A hand holding a magnifying glass over a petri dish containing a star-shaped microorganism. The background is a warm, orange-to-red gradient.

# cystinosis magazine

THE  
RESEARCH  
ISSUE

FOR FRIENDS AND SUPPORTERS OF THE CYSTINOSIS RESEARCH FOUNDATION

FALL 2018

TOGETHER WE SHINE BRIGHT

SHINE BRIGHT  
RESEARCH  
ISSUE



## TOGETHER WE SHINE BRIGHT

We have set our course, navigating by the light of a guiding star.

The research we support comes from the brightest minds, and our growing and compassionate community lights the darkness with an energy that shines a spotlight on a hopeful future.

We wish upon the same star, and we shine brightest when we come together creating our own constellation of hope. Together, We Shine Bright.

### CONTACT US:

Please send suggestions and comments regarding *Cystinosis Magazine* to [nstack@cystinosisresearch.org](mailto:nstack@cystinosisresearch.org).

To receive our e-newsletter, *Star Facts*, send your email address to [zsolsby@cystinosisresearch.org](mailto:zsolsby@cystinosisresearch.org).

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*Art Direction and Printing: Idea Hall*

FALL 2018

 **cystinosis**  
magazine

[CYSTINOSISRESEARCH.ORG](http://CYSTINOSISRESEARCH.ORG)

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Irvine, CA 92612

949 223 7610



The mission of the Cystinosis Research Foundation is to find better treatments and a cure for cystinosis by supporting bench, clinical and translational research. Since 2003, CRF has raised \$45 million for cystinosis research in an effort to find a cure.

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FALL 2018

DEAR  
*FAMILY*  
AND  
*FRIENDS*

*I*t seems like only yesterday that Natalie scribbled her birthday wish on a napkin, “to have my disease go away forever.” As parents, the years have flown by and we find ourselves reflecting on our lives and family. When we think of family, we think of you. We are incredibly grateful to all of you who have supported our efforts to find better treatments and a cure for cystinosis. The cystinosis journey has not always been easy — there have been ups and downs for our family and our community — but we have faced the struggles together. And from those struggles, we have found joy in living.

As we wind down 2018, we celebrate our researchers and clinicians who, through their dedication and commitment to the children and adults with cystinosis, have transformed our community.

When we founded CRF, there were only a handful of researchers in the world working on cystinosis. Today, there are hundreds, and that is a direct result of your donations and commitment to finding a cure for cystinosis. In this issue of Cystinosis Magazine, we focus on the researchers we support and the outstanding work they do every day for our children and adults with cystinosis.



Together we shine bright. It takes all of us working together, united in this cause, to make a difference. We will shine a light on several CRF-funded researchers and will share beautiful stories from families and patients in this issue that will inspire you and warm your heart.

## SHINING THE LIGHT ON OUR RESEARCH EFFORTS

The research we fund is broad in its scope because cystinosis affects every cell in the body; therefore, we focus research in the areas affected by cystinosis, including the kidneys, eyes, muscles and bone, brain and thyroid. We seek to know more about the pathogenesis of cystinosis knowing that it will help us unlock the mysteries of this disease. Every research study we fund is part of an overall strategy aimed at finding better treatments and a cure. We fund bench, clinical and translational research.

The bench research we fund is now moving from the lab to clinical trials. In this issue, you will read about six CRF-funded researchers who are very close to translating their studies to clinical trials in humans. Every day and every minute, there are CRF-funded researchers working on cystinosis. They work collaboratively, ensuring that information is shared in an effort to hasten discoveries and accelerate research.

Your donations are at work throughout the year because we issue grants biannually. Since 2003, CRF has funded 175 multiyear research studies in 12 countries. Our researchers have published 72 articles in prestigious journals as a result of CRF funding. Today, CRF is the largest private fund provider of cystinosis research in the world.

We have built a strong foundation for innovative research that is not only thriving, but producing extraordinary results. We could only accomplish this with you by our side. You have been there every step of the way, and we are eternally grateful.

## ELEVEN NEW GRANTS ISSUED IN FIVE COUNTRIES TOTALING \$2,391,837

We are pleased to announce that in the spring, we issued 11 new grants totaling over \$2.3 million in research awards. The grants went to researchers in the United States, Belgium, France, Italy and Switzerland. The recipients of the spring 2018 grants are listed on page 10, along with lay abstracts of their studies. The new grants focus on bones, the kidneys, development of a rat model of cystinosis, molecular mechanism of cystinosis, muscle dysfunction and a novel drug treatment for cystinosis.

## UPDATE ON STEM CELL AND GENE THERAPY

Dr. Stéphanie Cherqui at University of California, San Diego (UCSD) continues to work with the goal of submitting an Investigational New Drug (IND) application to the FDA this year. She has dedicated her career to our community, and we are thankful to her for working every day to find the cure. Dr. Cherqui's treatment for cystinosis will involve using the patients' own stem cells and gene-correct them to introduce a functional CTNS gene before transplanting them back in the patients. We are optimistic that the FDA will give their approval to begin a phase 1 clinical trial to treat the first patients with Dr. Cherqui's promising treatment before the end of the year.

## NOVEL TREATMENTS FOR CORNEAL CYSTINOSIS — THE NANOWAFER AND MICROSPHERES

Corneal cystinosis is the buildup of cystine crystals in the eyes that causes photophobia (extreme sensitivity to light), severe eye pain and, sometimes, blindness. There is an existing eye drop treatment, but the drops must be taken every waking hour and are painful for many patients. CRF is funding two very important studies that could revolutionize eye treatment for cystinosis.

CRF has been funding research at Baylor College of Medicine (BCM), and now, we are thrilled to report that we are full speed ahead with translating the research developed in the lab to clinical trials. NanoWafer, Inc., a CRF-owned company, hired a CEO, Ron Bache, to run the company with the goal of getting FDA approval for a new treatment for corneal cystinosis. We have completed the technology transfer and are producing nanowafers



for animal studies. The technology developed at BCM involves nano technology to deliver medication to the eye. The idea is for the nanowafer to be loaded with medication and placed in the eye, where it quickly dissolves but leaves medication in the eye for hours. We believe this might be a once-a-day treatment.

Another promising potential treatment is the work Morgan Fedorchak, PhD, is doing at the University of Pittsburgh. She had developed a hydrogel drop that is filled with small microspheres that are loaded with medication. The drop is placed in the eye and the medication is released. We believe this treatment is a once-a-day treatment that can deliver an entire day's worth of medication.

The nanowafer and the gel drop are two novel treatments that have great potential and are within a year of clinical trials.

## A NEW TREATMENT ON THE HORIZON!

One of the most exciting projects we are funding has the potential to change the way we treat cystinosis. Today, we use cysteamine in the form of two commercial medications, Cystagon® and Procysbi®, to treat cystinosis. Both medications use cysteamine, which is the only medication that helps slow the progression of cystinosis. Cysteamine causes severe gastrointestinal side effects, including nausea, vomiting, severe odor and headaches. For some, tolerating cysteamine is impossible, but it is the life-sustaining drug that must be taken by all children and adults with cystinosis.

We were motivated to find a better treatment for cystinosis by the horrendous side effects of cysteamine, as well as the high price of Procysbi®. For most patients with cystinosis, Procysbi® costs over \$1 million a year. We wanted to fund research that would not only improve the medication our children and adults take, but would be commercially available at a reasonable price.

Patrice Rioux, MD, PhD, and Vince Stanton, Jr, MD, (Thiogenesis Therapeutics, Inc.) are developing a cysteamine pro-drug, TTI-0102, which is slowly degraded into cysteamine in the gastrointestinal tract. Rodent pharmacokinetic studies suggest that this compound does not produce the very high peak blood cysteamine levels associated with cysteamine side effects. Therefore, it may be possible to deliver a higher amount

of cysteamine to patients and achieve a therapeutic response, without the gastrointestinal side effects and bad smell. The plan is to formulate TTI-0102 as a powder or a liquid, which should make drug ingestion more patient-friendly. Please read more about this significant study on page 18.

## THE IMPACT OF CRF-FUNDED RESEARCH HELPS OTHERS

The work we have funded has also resulted in new discoveries for other diseases and disorders. Dr. Cherqui's work has resulted in the successful treatment of Friedreich's ataxia and Danon disease in the mouse models. Dr. Fedorchak's work on corneal cystinosis could help others with inherited corneal dystrophies.

There are many more discoveries made by CRF researchers that have resulted from CRF funding, including discoveries for other corneal diseases, kidney diseases and genetic and systemic diseases similar to cystinosis. Our research could help diseases and disorders like Parkinson's disease and NASH, a fatty liver disease. Your support of cystinosis research has reached far beyond the cystinosis community. A cure for cystinosis will help find cures for other diseases, potentially helping millions of people. We are changing lives together, and you are giving hope to thousands and possibly even millions who will benefit from our research discoveries.

## WE ARE FOREVER GRATEFUL

We have so much to be grateful for — your unwavering support, your commitment to research and your compassion and love for our community. We have made extraordinary progress, and with your continued support, generosity and love, we will find a cure for cystinosis.

We are blessed by your encouragement, thankful for your prayers and eternally grateful for your steadfast commitment to finding the cure. You have helped us find joy along this cystinosis path, and for that, we are forever indebted to each and every one of you.

Thank you for supporting cystinosis research, for standing by our side and for embracing our community.

With heartfelt thanks and gratitude,

*Nancy & Jeff*



TOGETHER  
WE SHINE BRIGHT

---

## A LETTER FROM NATALIE



In early October, I started my new job as a case supervisor for Court Appointed Special Advocates (CASA), a non-profit organization. I work with the CASA volunteers who are committed to being the support system and advocates for children in the child welfare system. My new position will allow me to make a real and important difference in the lives of the most vulnerable, neglected or abused children by working to provide the children with a safe and healthy environment.

I am honored to be part of such a reputable and outstanding national organization that fights for and protects children. I am excited for the opportunity to reach the next level of my career goals at CASA and look forward to what the future holds for me.

Though having a full-time job takes a lot out of me physically, I am proud that I have continued to pursue my dreams and have never given up on my passion to help others. The medications are unbearable at times, and they take a toll on me; but I am hopeful that with better drugs, and possibly a cure soon, I can manage a full-time job more easily without having to worry about the medicinal side effects that I often experience at work. I also hope that improved medications might help with the extreme fatigue I often experience when I get home from work. The side effects often make it impossible to live my life as a normal and healthy 27-year-old woman.

I am committed to giving back to the community because I have been the recipient of so much support from others. Thank you to everyone who has supported me since I made my wish, “to have my disease go away forever,” so many years ago. Cystinosis is just a small part of who I am, and it will not stop me from living my life to the fullest.

Thank you to my family, my friends, the researchers and doctors, and most of all, the cystinosis community. I am blessed to be supported and loved by such an incredible group of people. I know a cure will be found soon, and I am hopeful that I will have a promising future.

With Love,

*Natalie Stack*



*I am committed to give back to the community because I have been the recipient of so much support from others.*



# WHAT IS CYSTINOSIS?

*Cystinosis is a rare, inherited, metabolic disease that is characterized by the abnormal accumulation of the amino acid dimer cystine in every cell in the body. Build-up of cystine in the cells eventually destroys all major organs of the body including the kidneys, liver, eyes, muscles, bone marrow, thyroid and brain.*

Medication is available to control some of the symptoms of this terrible disease, but cystinosis remains incurable. Cystinosis affects approximately 500 people, mostly children, in North America, and about 2,000 worldwide.

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

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

## WHO IS CRF?



Natalie Stack made a wish on the eve of her 12th birthday in 2003. That same year, the Cystinosis Research Foundation (CRF) was founded. It was established with the sole purpose of raising funds to find better treatments, and ultimately a cure, for cystinosis.

Today, **CRF IS THE LARGEST FUND PROVIDER OF GRANTS FOR CYSTINOSIS RESEARCH IN THE WORLD**, funding more than 175 studies in 12 countries. Since 2003, CRF has raised over \$45 million with 100% of donations going directly to support cystinosis research.

CRF's efforts have changed the course of cystinosis and given new energy to its investigators and scientists. CRF's commitment to research has given hope and promise to the global community of cystinosis patients and their families.



# YOU HAVE CHANGED THE COURSE OF CYSTINOSIS



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



We navigate by the light of a guiding star and have set our course closer to the cure with more new clinical trials than ever before. It is because of you that CRF has been able to fund extraordinary researchers across the globe.

# THE IMPACT OF CRF RESEARCH

AREAS OF RESEARCH FOCUS &  
GRANTS AWARDED SINCE 2002



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

29 GRANTS

### Stéphanie Cherqui, PhD

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

### Alan Davidson, PhD

THE UNIVERSITY OF AUCKLAND, GRAFTON,  
AUCKLAND, NEW ZEALAND

### Paul Goodyer, MD

MONTRÉAL CHILDREN'S HOSPITAL,  
QUÉBEC, CANADA

### Patrick Harrison, PhD

UNIVERSITY COLLEGE CORK, IRELAND

### Vasiliki Kalatzis, PhD

INSTITUTE GÉNÉTIQUE MOLÉCULAIRE  
MONTPELLIER, MONTPELLIER, FRANCE

### Daniel Salomon, MD

THE SCRIPPS RESEARCH INSTITUTE,  
LA JOLLA, CALIFORNIA

### Holger Willenbring, MD

UNIVERSITY OF CALIFORNIA, SAN  
FRANCISCO, SAN FRANCISCO, CALIFORNIA



## Molecular Study of Cystinosis in the Yeast Model

3 GRANTS

### Bruno André, PhD

UNIVERSITÉ LIBRE DE BRUXELLES,  
GOSSELIES, BELGIUM

### Anand Bachhawat, PhD

IISER MOHALI, MANAULI, PUNJAB, INDIA

### David Pearce, PhD

UNIVERSITY OF ROCHESTER MEDICAL  
CENTER, ROCHESTER, NEW YORK



## Skin, Muscle and Bone

11 GRANTS

### Justine Bacchetta, MD, PhD

**Irma Machuca-Gayet, PhD**  
HOSPICES CIVILS DE LYON  
UNIVERSITÉ DE LYON, LYON, FRANCE

### Robert Ballotti, PhD

**Christine Chiaverini, MD, PhD**  
FACULTÉ DE MÉDECINE, NICE, FRANCE

### Paul Grimm, MD

STANFORD UNIVERSITY SCHOOL OF  
MEDICINE, PALO ALTO, CALIFORNIA

### Mary Leonard, MD, MSCE

STANFORD UNIVERSITY,  
PALO ALTO, CALIFORNIA

### Robert Mak, MD, PhD

UNIVERSITY OF CALIFORNIA,  
SAN DIEGO, LA JOLLA, CALIFORNIA

### Richard Reimer, MD

**Jacinda Sampson, MD, PhD**

**Mary Leonard, MD, MSCE**

**Paul Grimm, MD**

**Trinh Tina Duong, MPT**

**Feliks Kogan, PhD**

STANFORD UNIVERSITY,  
PALO ALTO, CALIFORNIA



## Genetic Analysis of Cystinosis

5 GRANTS

### Katy Freed, PhD

TEXAS BIOMEDICAL RESEARCH INSTITUTE,  
SAN ANTONIO, TEXAS

### Sihoun Hahn, MD, PhD

SEATTLE CHILDREN'S HOSPITAL,  
SEATTLE, WASHINGTON

### Elena Levtchenko, MD, PhD

UNIVERSITY HOSPITAL LEUVEN, BELGIUM

### Eric Moses, PhD

TEXAS BIOMEDICAL RESEARCH INSTITUTE,  
SAN ANTONIO, TEXAS

### Minnie Sarwal, MD, PhD

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO,  
SAN FRANCISCO, CALIFORNIA



