cystinosis magazine

TOGETHER WE SHINE BRIGHT

Unlocking Endless Possibilities: Together, Let's Explore Beyond.

For friends and supporters of the Cystinosis Research Foundation

Winter 2024

CYSTINOSIS RESEARCH FOUNDATION

HISTORY IN THE MAKING

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 autologous stem cell and gene therapy clinical trial to test a new treatment for cystinosis.

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

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

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

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

2023
- CRF hosts the 8th Annual Cystinosis International Research Symposium in Irvine, CA, fostering continued innovation by connecting CRF researchers from around the world.
- Novartis purchases the cystinosis gene therapy program from Avrobio, guaranteeing the final phase of the stem cell transplant trial will soon become a reality.

2024
- CRF issues 8 research grants totaling $1,403,383.

WINTER 2024

UNLOCKING ENDLESS POSSIBILTIES: TOGETHER LET'S EXPLORE BEYOND

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

To view this edition digitally, visit *www.cystinosisresearch.org/cystinosis-magazine.*

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

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cystinosis RESEARCH FOUNDATION

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 $71 million for cystinosis research in an effort to find a cure.

CYSTINOSIS MAGAZINE IS A PUBLICATION OF THE CYSTINOSIS RESEARCH FOUNDATION

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100 percent of your donations go to support cystinosis research. All gifts are tax deductible as allowable by law.

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WELCOME

ANNOUNCEMENTS

RESEARCH NEWS

FAMILY STORIES

CYSTINOSIS RESEARCH IMPACT

UNLOCKING NEW POSSIBILITIES

WHAT IS CYSTINOSIS?

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

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

Federal funding for research on cystinosis and other rare diseases is virtually non-existent and most pharmaceutical companies remain uninterested because financial rewards are too small. Yet, while there are only a small number of patients who are affected by 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 cystinosis grants in the world and has funded 245 grants in 13 countries.

CRF has raised $71 million, with 100% of your donations going to support cystinosis research. CRF is the driving force of cystinosis research that has directly resulted in advances in treatment including the FDA-approval of Procysbi® and an FDA-approved stem cell and gene therapy clinical trial. We have accomplished milestones and given hope to the cystinosis community that a better quality of life and a cure for cystinosis is possible.

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cystinosis RESEARCH FOUNDATION

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WE CELEBRATE

AND ARE GRATEFUL EVERY DAY FOR YOUR SUPPORT

SINCE 2003, CRF HAS:

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

FUNDED
245
MULTI-YEAR GRANTS
in 13 Countries

PUBLISHED
112
ARTICLES
in Prestigious Scientific Journals by CRF-Funded Researchers

RAISED
$71
MILLION
for Cystinosis Research

IN SPRING 2024

CRF AWARDED
8
NEW RESEARCH GRANTS

TOTALING MORE THAN:
$1.4
MILLION

100% OF YOUR DONATIONS DIRECTLY SUPPORT CYSTINOSIS RESEARCH

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 $25 million in grants from other funding agencies. Not only does CRF research help our community, but our discoveries are applied to more prevalent diseases and disorders. CRF-funded research has the potential to help millions of others.

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

YOU HAVE CHANGED THE COURSE OF CYSTINOSIS - THANK YOU!

Dear Family & Friends,

DECEMBER 2024

It is hard to believe that 2024 is almost over - what a year it has been for CRF! We are wrapping up the year on a high note; the foundation is strong, the community determined to fund research and we are on the brink of new research milestones.

The Cystinosis Research Foundation was launched in 2003, just weeks after Natalie Stack wrote her 12th birthday wish on a napkin – "to have my disease go away forever." Her wish triggered a united and determined effort to find a cure for cystinosis. Natalie's wish has been heard around the world and has become the rallying cry for all those with cystinosis.

A LETTER FROM
NANCY AND JEFF STACK

We are incredibly thankful for your support throughout the years. Your steadfast commitment has resulted in new discoveries about cystinosis, multiple clinical trials, new areas of research focus and impressively, two FDA approvals. We have achieved milestones once unimaginable and today, our community is filled with HOPE. Hope for a brighter future and the promise of a cure for cystinosis.

CYSTINOSIS MAGAZINE

We heard you! We have returned to publishing a paper copy of the magazine! We received a lot of feedback and the overwhelming consensus was to return to a paper copy. Of course, the magazine will be available in a digital form so that it can be easily shared with family and friends.

In this issue you will read heartwarming stories about families and patients, you will read about current research, and you will learn about various CRF initiatives. We know that you will be moved by our family and patient stories of living life with cystinosis, the hope and the despair, the struggles, and the triumphs. Each story has its unique perspective and each story reminds us that we are not alone; we have each other.

The magazine also features an in-depth interview with Reza Seyedsadjadi, MD, at Massachusetts General Hospital in Boston. Dr. Seyedsadjadi is a neurologist, and he is doing ground-breaking research in the areas of myopathy and dysphagia which are common, often debilitating symptoms of cystinosis. This clinical study will continue Dr. Seyedsadjadi's earlier CRF study so that he can increase our understanding of what kind of treatments work best to maintain or increase quality of life. You will find the interview on page 32.

"When nothing is certain, anything is possible."
- Mandy Hale

IT'S ALL ABOUT THE RESEARCH!

CRF SCIENTIFIC REVIEW BOARD (SRB)

The reason our community has so much hope is that CRF has single-handedly created a synergistic, international research community that is working around the clock to find better treatments and a cure for cystinosis.

Our prolific and impactful research portfolio is a result of the strategic guidance from the CRF Scientific Review Board. The SRB is comprised of ten of the most recognized cystinosis researchers, scientists, and clinicians in the world. Their vision has helped us achieve important cystinosis research milestones. We are very thankful for their leadership and commitment to our community.

We are excited and honored to announce that Olivier Devuyst, MD, PhD and Benjamin Freedman, PhD have joined the SRB. They are both experts in the field and have dedicated many years to the cystinosis community as researchers. Please read more about their research and join us in thanking them for their dedication to the cystinosis community on page 16.

NEW GRANTS BROADEN OUR KNOWLEDGE

CRF's policy of reviewing research applications twice a year ensures that there are no gaps in the research cycle and that donations are being put to work throughout the year. Since 2003, CRF has awarded 245 grants in 13 countries creating a collaborative and synergistic community of dedicated scientists and researchers working every day on behalf of those with cystinosis. CRF is the largest private fund provider of cystinosis research in the world–we are the driving force of advances in treatment.

In June we awarded eight new research and fellowship grants totaling $1,403,384 in funding. The new studies are focused on important areas of research including bone disease, new cystinosis mouse models, prodrugs, and muscle wasting. We congratulate the eight newly funded researchers and thank them for their dedication. You can view the 2024 CRF award recipients and read their lay abstracts on our website: **www.cystinosisresearch.org/grants-awarded**. We will announce additional new research grants by the end of this year.

2025 CRF INTERNATIONAL CYSTINOSIS RESEARCH SYMPOSIUM – COLLABORATION IS ESSENTIAL!

We are pleased to announce CRF will host the ninth International Cystinosis Research Symposium on Thursday, March 6, and Friday, March 7, 2025 in Newport Beach, California. We are honored and privileged to announce that Stéphanie Cherqui, PhD, Francesco Emma, MD, and Julie Ingelfinger, MD, will co-chair the symposium. The symposium will be an opportunity for CRF scientific and medical experts to share current research discoveries, explore new ideas, and facilitate collaborations to advance cystinosis research.

>> CONTINUED

FROM BENCH TO BEDSIDE - STEM CELL AND GENE THERAPY CLINICAL TRIAL

The years have flown by – five years to be exact - since the first patient was treated with the stem cell and gene therapy treatment. There are very few bench research studies that result in an FDA-approved clinical trial but thanks to our partnership with Stéphanie Cherqui, PhD, and support from you, we accomplished that milestone! The path to the stem cell and gene therapy treatment is a remarkable story of determination, perseverance, extraordinary science, and a lot of hope.

CRF worked with the stakeholders in the community to ensure that the stem cell and gene therapy treatment would become a reality. Of course, it was Dr. Cherqui whose brilliance resulted in the treatment that we hope will stop the progression of cystinosis or be the cure. Our seed money provided Dr. Cherqui with the means to develop proof of concept which then attracted other funding sources. With the support of other funding sources, she was able to complete the clinical work and launch the FDA trial. CRF seed money was leveraged by the other funding sources by over $25 million!

The next phase of the clinical trial is being planned by Novartis. CRF is working with Novartis and is sharing the concerns and excitement as the voice of the community. We will continue to advocate the needs of the community and encourage Novartis to move quickly to commence the next phase of the stem cell trial. Our goal is to ensure that the stem cell and gene therapy trial is available to every person with cystinosis throughout the world.

DAY OF HOPE FAMILY CONFERENCE 2025

The CRF Day of Hope is co-chaired by five CRF family board members who are mixing things up! The 2025 family conference will be held at the Hyatt Regency Resort & Spa in Huntington Beach, California from April 10th through the 12th. The powerful relationships that are formed at the conference between cystinosis families and patients and the research community are life-changing. Together, we are strong and together, we will make a difference. We look forward to the conference which promises to be filled with hope and inspiration.

Thank you to CRF board members Jill Emerson, Clay Emerson, Stephen Jenkins, Kristen Murray, and Brian Sturgis who will undoubtedly create a memorable weekend for the entire cystinosis community.

CRF RESEARCH LEADS TO NEW DISCOVERIES IN OTHER MORE PREVALENT DISEASES

We are so pleased to know that discoveries made by CRF funded researchers are being applied to other diseases including Friedreich's ataxia, Danon disease, Alzheimer's disease, and other genetic and systemic diseases like cystinosis. CRF set out to find better treatments and a cure for cystinosis but we have impressively, and with great hope, impacted other disease communities who can now apply discoveries made about cystinosis to their diseases creating pathways to cures for their communities. We are changing lives and giving hope to people far beyond the cystinosis community.

THANK YOU FOR MAKING A DIFFERENCE

Our gratitude for your kindness and commitment to all our children and adults with cystinosis is boundless. Our lives have been immeasurably enriched by your constant support of our research efforts. With your support we are one step closer to the cure.

It has taken a village to accomplish the milestones CRF has reached and what a village we have – we are thankful for all of you who are part of our cystinosis village. We are forever grateful to you for embracing our beloved cystinosis community.

With heartfelt thanks and gratitude, Nancy & Jeff

LEADERSHIP. GUIDANCE. COMMITMENT.

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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 $71 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.

Zoe R. Solsby
Vice President

cystinosis RESEARCH FOUNDATION

a note from Natalie

2024 has been a wonderful year! There have been many joyful moments including living life as newlyweds in Chicago. My husband, Danny, and I have officially been married for one year! We celebrated our first anniversary on October 21, 2024. We often reflect on our magical wedding day with such awe and sweet memories. We are planning to move back to California next year and hope to start our family soon. Our dog, Wesley, is the love of our lives. He enjoys all seasons, however, we think he is ready to move back to California to hang out with all his doggy cousins and go to the beach!

I currently work at Lions International which is a service organization. They focus on global humanitarian service projects with over 1.4 million members world-wide. They help many groups and causes including the visually impaired, hunger alleviation, pediatric cancer, and disaster relief. I am the volunteer engagement and events specialist and I am working with a major healthcare organization to coordinate and execute their annual employee volunteer days. I have met some very wonderful people and I hope to find work in a similar organization once we move back to California.

