosis compared to healthy children and matched CKD controls and associated with impaired bone and muscular health in these patients. If so, musclin could be used as a novel biomarker and starting point for therapeutic interventions in cystinosis patients.

Evaluation of a novel drug combination treatment of CF10 and everolimus for nephropathic cystinosis in a new cystinotic rat model

Jennifer Hollywood, PhD and
Alan Davidson, PhD, *Principal Investigators*
UNIVERSITY OF AUCKLAND, NEW ZEALAND

Herbie Newell, CBE, *Collaborator*
UNIVERSITY OF SUNDERLAND, UNITED KINGDOM

OBJECTIVE/RATIONALE:

The only drug treatment available for cystinosis is cysteamine, which removes excess cystine from the cells. However, even if taken regularly and from birth, the kidneys will eventually stop working. Other organs will also eventually fail. This drug needs to be taken regularly and in large doses. It tastes bad and causes bad breath and body odor, as well as damage to the stomach. It is common for small children to vomit daily and for young people to try to stop their treatment to avoid having continuous bad breath, which negatively affects their health. To improve the lives of cystinosis patients there needs to be: 1) better versions of cysteamine that have fewer side effects, and 2) new therapies to reduce damage to the kidneys (as cysteamine does not stop this). Addressing the first point, a new version of cysteamine, CF10, has been developed that reduces cystine build-up in cells but lacks the side effects and can be taken in lower and less frequent doses. Tackling the second point, we have shown in cells in the lab that using a drug called everolimus, the damage to the kidneys can be addressed. Using cysteamine and everolimus together, all of the problems associated with cystinosis are corrected in these cell models. In this project we will test, in a rat model of cystinosis that we have developed, if the new drug combination of CF10/everolimus can provide a better treatment.

PROJECT DESCRIPTION:

The overall goal of this project is to conduct preclinical drug testing in cystinotic rats to determine whether a combination treatment of CF10 and everolimus is better at reducing cystine levels in blood and tissues and at preserving kidney function than either drug used alone. To do this we will treat the cystinotic rats with jelly pills containing CF10 (twice daily) and everolimus (twice weekly) for six months. We will collect blood and urine samples each month, measure body weight weekly and perform a number of kidney function experiments. At the end of the study, tissues will be collected to measure cystine levels and to examine the kidneys for damage. Over the course of the study, we will determine if this new drug treatment is more effective at slowing, and potentially stopping, the decline in kidney function.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

The advent of cysteamine therapy has extended life expectancy into adulthood for people with cystinosis. However, people with cystinosis face a highly challenging treatment regimen and may take dozens of pills a day on a strict dosing schedule. 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 based on CF10 and everolimus. If successful, this proposal will demonstrate that a combination therapy of CF10 and everolimus is a superior treatment for cystinosis than cysteamine. CF10/everolimus has the potential to be better tolerated, more potent at reducing cystine levels, more effective at reducing kidney damage, and provide greater longevity and better quality of life than cysteamine alone.

ANTICIPATED OUTCOME:

Our experimental design will allow us to robustly determine if CF10 is markedly superior to cysteamine in our cystinosis rat model. This will lay the foundation to developing a CF10 therapy in humans that requires less frequent dosing, whilst reducing the highly disruptive side effects of bad taste, odor, stomach problems and nausea. This potential improvement in treatment will also benefit the caregivers of these patients by enabling a regular night's sleep, rather than six hourly doses and sleep disruption. If this is the case, the proposed research will generate the required data needed to progress to clinical trials thereby expediting the clinical development of CF10.

Our experimental design will also allow us to determine if the combination treatment of CF10 and everolimus will be superior to CF10 alone at preserving kidney function in cystinotic rats. If this is the case, this result has the potential to greatly improve the lives of cystinosis patients and could remove, or substantially delay, the need for a kidney transplant. The evidence generated in this proposal will justify advancing the combination therapy of CF10 and everolimus to clinical trials in humans, where it is anticipated that it will deliver:

- A new and improved treatment option
- A reduced dosing schedule
- Fewer side effects, better taste, lower doses
- Prevent or further slow the progressive decline in kidney function
- Improve the quality of lives of patients and caregivers, as well as long-term health outcomes

JOIN OUR RESEARCH LEGACY

CALL FOR FALL 2022 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 220 multi-year research studies in 12 countries. Our researchers have published 103 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 $2.5 million was available for the Fall 2022 call for research and fellowship applications. The grant awards will be announced at the end of December 2022.