## New Drug Discovery Cysteamine, New Medications and Devices

25 GRANTS

### Ghanashyam Acharya, PhD

BAYLOR COLLEGE OF MEDICINE,  
HOUSTON, TEXAS

### Pierre Courtoy, MD, PhD

DE DUVE INSTITUTE, UNIVERSITÉ  
CATHOLIQUE DE LOUVAIN,  
BRUSSELS, BELGIUM

NEW

### Antonella De Matteis, MD

TELETHON INSTITUTE OF GENETICS AND  
MEDICINE, NAPLES, ITALY

### Ranjan Dohil, MD

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

### Francesco Emma, MD

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

### Paul Goodyer, MD

MONTRÉAL CHILDREN'S HOSPITAL,  
QUÉBEC, CANADA

### Vincent Stanton, Jr., MD

**Patrice Rioux, MD, PhD**  
THIOGENESIS THERAPEUTICS, INC.,  
SAN DIEGO, CALIFORNIA

NEW



## Eye-Corneal Cystinosis Research

8 GRANTS

### Ghanashyam Acharya, PhD

BAYLOR COLLEGE OF MEDICINE,  
HOUSTON, TEXAS

### Stéphanie Cherqui, PhD

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

### Morgan Fedorchak, PhD

UNIVERSITY OF PITTSBURGH SCHOOL OF  
MEDICINE, PITTSBURGH, PENNSYLVANIA

### Jennifer Simpson, MD

UNIVERSITY OF CALIFORNIA, IRVINE,  
IRVINE, CALIFORNIA

### Kang Zhang, MD, PhD

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA



## Thyroid

1 GRANT

### Pierre Courtoy, MD, PhD

DE DUVE INSTITUTE, UNIVERSITÉ  
CATHOLIQUE DE LOUVAIN,  
BRUSSELS, BELGIUM



## Rat Model for Cystinosis

NEW

### 1 GRANT

**Francesco Emma, MD**

BAMBINO GESÙ CHILDREN'S HOSPITAL,  
ROME, ITALY

**Olivier Devuyst, MD, PhD**

UNIVERSITY OF ZÜRICH, SWITZERLAND



## Cystine Measurement and Cysteamine Toxicity Study

### 9 GRANTS

**Bruce Barshop, MD, PhD**

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

**Thomas Jeitner, PhD**

NEW YORK MEDICAL COLLEGE,  
VALHALLA, NEW YORK

**Elena Levchenko, MD, PhD**

UNIVERSITY HOSPITAL, LEUVEN, BELGIUM



## Neurological

### 15 GRANTS

**Angela Ballantyne, PhD**

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

**Miriam Britt Sach, MD, PhD**

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

**Rita Ceponiene, MD, PhD**

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

**Florian Eichler, MD**

MASSACHUSETTS GENERAL HOSPITAL,  
BOSTON, MASSACHUSETTS

**Aude Servais, MD, PhD**

NECKER HOSPITAL, PARIS, FRANCE

**Amy Spilkin, PhD**

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

**Doris Trauner, MD**

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA



## Lab Equipment for Cystinosis

NEW

### 3 GRANTS

**Ghanashyam Acharya, PhD**

BAYLOR COLLEGE OF MEDICINE,  
HOUSTON, TEXAS

**Stéphanie Cherqui, PhD**

UNIVERSITY OF CALIFORNIA,  
SAN DIEGO

**Sergio Catz, PhD**

THE SCRIPPS RESEARCH INSTITUTE,  
LA JOLLA, CALIFORNIA



## Kidney Research

### 19 GRANTS

**Robert Chevalier, MD**

UNIVERSITY OF VIRGINIA,  
CHARLOTTESVILLE, VIRGINIA

**Pierre Courtoy, MD, PhD**

**Christopher Pierreux, PhD**  
DE DUVE INSTITUTE, UNIVERSITÉ  
CATHOLIQUE DE LOUVAIN,  
BRUSSELS, BELGIUM

**Olivier Devuyst, MD, PhD**

UNIVERSITY OF ZÜRICH, INSTITUTE OF  
PHYSIOLOGY, ZÜRICH, SWITZERLAND

**Allison Eddy, MD**

BC CHILDREN'S HOSPITAL, VANCOUVER,  
BRITISH COLUMBIA, CANADA

**Elena Levchenko, MD, PhD**

UNIVERSITY HOSPITAL, LEUVEN, BELGIUM

**Robert Mak, MD, PhD**

UNIVERSITY OF CALIFORNIA,  
SAN DIEGO, LA JOLLA, CALIFORNIA

**Tara McMorow, MD**

UNIVERSITY COLLEGE DUBLIN,  
BELFIELD, DUBLIN, IRELAND

**Philip Newsholme, PhD**

CURTIN UNIVERSITY,  
PERTH, WESTERN AUSTRALIA

**Daryl Okamura, MD**

SEATTLE CHILDREN'S RESEARCH  
INSTITUTE, SEATTLE, WASHINGTON

**Mary Taub, PhD**

UNIVERSITY AT BUFFALO, THE STATE  
UNIVERSITY OF NEW YORK,  
BUFFALO, NEW YORK



## Cellular and/or Molecular Studies of the Pathogenesis of Cystinosis

### 45 GRANTS

**Corinne Antignac, MD, PhD**

IMAGINE INSTITUTE (INSERM U1163),  
PARIS, FRANCE

**Francesco Bellomo, PhD**

BAMBINO GESÙ CHILDREN'S HOSPITAL,  
ROME, ITALY

**Sergio Catz, PhD**

THE SCRIPPS RESEARCH INSTITUTE,  
LA JOLLA, CALIFORNIA

**Antonella De Matteis, MD**

TELETHON INSTITUTE OF GENETICS  
AND MEDICINE, NAPLES, ITALY

**Liang Feng, PhD**

STANFORD UNIVERSITY,  
PALO ALTO, CALIFORNIA

**Bruno Gasnier, PhD**

**Rossella Conti, PhD**  
PARIS DESCARTES UNIVERSITY,  
PARIS, FRANCE

**Taosheng Huang, MD, PhD**

UNIVERSITY OF CALIFORNIA, IRVINE,  
IRVINE, CALIFORNIA

**Elena Levchenko, MD, PhD**

UNIVERSITY HOSPITAL, LEUVEN, BELGIUM

**Alessandro Luciani, PhD**

UNIVERSITY OF ZÜRICH, SWITZERLAND

**Gennaro Napolitano, PhD**

THE SCRIPPS RESEARCH INSTITUTE,  
LA JOLLA, CALIFORNIA

**Norbert Perrimon, PhD**

HARVARD MEDICAL SCHOOL,  
BOSTON, MASSACHUSETTS

**Giusi Prencipe, PhD**

BAMBINO GESÙ CHILDREN'S HOSPITAL,  
ROME, ITALY

**Matias Simons, MD**

IMAGINE INSTITUTE, PARIS, FRANCE

**Jess Thoene, MD**

TULANE UNIVERSITY SCHOOL OF  
MEDICINE, NEW ORLEANS, LOUISIANA



## Cure Cystinosis International Registry (CCIR)

### 1 GRANT

**Ranjan Dohil, MD**

UNIVERSITY OF CALIFORNIA, SAN DIEGO,  
LA JOLLA, CALIFORNIA

# SPRING 2018 CRF RESEARCH GRANTS FUNDED

IN SUPPORT OF SCIENTIFIC STUDIES ON  
CELL FUNCTION, NEW TREATMENTS AND THE QUEST FOR A CURE

## Cysteamine Toxicity on Bone: The CYSTEA-BONE Project

**\$ 126,000.00**

### TWO-YEAR GRANT

(November 1, 2018 – October 31, 2020)

---

**Justine Bacchetta, MD, PhD, Principal Investigator**  
**Irma Machuca-Gayet, PhD, Co-Principal Investigator**  
Hospices Civils de Lyon et Université de Lyon, France

## Evaluation of Ctns-/- Mice Protection by Oral Supplementation with Basic Amino- Acids: Focus on Kidneys – Extension to Another Colony

**\$ 165,045.00**

### TWO-YEAR GRANT

(September 1, 2018 – August 31, 2020)

---

**Pierre Courtoy, MD, PhD, Principal Investigator**  
**Christophe Pierreux, PhD, Co-Principal Investigator**  
De Duve Institute AISBL

## Novel Mechanistic and Translational Studies of Neutrophil-Mediated Inflammation in Cystinosis

**\$ 150,000.00**

### TWO-YEAR GRANT

(September 1, 2018 – August 31, 2020)

---

**Sergio Catz, PhD, Research Mentor**  
**Raquel Carvalho Gontijo, PhD, Research Fellow**  
The Scripps Research Institute, La Jolla, California

## Development and Characterization of a Rat Model of Cystinosis

**\$ 133,430.00**

### ONE-YEAR GRANT

(September 1, 2018 – August 31, 2019)

---

**Francesco Emma, MD, Principal Investigator**  
**Olivier Devuyst, MD, PhD Co-Principal Investigator**  
Bambino Gesù Children's Hospital, IRCCS, Rome, Italy  
University of Zürich, Zürich, Switzerland

## EnVision XCite Plate Reader Equipment

**\$ 62,233.18**

### EQUIPMENT GRANT

---

**Sergio Catz, PhD**  
The Scripps Research Institute, La Jolla, California

## Molecular Mechanism of Cystinosis

**\$ 150,000.00**

### TWO-YEAR GRANT

(September 1, 2018 – August 31, 2020)

---

**Liang Feng, PhD, Research Mentor**  
**Xue Guo, PhD, Research Fellow**  
Stanford University, Palo Alto, California



Total 2018 Spring Grants Awarded:

**\$2,391,837**

Evaluation of Ctns-/- Mice Kidney Protection by Oral Supplementation with Basic Amino-Acids: Extension to Another Colony with Sequential Analysis of Fanconi Syndrome and Renal Insufficiency

**\$133,083.00**

**TWO-YEAR GRANT**

(September 1, 2018 – August 31, 2020)

**Robert Mak, MD, PhD, Principal Investigator**  
University of California, San Diego

Impact of Leptin Signaling on Skeletal Integrity and Growth in Infantile Neuropathic Cystinosis

**\$206,466.00**

**ONE-YEAR GRANT**

(September 1, 2018 – August 31, 2019)

**Robert Mak, MD, PhD, Principal Investigator**  
University of California, San Diego

The Effect of Resistance Exercise on Muscle Dysfunction in Cystinosis

**\$159,680.00**

**ONE-YEAR GRANT**

(September 1, 2018 – August 31, 2019)

**Richard Reimer, MD, Principal Investigator**  
**Jacinda Sampson, MD, PhD, Co-Principal Investigator**  
**Mary Leonard, MD, MSCE, Co-Principal Investigator**  
**Paul Grimm, MD, Co-Principal Investigator**  
**Trinh Tina Duong, MPT, PhD Candidate, Co-Principal Investigator**  
**Feliks Kogan, PhD, Co-Principal Investigator**  
Stanford University, Palo Alto, California

Pharmacokinetic Evaluation and Optimization of Cysteamine Precursors

**\$153,900.00**

**ONE-YEAR GRANT**

(March 1, 2018 – February 28, 2019)

**Vincent Stanton, Jr, MD, Principal Investigator**  
**Patrice Rioux, MD, PhD, Co-Principal Investigator**  
Thiogenesis Therapeutics, Inc., Belmont, Massachusetts and San Diego, California

Synthesis and Human Testing of TTI-0102, a Cysteamine Prodrug

**\$952,000.00**

**TWO-YEAR GRANT**

(September 1, 2018 – August 30, 2020)

**Vincent Stanton, Jr, MD, Principal Investigator**  
**Patrice Rioux, MD, PhD, Co-Principal Investigator**  
Thiogenesis Therapeutics, Inc., Belmont, Massachusetts and San Diego, California



**SEE**

**LAY ABSTRACTS**

**STARTING ON  
PAGE 24**



# 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.

1

## Potential Use of Stem Cells as a Therapy for Cystinosis

Published online May 22, 2018

*Pediatric Nephrology*

by Stéphanie Cherqui, PhD, and Celine J. Rocca, PhD, Department of Pediatrics, Division of Genetics, University of California, San Diego

2

## A Genetic Screen for Investigating the Human Lysosomal Cystine Transporter, Cystinosin

Published online February 21, 2018

*Scientific Reports*

by Anup Arunrao Deshpande, PhD Student, Anjuj Shukla, MS Student, and Anand Kumar Bachhawat, PhD, FNA, FNASc, FASc, Indian Institute of Science and Education Research Mohali, Punjab, India

3

## Impaired Autophagy Bridges Lysosomal Storage Disease and Epithelial Dysfunction in the Kidney

Published January 2018

*Nature Communications*

by Olivier Devuyst, MD, PhD, and Alessandro Luciani, PhD, University of Zürich, Switzerland

4

## All-Purpose HSCs

Published November 30, 2017

*BIOCENTURY Innovations Journal*

highlights Dr. Stéphanie Cherqui's stem cell research at the University of California, San Diego

5

## Transplantation of Wild-Type Mouse Hematopoietic Stem and Progenitor Cells Ameliorates Deficits in a Mouse Model of Friedreich's Ataxia

Published October 2017

*Science Translational Medicine*

by Celine J. Rocca, PhD, Spencer M. Goodman, Jennifer N. Dulin, PhD, Joseph H. Haquang, Ilya Gertsman, PhD, Jordan Blondell, PhD, Janell L. M. Smith, Charles J. Heyser, PhD, and Stephanie Cherqui, PhD (Division of Genetics, Department of Pediatrics, UCSD, La Jolla, California)



# CYSTINOSIS RESEARCH FOUNDATION

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LEADERSHIP.  
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The Scientific Review Board (SRB) is composed of leading cystinosis scientists and experts from around the world. Members are actively involved in the grant-review process, evaluating and analyzing all research proposals that are submitted for potential funding, and advising the CRF on the scientific merit of each proposal.

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*Thank you for your dedication to the global cystinosis community.*



BY DENNIS ARP

Ron Bache has worked in the ophthalmology field for more than 25 years, helping to bring new ocular treatments to market and shepherding a wide range of innovative projects. But when his college-age son Carter's routine eye exam yielded a diagnosis of cystinosis, Bache reacted the same way so many other cystinosis parents have before.

"What is that, and what does it mean to my son?"

Like many others just getting introduced to cystinosis, Bache fought through the initial shock and concern to seek out as much information as he could find. In his case, the sources included corneal specialists he already knew as friends. One gave him the lowdown on the treatment regimen that might be in his son's future.

"It was a Sunday afternoon, and I was sitting in a parking lot at a mall speaking with my ophthalmologist friend and I said, 'I see there is a drop treatment, but they have to be frozen and then taken every hour while awake, and they only last for one week. How long does that one-week treatment last? A month? Longer?' My friend said, 'Ron once he starts the drops, he takes them every hour for the rest of his life.'" Bache recalls. "I literally sat there in stunned silence and was thinking, 'How does someone even comply with this? How is my son going to do this and go to class?' I immediately thought, 'There has got to be a better option.'"

The Bache family's journey with cystinosis had begun.

And while every such exploration has its own unique twists and turns, there's no doubt that Ron Bache's experience stands apart from all others. As he says, "I believe that with all of these events, God has led me to this place at this time — to be helpful with my knowledge and to take this forward, if that is possible."

For Bache, the tale took an exceedingly positive turn. Further testing revealed that his son, now a junior at USC, had a benign form of cystinosis. Carter has cystine crystals in his eyes, but they don't really bother him. He doesn't have to take the cysteamine drops, and the only real impact on his life is regular urine testing to ensure his status hasn't changed.

When the Baches got the results of the follow-up testing while at Stanford, "I went to the car and cried like a baby," Ron Bache says.

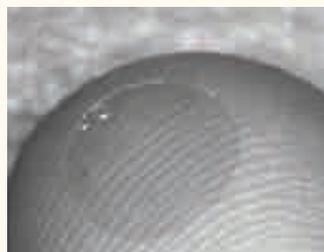
That moment of familial joy might have been the end of Bache's cystinosis story — except another ophthalmologist friend told him, "You know the Cystinosis Research Foundation is right in your backyard," and with that, Bache found his way to the Cystinosis Research Foundation website and then to a phone conversation with CRF president Nancy Stack. That's how Bache learned about the nanowafer technology that offers hope as a great advance in treating corneal cystinosis.