I wanted to share an update on my health. I am now 33 years old and doing relatively well; just a couple of challenges this year. In the last few months, my kidney function has deteriorated so my nephrologist suggested that I start the process of getting my name on the active waitlist for a kidney transplant. At first, I was devastated and in denial that this was going to be the next chapter in my life. I always thought that I would be in my 50s before I would need a transplant. However, after talking to my doctor and the transplant team, I know that this is the best option now. It is better to be proactive than to be in denial. I have come to terms with the fact that my kidneys are slowing down and they will not function for much longer. This next chapter in my life is scary and daunting, but I know I am in good hands with the transplant team and my support system.

As you might remember, I had the stem cell and gene therapy transplant two and a half years ago. Though my body has been responding slowly to the new stem cells, I do know it is working. My hair is much darker than before the transplant, even my eyelashes and eyebrows are slightly darker! Despite my kidney function declining, I feel good and generally healthy. My overall energy during the day is much better than it was prior to the transplant. The tests that measure the success of the transplant continue to show improvement which indicates that the engraftment worked, and the stem cells are slowly working their magic. I still have six-month check-ups which include blood draws, extensive eye exams, mole mapping, skin confocal tests, grip strength test, neurological functioning tests, bone density test, pulmonary function test, and a 24-hour urine collection. Though demanding on my body, the results are an important way to measure the success of the transplant and will help cystinosis patients who will be part of the next phase of the clinical trial. I remain hopeful that my body will continue to respond to the new stem cells and that my health continues to improve every day.

I am so thankful to the doctors and the cystinosis community for continuing to support the research and CRF. There is still more to be done and with the support of our community, everything is possible. I am beyond grateful to each one of you who not only helped save my life but who have given hope to others who have cystinosis. The stem cell treatment will help save the lives of others in our community – I know that will be a reality soon.

Thank you for never giving up and for making my wish become a reality.

love, Natalie

Natalie's WiSh 25

~The~ WISH that is CHANGING LIVES

APRIL 2025

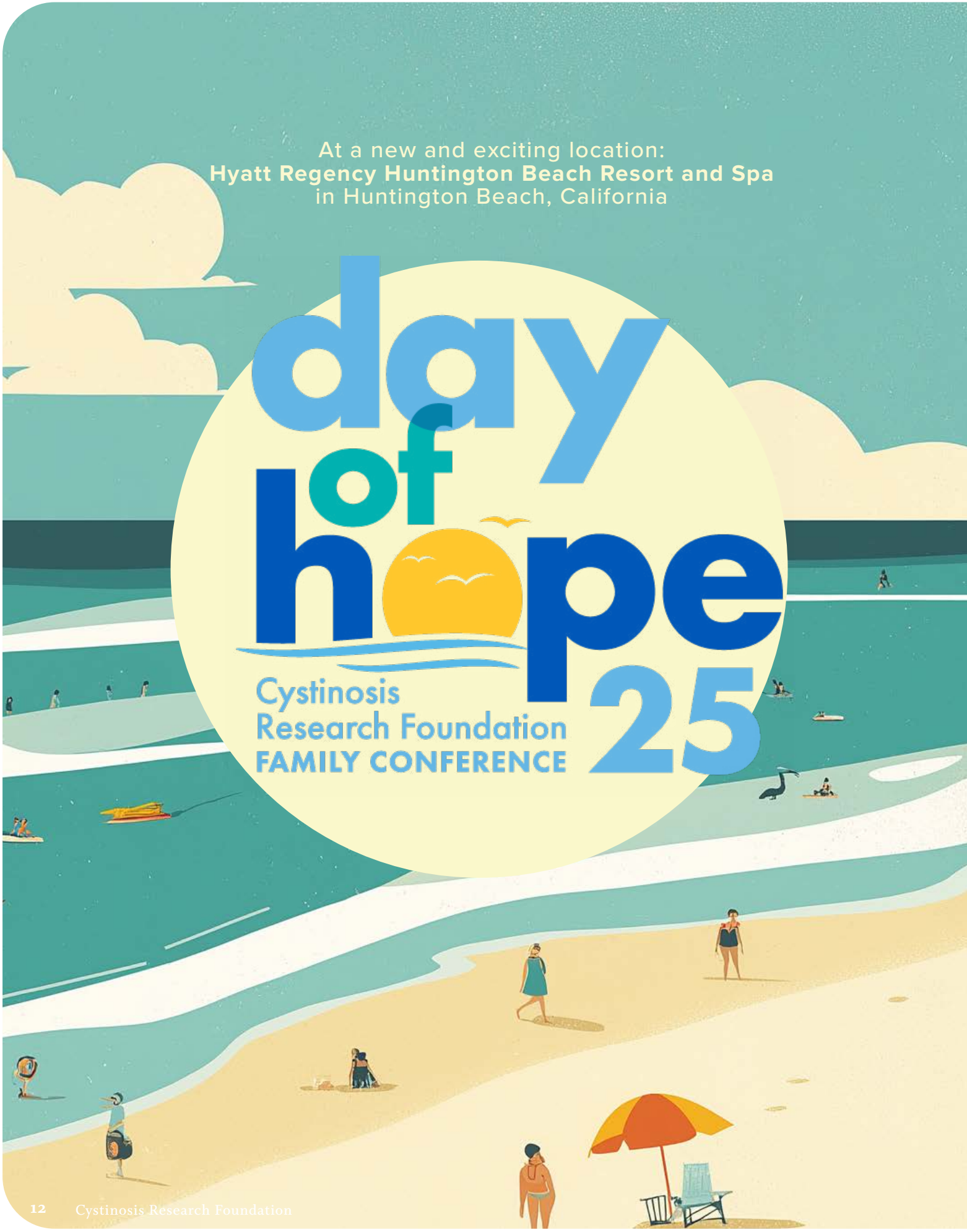
It all started with one girl's wish, *"to have my disease go away forever."* 21 years later, Natalie Stack's wish has grown from one girl's dream, to the rallying call of an entire, worldwide community. After two decades of research, 245 research grants, countless fundraisers, two FDA approvals and $71 million raised for cystinosis research, Natalie's wish has become the wish in all our hearts. And we've only just begun.

The Cystinosis Research Foundation's (CRF) Annual Natalie's Wish Fundraiser is back again, providing friends, families and supporters of the CRF community with the opportunity to renew their commitment to our children and adults living with cystinosis. The entire month of April will be dedicated to raising funds for life-saving cystinosis research and making Natalie's wish for a cure a reality for us all.

Join us in April 2025 for our month-long fundraiser to reflect on the incredible progress our community has made since Natalie Stack's 12th birthday and help us continue this momentum for all those born with cystinosis, today and in the future. Every contribution, big and small, brings us one step closer to finding better treatments, granting Natalie's wish, and changing lives for the entire cystinosis community.

cystinosis RESEARCH FOUNDATION

Watch the mail for this opportunity to fund the cure!


At a new and exciting location:
Hyatt Regency Huntington Beach Resort and Spa
in Huntington Beach, California
day of hope 25
Cystinosis
Research Foundation
FAMILY CONFERENCE

CRF Welcomes You To Day of Hope 2025
REGISTRATION IS NOW OPEN!

JOIN US FOR AN ENRICHING WEEKEND OF COMMUNITY, INSPIRATION, STRENGTH, AND HOPE!

Gather together with our special community of friends, families, and researchers. Gain new perspectives from leading scientists on the research that is improving lives. Celebrate the progress that we have made over the decades and the strength, and hope, that we have as a community.

Conference presenters will shed light on a range of topics including stem cell therapy for cystinosis, novel treatment possibilities and groundbreaking new research.

CONFERENCE AT A GLANCE:

THURSDAY, APRIL 10TH
Conference begins late afternoon with introductions and a welcome dinner

FRIDAY, APRIL 11TH
All-day sessions followed by a 'Dinner Under the Stars' celebration, a Day of Hope tradition

SATURDAY, APRIL 12TH
New this year! All-day sessions followed by a special sunset dinner celebration

- **Complimentary childcare program is available for infants and children up to age 12**
- **A special program is planned for teens!**
- **Join us for a weekend of friendship, inspiration and hope**

CONFIRMED SPEAKERS INCLUDE:

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



2025 Day of Hope Conference Co-Chairs

Clay Emerson, PhD, PE, CMF, Hope for Brooke, CRF Board Member
Jill Emerson, CPA, Hope for Brooke, CRF Board Member
Stephen Jenkins, MD, University of Utah Hospital, Sam's Hope for a Cure, CRF Board Member
Kristen Murray, Seth's Circle of Hope, CRF Board Member
Brian Sturgis, 24 Hours for Hank, CRF Board Member

Registration Now Open!

Questions? Email: jill.emerson@hotmail.com

Since 2016, Canadian families have funded over $1,321,762 in CRF research grant payments!

CANADA

When it comes to finding a cure, there are no country borders! Canadian cystinosis families are committed CRF partners who are dedicated to funding research that will lead to better treatments and a cure. We are grateful to our Canadian families who continue to organize and plan events to raise money for research. Working together, our two countries have united efforts to raise awareness about cystinosis, and to advocate on behalf of all children and adults with cystinosis.

The Cystinosis Awareness and Research Effort (CARE) has partnered with Canada Helps to establish the Canadian Cystinosis Research Foundation. Aqueduct Foundation administers this fund and allows for an efficient and effective fundraising process to ensure Canadians who donate will receive a charitable tax receipt. When you donate through Aqueduct Foundation be sure to select the Canadian Cystinosis Research Foundation from the dropdown menu after entering your donation amount.

www.canadahelps.org/en/charities/aqueduct-foundation/ Together, we are changing lives!

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

BARB KULYK at barbara_kulyk@hotmail.com **KRISTEN MURRAY at murraykristen@hotmail.com**

Ninth International Cystinosis Research Symposium

SPONSORED BY cystinosis RESEARCH FOUNDATION

THURSDAY, MARCH 6, 2025
FRIDAY, MARCH 7, 2025

SAVE THE DATE

The Symposium will be held at

THE PACIFIC CLUB IN NEWPORT BEACH, CALIFORNIA

Thursday, March 6th and Friday, March 7th, 2025

The symposium will be an opportunity for scientific and medical experts to share current research discoveries, explore new ideas, and facilitate collaborations to advance cystinosis research. Please save the date.

BY INVITATION ONLY

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

2025 SYMPOSIUM CO-CHAIRS

Stéphanie Cherqui, PhD

Francesco Emma, MD

Julie Ingelfinger, MD

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!

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THANK YOU FOR THE YEARS OF DEDICATION TO THE CYSTINOSIS COMMUNITY

CRF SCIENTIFIC REVIEW BOARD WELCOMES TWO NEW MEMBERS

CRF's successful global research program is a direct result of the expertise and guidance from the SRB. Last year, Stéphanie Cherqui, PhD, Professor, University of California, San Diego, accepted the position of the Chair of the SRB. Dr. Cherqui will continue to advance the CRF research program, and with the leadership of the entire Scientific Review Board, CRF will continue to fund the most promising research studies in the world aimed at finding better treatments and a cure for cystinosis.