In Spring 2022, CRF issued seven new grants totaling $1,287,127 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.

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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 $65 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.

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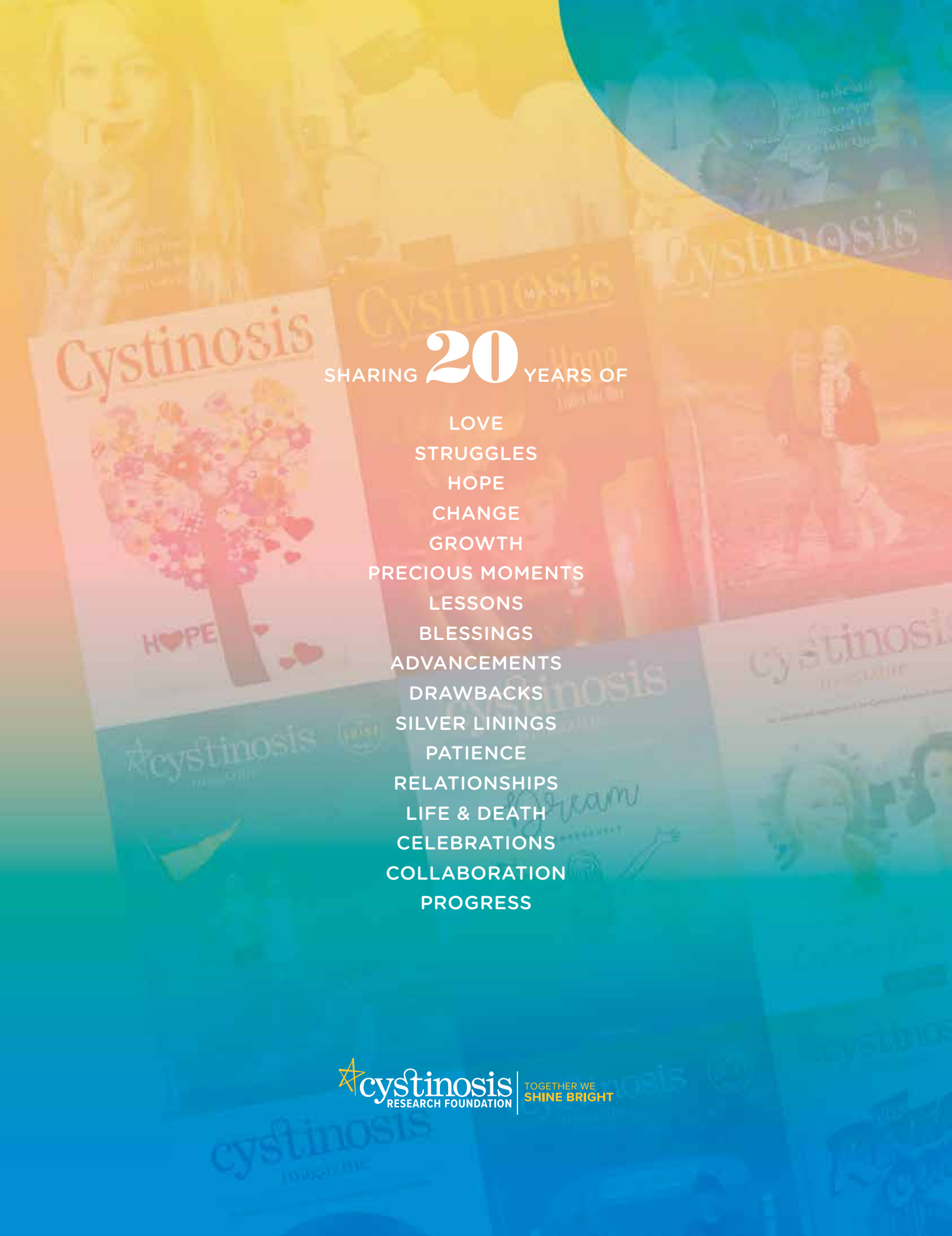

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