"Nancy told me the nanowafer project was at a crossroads, that they couldn't find someone to take it on," Bache says. It was also on this call that he said, "I see you are sponsoring a nanowafer once-a-day treatment. I have read the paper. How do I find one of the authors, Jennifer Simpson, MD?" Nancy replied, "You are from ophthalmology — do you know Ron Kurtz?" Bache said, "Of course, he is a friend and, in fact, we bought one of his companies years back — why?" Nancy said, "Because Jennifer is his wife and is one of the world's leading experts on ocular cystinosis, and she is right here at UC Irvine!" Nancy continued, "And Ron Kurtz is currently volunteering as CEO, and we are using Judy Gordon, D.V.M., for the FDA needs." As it turns out, Judy is also a longtime friend and the person who helped take Bache's previous company through the FDA process.

As it happened, Bache was at a professional crossroads of his own. For the past seven years, he had been the president and CEO of a startup called AqueSys, which had developed a minimally invasive stent that was a breakthrough for glaucoma patients. In 2015, the company was acquired by Allergan. The sale allowed Bache to sit back and consider the next steps in his career.

When he heard about the nanowafer project's need for leadership, he didn't hesitate.

"I said, 'I'll do it as a volunteer for now — let's just get this thing moving forward,'" Bache says. "It was very much a feeling of 'This is just meant to be.'"



This small transparent disc is placed on the surface of the eye and contains drug-loaded nanoreservoirs, delivering medicine more efficiently than eye drops.

As CEO of the new CRF-funded entity NanoWafer, Inc., **BACHE IS WORKING TO REALIZE THE GREAT POTENTIAL OF A TECHNOLOGY PIONEERED BY BAYLOR UNIVERSITY RESEARCHER GHANASHYAM ACHARYA, PhD, THANKS TO GRANT SUPPORT FROM THE CRF.**

The vision for the drug-delivery system features thin wafers packed with medication and then placed in the eyes of cystinosis patients. As the wafers dissolve, they continuously work to clear the eyes of cystine crystals, saving patients from the hassle of hourly eye-drop applications.

“I want to be careful not to overpromise, because these things are fraught with clinical and regulatory risk,” Bache says. “But the promise we are trying to attain is that this will be a once-a-day treatment that doesn’t need to be refrigerated.”

Now that the technology has transferred from inventors to corporate caretakers, “the goal is to secure funding and build out the company so it does what we hope it will,” Bache adds. “We feel confident in what we know, now that it’s worthy of our efforts.”

The CEO estimates it will take \$10 million to bring the nanowafer to market, so he’s reaching out to traditional venture capital sources. Usually, such investors are motivated by billion-dollar markets.

“We’re looking for a unique investor,” he says. “They exist, but it’s not a slam dunk.”

A positive development: Bache has found a world-class manufacturer and engineers to meet production goals, so that animal testing can progress. Future hurdles include approval for an FDA study, clinical trials for which to enroll cystinosis patients, and then follow-up with those patients — probably about 40 of them — to be tested at sites on both U.S. coasts as well as another location in between.

Because of those clinical and regulatory risks, as Bache mentioned previously, timelines are difficult to predict, he says. “But I estimate that we’re looking at somewhere in the range of two and a half to four years before this is available to patients in the U.S.”

Even as he acknowledges the variables and tries to manage expectations, Bache speaks with confidence about the future of NanoWafer, Inc.

“I’m banking on outreach to some of my previous investors, based on the good things we’ve done already,” he says.

In the end, his involvement with the project still revolves around a sense that he is answering a call to serve a greater good.

# RESEARCH BREAK-THRU

NEXT STEP CLOSER



Heeding an unexpected call,

**RON BACHE**

steps up to lead a project

full of hope for those with

corneal cystinosis.

“My whole business career, I’ve been involved in multibillion-dollar markets, with companies worth hundreds of millions,” he says. “Until I came in contact with the CRF, it seemed so obvious why working for large companies or in large markets made sense. Now I see how absolutely vital it is to have people like those at the CRF — people like cystinosis patients and their families and friends who drive forward new treatments for rare diseases. We all have abilities we bring to this effort. And that’s what it takes for these drugs to have a chance to be developed.”

“I totally had a veil lifted before my eyes. This is a labor of love to try and do the right thing.”

# PROMISING PATHWAYS

**In his quest to enhance cystinosis treatment, Dr. Emma finds two encouraging compounds as well as a reminder that every step matters.**

BY DENNIS ARP

Good things are happening in the lab of Dr. Francesco Emma, head of pediatric nephrology at Bambino Gesù Children's Hospital in Rome, Italy. The researcher and physician is investigating two compounds, in particular, that may deliver alternative or complementary treatments for cystinosis.

But before he gives an update on the research that's paving the way to progress, Dr. Emma wants us to join him on a side road lined with important lessons that illustrate, "In the work we do, there are no shortcuts."

Thanks to grants from the Cystinosis Research Foundation (CRF), Dr. Emma is exploring a library of small-molecule drugs that are already licensed for human use and show promise in treating cystinosis. Because the researcher is focusing on drugs that have already cleared regulatory hurdles, their path to approval as cystinosis treatments is likely to be more direct.

After narrowing the list of targeted drugs to about 25, he and his lab colleagues identified a smaller cohort with the greatest potential. These drugs have been shown to dramatically reduce the cystine content in cells — sometimes by as much as 70 percent. With a particular compound, the profile was compelling — until Dr. Emma and his team entered the phase of animal trials.

"It turned out that the compound was particularly toxic for cystinotic cells and animals, even though it was not for other cells and animals," Dr. Emma says.

Initial animal results revealed the toxicity, "but we didn't give up because the drug was so promising for cystinosis," Dr. Emma adds. "We tested lower doses, trying to find the right level of efficacy and efficiency."

Ultimately, that balance just couldn't be achieved. After investing three years in the search, the investigators had to abandon the testing and redirect resources to other promising compounds.

"This was a setback, and we were very disappointed," Dr. Emma says. "But sometimes, this is how research goes. However, as hard as these moments are, they also teach us. I tell of this experience when I speak with cystinosis families so they can better understand why we follow protocols. If we had not done the test in animals and instead administered this drug directly to cystinosis patients, it probably would have been extremely toxic."

Such setbacks are a reminder that even though drugs have been approved for human use, that doesn't mean all humans will benefit. The good news is that Dr. Emma and his research team work on multiple tracks, and they are masters at seamlessly transitioning to maximize other opportunities.



**"FROM THE START, THE CRF HAS BEEN THE MAJOR SPONSOR OF ALL THIS WORK... EVEN AS WE GOT SOME INSTITUTIONAL FUNDING FROM EUROPEAN AGENCIES, 80 PERCENT OF OUR SUPPORT HAS COME FROM THE CRF."**

# RESEARCH BREAK-THRU

NEXT STEP CLOSER



**Francesco Emma, MD**

*Head of Pediatric Nephrology  
Director of Nephrology Laboratory*

Bambino Gesù Children's Hospital, Rome, Italy

On another of these tracks, they are finding success with a natural compound called “genistein,” as well as a second discovery with similar properties. For now, the team is calling this second discovery “Compound No. 2” for proprietary reasons. In both cases, the compounds correct defects of cystinotic cells that are not corrected by cysteamine. Both have good safety profiles and have demonstrated efficiencies in treating conditions other than cystinosis.

Dr. Emma is excited that the compounds offer a new approach to clearing cystine from cells and organs. For most people, lysosomes in the body serve this clearance role. But because cystinosis is a lysosomal storage disorder, patients need cysteamine to serve as a cystine-depleting agent.

Genistein takes a different track.

“By activating this different pathway, we’re not trying to get cystine out of the lysosome; we’re trying to get rid of the lysosome that is full of cystine and create a new lysosome to take its place,” Dr. Emma says. “Genistein can activate this pathway, so it’s logical to see if it can benefit cystinotic cells.”

For more than a year, Dr. Emma has been testing the compound on cystinotic mice, with positive results.

“There’s a clear protective effect on the kidneys, which is a very good result,” he says. “Now we’re testing the different concentrations to validate the safety profile.”

Genistein has hormonal properties, so additional testing is needed with male mice in particular, to ensure there are no hormone-related side effects.

“So far, we’re seeing very encouraging results,” Dr. Emma says. “We’re still trying to find the best dose, and we still need to double-check for other side effects.”

As genistein and Compound No. 2 progress toward human trials, Dr. Emma’s lab will screen other similar compounds “for their ability to rescue metabolic pathways that are altered in cystinotic cells but not rescued by cysteamine.”

As he expresses optimism for this line of research, Dr. Emma notes that his investigations wouldn’t be possible without the support of the CRF.

“From the start, the CRF has been the major sponsor of all this work,” he says. “Even as we got some institutional funding from European agencies, 80 percent of our support has come from the CRF.”

The researcher also underscores that he’s working to give cystinosis patients more comprehensive treatment options but not to replace the ones they have.

“Cysteamine is a very good drug that has changed the lives of people with cystinosis,” he says. “But it has side effects, and it doesn’t correct every single aspect of cystinosis. My goal is to find something that acts on the pathways that are not corrected by cysteamine. These two drugs we are testing now seem to do exactly this.”

# PRECURSORS TO SUCCESS

**Less dosing, fewer side effects and an affordable price — that’s the vision for a new drug candidate soon to start human testing, thanks to CRF support.**

BY DENNIS ARP

When a new drug is approved, how should we measure its success? For investors, profitability is a critical component, to be sure. For patients, the yardstick is effectiveness and affordability, as well as a lack of harmful side effects.

Sometimes these considerations come into conflict. That’s when visionary industry leaders like Patrice Rioux, MD, PhD, and Vince Stanton, Jr, MD, step in.

The two are co-investigators on an exciting new project that carries considerable promise for cystinosis patients. If that potential is realized, patients and their families will get **A NEW TREATMENT THAT’S EXPECTED TO BE SUPERIOR TO CYSTEAMINE**, particularly with respect to the side effects they currently know and loathe.

“If their idea is real, it will be revolutionary,” says Nancy Stack, president and founding trustee of the Cystinosis Research Foundation (CRF).

Rioux and Stanton have formed a company called Thiogenesis Therapeutics, Inc. Rioux formerly worked as chief medical officer at Raptor Pharmaceuticals, where he helped pioneer Procysbi®, the delayed-release form of cysteamine. Now, with funding support from the CRF, Rioux and Stanton have taken up the challenge of providing a better treatment option to the cystinosis community.

The two are focused on success as seen through the lens of a singular measure.

“When we talked with Nancy and the CRF about the possibility of this new drug, we said, ‘If you commit to us, we’ll commit to you,’” Rioux said. “I’m nearing the end of my career — my goal is not to make a huge amount of money. The goal of this project is to produce a drug that improves lives at a fair price.”

The project is motivated by many of the same considerations that led to the development of delayed-release Procysbi® (early development of which was also funded by CRF), including twice-a-day dosing and reduced side effects. However, the researchers seek to change how cysteamine is administered and absorbed.

“What we’ve come up with is a cysteamine precursor — a molecule that is degraded into cysteamine in the

gastrointestinal tract,” Stanton said. “This is a multistep degradation process, and because each step takes time, the conversion of the precursor into cysteamine is spread out. That allows cysteamine to be absorbed throughout the gastrointestinal tract.”

In this way, the precursor concept replicates the best aspect of Procysbi® — that the delayed-release version of cysteamine requires only two doses each day, versus the typical four doses of Cystagon®. More time between doses makes a huge difference in the quality of life for patients and their families. But less dosing also means that those doses need to be stronger.

“You’re trading off the benefits of twice-a-day dosing against the downside of some patients seeing higher peak levels [of cysteamine], which is what drives the side effects,” Stanton said.

For many patients, those side effects are horrific. Sulfurous body odor and oppressive bad breath create great hardships, often derailing drug compliance.

The precursors Rioux and Stanton are studying help level out the peaks and valleys of cysteamine’s effects, the researchers say. That’s because of the slow-and-steady way the drug is degraded and subsequently absorbed into a patient’s bloodstream.

These precursors are taken orally, and as digestion breaks them down, they are naturally converted into cysteamine by chemicals and enzymes normally present in the gut.

“In the first part of the gastrointestinal tract, we see a limit in the rate of degradation, which prevents the spike in cysteamine levels observed with both Cystagon® and Procysbi®,” Stanton said. “This helps to spread out the absorption over many hours.”

By comparison, Cystagon® is entirely absorbed in the stomach and the first part of the small intestine, usually within three hours, Stanton noted. Meanwhile, Procysbi® “is pretty much dissolved and absorbed in the first third or first half of the small intestine,” he added.

“The rat data for our drug indicates that the drug is present all throughout the small intestine and into the colon. Other researchers have shown that cysteamine can be absorbed from almost the entire gastrointestinal tract,”

*Thiogenesis Therapeutics, Inc.*

Belmont, Massachusetts  
San Diego, California



Stanton said. “We are looking forward to testing to see if we can get this same pharmacokinetic effect in people.”

The researchers anticipate that by preventing the high transient concentrations of cysteamine in patients’ systems, their precursor drug will reduce or possibly even eliminate side effects, while still being able to deliver a therapeutic dose.

“Even if we increase the dose, we’re not seeing an increase in the peak concentration,” Rioux said of the rat data.

Another advantage of prolonged absorption is that the drug should accommodate twice-a-day dosing, the researchers note.

“It’s not inconceivable that there could even be a once-a-day formulation,” Stanton added. “But I don’t want to promise that.”

After more testing with rats, the next step will be clinical trials, which they plan to begin in Australia, where many first-in-man studies are done to take advantage of an expedited review process.

“It’s a way to move faster to approval,” Stanton said. “From there, we can bring our data to the FDA or the European Medicines Agency.”

The first phase of human testing will focus on healthy volunteers, who are typically the first population studied to establish a basic understanding of how a new candidate drug is absorbed, metabolized and excreted. The researchers will be particularly interested in tracking blood cysteamine levels over time. “We’ll learn an enormous amount from that study,” Stanton said. If all goes well, those trials could begin early next year, to be followed by a phase II trial later in 2019, and ultimately a phase III clinical trial involving about 40 cystinosis patients.

Though it’s hard to predict how fast the process will progress from there, the researchers hope to seek FDA approval as soon as 2020. As the testing continues, Rioux and Stanton also expect to learn more about possible uses for the precursors in treating other indications.

One thing they know for sure right now: The project wouldn’t be where it is without the assistance of the CRF. “That support is central to our company’s success to date,” Stanton said.

Working with the CRF as well as meeting cystinosis families at the Day of Hope Family Conference help reinforce the Thiogenesis team’s commitment to developing a drug that’s both effective and affordable.

# RESEARCH BREAK-THRU

**NEXT STEP CLOSER**



**Vincent Stanton, Jr., MD**



**Patrice Rioux, MD, PhD**

“I’ve been to many scientific and medical conferences, but I’ve never seen one that did such a good job of capturing the patient’s point of view,” Stanton said. “I found the whole experience inspiring. The support we’ve gotten is a tremendous source of energy and motivation to move this project forward.”



# STEM CELL GENE THERAPY

Stéphanie Cherqui, PhD  
Department of Pediatrics, University of California, San Diego



My research goal is to develop a gene-therapy approach for cystinosis using bone marrow stem cells called hematopoietic stem cells (HSCs) isolated from the blood of patients and gene-correct them before transplanting them back to the patients. We showed that this approach was efficient in the mouse model of cystinosis, and could lead to the decrease of tissue cystine levels and kidney function improvement. We are now finishing pre-clinical safety studies required by the U.S. Food & Drug Administration (FDA) and assembling an Investigational New Drug (IND) application to be able to start a phase I/II clinical trial for cystinosis at UC San Diego; we will submit the IND in December 2018. Stem cell and gene therapy might become a new treatment for cystinosis. If successful in humans, it would represent a one-time treatment that would last for the life of the patients and prevent tissue damage.

In parallel, we are investigating the mechanisms by which HSCs, which are generating blood cells, could rescue a disease like cystinosis and lead to long-term tissue repair. We showed for the first time that HSCs differentiated into macrophages within the tissues and led to the transfer of healthy lysosomes to the adjacent disease cells via long cellular protrusions called “tunneling nanotubes.”