Given where we are today with our impressive global research program, it is hard to believe that we had such humble beginnings. Over the years our research program has grown as a result of the generous donations from our families and large community of friends, who have partnered with us to find a cure for cystinosis. Since 2003, we have awarded 245 research grants in 13 countries which has resulted in two FDA approvals, numerous clinical trials, and new discoveries about cystinosis and its complications.

We are pleased to announce the addition of two outstanding scientists to the CRF Scientific Review Board (SRB). Both new members are experts in the field of cystinosis and have a deep commitment to the CRF community. We are honored to welcome Benjamin "Beno" Freedman, PhD, Associate Professor, University of Washington, Department of Medicine, Division of Nephrology, and Olivier Devuyst, MD, PhD, Professor, University of Zurich, Switzerland, Institute of Physiology, Group Leader of Mechanisms of Inherited Kidney Disorders. Dr. Freedman and Dr. Devuyst are dedicated researchers and pioneers in the field. Please read about their outstanding contributions to research.

We thank every member of the SRB board for their dedication to our community and their commitment to research. We are changing the future of cystinosis through our focus on research, and we are giving the children and adults with cystinosis hope for a brighter future. Please join us in welcoming Dr. Freedman and Dr. Devuyst to the 2024 Scientific Review Board!

Visit www.cystinosisresearch.org/crf-srb-welcomes-two-new-members/

RESEARCH UPDATES

UPDATE ON THE

Stem Cell and Gene Therapy Clinical Trial

The Phase 1/2 of the stem cell gene therapy clinical trial at University of California San Diego (UCSD) was fully enrolled with 6 patients treated from 2019 through 2022. Last year, Novartis acquired the stem cell gene therapy clinical program and will sponsor the next phase of the clinical trial and seek FDA approval.

The phase 1/2 clinical trial at UC San Diego has successfully completed patient enrollment with six treated patients, who received autologous gene-modified hematopoietic stem cells. Five patients have enrolled to the long-term follow up study and will be followed for 15 years post-stem cell transplantation. The patients are now between 22-month post-stem cell infusion for Patient 6 to almost 5-year post-stem cell infusion for Patient 1.

Continuing to monitor the progress of the five patients participating in the long-term follow-up after their stem cell transplants is very important as we keep collecting data and learning about the impact of the gene-modified stem cells for cystinosis over time.

We report that the genetically modified cells have been stable so far. Patients 4 and 5, who had the fewest stem cells that possess the healthy CTNS gene, have resumed low dose cysteamine treatment. Nonetheless, for patients 4 and 5, there is still expression of the CTNS gene in a portion of the stem cells, resulting in a reduction of cystine and cystine crystal levels compared to baseline.

BY STÉPHANIE CHERQUI, PhD
UNIVERSITY OF CALIFORNIA, SAN DIEGO

Indeed, most patients have shown reductions in cystine and crystal levels. White blood cell cystine levels have decreased in the five patients compared to baseline. Cystine crystals in the skin are monitored using a skin confocal microscope, showing a consistent decrease compared to baseline levels in most patients. In particular, Patient 1 and Patient 3, who received stem cells more than 3 years ago, have reached low levels.

These initial results highlight the promising therapeutic potential of gene therapy for cystinosis. The next phase of the clinical trial is being organized by Novartis, and we are confident they will manage the program effectively.

STÉPHANIE CHERQUI, PhD

CYSTINOSIS RESEARCH FOUNDATION

SPRING

2024 RESEARCH & FELLOWSHIP GRANT AWARDS

8 RESEARCH GRANTS AWARDED

TOTAL AMOUNT AWARDED :
$1,403,383

FROM 2 COUNTRIES

FRANCE and the UNITED STATES

CRF IS THE LARGEST FUND PROVIDER OF GRANTS FOR CYSTINOSIS RESEARCH IN THE WORLD, ISSUING 245 GRANTS IN 13 COUNTRIES SINCE 2003.

CRF IS FUNDING A FUTURE WITHOUT CYSTINOSIS
SPRING 2024

Justine Bacchetta, MD, PhD (Principal Investigator, Mentor)
Claire Dumortier, PhD (Fellow)
Hospices Civils de Lyon, Bron, France

"THE 2024 CYSTEA-BONE PROJECT"

$123,000 TWO-YEAR FELLOWSHIP

Bruce Barshop, MD, PhD (Principal Investigator)
Jon Gangoiti, MS (Co-Principal Investigator)
University of California, San Diego, La Jolla, California

"TRIAL OF A HYDROLASE-ACTIVATED THIOL PRODRUG IN CYSTINOSIS FIBROBLASTS"

$67,615 ONE-YEAR STUDY

Sergio Catz, PhD (Principal Investigator, Mentor)
Danni Chen, PhD (Fellow)
Scripps Research Institute, La Jolla, California

"NOVEL MECHANISTIC AND TRANSLATIONAL STUDIES OF INFLAMMATION IN CYSTINOSIS"

$150,000 TWO-YEAR STUDY

Sergio Catz, PhD (Principal Investigator, Mentor)
Aparna Shukla, PhD (Fellow)
Scripps Research Institute, La Jolla, California

"TRANSLATIONAL APPROACHES TO REPAIR CHAPERONE MEDIATED AUTOPHAGY IN CYSTINOSIS"

$150,000 TWO-YEAR STUDY

Stéphanie Cherqui, PhD (Principal Investigator, Mentor)
Veenita Khare, PhD (Fellow)
University of California, San Diego, La Jolla, California

"TO CHARACTERIZE TWO NEW Ctns -/- MICE MODELS"

$150,000 TWO-YEAR STUDY

Liang Feng, PhD (Principal Investigator)
Stanford University, Stanford, California

"PROBING PROTEIN MUTAGENESIS AND MODULATION IN CYSTINOSIS"

$245,000 TWO-YEAR STUDY

Norbert Perrimon, PhD (Principal Investigator, Mentor)
Ting Miao, PhD (Fellow)
Harvard Medical School, Boston, Massachusetts

"PROFILING DYSREGULATION OF KIDNEY COENZYME A (CoA) BIOSYNTHESIS IN CYSTINOSIS"

$75,000 ONE-YEAR STUDY

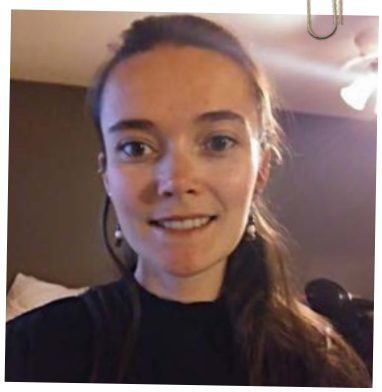
Reza Seyedsadjadi, MD (Principal Investigator)
Massachusetts General Hospital, Boston, Massachusetts

"FURTHER CHARACTERIZATION OF DYSPHAGIA IN NEPHROPATHIC CYSTINOSIS"

$442,768 TWO-YEAR STUDY

SEE LAY ABSTRACTS STARTING ON NEXT PAGE >>>

Pathophysiology of Bone Disease in Cystinosis: 2024 Cysteabone Project



Justine Bacchetta, MD, PhD, Principal Investigator/Mentor
Claire Dumortier, PhD, Fellow
HOSPICES CIVILS DE LYON, FRANCE

OBJECTIVE/RATIONALE:

Cystinosis metabolic bone disease (CMBD) has a significant impact on patients' quality of life because of an increased frequency of bone pains, deformations, and fractures. Local bone cell dysfunctions contributing to CMBD are still poorly understood, and the goal of the 2024 project is to keep dissecting the molecular mechanisms underlying the intrinsic defects not only in osteoblasts (Ob), the bone forming cells of mesenchymal origin but also in osteocytes, that represent 80% of the cell content of cortical bone.

PROJECT DESCRIPTION:

The first aim is to develop an accessible human model of bone forming cells carrying several Ctns mutations to study their impact on bone resident cells. We will differentiate induced pluripotent stem cells (iPSC) obtained from cystinotic patients into MSCs; this will allow us to have a closer model to mice models responding to 1,25VD3 and to produce the full range of mesenchymal cell types affected by cystinosis including Obs, myocytes and adipocytes.

The second aim is to study the osteocytes, by exploring lacunar and canalicular network in cortical bone of Ctns deficient mice. In order to support the hypothesis of a premature transition shift from osteoblast to osteocyte phenotype of Ctns -/- mice Obs, osteocyte and bone aging markers expression will be analyzed, bone formation dynamic parameters being quantified on 3D-reconstruction images.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

This model will allow us to better understand the relation between each Ctns mutation and specific bone resident cells phenotype. Understanding the premature transition shift from osteoblast to osteocyte phenotype may explain altered bone growth and quality leading to inadequate bone dimension and shape observed in cystinosis, as recently reported in patients.

These new models will keep gathering evidence to propose in the future to cystinosis patients with severe bone phenotype therapeutic perspectives based on antagonizing IL1.

ANTICIPATED OUTCOME:

The study of several mature cells affected by Ctns mutations will give information on mediators secretion and intra-cellular communication in bone. If proved to be true, the deregulation of sclerostin and osteocalcin in the bone/endocrine axis may open new therapeutic perspectives, especially since osteocalcin has also a crucial role in regulating glucose and energy metabolism, fertility and muscular adaptation to exercise, all fields in which cystinosis induces specific impairment. This is one further step to personalized medicine in CMBD.

Trial of a Hydrolase-Activated Thiol Prodrug in Cystinotic Fibroblasts

Bruce A. Barshop, MD, PhD, Principal Investigator
Jon A. Gangoiti, MS, Co-Principal Investigator
UNIVERSITY OF CALIFORNIA, SAN DIEGO

OBJECTIVE/RATIONALE:

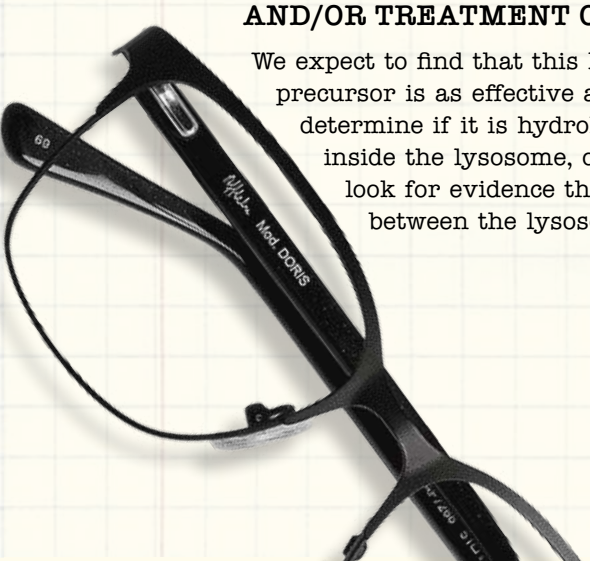
The mainstay treatment for cystinosis for more than two decades has been cysteamine. Cysteamine is known to reduce intracellular cystine and its effectiveness has been shown to be related to good compliance. However, there are problems with all available formulations of cysteamine, including stomach upset or ulcers, bad breath and body odor, and these side effects often make it difficult to take the full prescribed dose. There is a drug candidate which is designed to release cysteamine only inside of cells, and we will test if that candidate will reduce the cystine content in cultured skin cells from patients with cystinosis.

PROJECT DESCRIPTION:

The prodrug will be added at various concentrations to fibroblasts (cultured skin cells) from patients with cystinosis. After a series of time intervals, the intracellular cystine content of those cells will be measured by tandem mass spectrometry, following our standard lab methods. We also plan to measure the concentrations of the prodrug, LL-244, in the cells and the growth medium, as well as the cysteamine which is released in the medium and inside the cells. We will also attempt to isolate intact lysosomes.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

We expect to find that this hydrolase-activated precursor is as effective as cysteamine. We will determine if it is hydrolyzed in the fibroblast, inside the lysosome, or in the medium. We will look for evidence that cysteamine is recycled between the lysosome and cytoplasm.



ANTICIPATED OUTCOME:

This study would be a useful first step for possible future development of an agent which potentially could eliminate or reduce the troublesome side effects of cysteamine therapy.

Translational Approaches to Repair Chaperone-Mediated Autophagy in Cystinosis

Sergio D. Catz, PhD, Principal Investigator/Mentor
Aparna Shukla, PhD, Fellow
SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

OBJECTIVE/RATIONALE:

The objective of our research is to identify small molecules that can improve the localization and multimerization of the lysosomal membrane protein LAMP2A and enhance Chaperone-Mediated Autophagy (CMA) in cystinosis cells. By improving LAMP2A function and CMA, we seek to restore lysosomal malfunction that leads to cystine accumulation in cystinosis. To achieve this, we aim to screen the ReFRAME drug repurposing library and the commercial Maybridge library for potential drug-like small molecules.

PROJECT DESCRIPTION:

In cystinosis, cells are negatively impacted by malfunctioning lysosomes, which are responsible for degrading and recycling cellular components. One major issue leading to this lysosomal malfunction is a reduction in Chaperone-Mediated Autophagy (CMA). CMA is a selective autophagy process where KFERQ motif-containing proteins bind to a chaperone and are then delivered to the lysosomal membrane protein LAMP2A, which helps translocate them into the lysosome for degradation. In cystinosis, reduced LAMP2A expression and multimerization prevent proper protein degradation, causing cystine to build up in the cells. Based on our previous work, we aim to identify small molecules that can help LAMP2A localize and multimerize correctly at the lysosomal membrane. To accomplish this, we will apply a translational approach that includes computational modeling and screening, in-vitro testing, and in-vivo confirmation. Our goal is to identify a small molecule (drug-like candidate) to correct LAMP2A localization and multimerization at the lysosomal membrane in cystinosis cells.

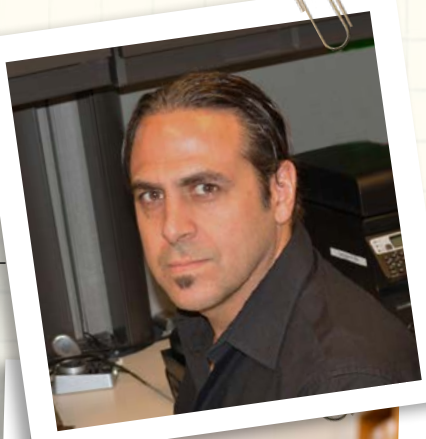
RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

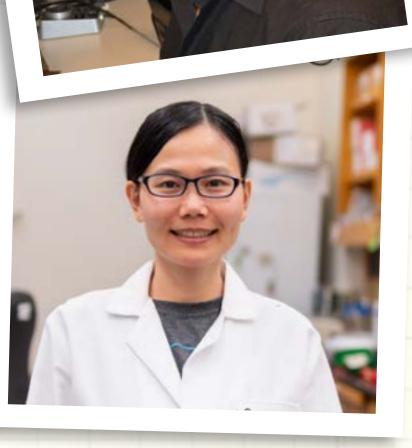
In our previous work, we demonstrated that enhancing CMA using small molecules improves LAMP2A expression, localization, and multimerization in cystinosis cells. Based on these findings, our current research focuses on identifying small molecules that can directly influence LAMP2A multimerization. By targeting LAMP2A, we aim to enhance CMA and restore cellular homeostasis in cystinosis.

ANTICIPATED OUTCOME:

We anticipate that our research work will identify potent small molecules that can enhance LAMP2A multimerization and improve CMA in cystinosis cells. These compounds are expected to restore cellular homeostasis, reduce cystine accumulation, and improve cellular and kidney function in cystinotic mice.

Novel Mechanistic and Translational Studies of Inflammation in Cystinosis





Sergio Catz, PhD, Principal Investigator/Mentor
Danni Chen, PhD, Fellow
SCRIPPS RESEARCH INSTITUTE,
LA JOLLA, CALIFORNIA

OBJECTIVE/RATIONALE:

Lysosomal damage induces alteration in immune cells leading to inflammation. Our preliminary data show that a subtype of specialized white blood cells, neutrophils, inflammatory components that have the potential to contribute to tissue damage in cystinosis. Our work focuses on the characterization of this process and the development of approaches to counteract inflammation in cystinosis.

PROJECT DESCRIPTION:

We found altered posttranslational modification and lysosomal localization of a regulatory kinase in cystinotic neutrophils. Inhibition of this protein with specific inhibitors decreases the secretion of toxic components in Ctns-/- neutrophils. We will study a) The mechanisms of action of this kinase in cystinosis, in association with the regulation of small Rab GTPases; b) The mechanisms mediated by this kinase to induce secretion in cystinosis and c) The cross-regulation of the kinase with other inflammatory processes including the inflammasome. To test these hypotheses, we will use state-of-the-art technical approaches including Elisa, flow cytometry, immunoblotting, CyTOF, and immunofluorescent staining. These assays will be complemented with comparative phospho-proteomics to identify potential kinase substrates that are affected in cystinotic neutrophils.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Proximal tubule cell de-differentiation is associated with increased pro-inflammatory signaling and increased neutrophil infiltration into cystinotic kidneys. We found altered posttranslational modification and mis-localization of regulatory kinases in cystinosis. We will utilize a pharmacological approach to inhibit this regulatory protein in cystinosis mouse models. We propose that specific inhibitors of this process will decrease kidney inflammation and possibly improve renal function in cystinosis patients.

ANTICIPATED OUTCOME:

We expect to identify new dysregulated mechanisms in cystinosis. We also anticipate that the manipulation of upstream lysosomal damage sensors could help reduce neutrophil-mediated inflammation in cystinosis mouse models.

To Characterize Two New Ctns-/- Mice Models

Stéphanie Cherqui, PhD, Principal Investigator/Mentor
Veenita Khare, PhD, Fellow
UNIVERSITY OF CALIFORNIA, SAN DIEGO

OBJECTIVE/RATIONALE:

Animal models play a crucial role in understanding the pathophysiology of any disease condition. The widely utilized C57BL/6 Ctns-/- mouse model has been instrumental in understanding the mechanisms underlying cystinosis. However, this model has exhibited progressive decrease of kidney phenotype, especially the renal Fanconi syndrome (FS). We have two new mouse models on a pure C57BL/6 background. One harbors a 5bp deletion in exon 5 of Ctns. The other model carries a ~50kbp deletion in the entire Ctns gene and part of the Trpv1 and Carkl genes, closely mirroring the ~57kbp deletion the most common mutation in cystinosis patients. We aim to characterize these mice models and study how closely they resemble the human disease characteristics.

PROJECT DESCRIPTION:

We aim to do detailed characterization of both the mice models to monitor their breeding efficiency, survival, and growth rate. Analysis of their kidney function will be done by collecting 24h-urine and blood samples at 3, 6, 9, and 12 months. Following explant at 12 months of age, the kidneys will be used to measure cystine and for histopathology. Analysis of the non-renal phenotype in these two mice models like eye, bone, muscle, neurocognitive defects will be done by conducting behavior studies, followed by molecular characterization by performing several molecular assays, as well as cystine content determination and histopathological studies.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

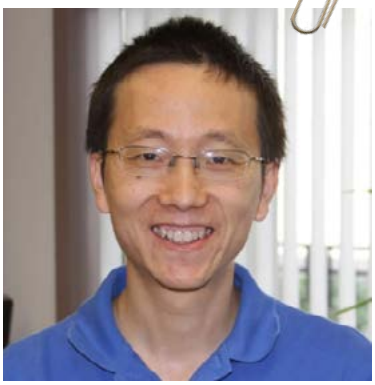
These models may serve as invaluable tools for researchers, enabling the exploration of novel treatments based on mutations in the Ctns gene. We will also be able to determine if the 57 kb deletion led to different phenotype in cystinosis. It holds significant interest to observe how these two models mimic the human phenotype and whether variations arise due to the unique mutations in the Ctns gene, and these models will be shared with the community for research.

ANTICIPATED OUTCOME:

Our objective is a comprehensive characterization of these models, encompassing renal and non-renal aspects, breeding characteristics, and survival, to understand their resemblance to human disease pathophysiology. Our initial finding shows positive indications in both mouse models, reflecting characteristics observed in human patients affected with cystinosis. Our preliminary data show that these mice exhibit as early as 3 months of age characteristics of renal Fanconi syndrome and neurobehavioral anomalies. Cystine storage and cystine crystals, hallmarks of cystinosis, are present in the new models. Additionally, we aim to explore potential differences between the two models, considering the distinct nature of their mutations and their impact on disease onset or progression.

Probing Protein Mutagenesis snd Modulation in Cystinosis

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



OBJECTIVE/RATIONALE:

Lysosomal membrane transport proteins play a crucial role in maintaining cystine homeostasis within lysosomes. The dysfunction or dysregulation of these proteins is the underlying cause of cystinosis. The biophysical properties of these transport proteins are key to their function. Understanding how alterations in these proteins affect their biophysical properties is vital for elucidating the molecular basis of cystinosis. This knowledge is fundamental for developing targeted, mechanism-based therapies.

PROJECT DESCRIPTION:

The functions of lysosomal membrane transport proteins are tightly linked to their fundamental biophysical properties. To assess the impact of alterations in these key proteins in cystinosis, we will develop and implement robust assays designed to efficiently measure their critical biophysical properties. These measurements will provide crucial insights into the modulation of these proteins' function. Additionally, we aim to develop highly selective methods to modulate the activity of these transport proteins based on our molecular understanding. This approach may potentially lead to the development of novel therapeutic strategies for treating cystinosis.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Defective lysosomal membrane transport is the cause of cystinosis. Understanding the molecular mechanisms by which alterations in key membrane transport proteins involved in cystinosis affect their function will provide crucial insights into the underlying causes of cystinosis. This knowledge will enhance our ability to assess the risk of cystinosis and guide the development of novel therapeutic strategies specifically aimed at mitigating the detrimental effects of defective membrane transport proteins.

ANTICIPATED OUTCOME:

The proposed research will provide new approaches to better understand the fundamental properties of key membrane transport proteins in cystinosis, uncover how alterations in these proteins' biophysical properties affect their function, and explore new ways to modulate their activity for potential therapeutic purposes. These studies will deepen our understanding of lysosomal membrane transport and the underlying causes of cystinosis, ultimately aiding in the development of novel, selective therapeutic strategies to treat cystinosis.