This discovery opens new perspectives in regenerative medicine and in the application to other genetic disorders. Thus, we tested the impact of HSC transplantation in Friedreich’s ataxia, a neuromuscular degenerative disorder for which there is no treatment, and in Danon disease, which is a cardio-muscular degenerative disorder. In both cases, the stem cell therapy was successful in the mouse models, and we are now following the path we paved with cystinosis to develop the stem cell gene-therapy approach for these disorders. Based on our work, Dr. Olivier Devuyst in Switzerland also successfully treated the mouse model of Dent disease, a hereditary kidney disorder.

I began studying cystinosis 20 years ago when I was a graduate student in Dr. Corinne Antignac’s lab, and I started working on the project “Stem Cell and Gene Therapy for Cystinosis” in 2006 when I got my first grant from the Cystinosis Research Foundation.

My main inspiration is the families impacted by cystinosis. I admire the strength and courage of the patients and parents affected by this disease, and I hope to be able to make a difference in their lives.

# EYE DROP GEL



Morgan Fedorchak, PhD  
University of Pittsburgh School of Medicine

We are in the process of developing a topical controlled release eye drop for cystinosis. This unique system includes a liquid carrier that transitions at body temperature to a stable gel. Suspended within that carrier are the drug-loaded microspheres that provide higher drug levels over time without the need for readministration. Our primary objective is to decrease the burden on patients for eye drop administration and improve the overall tolerability of the drug. We strongly believe based on our preliminary work that this will achieve better therapeutic results with less irritation for patients. The goal is to validate the drop for once daily use.

A lot of the work we are doing is relevant for other drugs and diseases, too. There has been a lot of research

on long-term drug releasing systems for glaucoma and other very common ocular diseases. One of the things we are hoping to raise awareness about with these studies is the potential for improved treatment of less common diseases with controlled release technologies. The materials we use are designed to decrease dosing frequency and increase safety, which is widely applicable to many orphan drugs.

Since starting this work, we have hit several major milestones. We have exhaustively refined the microsphere formulation to provide sustained drug release at high concentrations. We completely overhauled our fabrication methods to find the right balance of drug release and compatibility with the gel carrier. We are currently testing

this formulation in large animal studies and are preparing a colony of CTNS +/- mice for efficacy testing. These will be pivotal data that determine the timing and potential for a clinical trial, and we hope to have those data within the year. Fortunately, our current formulation is being made at a GMP facility. This will streamline the clinical trial, as the transition from bench scale to large scale is a common bottleneck in testing drug delivery systems.

My inspiration comes from personal experience with my mother's chronic illness and also from the families I have met in the cystinosis community. I feel very fortunate to have the chance to work in this area and find constant motivation in the hope of offering patients a better quality of life.



# A NO-NONSENSE APPROACH TO CYSTINOSIS

Paul Goodyer, MD  
Montréal Children's Hospital, Québec, Canada



My lab has been funded by the Cystinosis Research Foundation (CRF) to develop a new strategy for therapy of cystinosis caused by a particular type of CTNS gene mutation, termed “nonsense mutations” (NSM). Our project arose from two observations: a) Nearly half of the cystinosis patients in Québec carry a specific NSM (W138X) of Irish origin; b) a series of new compounds related to the aminoglycoside antibiotic gentamicin was recently developed by Eloxx Pharmaceuticals that trick cells into overlooking NSMs. We contacted Eloxx Pharmaceuticals and proposed a collaboration in which we would test their compounds in the lab, using skin fibroblasts from our patients. The project has evolved over the past five years with CRF studentship support for my graduate student, Emma Brassell (2013–2016), and an operating grant (2017–2019).

In cells from our patients carrying the W138X mutation, we were delighted to find several Eloxx compounds that overcame the W138X mutation, permitting expression of the CTNS protein. This reduced cystine accumulation in cultured cells. We also generated a mutant NSM mouse model and showed that ELX-02 also reduces cystine accumulation in the kidneys. There were no signs of toxicity in cells or mice.

In a genetic survey of cystinosis patients, we found that the W138X mutation is dispersed widely across North America, so the strategy should also be applicable to 10–15% of patients outside of Québec. Based on our observations, Eloxx is submitting applications to Health Canada and the FDA for a Phase II clinical trial anticipated at three U.S. and Canadian sites in 2019. If the drug is effective in cystinosis, it should be useful in many other genetic diseases involving NSM.



Doris Trauner, MD  
University of California, San Diego

REPORTING PERIOD  
2/1/18 — 8/31/18

The specific aims of the study are:

**A / TO DETERMINE THE OCCURRENCE AND TYPE OF SLEEP DISORDERS IN ADULTS WITH NEPHROPATHIC CYSTINOSIS.**

**B / TO EXAMINE ATTENTION AND MEMORY FUNCTIONS IN THE SAME INDIVIDUALS.**

**C / TO DETERMINE WHETHER SLEEP DISTURBANCES ARE ASSOCIATED WITH ATTENTION AND MEMORY DYSFUNCTION IN INDIVIDUALS WITH CYSTINOSIS.**

**D / TO DETERMINE WHETHER SLEEP DISTURBANCE AND MEMORY PROBLEMS ARE SPECIFIC TO CYSTINOSIS OR ARE NON-SPECIFIC BY STUDYING INDIVIDUALS WITH CHRONIC RENAL DISEASE (CRD) OF OTHER CAUSES.**

## SLEEP DISORDERS AND MEMORY IN ADULTS WITH CYSTINOSIS AND CHRONIC RENAL DISEASE



The hypothesis to be tested is that sleep disturbances in nephropathic cystinosis are common, and are associated with deficits in sustained attention, working memory and long-term memory.

The research plan includes overnight sleep studies, neurological and cognitive testing of memory and attention in 30 adults with cystinosis and 10 adults with chronic renal disease from other causes.

To date, we have completed testing of 18 adults with cystinosis. The age range of the participants is 26 to 38 years, with an equal distribution of males and females. All participants were in good general health at the time of the study with adequate renal function. None were in renal failure or on dialysis.

Our findings to date indicate a high incidence of obstructive sleep apnea in cystinosis, but somewhat surprisingly, little evidence of memory impairment even in those who have severe sleep apnea. This may be related to a number of factors. First, the individuals we have tested are in good general health with good renal function and taking cysteamine on a regular basis. Second, they are all relatively young, and the long-term effects of sleep apnea may not be present as yet. All of these factors may explain our good results in terms of memory functioning. Those results do not preclude future problems associated with prolonged sleep apnea, however, and it is important that this condition is diagnosed and treated early before cognitive complications arise.



## Cysteamine toxicity on bone: the CYSTEAMINE-BONE project

**Justine Bacchetta, MD, PhD, Principal Investigator**

**Irma Machuca-Gayet, PhD, Co-Principal Investigator**

HOSPICES CIVILS DE LYON, UNIVERSITÉ DE LYON, LYON, FRANCE

### OBJECTIVE/RATIONALE:

As patients with nephropathic cystinosis (NC) receive cysteamine and improve survival, bone impairment was recently recognized as a complication of NC, occurring during teenage or early adulthood. Even though the exact underlying pathophysiology is unclear, at least six hypotheses are discussed, and notably cysteamine toxicity and/or direct bone effect of the CTNS mutation. Because of the potentially dramatic impact on quality of life of this novel complication, research should aim to better understand bone disease in NC.

### PROJECT DESCRIPTION:

This application is based on our recently published data on cystinosis deficiency in human osteoclasts and cysteamine effects in bone cells. The aims are to dissect the underlying mechanisms behind cysteamine toxicity on bone cells. First, we propose to evaluate in a murine model whether and how cysteamine and cystinosis modify the crosstalk between the bone-forming cells (i.e., osteoblasts) and the bone-resorbing cells (i.e., osteoclasts). Second, we propose to expand our preliminary results observed in human osteoclasts with more samples from different European centers in order to perform a genotype/phenotype analysis on osteoclastic differentiation and resorption activity. Last, we propose to use a very innovative animal model in the field (namely the zebrafish model) to assess bone toxicity of cysteamine.

### RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

This application is aimed at improving the general understanding of bone disease in NC, with a specific focus on bone toxicity of cysteamine. In order to answer these questions, we will use novel animal models, cell cultures from murine models and cell cultures from patients in addition to a thorough clinical and biological assessment. Therefore, we should be able to modify NC management by improving the understanding of the underlying mechanisms behind cysteamine toxicity on bone.

### ANTICIPATED OUTCOME:

First, we hypothesize that cysteamine and/or cystinosis deficiency alter secretion and crosstalk between osteoblasts and osteoclasts, and vice versa. Second, we hypothesize that the different mutations in CTNS induce different effects on osteoclastic resorption, with and without cysteamine, thus providing additional evidence to explain different clinical bone phenotypes depending on the genetic background. Last, we hypothesize that CTNS +/- zebrafish display impaired bone mass in comparison to wild-type peers and that cysteamine restores bone quantity at low doses although inducing toxicity at high doses.



## Novel mechanistic and translational studies of neutrophil-mediated inflammation in cystinosis

**Sergio Catz, PhD**, *Research Mentor*

**Raquel Carvalho Gontijo, PhD**, *Research Fellow*

THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

### OBJECTIVE/RATIONALE:

Neutrophils are white cells that circulate in the blood and play an essential role in protecting us from microbial infections through the production and release of substances that are toxic to invading microorganisms. These toxic products, when released in large amounts or in an uncontrolled manner, can be harmful to the host (humans). We propose to study the mechanisms that lead to neutrophil dysregulation and to test compounds (drugs) that have the potential to attenuate the neutrophil-mediated inflammation in cystinosis disease.

### PROJECT DESCRIPTION:

Preliminary data from our laboratory uncovered a dysregulated mechanism of neutrophil granule cargo exocytosis (secretion) in cystinosis. We found that cystinotic neutrophils have increased secretion of pro-inflammatory components and, consequently, high levels of these pro-inflammatory factors were found in circulation in cystinotic animal models. We hypothesize that these factors contribute to the pro-inflammatory phenotype observed in cystinosis. To elucidate the mechanisms that drive neutrophil dysregulation and induce the increased inflammatory process in cystinosis, our group will analyze neutrophil migration and infiltration into tissues in animal models. Besides this, we will investigate the mechanisms that are responsible for increased organ injury in cystinosis induced by exacerbated molecules released by neutrophils. Finally, we will test the ability of novel compounds (drugs) to decrease inflammation in cystinosis.

### RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Inflammatory disorders are emerging as novel, previously unidentified, dysregulated processes in cystinosis. It is anticipated that controlling these processes would have beneficial effects for cystinotic patients. In particular, the study of uncontrolled activation of white blood cells would lead to the identification of novel mechanisms to complement current treatments. The study of the mechanisms that control the release of toxic products by neutrophils will lead to the design of new therapeutic strategies for the control of inflammatory disorders in the lysosomal storage disease cystinosis.

### ANTICIPATED OUTCOME:

The completion of this study will identify novel possible target molecules to avert inflammation in cystinosis. We anticipate that once these targets are identified, we will be able to design more efficient therapies for cystinosis, thus enabling an improvement in quality of life and life expectancy for patients with cystinosis.



## Development and characterization of a rat model of cystinosis



**Francesco Emma, MD, *Principal Investigator***

**Olivier Devuyst, MD, PhD, *Co-Principal Investigator***

BAMBINO GESÙ CHILDREN'S HOSPITAL, IRCCS, ROME, ITALY

UNIVERSITY OF ZÜRICH, ZÜRICH, SWITZERLAND

### OBJECTIVE/RATIONALE:

The aim of this project is to develop and characterize a new rat model of cystinosis to study aspects of the disease that cannot be satisfactorily studied with the currently available mouse model. Specifically, the mouse model that most researchers in the field of cystinosis are using was generated in Prof. Antignac laboratory in 2010. This model has allowed for key discoveries in the understanding of the disease but has limitations. In particular,

- the renal Fanconi syndrome, which is the main characteristics of renal involvement in humans, is mild;
- mice have little muscular and neurological defects, yet these aspects are of major concern in adults with cystinosis;
- bone defects are also considerably milder, compared to humans.
- Moreover, mice are not ideal models to test drugs because their size prevents regular blood testing to measure drug levels and toxicity.

### PROJECT DESCRIPTION:

To overcome these limitations, a Swiss-based company was contracted in 2016 to generate rats harboring mutations in the *ctns* gene, in order to obtain a new model of cystinosis. After 1 year of work using a specific technology termed "CRISPR/Cas9", we have obtained five mutated ratlines, two of which are breeding very well and have generated homozygous animals. These animals have *ctns* gene mutations on both maternal and paternal chromosomes and are therefore expected to have cystinosis. They are currently being tested. In this project, the renal disease will be characterized in the Zürich laboratory, while the Rome laboratory will characterize all other aspects of the disease.

### RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Should the rat model have relevant signs of cystinosis, it will allow a better understanding of certain characteristics of the disease, in particular at the renal and muscular levels. In addition, rats can be used advantageously to test new drugs for the treatment of cystinosis.

### ANTICIPATED OUTCOME:

The ultimate goal is to provide the cystinosis research community with a new model of cystinosis.



## Evaluation of Ctns $-/-$ mice protection by oral supplementation with basic amino-acids: focus on kidneys – extension to another colony



**Pierre Courtoy, MD, PhD**, *Principal Investigator*

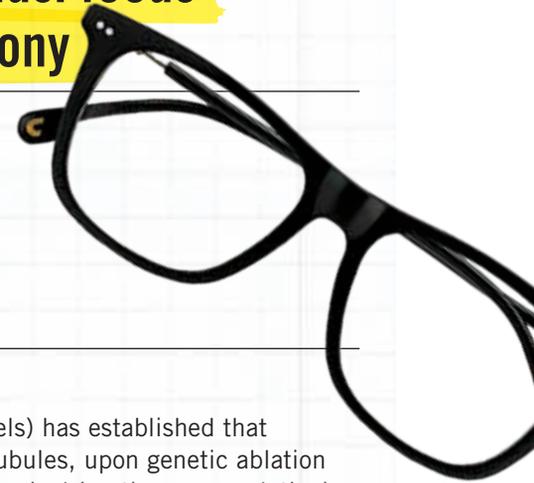
**Christophe Pierreux, PhD**, *Co-Principal Investigator*

DE DUVE INSTITUTE AISBL, BRUSSELS, BELGIUM



**Robert Mak, MD, PhD**, *Principal Investigator*

UNIVERSITY OF CALIFORNIA, SAN DIEGO



### OBJECTIVE/RATIONALE:

Previous work from Courtoy's-Pierreux's laboratory (UCL/DDUV, Brussels) has established that suppression of endocytosis in mouse cystinosis KO kidney proximal tubules, upon genetic ablation of the endocytic receptor, megalin, almost completely prevents biochemical (cystine accumulation), subcellular (crystal deposition, lysosomal enlargement) and tissular disease hallmarks (swan-neck atrophy) *despite absence of cysteamine*. New preliminary results suggest that *megalina inhibition* by a simple basic amino acid (bAA) oral supplementation offers similar *structural* kidney protection. This new application aims at testing for *functional* protection against Fanconi syndrome and renal insufficiency.

### PROJECT DESCRIPTION:

Unlike other settings, cystinosis KO mice at Dr. Mak's UCSD colony still develop predictable renal Fanconi syndrome at 6 months followed by renal insufficiency at 9 months. These cystinosis KO and WT mice as controls will be fed from 2 months of age with a 5-fold supplementation by lysine or arginine as bAA, or glycine as non-bAA control. They will be regularly monitored for growth, metabolic balance (body composition, energy homeostasis) and kidney function (Fanconi, renal insufficiency, etc.); then euthanized at 6 or 9 months of age. Kidney cystine level will be measured by Dr. Barshop, UCSD. Other kidney and liver samples will be shipped to UCL/DDUV and analyzed for expression and localization of endocytic receptors and exemplary solute transporters as well as possible signs of bAA-related toxicity.

### ANTICIPATED OUTCOME:

We expect the dietary supplementation by basic amino acids will offer beneficial effects in terms of ameliorating the Fanconi syndrome and chronic kidney disease manifestation in the cystinosis mice. We will document the changes with detailed measurement of tubular and glomerular function as well as improvements in muscle function and energy homeostasis. If the results are as expected, we hope to be able to proceed to bring this novel therapy to the clinic.

### RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

This study should provide a proof-of-concept that dietary supplementation by basic amino acids, currently used by body builders, offers structural and possibly functional protection of cystinotic kidneys in the mouse model even without cysteamine, and evaluate potential toxicity. If clearly beneficial, such a *simple diet could represent an effective, safe, flexible and cheap adjuvant therapy to cystinotic patients*. Further refining studies should then evaluate dosage titration, synergy by combination, effectiveness of intermittent use, and likely benefits on muscle as well.



## Synthesis and human testing of TTI-0102, a cysteamine pro-drug



**Vincent P. Stanton, Jr, MD, *Principal Investigator***

**Patrice P. Rioux, MD, PhD, *Principal Investigator***

THIOGENESIS THERAPEUTICS, INC.,  
BELMONT, MASSACHUSETTS AND SAN DIEGO, CALIFORNIA



### OBJECTIVE/RATIONALE:

Cysteamine is a life-extending medicine for patients with cystinosis, particularly those able to rigorously adhere to the challenging treatment regimen. Unfortunately, compliance with therapy is difficult because of side effects, including stomach pain, nausea, vomiting, and bad smell, all of which occur around the time of peak blood cysteamine levels. If cysteamine could be delivered to the body at a steadier rate — rather than quickly absorbed and then quickly eliminated — the frequency of side effects should be reduced. This project will test whether a new cysteamine precursor, designed to be slowly degraded into cysteamine in the gastrointestinal tract, can produce a steady cysteamine concentration in the blood of healthy volunteers.

### PROJECT DESCRIPTION:

This is a four-step project: (1) Transfer the technology for producing the experimental cysteamine precursor TTI-0102 from a research laboratory to a drug manufacturing plant. The TTI-0102 synthesis procedure will be scaled up from a few grams to hundreds of grams. (2) Make enough TTI-0102 for human testing. The compound has to be manufactured under good manufacturing procedures (GMP), and shown to be of high purity. (3) Formulate TTI-0102 for human administration. This process involves testing to show that the procedures involved in transporting, storing and administering the compound do not affect its chemical structure. (4) Administer TTI-0102 to healthy volunteers and test their blood cysteamine levels for up to 48 hours afterward. The volunteers will also take a dose of Cystagon®, on another day, to provide a basis for comparison.

### RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

TTI-0102 was designed as a potential treatment for cystinosis. In rat studies, TTI-0102, compared to cysteamine, produced lower peak blood levels of cysteamine, even at three-fold higher doses, while simultaneously extending the duration of elevated blood cysteamine levels (i.e., cysteamine levels remained in the therapeutic concentration range for hours longer). The latter effect should translate into less frequent dosing. However, rat gastrointestinal physiology differs in important respects from humans, so a phase I trial is necessary to assess human metabolism of TTI-0102.

### ANTICIPATED OUTCOME:

The phase I trial in healthy volunteers will show whether the pattern of TTI-0102 degradation and subsequent cysteamine absorption observed in rats can be replicated in humans. If successful, there is a strong rationale for testing TTI-0102 in cystinosis patients. The trial will also provide important information about the relationship between TTI-0102 dose and cysteamine blood levels and reveal the extent of inter-individual variation in TTI-0102 metabolism, information that will be useful in designing subsequent human trials.



## Molecular mechanism of cystinosis

**Liang Feng, PhD, *Research Mentor***

**Xue Guo, PhD, *Research Fellow***

STANFORD UNIVERSITY, PALO ALTO, CALIFORNIA

### OBJECTIVE/RATIONALE:

All forms of cystinosis are caused by the deregulation or malfunction of cystinosin, a membrane transporter protein primarily localized on the lysosome membrane. Elucidating how membrane transporters work to export small molecules from lysosomes is essential for us to understand the cause of cystinosis. Currently, little is known about the molecular mechanism of cross-lysosome membrane transport. In this study, we aim to understand the transport mechanism of lysosomal membrane transporters by biophysical, biochemical and structural approaches.

### PROJECT DESCRIPTION:

We plan to establish a blueprint for the lysosomal membrane transporter at an atomic level through X-ray crystallography. First, the membrane transporter will be isolated and purified to homogeneity. Then the purified protein will be induced to form ordered crystals. After that, the crystals will be subjected to a bright X-ray beam to obtain diffraction images. We will then deduce the structural information from the diffraction pattern and build an atomic level model for the membrane transporter. We also plan to generate highly specific antibodies that bind to membrane transporters tightly, which will provide a valuable tool to probe their physiological functions. In the meantime, we will establish a method to measure the protein's transport activity in a well-defined system and pinpoint key components that are critical for function.

### RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Defects in transporter function cause abnormal cystine accumulation, a characteristic manifestation of cystinosis. Despite its critical role in cystinosis, very little is understood regarding how lysosomal membrane transporters transport cystine and other related small molecules. Our proposed study will fill in the knowledge gap in the fundamentals of cystinosis and will provide insights into our understanding regarding both pathogenesis and therapies for cystinosis.

### ANTICIPATED OUTCOME:

Our proposed research will shine a light on how cystine and related small molecules are transported across the lysosomal membrane and will reveal at the atomic level how membrane transporter proteins fulfill their function. We will also provide a molecular explanation for disease-causing mutations. These studies will help us to better understand the cause of cystinosis and to aid in the development of better therapeutics.





## The effect of resistance exercise on muscle dysfunction in cystinosis



**Richard Reimer, MD**, *Principal Investigator*

**Jacinda Sampson, MD, PhD**, *Co-Principal Investigator*

**Mary Leonard, MD, MSCE**, *Co-Principal Investigator*

**Paul Grimm, MD**, *Co-Principal Investigator*

**Trinh Tina Duong, MPT, PhD Candidate**, *Co-Principal Investigator*

**Feliks Kogan, PhD**, *Co-Principal Investigator*

STANFORD UNIVERSITY, PALO ALTO, CALIFORNIA

### OBJECTIVE/RATIONALE:

Muscle disease (myopathy) is a debilitating complication of cystinosis that causes weakness and swallowing problems, and effects up to three-quarters of patients. Although the progression of the myopathy is slowed, it is not stopped by treatment with cysteamine. Little is known about other factors that might influence the development and progression of muscle dysfunction in patients with cystinosis. In this study, we will test the effect of a short, high-intensity interval training (HIIT) exercise program on individuals with cystinosis.

### PROJECT DESCRIPTION:

In our initial study of children and adults with cystinosis, we found a decrease in lean mass, strength, and endurance. We now propose to establish a longitudinal data set for muscle function in patients with cystinosis from our original study who are able to participate in a follow-up study. In a subgroup of adult participants, we will also assess the effects of a six-week high-intensity interval training (HIIT) regimen. Assessments pre- and post-HIIT regimen will include strength measurements, metabolic testing, pulmonary function tests, and imaging, including MRI with creatine chemical exchange saturation transfer (CrCEST), a state-of-the-art noninvasive measure of muscle mitochondrial function. Optional skin and muscle biopsies will also be included in our current cystinosis biobank for future metabolic and genetic studies.

### RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

We don't know why muscles deteriorate in cystinosis or whether anything can be done to stop or slow down the process. While some with cystinosis exercise regularly, others see the muscle weakness as inevitable and feel helpless. Our study will test whether HIIT can reverse or slow the progression of muscle weakness. If we can prove this hypothesis, it could provide the rationale for members of the cystinosis community to embrace exercise as a way to take charge of their disease.

### ANTICIPATED OUTCOME:

The completion of our study will provide the first set of longitudinal data for muscle and bone health in a large group of cystinosis patients. It also will provide data on the benefits of exercise as an intervention for muscle disease in adults with cystinosis and may provide a rationale for members of the cystinosis community to make informed decisions about exercise as a way to take charge of their disease.

FALL 2018

# CALL FOR RESEARCH • PROPOSALS •

RESEARCH IS OUR HOPE

When Nancy and Jeff Stack established the Cystinosis Research Foundation in 2003 they were committed to aggressively funding cystinosis research to ensure the development of new and improved therapies and a cure for cystinosis. But never in their wildest dreams could they have imagined what has been accomplished in 15 short years. Since its inception, CRF has funded 175 multi-year research studies in 12 countries. Our researchers have published 72 articles in prestigious journals as a result of CRF funding. Every dollar donated goes directly to support cystinosis research.

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

In September, CRF announced \$2.5 million was available for the 2018 Fall call for research proposals and fellowship grants. The grant awards will be announced in December 2018.

In Spring, CRF issued 11 new grants for \$2.39 million which brings us closer to better treatments and a cure. All research applications received by CRF are evaluated by CRF's Scientific Review Board (SRB) comprised of the leading international experts in the field of cystinosis. The SRB provides independent, objective reviews and recommendations for each research proposal submitted based on the NIH scale of standards. Additionally, the SRB follows grant review guidelines established by the CRF and advises the foundation on the scientific merits of each proposal.



In 2010, CRF established the **Cure Cystinosis International Registry (CCIR)** to serve as a hub of information about cystinosis and its complications. Currently, CCIR has 576 registrants from 44 countries. The site, which includes a Professional Research Portal, is a critical resource for researchers and scientists who register to access and view de-identified, aggregate cystinosis patient information. The portal can be accessed at [www.cystinosisregistry.org](http://www.cystinosisregistry.org).

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[www.cystinosisresearch.org/research/for-researchers](http://www.cystinosisresearch.org/research/for-researchers)

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



## Canadian Families Working for a Cure

Cystinosis families from north of the border have contributed to research efforts with the Cystinosis Research Foundation since 2009. Our partnership with Canadians affected by cystinosis has funded research grants, through popular events such as the Swing, Shoot & Liv Golf Classic (Ontario), the JCFG Memorial Golf Tournament (“the most fun you will have on a golf course” - Alberta), and the Hope for James tournament (Saskatchewan). Events like Shoot for Abbi (Ontario), the de Bruyn family’s candle-lighting ceremony at Seth’s Circle of Hope (Alberta), and the Little family’s Paint the Town Purple (Ontario) lend uniqueness to fundraising efforts in Canada and help expand Canadian support for CRF’s mission to find a cure for cystinosis.

Since 2003, CRF has issued 175 multi-year grants in 12 countries. Today, CRF is the largest fund provider of cystinosis research in the world. Canadians funnel their colorful dollars through Canada Helps, managed by the Aqueduct Foundation, and administered by Cystinosis Awareness Research Effort (CARE). Through Canada Helps, CARE has created an efficient and effective fundraising process, allowing Canadians to fundraise and ensure their donors receive a charitable tax receipt. Since 2016, **Canadian families have directly funded research for CRF totaling \$538,012 in grant payments.**

Working together, our two countries have united in their effort to raise awareness about cystinosis, to advocate on behalf of all children and adults with cystinosis and to ensure that we will fund the most qualified researchers in the world. *Unlimited hope and boundless determination for a cure crosses borders and magic happens when countries work together!*

*The CARE and Liv-A-Little Foundations have a strong working relationship with CRF. Erin Little (Liv-A-Little) is a CRF board of trustees member. Karen McCullagh, Crystal Walker and Chad Little are co-chairs of CARE and help guide the funding process. Canadians can donate directly to CRF or contribute to CRF Scientific Review Board approved research studies through Canada Helps.*

## Moms on the Hill – Uniting for Change

In the summer of 2017, Horizon Pharma acquired approval for Procysbi® by Health Canada, the federal department responsible for national public health. The Canadian medical system is divided into 13 provincial and territorial insurance plans, and each province ensures all medically necessary services (hospital, physician and dental) to all Canadian residents. Approval of new medications is done by the federal government, but funding comes from the provinces.

The approval of Procysbi® created a significant and unexpected battle for Canadian families with cystinosis. Firstly, Cystagon®, the original life-sustaining drug for cystinosis, was never approved by the government. For the past 27 years, it was accessible to Canadians through a special access program. When Procysbi® was approved, it resulted in the removal of Cystagon® from the access program, leaving Canadians without Cystagon® even before Procysbi® had been assigned a price point. Needless to say, patients and families scrambled for answers and sought access to the life-sustaining medication.

Canadian cystinosis mama bears are ferocious, and they advocate purposefully and united in spite of 3,000 km of distance between them! **Erin Little, Karen McCullagh and Crystal Walker headed to Parliament Hill in March to meet with various members of parliament regarding these access issues, and their voices were heard.** Currently, a study is underway, investigating Health Canada’s efficacy for patients with rare diseases and Canadian families are determined to have fair costs, availability and access to the medication options for cystinosis. We support the CRF because we know the heart and soul behind it. CRF advocates for all cystinosis patients, regardless of nationality, and although our systems are vastly different from country to country, the cystinosis communities know it is urgent that we advocate for each other.

Canadian families affected by cystinosis continue to warrior on, contributing to the amazing research done through the CRF.

If you would like to learn more about how to fundraise in Canada or make a donation, please contact: CRF Board Member Erin Little ([erin.little@livalittlefoundation.com](mailto:erin.little@livalittlefoundation.com)) or Karen McCullagh ([kcmccullagh@gmail.com](mailto:kcmccullagh@gmail.com)).

# Thank you

# Canada



  
Since 2016,  
Canadian families  
have directly funded  
CRF research with  
**\$538,012**  
in grant payments  
through Aqueeduct and  
Liv-A-Little Foundation.



## Canadian Donations Fund Grants

**Liang Feng, PhD**  
STANFORD UNIVERSITY

*Molecular Mechanism  
of Cystinosis*

**\$37,500**  
*Funded through Aqueeduct*

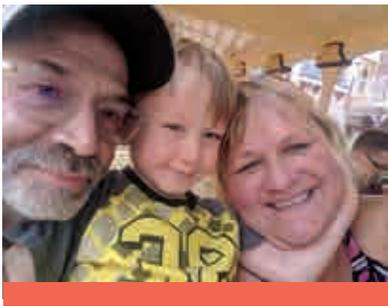
**Paul Goodyer, MD**  
MCGILL UNIVERSITY  
HEALTH CENTRE

*ELX-02 therapy for  
cystinosis caused by  
CTNS nonsense mutation*

**\$37,500**  
*Funded by Liv-A-Little  
Foundation*

# RESILIENCE, MIRACLES, AND KETCHUP!

By Denise Brown, Noah's mom  
SPOKANE, WASHINGTON



## Noah is our miracle in so many ways!

I was never supposed to be able to have children. We had adopted our daughter and were in our second year of fostering two grandchildren. Our lives were crazy, full and happy.

Yet, in 2012, soon after my 44th birthday, I suffered from a pulmonary embolism. Two months later, I still couldn't get my feet under me. I went in for an ultrasound because we thought I might have been facing a bladder cancer diagnosis — instead, we found Noah! I was 15.5 weeks along, and to say we were surprised would be a huge understatement. Twenty weeks later, Noah was born at 35.5 weeks on September 1, 2012 — and 16 days later, he got to come home to our busy household. It was a wonderful miracle.

Noah is a happy, smiley, little boy. His journey with cystinosis seems to be different from many others we've heard.

He did not have hospital stays. In fact, except for one trip to the emergency room for stitches due to an amazing dismount off one of the kids' beds, he hadn't returned to the hospital since his birth. However, like so many others, we noticed that his growth stopped somewhere between ages 2 and 3. We also noticed that he loved water! We joked that he could drink his body weight in water from a really young age. We had talked to our doctor about our concerns, and he kept reassuring us that we had nothing to worry about and he would soon catch up. We had tested him for diabetes twice — both tests came back negative. And although we felt something wasn't right, we couldn't put our finger on it.

February 9, 2018, will be a day that Scott and I will never forget. Noah had an eye appointment with a geneticist to confirm a diagnosis of retinitis pigmentosa, a genetic disorder that runs on my side of the family. During that appointment, Dr. Weed delivered the news that would knock our whole world on its side. He suspected Noah also had cystinosis. Neither of us knew what that meant for sure but would soon learn that the damage done to his eyes was the least of our worries. I begged and pleaded with God to let this be a mistake, to set my life back on its axis, while we waited for test results to come in.

On March 1, the diagnosis was confirmed. It is still amazing to me how

quickly our lives stop and crumble into a million fragmented pieces while the rest of the world continues to move along at a terrifying pace. The next couple of months were a total whirlwind. In fact, much of our life still feels like that. Many people we've connected with through the CRF have assured us that it will slow down and not be so hard. We look forward to that day.

Through it all, Noah has been a trooper. He is confused about why he has a G-tube, and he doesn't understand why he has to take so many meds every day. He also is trying to make peace with the fact that he feels nauseous and throws up almost daily. He mourns his old life but is resilient and a fighter! He loves to play with his siblings, and he has become an excellent swimmer and joke teller. He is always hungry for anything that "goes with ketchup." Noah will start kindergarten soon and is still unsure about how he feels about it. We know he will do great.

We know Noah was given to us for a reason. He has gone through so much in his short little life. We are so thankful for all of those we have met through the Cystinosis Research Foundation and the cystinosis community. We don't know how we would have gotten through all this without the resources they have provided us. Like everyone else in this community, we are waiting for the cure and holding on for Noah's miracle.



HE LOVES TO  
PLAY WITH HIS  
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SWIMMER AND  
JOKE TELLER.



HE MOURNS HIS  
OLD LIFE BUT HE  
IS RESILIENT AND  
A FIGHTER!

# BIG HAIRY DEAL: A FAMILY'S QUEST TO PAY IT FORWARD

Andrew was diagnosed with cystinosis at 17 months, and we have been blessed by the love and support of the cystinosis community for the last 14 years. As we have been on the receiving end of so many “silver linings,” it is important for us as a family to pay it forward to others facing battles of their own.

Donating hair has become a bit of a family affair for us. Starting back in 1999, Andrew's big sister Kelsey donated almost two feet of her hair to Wigs for Kids. Over the last few years, Andrew's cousin Aisling and his uncle Alan's wife Naoko (Coco) have also sheared their lovely locks in support of patients battling cancer.

In a world where we could easily become consumed in the day-to-day struggles of living with cystinosis, recognizing that others are fighting their own battles can be humbling and can help keep things in perspective. Our cystinosis community is so blessed to have an incredible support system, amazing researchers, doctors and nurses. We have incredible families forging ahead with ways to raise funds for research and lift the spirit of others who may be struggling.

In 2012, what started out as a bet between friends, grew (literally) into an epic commitment to raise funds for cystinosis research and pay some of that good will forward. Andrew's uncle Alan and a friend from work placed a bet with each other to see who could grow the most ridiculous mop of hair. Seven months into their challenge, his competition conceded.



As Alan recounts it: **“The next day, a woman we worked with showed up bald, having just donated her once beautiful long hair to the Canadian Cancer Society. I figured, ‘I’ve looked ridiculous for this long — I suppose I can grow it a little longer and see that it goes to a good cause.’ Five years and a couple feet of hair later, we auctioned off the rights to shave my head at our 2016 annual charity event [Forefather’s JCFG Memorial Charity Golf Tournament]. The money raised went to the Cystinosis Research Foundation, and the hair went to the Cancer Society.”**

# Before and Afters



Uncle Alan



Coco



Cousin Aisling



Andrew!

Andrew, who adores his uncle, decided he would also grow his hair in support of Alan, but was not quite ready to say goodbye to his lovely locks in 2016. So, the “grow-a-thon” continued for another two years.

Andrew started 10th grade this year, and as part of the transition into a new high school, he decided it was time to cut his hair and donate it to Angel Hair for Kids. Over the long weekend in September, the deed was done. Andrew’s beautiful mane was sheared off and sent away to make a wig for a child battling cancer. He started school with the shortest haircut any of his schoolmates have ever seen him wear. While it is still strange to see him without his infamous locks, he sure does look handsome sporting his new look.



By Karen McCullagh-Cunningham, Andrew’s mom  
LANGDON, ALBERTA, CANADA

# MY GRATITUDE RUNS DEEP

By Jenni Kloete, Katie's mom  
FRANKLIN, TENNESSEE

When I was a little girl, I had a big brother named Jeff. He would ride his tricycle while I stood on the back of it, and he peddled both of us up and down the driveway. We played Batman and Robin, and sometimes he'd let me be Batman, which made him the best big brother ever. We pretended to fish while standing on the coffee table, because who needed a lake full of bass when you had tons of imagination? We laughed and giggled a lot. He was the coolest little guy I knew.

I had a younger sister. Her name was Jan. Jeff and I wanted her to play with us, but mom was always holding her and would tell us she was too tired to play. Then one day, mom took Jan to the hospital. Jan never came home again. Every time I asked about her, mom and dad's eyes would swell up with tears.

Jeff and I were playing one day, and I noticed he was shorter than me. I thought that was weird because he was the oldest. When I asked mom why, her eyes would tear up. Not long after that, Jeff went to the hospital. He didn't come home either.

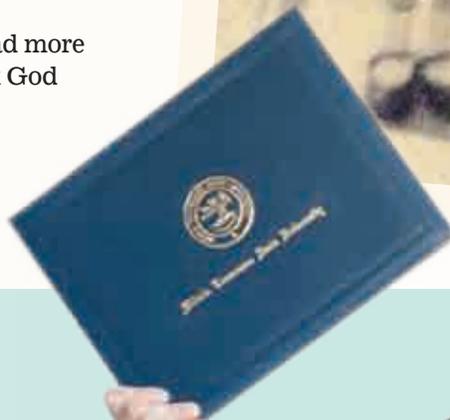
A few months later, mom had another baby. A girl. They named her Hope. She had big blue eyes and smiles for days. I was so happy to have a little sister. She loved to make noise. She would sit in the kitchen floor with pots and pans and bang them together to make the loudest clang and clatter I'd ever heard. Then she would laugh and laugh. I can still hear it. We were all so excited to have her in our lives. But that dreadful day came. The day she went to the hospital. I cried and cried because I knew she wasn't coming home — and she didn't.

I don't have cystinosis, but I have lived with it my whole life. I've been scared of it. I've been angry at it. Mostly, I've prayed for it to just go away.



I grew up, got married and had three daughters. My middle girl was born with spina bifida. So one day, I picked up a magazine for special needs moms, as I had become one. I found a tiny article about cystinosis. I saved the magazine, as I intended to inquire if there was a cure yet. I just wanted to know. But life got busy raising three little girls, and I didn't inquire. When my baby was 2, I began to notice some changes. She only wanted to drink water and she wasn't eating much, and potty training was not working. My mom was growing more and more concerned, but I wasn't going to let cystinosis back in our lives. No way! This is not what she had! But it was. I was right back in the middle of the cystinosis nightmare. I've often wondered if God led me to that article in the magazine as a heads up.

My baby, Katie, who is now 26, has had more hospital stays than I can count. I thank God she came home after each one. And I thank cystinosis research for making it possible. Without the research and the advances in treatment, she wouldn't be here. I'm still scared of cystinosis, and I'm still angry at it — but my focus is on finding a cure. I didn't know how to contribute or where to start with fundraising. My husband, Katie's stepdad, came up with the idea. He's a New Orleans native living in Nashville who misses his hometown traditions. So we started hosting a small neighborhood crawfish boil benefitting cystinosis research. We're still pretty new at this, but as we learn, we hope to increase our annual donation. It's all about starting somewhere to help the end goal, finding a cure! Next month marks 16 years since giving Katie my kidney. She has done remarkably well. She recently earned a bachelor's degree from Middle Tennessee State University, and this mom couldn't be more proud. Our family is extremely grateful for the cystinosis community, the doctors, the research and the hope for a cure.



READ ABOUT  
THIS YEAR'S  
CRAWFISH BOIL  
ON PAGE 75

Katie Roy  
celebrating her  
Bachelor's  
Degree.



OUR FRIENDSHIPS  
WITH THESE  
FAMILIES EXTEND  
BEYOND CYSTINOSIS,  
WHICH IS BY FAR THE  
MOST IMPORTANT  
PART OF THIS.

# Cystinosis Silver Lining:

## Our 2018 Cystinosis Vacation

By Jill Emerson, Brooke's mom

HAMMONTON, NEW JERSEY

One of the hardest things about my cystinosis journey has been the loss of pre-cystinosis friendships — friends who didn't understand why I had to cancel so frequently because of doctor appointments or rough mornings, friends who didn't know what to say about our situation, and friends whose paths diverged from Clay's and mine while their children took a different direction than Brooke did. So, not surprisingly, one of the biggest blessings of my cystinosis journey has been the friendships that both Clay and I have forged with parents within the cystinosis community — and the resultant friendships that Brooke has made with their children.

**We first met the Coe family, Megan, Michael and Charlotte, at the Day of Hope 2016, only a couple months after both Brooke and Charlotte were diagnosed. Fast-forward a year and a half, and we had the pleasure of hanging out with the Beauregard family, Courtney, Kevin and Lily, in Delaware at a cystinosis event. And both Charlotte and Lily have the same nephrologist, so it was only natural for us to all plan our 2018 cystinosis summer vacation together. We decided to rent a house on a farm in upstate New York, a location relatively central for all of us.**

The girls instantly took to the house (as did the Coe's newest addition, baby Alex) and made it their home for the next few days. They played ball and ran up and down the large hill in the backyard until they reached exhaustion, thirst or both. The girls also loved swimming in the pool and fishing together with their daddies. After long days in the sun, they could often be found curled up on the couch together for a movie or cartoon show.

Meanwhile, while the kids played, we adults loved hanging out poolside and cooking wonderful dinners together, which we enjoyed while chatting and laughing until we cried.

Our friendships with these families extend beyond cystinosis, which is by far the most important part of this. We understand each other's lives, our fears and frustrations, and our joys at seemingly little victories. Our cystinosis friends are our "safe place," and we love spending time with them.

The first two years of diagnosis, I kept telling myself that being part of the cystinosis community was a good way for Brooke to meet kids like her — friends who understood what



she was going through and who could walk her journey with her. Now I realize that the community is a great place for Brooke to make friends, period. It's a great place for me — and Clay, too.

We have met amazing lifelong friends who understand and accept us for who we are and for what we have going on in our lives. We look forward to vacationing again with the Beauregard and Coe families, and continuing to develop genuine friendships with even more families in the community!



By Diane Neumann,  
Brooke's grandmother  
DOYLESTOWN,  
PENNSYLVANIA

## Cystinosis from a **Mom-Mom's Perspective**

Before diagnosis, I would wake up in the middle of the night and go through the list of possibilities. I knew something was wrong, but the doctors (and there were many) kept telling my daughter Jill and son-in-law Clay, "Brooke will grow at her own rate." But Brooke wasn't growing, and she kept slipping down the growth chart. My brain kept repeating, "No baby intentionally starves itself" — something I learned in nursing school many years ago — but Brooke would not eat. Then came the diagnosis, one I had never learned about in school. What is it? And what will it mean for our precious Brooke and her parents?

After diagnosis, we began to accept that our daughter would have a different life with Brooke than her brothers do with their children. The parenting of a child with cystinosis requires not only learning how to dispense medicine and handle a feeding tube but also how to provide as normal a life for your child as you can under the circumstances. Jill and Clay have found that involvement with the Cystinosis Research Foundation and the community is a great way to

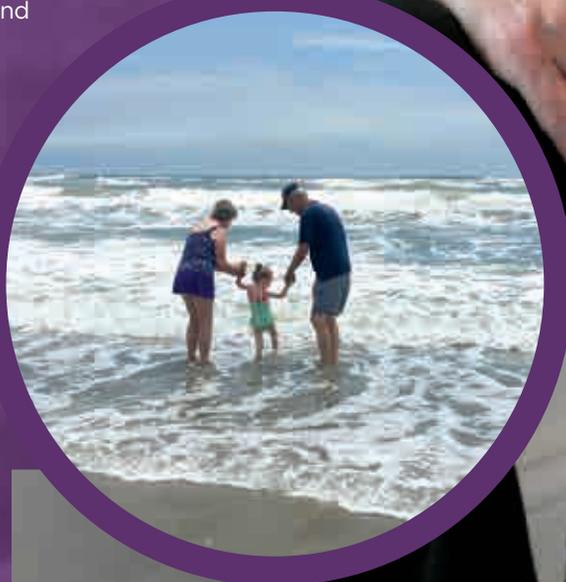
develop an understanding of what to expect and a way to participate in groups that are seeking new ways to handle and hopefully cure this disease.

Brooke may have cystinosis, but it doesn't define her. **At 4 years old, she is a bright, spirited girl with boundless energy and a great big personality.** She knows what she wants and knows how to get it. She chirps away in her Minnie Mouse voice, always asking, "Why, why?" and "How did that happen?"— often referring to herself in the third person. Even though Brooke has a feeding tube, her favorite place to eat is McDonald's (where she always orders extra fries!), and she loves bacon and eggs, spaghetti and meatballs, strawberry ice cream, Popsicles and chocolate.

Brooke knows a trip to Target means a new toy, and she has amassed a large collection. She knows the names of every one, and she panics if one is missing in action! Mountains of stuffed animals fill her room and occupy her bed, and she always brings at least three or four of them everywhere she goes!

Grandchildren are always welcome at the retirement community where we live. In fact, Brooke is the unofficial mascot at Pine Run, where on a regular basis she can be seen playing kickball and walking around the campus with her Pop-Pop, chit-chatting (to herself, or to anyone who will listen) all the while. She loves to play in the small pool we set up outside our cottage, and she fills it with her toys and flowers that she's handpicked from my garden. Brooke has just started ballet lessons and loves posing for us in her tutu and ballet slippers.

The little girl who used to walk under our living room table has grown leaps and bounds in the past year, and we always marvel at her progress. It is a joy to see her thrive in spite of cystinosis. This September, Brooke started pre-K in her school district. Another chapter in the book of her life. She has had so many experiences in her short time here on this earth, so many we would not have wished for, but ones she and her parents have met with grace and determination. There are many things that make her different than other children her age, but there are more things that make her a typical 4-year-old toddler!



# Getting Life on Track



**For many years, we prayed and wished for a fourth member of our family, a second child to add to our tribe and a forever friend for our 6-year-old son, Brendan.**

In February 2017, we received an answer to our prayers. Our Josephine “Josie” Marie joined our family. She fits perfectly and has brought us endless amounts of joy.

Although, as time progressed, around 6 months old, we began to notice other trends and became increasingly concerned. At a mere 16 pounds, Josie’s weight had plateaued. At night, she started dry heaving and having intense cravings for water, paired with severe constipation. Our family pediatrician thankfully took quick action. After several blood tests and outpatient assessments, Josie was admitted to Advocate Children’s Hospital in Oak Lawn, Illinois, for further testing. Following a fairly quick stay in the hospital, in which the doctors were able to balance her electrolytes, Josie was discharged just in time for her first Christmas.

A week into 2018, we received a call that changed everything and confirmed our worst fears: cystinosis. This was scary and overwhelming. Words will never be able to adequately describe our feelings those first few months as this all set in. It was then that we dedicated ourselves to finding out as much as we could about this disease.

Later that month, Josie had G-tube surgery for easier administration of her seven daily medications, as well as extra nutrients. After Josie’s first birthday, it was apparent that further action needed to take place. She was still vomiting several times a day and had yet to gain much weight. We then decided to bring her to Dr. Craig Langman at Lurie Children’s Hospital in Chicago. Langman and his team’s vast knowledge of cystinosis has been lifesaving and life-changing.

In the midst of finding out such news and attempting to research as much as we could about the disease, we also found a community of people online. We will always remember and forever be grateful for the welcome we received when we shared our diagnosis with the cystinosis parents group on Facebook and also our correspondence with Nancy Stack.

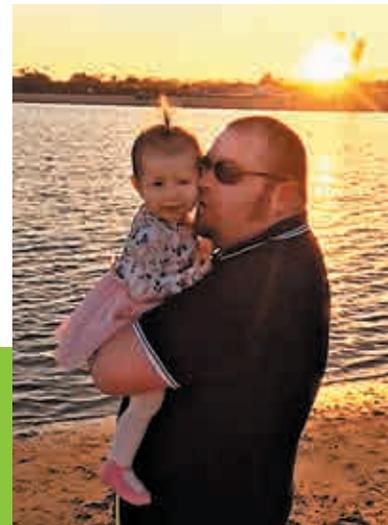
Knowledge is power, and we spent endless amounts of time compiling as much information as possible to ensure that we could give Josie the best care possible. We were informed about an annual meet-up called Day of Hope that was held in California. It was an incredible weekend in a beautiful location. My family and I gained so much from this convention through the information shared and the connections made. Upon looking back on the weekend, seeing all the kids affected by this disease just playing and being “normal” was the best part.