Profiling Dysregulation of Kidney Coenzyme A (CoA) Biosynthesis in Cystinosis

Norbert Perrimon, PhD, Principal Investigator/Mentor
Ting Miao, PhD, Fellow
HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS

OBJECTIVE/RATIONALE:

Cystinosis, a genetic disorder caused by mutations in the CTNS gene, leads to the accumulation of cystine in the kidneys and other organs. This buildup causes cellular stress and metabolic disturbances. Recent research from our laboratory indicates that cystine transport is crucial for Coenzyme A (CoA) biosynthesis, a vital metabolic process. This project aims to explore how CoA biosynthesis is affected in the kidneys of cystinosis patients, potentially uncovering new treatment strategies. Using Drosophila models, we will investigate the role of CoA biosynthesis in kidney function and overall metabolic health.

PROJECT DESCRIPTION:

To carry out this project, we will use Drosophila (fruit flies) to model cystinosis due to their genetic similarities to humans and ease of genetic manipulation. First, we will create Drosophila models with mutations in the CTNS gene to mimic cystinosis. We will then study these models to understand how these mutations affect kidney function and Coenzyme A (CoA) biosynthesis. Advanced metabolomics techniques will be employed to measure metabolite levels in the kidneys, identifying disruptions in metabolic pathways. Additionally, we will use genetic and biochemical methods to assess how changes in CoA biosynthesis impact kidney function and overall metabolic health. By comparing the results with healthy flies, we aim to uncover the specific metabolic alterations caused by cystinosis, potentially leading to novel therapeutic strategies.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

This project will enhance our understanding of the metabolic disruptions caused by cystinosis, specifically focusing on the role of Coenzyme A (CoA) biosynthesis in kidney function. Recent metabolomics analyses have reported significant alterations in the CoA biosynthesis pathway in individuals with cystinosis, suggesting a link between cystine transport deficiency and CoA imbalance. Given CoA's pivotal role in cellular metabolism, dysregulated CoA biosynthesis may underlie systemic metabolic abnormalities in cystinosis. By uncovering these mechanisms, we may identify new therapeutic targets, potentially leading to more effective treatments and improved outcomes for cystinosis patients.

ANTICIPATED OUTCOME:

We expect to discover how the disruption of Coenzyme A (CoA) biosynthesis in the kidneys contributes to the symptoms and progression of cystinosis. Using Drosophila as a model, we will investigate: 1) the impact of dCTNS deficiency on kidney CoA biosynthesis; 2) the role of CoA biosynthesis and dCTNS in renal function; and 3) the influence of kidney CoA biosynthesis on whole-body metabolic homeostasis. This research aims to identify new treatment targets to better manage the metabolic abnormalities in cystinosis, ultimately improving patients' quality of life.

Further Characterization of Nephropathic Cystinosis

Reza Seyedsadjadi, MD, Principal Investigator

MASSACHUSETTS GENERAL HOSPITAL,

BOSTON, MASSACHUSETTS

OBJECTIVE/RATIONALE:

Myopathy and dysphagia are common symptoms of nephropathic cystinosis. Preceding research has been done to assess which swallowing phases are most affected in patients experiencing these manifestations. The past phases of this project have shown that patients had the most improvement with bolus transport, timing of their pharyngeal swallowing response, and laryngeal elevation with respiratory training and exposure to their physiology. These improvements may be related to the focused effort from the patients who received the respiratory treatment and education on swallowing mechanics.

PROJECT DESCRIPTION:

Patients will come on site to Massachusetts General Hospital (MGH) to meet with a neurologist and speech pathologist who will perform baseline procedures such as a neurological exam, muscular ultrasound, and MBSImp. After the conclusion of these procedures we will randomized the patients into three cohorts, each with a different treatment targeting different muscular groups. The patients will be educated on their treatment method and how to progress their training in-between visits. They will report progress with the study coordinator every three months and receive any necessary feedback on their exercise program. The patients will return to MGH one year after their baseline visit to complete the same procedures. The study team will compare the data from both visits across all three treatment arms to assess improvements in function and quality of life.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

The imaging methods – MBSImp and muscular ultrasound - will be used to identify and compare which muscles are most affected by myopathy and dysphagia in this patient population. In the interim between on-site visits, the patients are in three separate cohorts using treatments that strengthen three different groups of muscles involved in swallowing. After they complete the second visit, we will be able to increase our understanding of what kind of treatments work best to maintain or increase quality of life.

ANTICIPATED OUTCOME:

Prior research has shown that when patients are exposed to their physiological data and make educated, focused efforts to improve function, it may influence their ability to swallow. Given that these patients are practicing their treatment over the course of the year, we expect them all to improve their swallowing function as their musculature is strengthened. We are hoping to discover differences in improvements between the groups with data showing one treatment arm had better/more improvement between baseline and the last on-site visit.

RECENTLY PUBLISHED STUDIES

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

JASN '24

Francesco Bellomo, PhD
Francesco Emma, MD

Bambino Gesù Children's Hospital, Rome, Italy

Ketogenic Diet and Progression of Kidney Disease in Animal Models of Nephropathic Cystinosis

The Ketogenic diet, when used in cystinotic mice and rats, showed nearly complete prevention of Fanconi syndrome, including low molecular weight proteinuria, glycosuria, and polyuria. Moreover, the diet seemed to contribute to healthier kidney function by changing the metabolism in the body to help restore the function of altered pathways in cystinosis. It appears that the Ketogenic diet could help prevent kidney damage.

Molecular and Cellular Biology '24

Sergio Catz, PhD

Scripps Research Institute
San Diego, California

Reconstitution of Rab11-FIP4 Expression Rescues Cellular Homeostasis in Cystinosis

Summary by CRF Board Member, Clay Emerson, PhD, PE, CFM

Current research on cystinosis is uncovering new cellular-level disease manifestations and in the process the research is revealing potential new therapeutic targets beyond lysosomal cystine clearance; a job that is largely addressed by cysteamine. This recently published CRF-funded study focused on the role that one specific protein may play in intracellular molecular transport. The protein known as "Rab11 Family Interacting Protein 4 (Rab11-FIP4)" was found to be suppressed in cystinosis. The researchers theorized that the restoration of Rab11-FIP4 in cystinosis might improve various measures of cellular function as they relate to molecular transport and the overall maintenance of stable conditions within the cell. The researchers used the drug known as QX77 as well as genistein, a naturally occurring compound found in some vegetables, to restore Rab11-FIP4 levels. Using both a mouse model of the disease as well as human proximal tubule cells, researchers found evidence that both QX77 and genistein increased the expression of Rab11-FIP4.

Importantly, the study also documented evidence showing improvements in multiple independent measures of cellular function due to the restoration of Rab11-FIP4. Whether through the drug QX77, genistein or some other approach, the study concluded that Rab11-FIP4 offers a potential new therapeutic target for the disease.

biomedicine AND PHARMACOTHERAPY '24

Ester De Leo, PhD
Francesco Emma, MD

Bambino Gesù Children's Hospital
Rome, Italy

Long-term effects of luteolin in a mouse model of nephropathic cystinosis

Summary by CRF Board Member, Clay Emerson, PhD, PE, CFM

Prior to the development of modern cysteamine-based treatment, some of the earliest research into treatment strategies for cystinosis focused on potential dietary interventions for the disease. However, those early dietary studies never provided the lysosomal cystine depletion necessary to delay the progression of the disease. Flash forward 50 years and our understanding of the disease has dramatically improved. Lysosomal cystine accumulation is the most serious manifestation of the disease, however modern research into the cellular metabolism impairments caused by cystinosis have revealed that other important cellular functions are also impaired by the disease. While cysteamine depletion is the current standard of care, new research has shown that there may be a role for dietary supplements to complement the standard cysteamine treatment.

Following their recent investigations into the potential therapeutic effects of genistein, researchers from the Bambino Gesù Children's Hospital in Italy conducted similar research into another naturally occurring flavonoid called luteolin. Luteolin is a compound that is found in many fruits, vegetables and herbs. In the study conducted in a mouse model of cystinosis, the researchers found that treatment with luteolin provided evidence of improved cellular functions including autophagy, lysosomal homeostasis and apoptosis. However, treatment at the levels used in the study did not prevent nor delay the development of Fanconi syndrome in the mouse model of the disease. Although the study did not result in significant clinical improvements for this particular compound, it provided critical insight into potential treatments which will one day address cystinosis-related cellular dysfunction beyond cystine accumulation alone.

Published articles and their summaries provide insights into CRF's research progress and are available on our website in the 2024 section.

WWW.CYSTINOSISRESEARCH.ORG/PUBLISHED-STUDIES

CCIR IS OUR LINK BETWEEN PATIENTS AND RESEARCHERS

In less than four years, patients from 15 countries around the world have participated in the Cure Cystinosis International Registry (CCIR). The registry also includes patients representing 24 states across the United States. The registry is critically important as it provides an important link between patients and researchers. Due to the ultra-rare nature of the disease and the wide variety of complications it presents, progress towards improved treatment and an ultimate cure for cystinosis is only possible with input from our small patient community.

The full value of the registry will only be realized with widespread participation from our community. We strongly encourage patients or caregivers to pitch in, sign up, and be part of our mission to identify the unmet needs of patients and accelerate research. The questionnaire takes about 40 minutes to complete, and registration is simple. Please visit the CRF website to sign up today!

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

15 COUNTRIES HAVE REGISTERED:

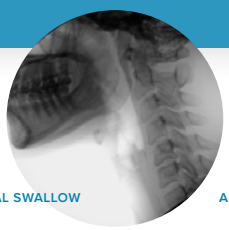
- Australia
- Brazil
- Canada
- China
- France
- Ireland
- Italy
- Mexico
- Netherlands
- Pakistan
- Portugal
- Saudi Arabia
- Sweden
- United Kingdom
- United States of America

ADDING MUSCLE TO UNDERSTANDING

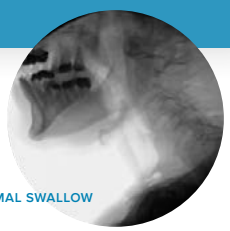
IN THIS NEXT PHASE OF HIS CRF-FUNDED RESEARCH INTO CYSTINOSIS AND SWALLOWING, DR. REZA SEYEDSADJADI PLANS TO FURTHER EMPOWER PATIENTS TO JOIN IN THE SEARCH FOR SOLUTIONS.

REZA SEYEDSADJADI, MD

NEUROLOGIST - Massachusetts General Hospital
DIRECTOR - Charcot-Marie-Tooth (CMT) Center of Excellence
ASSISTANT PROFESSOR OF NEUROLOGY - Harvard Medical School



NORMAL SWALLOW



ABNORMAL SWALLOW

As a researcher and physician, Reza Seyedsadjadi, MD invests vast amounts of time exploring something most of us never give a second thought.

He's deeply committed to understanding the muscles used in swallowing – not as some secondary research exercise, but to unearth insights that hold the promise of improving the daily lives of cystinosis patients.

Those patients cannot take the act of swallowing for granted. So, neither does Dr. Seyedsadjadi.

"We want to know much more about what muscles are not working well for those who experience difficulty swallowing," says Dr. Seyedsadjadi, a neurologist at Massachusetts General Hospital and an assistant professor of neurology at Harvard Medical School.

"This is an area of cystinosis impact that is still not well understood. Not only do we want to answer more of these questions, but we want to give cystinosis patients more agency over their condition and their lives."

Throughout years of research and clinical practice, the doctor has gained expertise in treating cystinosis patients for myopathy (muscle weakness) and dysphagia (difficulty swallowing). Because cystinosis attacks all the muscles and organs of the body, it's inevitable that smaller muscles like those used in swallowing eventually will be affected. Especially for patients who must take dozens of pills a day, the impact becomes immense and immediate.

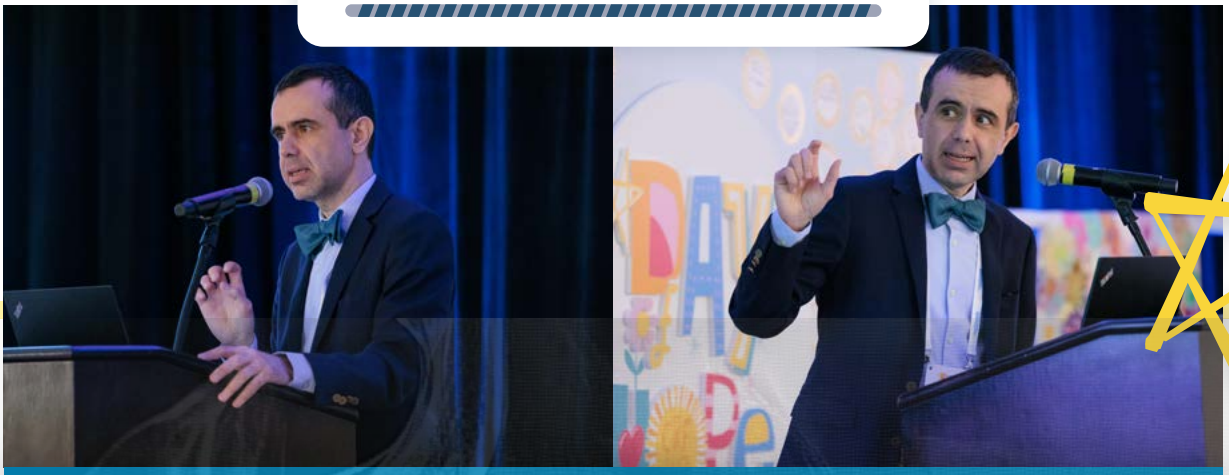
CRF SUPPORT HELPS PRODUCE INSIGHTS

Over the past four years, the progress of Dr. Seyedsadjadi's research has accelerated, thanks to the financial support of the Cystinosis Research Foundation. A CRF-funded study allowed the research team to establish baseline measures for clinical outcomes and define measures of muscular function specific to cystinosis.

Recent phases of the project show that most patients can improve function by coordinating chewing, swallowing and breathing.

"These improvements may be related to the focused effort from the patients who received respiratory treatment and education on swallowing mechanics," Dr. Seyedsadjadi says.

Now the doctor and his colleagues want to build on these advances. Additional CRF grant support will allow more patients to travel to Massachusetts General Hospital to participate in baseline procedures. It's hoped that these neurological exams, muscular ultrasounds and other tests will enhance the overall understand of the ways cystinosis affects swallowing.



DR. REZA SPEAKING AT THE 2024 DAY OF HOPE CONFERENCE

After study participants undergo the tests, they will be randomized into three groups, with each receiving a specific treatment that targets different muscular functions. The patients will be given exercise regimens and then return to Boston about a year later so the study team can compare results across all three treatment arms to assess improvements in function and quality of life.

"When we began, we wanted to better define the pathology – what's wrong, what can we fix and what changes can we mitigate over time?" Dr. Seyedsadjadi says. "With the wealth of knowledge we've gained, we've found that the glass is not half empty but half full. In some cases, patients did better on swallowing function when tested over time, when we might have expected further deterioration over time."

GIVING PATIENTS AGENCY OVER THEIR CARE

A key component of this new phase of research is the one-on-one care participants receive from specially trained speech pathologists and those with expertise in cognitive behavioral therapy. In between their two hospital visits, patients will meet virtually with a study coordinator to report progress and receive feedback on their specially designed exercise programs.

The researchers have learned that patients benefit when they become more invested in their particular treatment protocols. So, Dr. Seyedsadjadi and his colleagues are leaning into this source of patient motivation.

"You can learn a lot about yourself from the studies and testing and by applying adaptive steps that help with swallowing function," the doctor says.

By meeting with therapists while looking at testing images on a screen, patients get to work through the nuances of response to swallowing difficulties, Dr. Seyedsadjadi says. "Try turning your head to the right as you swallow," a therapist might advise one patient.

"If you know what's happening, it empowers you to know what to do," the doctor says.

SMALL STEPS CAN HAVE A BIG IMPACT

Even minor improvements in swallowing can have a major effect on treatment compliance when so many pills are involved, he adds.

Overall, the impact of the team's research project can be just as substantial.

As they prepare to welcome about 30 new patients to this next phase of their research, Dr. Seyedsadjadi and his colleagues see both immediate applications and expanding possibilities. For instance, their partnership with Harvard's Stem Cell Institute is providing muscle biopsies from patients and other insights that they hope will lead to effective interventions.

"As we start correlating the data, we expect to have a better idea of what groups of muscles are not working and why, and then it's a matter of whether we apply some targeted treatment that might restore muscle function for patients," Dr. Seyedsadjadi says.

Even with all those possibilities before him, the doctor is quick to note that none of the progress would be possible without the committed participation of the cystinosis community and the financial support of the Cystinosis Research Foundation.

"CRF makes this research possible," he says. "How else could we recruit globally? How else could we create these connections that bring together investigators and patients? It's hard for me to express just how important it is to have CRF's support all throughout this process."

THE IMPACT of CRF RESEARCH

EXPANDING NEW FRONTIERS!

AREAS OF RESEARCH FOCUS & GRANTS AWARDED SINCE 2003

SINCE 2003, THE CYSTINOSIS RESEARCH FOUNDATION HAS RAISED AND COMMITTED MORE THAN $71 MILLION FOR CYSTINOSIS RESEARCH, MAKING THE CRF THE LARGEST PROVIDER OF GRANTS FOR CYSTINOSIS RESEARCH IN THE WORLD. OUR DEDICATED RESEARCHERS AND SCIENTISTS ARE WORKING IN 13 COUNTRIES AROUND THE WORLD TO FIND BETTER TREATMENTS AND A CURE FOR CYSTINOSIS.

VISIT OUR CRF WEBSITE TO SEE EACH AREA OF RESEARCH FOCUS & GRANTS AWARDED IN DETAIL:

WWW.CYSTINOSISRESEARCH.ORG/IMPACT

	Cystine Measurement and Cysteamine Toxicity	10 GRANTS
	Cellular and/or Molecular Studies of the Pathogenesis of Cystinosis	68 GRANTS
	Stem Cells and Gene Therapy: Bone Marrow Stem Cells, Induced Pluripotent Stem Cells, Gene Therapy and Gene Editing	35 GRANTS
	New Drug Discovery: Cysteamine, New Medications and Devices	32 GRANTS
	Neurological	17 GRANTS
	Eye-Corneal Cystinosis Research	11 GRANTS
	Kidney Research	28 GRANTS
	Thyroid	1 GRANT

CONTINUED ON NEXT PAGE >>

THE IMPACT *of* CRF RESEARCH

AREAS OF RESEARCH FOCUS & GRANTS AWARDED SINCE 2003

<< CONTINUED

Skin, Muscle and Bone	21 GRANTS
Molecular Study of Cystinosis in the Yeast Model	3 GRANTS
Genetic Analysis of Cystinosis	5 GRANTS
Cure Cystinosis International Registry (CCIR)	1 GRANT
Rat Model for Cystinosis	4 GRANTS
Lab Equipment for Cystinosis	9 GRANTS

CLICK TO SEE EACH AREA OF RESEARCH FOCUS & GRANTS AWARDED IN DETAIL: WWW.CYSTINOSISRESEARCH.ORG/IMPACT

The
deBruyn Family

The
Fehr Family

Shannon
Keizer-Henderson

The
Suetta Family

WINTER 2024

FAMILY STORIES

COMMUNITY FUNDRAISING

FROM HERE
DONATE
WE CAN SEE A CURE

INDEPENDENCE, SUPPORT & PERSEVERANCE

A CHAT WITH SETH

By Kristen Murray, Seth's mom
CALGARY, ALBERTA, CANADA
CRF BOARD MEMBER FAMILY

With a new and busy school year underway, I welcomed a few moments to chat with my son Seth on topics ranging from middle school to hope, with much in between.

How is Grade 7 so far?

It's my second year in middle school, I know how things work and I have some good friends, so it's pretty good.

Taking the bus home from school with kids from the neighbourhood is new and fun. It's also fun that we're now allowed to go off campus for lunch. It seemed like a big deal at first to go places like the candy store across the street, but now Leif and I mostly play soccer in the school field like we've always done because it's more fun.

You and I worked with your teachers to set up your Individual Program Plan (IPP) to make sure you have accommodations, like permission to go to the bathroom or for water whenever you need. This year you also have extra time on tests if you need it. What are your thoughts about this?

Since I know that all my teachers know about it, I feel more comfortable to ask for the extra time that I need. I used to feel rushed to finish tests, and with extra time, I'll be able to check my work. I haven't needed it yet this year, but it's good to know that it's there when I need. I have a symbol (crossing my fingers) to show my teachers when I need to leave class to go the bathroom, get a drink, or honestly, just go for a walk, which I sometimes need to do too. It's great to have that freedom.

Cystinosis is complex and there's, you know, a lot to it. It's OK with me that teachers know that I have a rare disease and that I sometimes need extra time and breaks. I still just want to be a regular kid like everyone else, though. I don't want to be known as "the kid who has a disease that no one else has." Lots of kids in my class have IPPs and it's no big deal, so I think I can have an IPP and also be like all the other kids.

Tell me about the medications that you are taking.

I just switched to taking delayed release pills (cysteamine) twice a day. So now I take a total of 16 pills in the morning and 18 at night. And then there's liquid supplements too, eye drops and a needle every night. The new pills bugged my stomach in the morning for a bit, but it's not as bad now. I like not interrupting my day at school to take pills and that they smell a lot better than the old ones.

→

We often talk about adversity and the opportunity that it offers for growth....

There can be a lot to learn from difficult situations. Good things and even big wins can come from losses. Like with the cross-country running team at school. In the first race of the season, I started too fast, got cramps and didn't finish as strong as I wanted. I felt upset and didn't know if I wanted to run in the next race.

After talking about it as a family, I remembered that challenges make us stronger and that "victory" is more about trying my best than winning. I decided to give it another shot. I paced myself better and ended up finishing the next two races in the top twenty of about two hundred kids. I did my best, finished strong and that felt like a "win". We got ice cream after, too – soft serve, my favorite.

This seems to be an example of your determination and perseverance in other areas of your life.

Yeah, especially in sports, I guess. I'm competitive, and when I've started new sports, like cross-country skiing, mountain biking and soccer, I didn't like not being "good" right away. I'm learning that if I focus on doing my best and on improvement more than trying to be better than other people are, it feels better. I also like mixing it up with the non-competitive adventures that our family has, like hiking and canoeing, where it's pretty chill and more about being together and out there in nature.

What has cystinosis taught you about determination and perseverance?

Well, I guess just like all kids with cystinosis, I've had a lot to get used to, like pills, eye drops, needles and new medications. Sometimes it's not easy, but I push through and it always seems to get better. Maybe all this "experience" makes other hard things that happen seem like not such a big deal after all.