It’s late August now, yet it feels as though it has been years since this all began. So many of the days blended together as we were able to do nothing more than wait. Waiting on insurance approvals, waiting to be discharged from the hospital, waiting for blood work results, waiting on weight gain, waiting on the vomiting to end. We have felt a plethora of emotions throughout this whole process, and it has taken its toll on everyone.

Many times, throughout the years we have heard the proverb that “it takes a village to raise a child,” and we couldn’t agree more. Thankfully, we have an incredible family and friends that help us consistently. They too are becoming more comfortable administering Josie’s food and medications, which has been extremely helpful.

To say that Josie is a different baby now is an understatement. She has gained weight, stopped vomiting, has worked with a speech therapist, thus improving her ability to eat orally, and most importantly — her cystine level has dropped. With the knowledge we have of this disease, we are aware that the journey ahead of us is long and winding. But together, as a family, we are beginning to get our lives back on track.

Josie’s vivacious and determined spirit has carried her through it all and has helped to get us where we are today. She strives to be Miss Independent and is the “Boss Baby” of our home. Josie tries to keep up with her older brother every day, and we are so thankful for this. During one of her hospital stays, we



By Tom and Katie Kanupke, Josie's parents  
OAK FOREST, ILLINOIS

were told by a nurse how lucky Josie is to have an older brother to look up to — and to be honest, we couldn't agree more. He is her motivation, and she is without a doubt, the apple of his eye.

As parents of a child with an incredibly rare disease, we know how lucky we are. While “lucky” may seem like an outlandish adjective to apply within the context of our child's diagnosis, it is fitting. We are lucky that we have the availability of treatment options and the determination of the Cystinosis Research Foundation to continually find better treatments — and hopefully one day, a cure.

As Josie's parents, the hope of finding a cure is what gets us through each day and keeps our hopes and dreams for her future alive. We have been beyond impressed with the generosity, support and fundraising efforts of the Cystinosis Research Foundation. The CRF's ability to not only help our family, but hundreds of others, has inspired us also to want to fundraise. With that said, we have decided to host our first fundraiser for the CRF in our daughter's name. **“Getting Jolly for Josie” will be held on December 8, 2018, in Blue Island, Illinois.** We are excited to host this event and are determined to end this year in a completely different way than how we started.

Thanks for taking the time to read and share in our story.

GETTING **Jolly** FOR Josie

JOSIE'S VIVACIOUS  
AND DETERMINED  
SPIRIT HAS CARRIED  
HER THROUGH IT ALL  
... SHE IS THE 'BOSS  
BABY' OF OUR HOME.

For more information about “Getting Jolly for Josie,” please contact Laura Christopherson at [lmchristophers30@gmail.com](mailto:lmchristophers30@gmail.com).



# FIRST FUNDRAISER FOR THE WIN

By Erin and Jim O'Leary, Aidan's parents

CHICAGO, ILLINOIS

Dear Friends,

Last month, we successfully launched our first-ever charity event for Aidan — Aidan's Army Golfs Fore a Cure. Thanks to the generosity of our amazing donors, friends and family, we were able to raise \$63,133 in proceeds for the Cystinosis Research Foundation!

Participants from across the country gathered at Forest Lake Country Club in Bloomfield Hills, Michigan, to join Aidan's Army. Our supporters' generous contributions will fund pivotal research, which will lead to better treatments — and hopefully the cure — for cystinosis in the near future.

We are so unbelievably thankful to Katie and Bob Emerine, Mike O'Leary and our dedicated team of volunteers. Your tireless efforts made this fundraiser possible, and we are forever grateful for everything you've done to help our Aidan.

Aidan is an extremely active and happy 2-year old. He particularly loves to wrestle, play with his Hot Wheels, attend swim class and play with his dog Gus. He now weighs more than 30 pounds and grows taller every day, and we feel very blessed that he is thriving. Of course, there are challenges, but Aidan remains very stable and healthy within his disease. We continue to be astounded and proud of his unwavering strength and determination.

We are very hopeful for the future, mainly due to the outstanding work being funded by the CRF. Thank you again to everyone who joined Aidan's Army, and we look forward to hosting you again next year. We will continue to fight until the cure is found.

Love,  
Erin and Jim O'Leary



A young child with red hair, wearing a white short-sleeved shirt and blue and white striped pants, is walking barefoot through a fountain of water. The child is smiling and looking back over their shoulder. The background is a blurred outdoor setting with trees and a fence.

WE CONTINUE TO  
BE ASTOUNDED AND  
PROUD OF AIDAN'S  
UNWAVERING  
STRENGTH AND  
DETERMINATION.

## *Our sweet girl,*

Stella Grace, entered this world a happy and seemingly healthy baby on January 30, 2017. Her first year of life was everything we had hoped for and more. She was meeting her milestones as expected and loved learning about the new, big world around her.

Her 12-month wellness check with the pediatrician seemed like a typical visit; however, one thing stood out to the doctor that was concerning. Stella had not grown in height or weight since her 6-month wellness check. Because her big sister has always been small compared to other children her age, we weren't too concerned. The doctor wasn't too concerned either, as he noted the small stature of the rest of the women in Stella's family. But he asked to see us back a few months later to ensure Stella was growing and continuing to meet her milestones.

March 14, 2018, will forever be a life-altering day for our family. On this day, we visited the pediatrician and learned Stella had not grown and actually lost weight. Many different, possible diagnoses were suggested to us — diabetes being one of them — but ultimately, blood work would be the true test to give us clear answers. It wasn't until that night that we received the heartbreaking news. Our baby girl was, in fact, in great danger of a serious illness. That same evening, we were rushed to the nearest children's hospital, where we spent the next 28 days. After many days of testing and lots of blood work, Stella was finally given a diagnosis, nephropathic cystinosis.

We had no idea how serious this disease was until we began to educate ourselves. Cystinosis is a terminal metabolic disease in which the amino acid cystine gets into the cells but has no transporter out. Because of the defect in transportation, the cell crystallizes, causing early cell death. Cystinosis slowly destroys the organs in the body including the kidneys, liver, eyes, muscles and the brain. Current treatments to slow the progression of cystinosis require a strict regimen of medicines every hour of every day. The treatments must also be adjusted often based on the results of kidney function, frequent blood work to monitor nutrient levels, eye exams and much more.

Since her diagnosis, she has begun a rigorous medicine schedule. These meds have improved her quality of life. Her muscles are stronger, she's more energetic, she's slowly gaining weight (thanks to her gastrostomy tube), and she's beginning to meet her milestones. As we are well aware of the devastation this disease can cause to Stella's body, we are hopeful she will continue to be a bright, happy, playful little girl through it all — because that's what she's been since day one of her diagnosis.

Because cystinosis is such a rare disease — only 500 diagnosed in the United States (2,000 worldwide) — the Cystinosis Research Foundation (CRF) is vital to those living with this disease. The CRF is dedicated to finding better treatments to improve the quality of life for those with cystinosis and to ultimately find a cure for this devastating disease. This foundation has already done so much for my family, and we truly believe this foundation will save our baby girl's life. Nancy Stack, the founder of the CRF, is a positive light in our cystinosis community and brings us hope for a better future for our loved ones.



STELLA LOVES  
LEARNING ABOUT  
THE NEW, BIG WORLD  
AROUND HER.

# STELLA GRACE

By Christine and Nate Miller, Stella's parents  
PORT CLINTON, OHIO

# accepted and understood

By Jenny Raycraft  
CALGARY, ALBERTA,  
CANADA

Cystinosis has affected my life in a way that I consider to be both a blessing and a demanding obstacle. Cystinosis has made me realize how precious life is and to never take anyone or anything for granted.

What I have been through in the past 24 years of my life, most people don't encounter in their entire lifetime. The countless appointments, medications and surgeries are a difficult burden, especially now as an adult with cystinosis. The time commitment to manage cystinosis is challenging, especially with a full-time job or while being a student. I try to remain positive and resilient every day. Having a strong support structure around me is the key.



I have the world's most supportive parents who have always been there for me and continue to give me unconditional love, which has helped me in a bigger way than words can even begin to explain. Not only do I have my parents, but I have my partner who has been the most supportive, nonjudgmental, loving and caring individual I have ever met. I never thought I would have someone like Steven in my life, and I can't thank him enough for being that person for me.

When we attended the Day of Hope conference earlier this year, I felt totally accepted and understood, and now I have the support of the cystinosis community, which has greatly impacted me. I so appreciate the support of the Cystinosis Research Foundation and everything they continue to do for me and the cystinosis community.

People who meet me and who are unaware of my affliction, often remark how mature I am for my age. The challenges of cystinosis; multiple painful leg surgeries as a teenager; the responsibility of adhering to daily medication regimens, the social discriminations, etc., to name a few, have forced me to develop characteristics of personality that have helped me cope accordingly.

I feel extremely blessed to be where I am today with the people I have in my life and very fortunate that at the age of 24, I have yet to have a kidney transplant.

I am forever grateful to my caring nephrologist, Dr. Julian Midgley, and to my dedicated parents for their contributions in facilitating responsible management of my health and well-being.

Lastly, after going to my first Day of Hope in March, I feel more "hopeful" than ever that there will be a cure for cystinosis.



I FEEL EXTREMELY  
BLESSED TO BE  
WHERE I AM TODAY  
WITH THE PEOPLE I  
HAVE IN MY LIFE.



As Jenny's parents, it's often been painful to witness her daily struggles through life, and yet it has seemingly afforded her with a unique perspective that has helped shape who she is as a person. Witnessing her resilience and perseverance is heartwarming. And her unique ability to balance fragility with braveness has always been an inspiration.

We are grateful for the hard work and dedication of the CRF and the health care professionals committed to bettering the lives of cystinosis patients. We are especially hopeful for the research being done by Dr. Stéphanie Cherqui and her team to maybe one day make cystinosis go away forever.

—Brent and Jodi Raycraft



SEE THE BIG  
RESULTS FROM THE  
7TH ANNUAL LOTS OF  
LOVE FOR LANDON  
GOLF OUTING ON  
PAGE 74

# TIME FLIES

By Lauren Hartz, Landon's mom

PITTSBURGH, PENNSYLVANIA

There are moments when I think back to those days, soon after diagnosis, when Landon was 14 months, and I feel so much gratitude for where we are right now. Jimmy and I reflect on those times and say to each other, "I don't know how we did that." There are many moments that were lived in a state of survival. The brain has a way of helping us to get through challenging times. We don't feel or process — we just go. It does catch up, but the catch-up is an adventure for a future time.

My childhood neighbor used to tell my mom that "once the kids start school, the time flies by." Her experience feels very true to me. Landon is 8 years old and in second grade. He is the big man on campus in his school, which includes kindergarten through second grade, so the nurse and his medication routine is already established. I have had one or two email exchanges with his teacher, and I have not yet seen his classroom. But he continues to thrive, despite mom not having control or insight into his day-to-day adventures in school. He has found his own best friend, again, and has decided, at least for the past week, to do extra math homework so that he can clip up on his color chart. "It doesn't matter to me, buddy, where you end up on the behavior chart. As long as you are being helpful, kind and listening to the grown-ups, I am happy." He responded, "I know, mommy. I want to do it because I want to do it." He still loves and wants me to write notes to put in his lunch box, so I'm holding onto that for now.

Landon has not only found his place in school, but year after year, fall after fall and spring after spring, when we ask him what extracurricular activity he is interested in doing, he reminds us that he plays soccer and wants to continue to do that. "Soccer is my sport," he proudly tells us.



I have to admit that my anxiety presents at times, and I find myself saying, "I just hope that he can keep up and that he can play as long as he wants to play." And then I remember a conversation that Landon had with his dad last year. "Daddy, I really want to score a goal," he told Jimmy. I was waiting for the "keep practicing and working hard"

— which is the usual message in our house. Jimmy responded, "Buddy, if you want to score a goal, you have to play smart. Most of those kids are bigger and faster than you." My heart sank, and I thought, "What if he doesn't realize that yet? What are you doing?!" Landon shook his head up and down, "I know." Jimmy continued, "You have to get open so that they are running behind you. You probably aren't going to be able to catch them." Landon lit up, "Oh, yeah! That's a good idea." So you see, I have learned to keep my mouth shut sometimes. He hasn't yet scored a goal, but the new season is beginning!

As he grows and matures, Landon is finding his way. And rather than relying on his dad and me to stay slightly ahead of him and guide him, we are now in a place of standing slightly behind him and trusting him. Challenges will no doubt present themselves, and I know that we are not on an easy path for the rest of our lives. None of us can say that, and we certainly can't say that for our other child, Jordan, who does not have cystinosis, either.

I don't know what the future holds for our family, but I trust that all of us will do our best and that we will move through adventures and challenges. We will cheerlead through the fun stuff and support each other through the difficult times. And now that I have two little boys who go to school all day, I am going to enjoy more silence and hot coffee.

CHECK OUT THE  
STANDINGS FROM  
THE 2ND ANNUAL  
24 HOURS FOR HANK  
GOLF TOURNEY ON  
PAGE 75



# Henry turned 12 in July! SUMMER FUN

By Tricia Simms, Henry's mom

SANDPOINT, IDAHO



In the past year, Henry has become very responsible with his med schedule, often reminding us that it is “med time.” I’m proud of his maturity and dedication to his health but saddened that at 12 years old, this is something that he must think about.

Henry also has become much more aware of cystinosis and how it affects him. One week before his 12th birthday (on July 19), he asked me what the status of the cure was. I gave him the best update I could. I was questioned on if I think the cure would work, the what-ifs and what the plan is if it doesn’t work. All tough questions for sure. He followed up the conversation with, “Well, my birthday is next week, and that just means that I could be getting closer to dying.”

My first thought was to crush this thought, tell him to not worry about that, tell him that everything will be ok, but I didn’t. I did reassure him that we are doing everything possible to find a cure quickly and pointed out all the people much older than him and how well they were doing. It is his right to worry about these real things in his life though. Henry is looking forward to the new delivery system for eye drops. He asks me for updates every couple of months. He knows how important taking the hourly eye drop is, but getting them in five times a day is a struggle.



Henry had a great summer starting with a quick trip to Seattle in June for his semi-annual checkup at Seattle Children’s Hospital. All levels looked good, and they were able to decrease a couple of doses of medicine. Henry spent a lot of time at the lake this summer, played with his friends, went to summer camps and traveled with his grandparents for a week to visit the Oregon coast. He also was able to spend four days with Tina Flerchinger and her family in Clarkston, Washington. He loves to visit them and spend time with Tina.