Tell me about the role that hope plays in your life.

Well, I hope for a cure. It doesn't feel urgent to me though. I'm not super excited about staying in the hospital for a long time. I kind of focus on what I'm doing right now, so I'm not always thinking about the future. It would be nice to not have cystinosis one day, that's for sure.

Are there any other thoughts that you'd like to share?

I think that anything is possible if you just put your mind to it. Set personal goals, don't compare yourself with others, keep persevering and never give up.

You inspire me every day Seth. Thank you.

"IN EVERY ADVERSITY THERE LIES THE SEED ON AN EQUIVALENT ADVANTAGE. IN EVERY DEFEAT IS A LESSON SHOWING YOU HOW TO WIN THE VICTORY NEXT TIME."

– ROBERT COLLIER

JAMES FEHR

UNstoppable James

By Leah Klaassen and Devin Fehr, James' Parents
ROSTHERN, SASKATCHEWAN, CANADA

Early days!

Our cystinosis journey began in June 2017 when our son James was diagnosed at the age of 10 months. He was born a healthy weight of 8lbs 13oz on July 29th, 2016, and until about 8 months, he was growing well. It was around then that we started noticing he didn't want to try food, and anything he had been eating previously, he was no longer interested in. His appetite for food disappeared and his interest in nursing skyrocketed. For fear of some food aversions, we brought him in to see a pediatrician. She urged us to head to the ER for further investigation.

As many of you already know, the story from here looks something like: a bunch of tests, a lot of questions, medical terminology that we were not (yet) familiar with, and a whole lot of stress and grief. We admittedly weren't always kind to the nurses or doctors helping us along the way. In fact, we were convinced at the time that they were all the worst. My perspective has since shifted, and we are so grateful to them for their patience with us and for their help during that hospital stay.

James was then equipped with an ng-tube for the next 6 months, and we were fully UN-equipped to deal with this new diagnosis. At least that's how it felt. A few months, a few meltdowns and more than a few visits for bloodwork later, James was stable, and we were starting to see the fog lift.

That part of the story really sucks a lot, and honestly, we don't love telling people about it. It was traumatic and retelling it can bring up a lot of things we don't love to think about. However, there is a part of our story we love to tell people about, and it's how the community around us showed up.

Devin and I both grew up near small Saskatchewan farming towns – small communities where people show up for each other in big ways. And while we had always known this, this time in our lives is when we got to experience it firsthand. Our family and friends carried us because we couldn't carry ourselves.

At the time of James' diagnosis, I was just finishing up my 12-month maternity leave, so when James got sick, I was suddenly unable to return to my job. While this was incredibly stressful, I was fortunate to have a boss who cared and who held my job for me for as long as I needed. We had friends and family show up with meals and groceries, and to do the dishes or wash this new collection of syringes we had taking over our kitchen. We had family members learn the medication schedule right away, and friends reading up on cystinosis so that we didn't have to explain it all to them. Allowing people into this mess was how we survived, and now we know, that for the people closest to us who got to witness the ugly cries and hold our grief, that that was somehow beautiful for them, too.

Just a few weeks after diagnosis, we were introduced to CRF. At first the idea of a group of cystinosis families felt daunting and we didn't think that talking to anyone or seeing anyone else with cystinosis was anything we could bear. We started to receive the CRF magazine in the mail, and truth be told, the first time we got it, we hid it away because looking through it felt like one step closer to us believing this was real, and not just a bad dream. We weren't ready to leave that state of denial quite yet. Little did we know, this would be yet another community of people who show up for one another, and once we saw that, our perspective changed dramatically. We heard about the fundraising efforts made by the foundation and by the families and we were eager to take part.

For several years, Devin worked in the golf industry as an assistant golf professional where a lot of his time was spent helping organize and lead tournaments. A golf tournament felt appropriate and "easy" for our first-ever fundraiser. In May 2018 we held our first annual Hope for James golf tournament. We knew our friends and family cared, but that day was proof of it. We were completely overwhelmed by the support and love we felt that day. Ideas for more events started to flood in.

In 2019 Devin's oldest brother Matt, came up with the idea to host a crokicurl tournament on his acreage. For anyone confused by the word "crokicurl", you must imagine the board game crokinol and curling, combined. Matt made the ice rink with the crokinol lines and made curling rocks in place for cookies. It was March 1, and quite literally 50 below zero (-58^{0}F), but everyone showed up. A huge bonfire, some homemade chili and buns, and the group was quite happy. Just a few ice fishing tents and a few drinks to keep the group warm while they weren't playing.

Matt is the kind of guy who just doesn't quit, so next up he planned a Bones tournament (popular lawn game). Held in the riding arena on their yard, more people showed up for a full day of games, food, live music and raffle items. We've now had two Bones tournaments and we've got a waitlist for teams. These events have been a lot of fun for the winter months when people are often less social. We are surprised at every event how interested people are in James and how we are all doing managing his health.

During the last seven years, we've been able to move from intense grief and fear to a place of hope. We know now that we cannot do it on our own, and that it really does take a village, medical-needs kid, or not. We have had to set our pride aside and let people help us. That's hard sometimes. We've opened up and asked questions to strangers about things we didn't think we ever would, like, "Do we have another baby?" "What does that look like"? etc. Growing our family was something we desperately wanted, but at the time didn't know how to make that choice. I am beyond grateful for the honest answers I got when I so boldly approached people with that question. It's not something you typically lead with when you first meet someone, but I quickly learned that at Day of Hope there are few things you can't ask about. Everyone wants to help everyone. We all know the challenges and fears that come along with this new life, and it's been invaluable to us to have this group of people who so closely relate.

We are aware that not everyone has a community like this. From good bosses who give you the time you need, strangers showing up at events, siblings who plan and carry out events on their yard, or the people showing up over and over, donating their time and money to a cause that only affects one child in the province that they live. Allowing people to do this for us has been challenging at times and will likely continue to be so. Admitting you need help isn't always easy.

I'm sure we aren't the only ones who struggle to ask for or accept help. It can feel uncomfortable and even embarrassing at times to admit that you don't have the skills, experience, or knowledge to deal with the situation in front of you. I know I felt a lot of shame for not being able to care for my own child without help. We each come into all this having different lived experiences that shape how we respond to these things. You may have grown up around people who want to help, as we did, or you may have had to live more independently to survive. Our hope for those new or old to this cystinosis life, is that they find community and support, ideally close to home, but if not, here with CRF. If you do not have that support close to home, I can promise you there's another cystinosis family eager to be there for you. I've had more than a few text or messenger conversations at all hours of the day with a few of the moms I've met at the Day of Hope conference. Friendships are made and the road gets a little less bumpy. Sharing it with all of you makes it easier somehow. Less isolating. Less overwhelming. More hopeful. More fun. It's all just better when we're together.

First day of Kinder

A little more about James:

James is 8 years old and in 3rd grade. He's highly energetic, goofy, distracted, and witty. He's jam-packed with attitude, and once he's comfortable, he's making everyone around him laugh. He's got some sweet basketball skills and he loves to swim. He seems to have no fear; in fact, last year after breaking his arm falling from the monkey bars, he was eager to get back on them. Climbing trees or jungle gyms feels natural to him. James loves the outdoors, particularly during harvest time in the garden, because there's nothing better than a carrot right out of the dirt. He'll take any chance he can get to go into the forest foraging for mushrooms with his Auntie Emily. Ask him for facts about mushrooms and he'll teach you a thing or two. He loves Rubik's Cubes of all varieties and his little sister Maya. He is a good friend and big brother. We feel lucky to be his parents and we feel he's taught us how to be strong through all the hard stuff. We look forward to seeing him build friendships within the cystinosis community, and we hope he feels as cared for as we do when he's surrounded by all of you.


Golf pro!

By Shannon Keizer-Henderson
WAYLAND, MICHIGAN

A Season of Gratitude

Remember the scene in 13 Going On 30, when Jenna wishes to be “thirty, flirty, and thriving”? That line has become a cultural standard for a woman’s 30th trip around the sun. Looking back on my 30th year, this was not the case. In fact, at 29, I went on a date with my now husband, and nothing came of it for another five years. Ages 30-31 were an all-time low with many physical and emotional struggles. You may recall my giant kidney stones, nine hospitalizations, sepsis, c-diff, and the story of me crying on my parent’s basement floor on Christmas morning.

Fast forward five years. I’m now married, an RN working as a school nurse, own a home with my husband, and a devoted aunt. Looking back, I see how those trials helped prepare me for my present-day reality. I still have challenges, as my kidney function sits around 25%. But with new perspective, I live out each season with gratitude and joy.

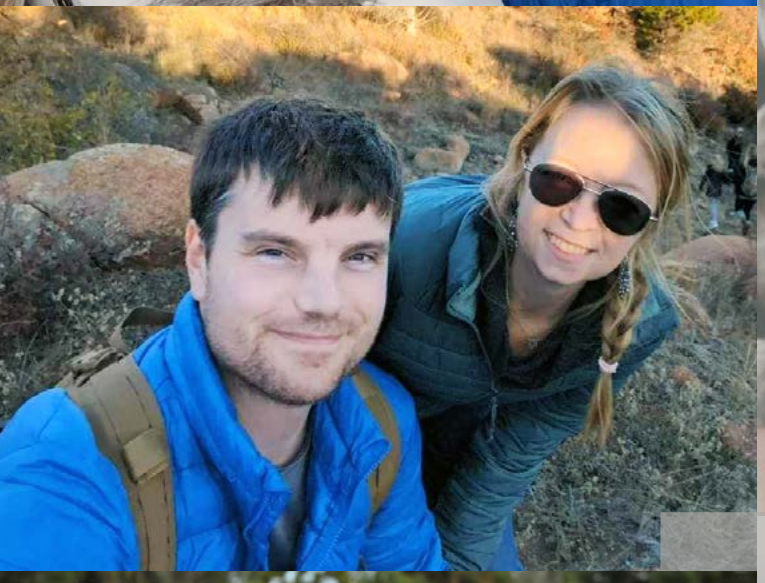
My husband and I agree, six years ago I would have been too spontaneous, and he would have been too structured for our partnership to thrive. We are actually 100% opposite on the Myer’s Briggs personality profile, him being ISTJ and me ENFP. While this can sometimes cause “sparks on the railroad track”, we see it as a superpower for a well-rounded relationship.

Dylan loves making sure I’m taken care of. He stocks my car with water, and my “big blue” Stanley is filled nightly. Even if he is met with an eye roll, I adore that he sets Google alarms to help hold me accountable for things like meds and ordering refills. And bonus... Dylan has no sense of smell. He couldn’t identify cysteamine odor if a bottle was placed under his nose.

Rather than give you a narrative of married life, I thought it would be fun to interview Dylan. Here are his responses...

How did you and Shannon meet?

At church. We went out with my sister and brother-in law in 2018. There were no sparks at the time, but through that, Shannon became close with my family.



Did you know she had cystinosis before pursuing her?

Yes, but not many details. My mom told me she feels sick many mornings, and I felt bad about that.

How soon into the relationship did you talk about cystinosis?

During our first official date in April 2023, we talked for four hours about goals, dreams, cystinosis, and other deep topics.

What were your thoughts after attending your first cystinosis conference just 3 months into dating?

My empathy increased once I better understood cystinosis. It opened my eyes to the daily struggles and why treatment is so important.

What is the hardest thing for you as you walk alongside Shannon?

Watching her feel cold and sick often. I'm empathetic and want to take the suffering away from her.

What is something you've learned from Shannon?

Limitations do not have to stop anyone from living their best life.

What is one favorite thing about your relationship?

How much we laugh together.

What has been your favorite adventure together?

Being extras on "Heartland" in Calgary! And staying in a tree house in the Ozarks.

I hope you enjoyed this glimpse into our life, and I'd love to share more with anyone who is interested. I tell these stories with hopes that they will encourage someone going through a rough season, or a teenager or parent wondering what dating/marriage with cystinosis looks like. Cystinosis doesn't have to be awkward or a limitation. The vulnerability that comes with sharing your story can create deep connections. Your current season of life is preparing you for the next. Without a doubt, your resilience, the way you bounce back after a rough patch, and how you show faith and gratitude will be an inspiration and encouragement to everyone in your life.

Everything Happens for a Reason

BY SHELLY SUETTA, EMMA'S MOM
ETNA, CALIFORNIA

"Everything happens for a reason!" This is a quote that I have lived by. It has been nine years since Emma spent a month in UCSF children's hospital. This hospital is six hours from our home. Our lives were turned upside down on June 17th, 2015. This is the day that we got the official diagnosis of cystinosis. Within a week, I was connected to the very small community of other cystinosis families. We are so thankful for social media. I'll never forget the call I got from Zeke to walk me through life with this new diagnosis and how to move forward. His daughter, Zylar, was a few years older than Emma, so he had already walked in our shoes. We talked about medications and how to avoid making Emma sick. We discussed the best foods to feed her to keep her tummy happy. Since that day, we have become a part of a new Cysta family. Zeke, Taishia, and their family drove 12 hours to come and stay with us in 2017. Ever since then, we have gone to visit their family multiple times and made many trips to Disneyland together.

"Every cloud has a silver lining!" We attended our first "Day of Hope" conference in the spring after Emma's diagnosis. It was overwhelming and heart wrenching, but amazing and welcoming at the same time. We met our new forever friends and family that weekend. We met Emma and Gracie, twins with cystinosis, connected to my Emma Grace by name and diagnosis. We also met Jenna and Patrick, whose mom, Teresa, visited us in UCSF during one of our many hospital stays. Emma has built lifelong friends whom she calls her "Cystas". She met her best friend Emma D. two years ago at the Day of Hope Family Conference. Since they met, there are very few days that go by that the two Emma's don't talk on video chat and play together. They are already planning our next trip to Day of Hope and all the possible ways they can be together, including a hopeful sleepover.

My oldest daughter, Lillyanna, has also made deep connections with friends and siblings of children with

cystinosis. She talks daily to her best friend, Peytan, who is 14 with cystinosis. They have not yet met in person but had an instant connection because of cystinosis. I think it helps her to understand her sister's struggles a bit more, having friends that are going through the same disease. She looks forward to Day of Hope just as much as the rest of us because she gets to see all her friends that she would never have met without her sister's diagnosis.

"My life is perfect, even with cystinosis!" Emma has said this to me a couple times this past year. Recently, we have talked about the possibility of a "Make a Wish" for Emma in the future. When I asked Emma what her wish might be, she responded, "Nothing, my life is perfect, and I don't need to change anything." She knows all about her medications and knows how to do them all via her G-tube. She doesn't yet eat by mouth but plans to be a chef after attending culinary school. She knows more about food and cooking than most adults she talks with. It makes my heart so happy to know she is so happy with her life despite her struggles.

Nine years ago, our hearts were broken with our new diagnosis and for all the changes our lives had. The round-the-clock care, doctors appointments, blood draws, blended food, therapy, medication, pharmacies and so much more were unimaginable. Since then, our lives have found a new normal. We have made lifelong friendships that we consider to be family. We have found so many silver linings to be thankful for. There would be so many things we would not have, and would not have the opportunity to do without cystinosis.

TOGETHER, WE ARE one

COMM
UNITY
FUND
RAISING

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

1 PURPOSE. 1 JOURNEY. 1 CURE.

RAISED over $3,000

SIXTH ANNUAL CHILI COOK-OFF

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

The sixth Annual Chili Cook-off for cystinosis research was held on October 6, 2024, in honor of Lily Beauregard in River, Massachusetts. The successful event was organized by Shelli Pereira, a dear friend of the Beauregard family, and Pat Freitas, Lily's grandmother. The enthusiastic community attending to support Lily included the creative chili chiefs, the dedicated volunteers, entertaining musicians, and very generous donors. The afternoon festivities and competition resulted in $3,495 raised for CRF and cystinosis research. Thank you to Shelli and Pat for their time and energy to organize and host the fun-filled event. Since the first chili cook-off, more than $26,341 has funded important cystinosis research. We are grateful to the Beauregard family, their friends, and community for creating a brighter future for Lily and all the children and adults affected by cystinosis. Thank you!

SACRAMENTO L5 CAPITAL CUP GOLF TOURNAMENT

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

The Capital Cup is one of Sacramento's largest fundraisers, with 100% of the money raised going directly to the featured charities. The three-day competition, held September 13 – September 15, challenges 32 of Sacramento's most prominent CEOs against each other in a Ryder Cup format to raise funds for charity. Shannon Deary-Bell, CEO of Nor Cal Beverage, a long-time friend and advocate for Jenna and Patrick's Foundation of Hope, participated for the eighth time in the 2024 L5 Capital Cup Golf Tournament, raising more than $62,000 for cystinosis research. CRF and the Partington family are honored and grateful for the years of support from the Sacramento community. The Capital Cup and its generous participants have raised over $400,000 for Jenna & Patrick's Foundation of Hope and CRF. Together we are providing hope for a future without cystinosis!

RAISED over $62,000

CELEBRATING THE CIRCLE OF HOPE

The deBruyn Family, Kristen, Nathan, Leif, and Seth - Calgary, Alberta, Canada

Each year, on October 21, Kristen and Nathan deBruyn mark the anniversary of their son Seth's cystinosis diagnosis by lighting a candle, creating a Circle of Hope. In 2024, Seth's Circle of Hope candle-lighting remembrance spread throughout the cystinosis community and beyond, sending a message of hope and gratitude. CRF's partnership with the deBruyn family and the Canadian Cystinosis Research Foundation ensures that donations will be used for CRF-funded research projects. Each year for the past 11 years the deBruyn family has raised $25,000 during their Circle of Hope campaign to contribute over $275,000 to Canada Helps through the Aqueduct Fund to support CRF and cystinosis research.

RAISED over $275,000 SINCE 2013

Thank you to the deBruyn family and the Canadian cystinosis community for raising awareness and helping fund ongoing cystinosis research for a brighter future for our children and adults with cystinosis.

THE COLLINS CURE CUP

A message from the Galloway Family - Cumming, Georgia

RAISED over $100,000

We are absolutely overwhelmed with the generosity and support that we received at the 4th Annual Golf Tournament this past weekend. We couldn't have asked for better weather or a better group of people to spend the day with.

Thanks to the collective effort of our amazing community, we are thrilled to announce that we raised just over $100,000. The funds raised will play a crucial role in advancing research, treatment options, and ultimately bringing us closer to finding a cure.

The spirit of generosity and compassion displayed by individuals like you inspires us to continue our mission and reinforces the power of community when we come together for a common cause. Your support goes beyond the financial contribution—it symbolizes hope, unity, and the belief that positive change is possible.

We want to extend our appreciation to everyone who participated, donated, volunteered, and contributed in any way to the success of this event. Your kindness has a lasting impact, and we are honored to have you as part of the Collins' Cure family.

As we move forward in our journey to improve the lives of those affected by cystinosis, we remain grateful for your ongoing support. Please stay connected with us through our website and social media channels for updates on the impact of your generosity and the progress we are making together.

Thank you, Christina, Hunt, Rowyn & Collins

4TH ANNUAL

ALL OUT FOR AYLA AND OTTO

The Maher Family, Amelia, Tim, Otto and Ayla - Roslindale, Massachusetts

When the Maher family attended their first Day of Hope Family Conference this year, they received encouragement from other cystinosis families to host a simple fundraiser, the results were extraordinary!

On Sunday, October 13, more than 100 friends and family gathered with the Maher family for their first fundraiser to go "All out for Ayla and Otto" at the Roundhead Brewery in Boston, MA. Guests shared a variety of delicious pizzas and refreshments as the children (and adults) participated in some face painting and games. Ayla and Otto proudly handed out CRF brochures with their picture on the cover and were happy seeing their friends, and even a few teachers in A+O event t-shirts.

During the festivities, Amelia and Tim were surrounded by the love and support from their community. As donations continued to arrive they were astounded to learn as first-time fundraisers they raised over $74,480! We are grateful to the Maher family for their time and efforts in organizing your first fundraiser and for the support of your generous community in honor of Ayla and Otto and cystinosis research. Together, we are changing lives, thank you!

SAM & LARS JENKINS HALLOWEEN FUNDRAISER

The Jenkins Family, Ashton, Stephen, Sam, Lars and Birdie - Salt Lake City, Utah

On October 26, the Jenkins family hosted their annual Haunted House fundraiser. They created an elaborate and spooky alley in the backyard that included a funeral, animatronic monsters, and a cemetery with a tunnel of terror. Sam, Lars, and eight of their friends hid throughout the area to startle and scare the Halloween partygoers. Hot chocolate and treats were offered, and tickets were sold to play a haunted shooting gallery game. Nearly 160 family, friends, and neighbors attended the event this year to raise over $4,000. Special thanks to Stephen's siblings, Seth Jenkins and Lauren Larsen, for managing the large crowd and selling tickets and goodies. Thank you to the Jenkins family for their commitment to CRF and cystinosis research and for providing another spooky night to remember!

GIVING TUESDAY MATCHING GIFT CHALLENGE

December 3, 2024

The generosity and dedication of our community continue to amaze us! A huge thank you to all the friends, families, coworkers and neighbors who offered tremendous support for the Cystinosis Research Foundation's Giving Tuesday $100,000 Matching Gift Challenge. We are so proud to be able to say that 100% of all donations made to CRF go directly toward funding research studies focused on finding novel treatments and a cure for cystinosis.

With your ongoing commitment and support, CRF continues to be the largest fund provider of cystinosis research in the world. Since 2003, CRF has raised over $71 million and funded 245 research studies which have led to new discoveries about cystinosis, new clinical trials, two FDA approvals and – ultimately – hope for a cure for the cystinosis community. Thanks to all of you, we're unlocking doors to endless possibilities for our children and adults with cystinosis!

If you'd still like to support critical cystinosis research, it's not too late! Scan and Share this QR code to donate today.

It all started with a diagnosis,
The first of many doors
Blocking our path
To a world without cystinosis.
But from one girl's wish,
We were given the key -
The key to possibilities.
The key to hope.
Wishes, research, community, family.
Keys we all hold dear,
To unlock a world of endless possibility.
Together, let's explore beyond.

cystinosis RESEARCH FOUNDATION

Unlocking endless possibilities:
Together, let's explore beyond.

FROM HERE
DONATE
WE CAN SEE A CURE