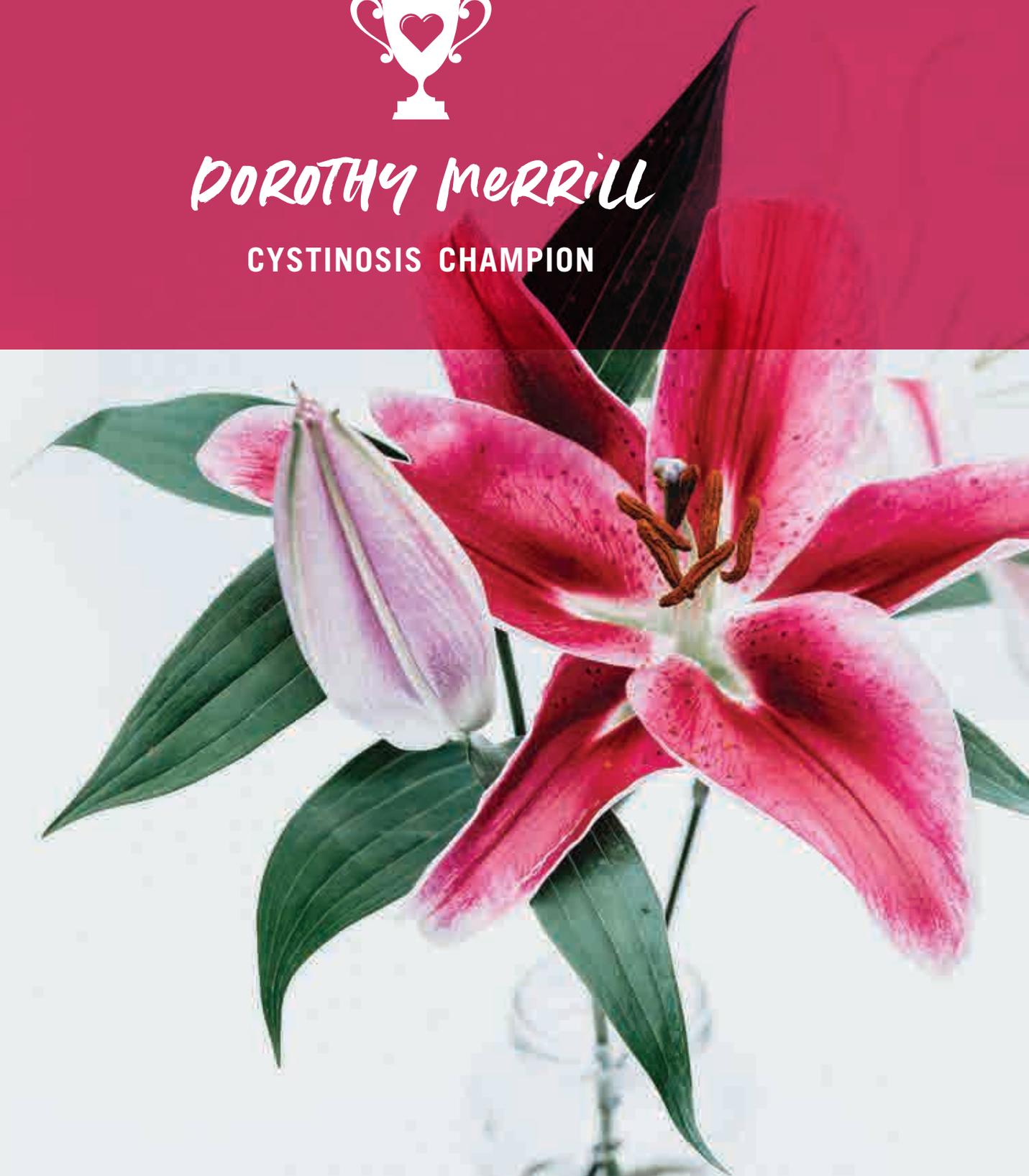
Fall finds us busy with school starting, flag football and Henry’s first year of band! And we are excited about the upcoming ski season.

Our next fundraiser, 2400 Feet of Schweitzer, is scheduled for March 23, 2019. The new format for this fundraiser was an enormous success last year, and we are looking forward to doing it again.



*DOROTHY MERRILL*

**CYSTINOSIS CHAMPION**



# Charity Never Faieth



By Stephen Jenkins, MD, Sam and Lars' dad

SALT LAKE CITY, UTAH

For this issue of the magazine, I wanted to write about one of our heroes, Dorothy Merrill. We first met Dorothy when we moved to Salt Lake City, Utah, for medical school. She was a nice, older lady in our congregation at church. Samuel was diagnosed with cystinosis shortly after we moved to Salt Lake City, at the age of 1. We would bring him to Sunday school with us, and he'd sit on our laps, usually hooked up to his feeding tube. Sometimes we sat in front of Dorothy, and she always took an interest in Sam. It was clear she really liked kids, and had a good sense of humor.

In 2014, we had our first big fundraiser at a park near our house. We invited everyone we knew in the neighborhood, including many of our friends from church. We had a silent auction, bake sale and cream soda cart for our first event. Dorothy came with some other ladies from church, and she surprised us with a check for \$500. My eyes filled with tears, as I was overwhelmed by her generosity. At that time, we didn't know Dorothy very well, but that didn't stop her from showing us her love for our family.

Dorothy was born and raised in Davis County, Utah. She was a child of the Great Depression era. Her father ran a canning factory. She was the oldest of five children. She came of age during World War II. She went to college at Utah State University and studied education. Dorothy took her first job teaching elementary school in Clearfield, Utah, where she was a teacher for 27 years and taught kindergarten through third grade.

At the age of 49, Dorothy married Doug Merrill. He was also a teacher and a World War II veteran, and

received the Purple Heart as an officer of the U.S. Navy. He was a widower with six grown children from his first wife. Although Dorothy never had children of her own, she loved being a grandmother to 28 grandchildren. By her estimate, she now has over 100 great-grandchildren and 10 great-great-grandchildren.

Shortly after marrying Doug, they left their home to serve a mission for the Church of Jesus Christ of Latter-day Saints in Vermont. They were married for 27 years, until Doug died at the age of 95 of leukemia.

After Doug passed away, Dorothy continued to live in the same home in Salt Lake City, where she has been a loving neighbor and friend to those around her. She has taken a special interest in a family from church, a mother named Yheily and her son Daniel. Yheily is from Venezuela, where all her family still resides. Dorothy invites them to all her family activities, and they celebrate holidays together.

Since 2014, Dorothy has donated \$100 a month to our nonprofit organization, Sam's Hope for a Cure, and is one of our biggest (if not the biggest) donors. And she gives it all with love and no expectation of anything in return. We get together with Dorothy, Yheily and Daniel every so often for dinner at Café Rio or the boys' new favorite restaurant, Chuck-A-Rama. We love to hear stories about her life, and she always asks us about all our latest adventures. I'm so grateful she has become part of our lives. While I wish my sons, Sam and Lars, didn't have cystinosis, it has been a blessing to get to know and love people like Dorothy Merrill.



By the time you receive this issue of Cystinosis Magazine, our major fundraising events for the year will be wrapped up. Pictured here is the playful logo advertising this year's Swing & Bling golf and dinner events at Catta Verdera Country Club in Lincoln, California, and Kimpton Sawyer Hotel in Sacramento.

Jenna and Patrick will be 14 years old on December 7. They have excitedly taken part in some of the Swing & Bling event planning this fall, and it's been fun to include them on committees as they participate and learn how it all comes together. The kids have joined me for meetings at the hotel and made suggestions that influenced much of the decoration, food and auction item choices. Having their help and sharing in their excitement for the annual benefit in their name breathes new life into the planning portion for Kevin and me! It is our goal to raise \$300,000 this year, which will once again be passed along to the Cystinosis Research Foundation. Please check out our website at [www.jpfh.org](http://www.jpfh.org) to see a summary of events and funds raised for cystinosis research.

We are grateful to Shannon Bell once again for choosing Jenna & Patrick's Foundation of Hope as her charity of choice, as she participates in Sacramento's Capital Cup 2018 Golf Tournament. Shannon, a dear friend and avid JPFH supporter, will compete with other CEOs in the Sacramento business community for a percentage of an impressive fundraising pot, which will be shared with other local charities. Two years ago, Shannon competed and raised over \$20,000 for JPFH. She has made \$30,000 her goal for this year! Check out the JPFH website at [www.jpfh.org](http://www.jpfh.org) to see how Shannon did this year!



*Jenna, Shannon Bell, and Patrick with Boomer-the-Dog*

We appreciate our friendship with the families we've come to know as a result of cystinosis. We spent time in Idaho with the Alexander family this summer and attended their Hearts for Hadley fundraiser in Boise. We are grateful to be able to work together with other families in various regions of the U.S. and abroad, to raise funds for the Cystinosis Research Foundation.

This summer saw the four of us healthy enough to enjoy our first travels abroad together. Thank you to Ted and Sue Olson for hosting us at their lovely home in Italy! We made memories that will last a lifetime. We hope the trip was the first of many that the kids will be able to enjoy in their lifetimes. There is so much about the way we live, which can be learned by seeing how others live.

In order to convey some of the travel preparations unique to a family dealing with cystinosis, I thought I'd share some of what we needed to consider ...





# PARTINGTON FAMILY UPDATE

By Teresa and Kevin Partington, Jenna and Patrick's parents  
SACRAMENTO, CALIFORNIA

- 1 We packed 48 doses of medication, a total of 1,680 pills and 16 shots (which needed to be on ice, or refrigerated, at all times).
- 2 An entire suitcase was dedicated to absorbent bedding and mattress protection for the management of overnight incontinence.
- 3 Wheelchairs were arranged for airports and hotels whenever possible, as the kids are still healing from the knee surgeries the past two years.
- 4 Documentation pertaining to every medication for customs clearance, should it be necessary (thankfully, it wasn't).
- 5 Sunglasses and more sunglasses. I took a photo one day after clearing my purse of them. The kids cannot face the sunlight without them, due to cystine crystals on their corneas, so we always grab a pair on the way out the door. (Perhaps we will try the less-is-more approach going forward. This is ridiculous!)
- 6 The village of Altino, where we were so fortunate to spend some of our vacation, has a diuretic in the water, which is unsafe for anyone with chronic kidney disease. For this reason, we had to purchase bottled water for the kids for the duration of our visit. The kids went through 150 three-liter water bottles in five days. Between water bottles, medicine bottles, four styrofoam coolers per month for specialty medication delivery and, finally, absorbent disposables, the impact of two kids with cystinosis on the environment can make me sick to my stomach, if I think about it too much.

Overall, we are in a good place these days. The kids are enjoying 8th grade and their last year at Holy Spirit School, which has become a very special place to our family. Next year, at this time, Jenna and Patrick will be in high school! Kevin and I have had many discussions about what the next five years will hold for our family, as we watch our peers and the kids' peers navigate their education and prepare to move away from home. This morning, Kevin mentioned that it seems like the "age of innocence" is coming to a close. In so many ways, we are just getting started on this journey that is cystinosis. In the next four years, it is imperative that Jenna and Patrick learn to not only live with cystinosis, but how to care for a person with cystinosis. In addition to dealing with adolescence, romance, social pressures, high school and driving, in order for our kids to succeed in their next decade of life, our responsibilities around cystinosis need to become theirs.



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## THE 5TH ANNUAL HEARTS FOR HADLEY BENEFIT

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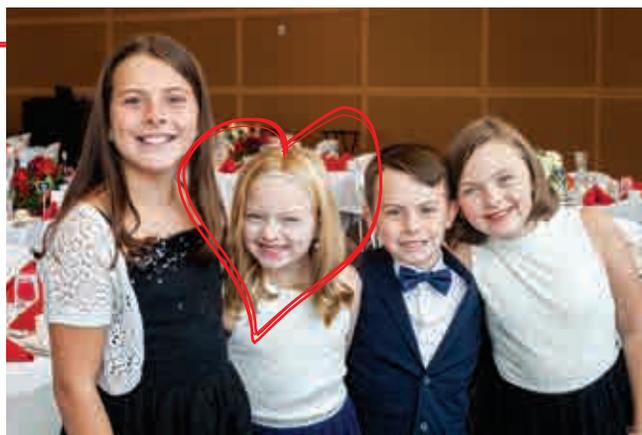
By Marcu Alexander, Hadley's mom  
BOISE, IDAHO

# Hearts for Hadley

The 5th Annual Hearts for Hadley Benefit took place on Saturday, September 15, at JUMP (Jack's Urban Meeting Place) in Boise, Idaho. Nearly 300 guests gathered together in honor of our 8-year-old daughter Hadley Alexander and raised over \$105,000 for cystinosis research!

The evening kicked off with drinks and appetizers, while guests mingled and bid on over 30 silent-auction items. Some of the generously donated items included original artwork, a signed Alice in Chains CD and band swag, spa certificates, and an overnight dinner and hotel package. There was also a wine wall where more than 50 bottles of wine were available for purchase. Tickets to the wine pull were \$20 each and guaranteed the participants a bottle of wine valued at \$15 or much higher.

Hadley and big sister Stella were on site to greet everyone as they arrived. The ballroom was decorated in accents of black, white, and red, and the tables were adorned with beautiful floral arrangements designed by K. Costa Floral. We are blessed to have so many



talented friends and family who are willing to donate their time to create a beautiful space for our event.

The evening included a delicious dinner, followed by an exciting dessert auction! The desserts raised over \$14,000, and the friendly competition was one of the most fun parts of the night. Some of the dessert offerings included ombre peach layer cake, huckleberry poppy seed cake with lemon curd, tiramisu, trifle with fresh berries, chocolate hazelnut dacquoise, and peanut butter brownies.

"Uncle" JJ was back in action as the emcee and co-auctioneer alongside Mark Johnson, news anchor for KTVB. The two guys kept the audience entertained, excited and inspired. The live auction was action-packed and

included a stay at the Diamond D Ranch for three nights, with fly fishing, a weeklong guided rafting trip for two on the Middle Fork, a five-course gourmet dinner for 12, a Yeti cooler filled with beer and booze, and a weekend Goat Yoga retreat, to name a few.

We were grateful to have the Partington family (Kevin, Teresa, Patrick and Jenna) from Sacramento join our family at the event for the second year in a row. Before the event, the Partingtons took Stella and Hadley on an adventure through Boise, while Ben and I helped set up for the evening's festivities. I think they may have had more fun hanging with the Partingtons during the day than they did at the event that night!

The speaking kicked off with Jenna doing a fantastic job

introducing Uncle JJ. I was then introduced and spoke about Hadley's health and the ups and downs she's experienced this year due to cystinosis. Fortunately, right now she is doing very well, thanks to the additions of a few new medications. I also provided an update on the latest research findings and specifically shared information regarding stem cells and gene therapy. Plus, I had the honor and privilege of introducing Kevin Partington who shared what cystinosis is like for their family. Kevin spoke from the heart, and there wasn't a dry eye in the house by the end of his speech. We are so grateful for the Partington family and their involvement in our lives!

We are also grateful for the outpouring of love and support provided by our family, friends and the city of Boise. We continue to raise awareness and money for cystinosis research and are already busy planning some other exciting Hearts for Hadley events over the next few months, including a holiday pub crawl and benefit concert. We will never give up hope!



# OLIVIA'S FIVE TO THRIVE



On September 8, 2018, our friends and family, as well as people we didn't know, gathered together for one reason: to help us on our mission to find a cure and better treatments for cystinosis.

We had a full course with 216 golfers. Our mission on the course this year was to educate our guests about cystinosis and to share Olivia's story with them. We called the tournament, "Olivia's Five to Thrive." We wanted to share the way Olivia thrives so throughout the course, we had different holes set up to educate the players about the five things that help Olivia thrive.



Our sponsors helped make the educational holes possible on the course. For instance, our local retreat center set up a hole to educate the players on the role yoga and deep breathing play in Olivia's life. Olivia experiences a lot of poking and prodding throughout the year, so we incorporate deep-breathing exercises, which has given her a tool to help with the anxiety and stress of getting poked by a needle. Yoga plays a huge part by strengthening her core. Since muscle wasting might potentially be part of her future, we want her to make yoga a lifestyle and to be physically active.

One of our local gyms set up a circuit station on a hole to demonstrate the importance of physical fitness and building muscle. The research that is being funded by the Cystinosis Research Foundation has allowed us to gain insight into what might happen in the future. We have been fortunate enough to listen to research updates and talk to the researchers at the Day of Hope family conference. The research gives us enough information to make us proactive with Olivia's health. After hearing the research progress reports, we take what we have learned and make a plan to do our best for Olivia's future.

Our golfers also threw back shooters, but they were not typical shooters! These shots were filled with celery juice to emphasize the importance of a healthy and balanced diet and the role a healthy diet plays in Olivia's life. As golfers approached the putting green, their lips puckered from the bitter taste of downing an ounce of celery juice.

Although our golfers joined us to support a very serious cause, they also enjoyed a day of fun. There was a DJ on the course taking requests by donation, followed by syringes filled with "vitamins." We wrapped up the evening with dinner and speeches to a group of over 250 people who all came together because of their love and hope for Olivia.



One of the highlights of the evening was celebrating Nora Campbell's first birthday. Katelyn and Adam Campbell have two beautiful children, Alan and Nora, both with cystinosis. They have joined us at the golf events in the past, but this year it happened to be Nora's first birthday. We surprised Nora and her family with a birthday celebration; it's a day Nora probably won't remember, but a day we will never forget.

If anyone will find a cure for cystinosis, it will be the families, friends and complete strangers who come into our lives and fall in love with our beautiful children. We raised over \$110,000 that day on the course, and it all comes from the love our supporters have for our children. Together we will find a cure, and Olivia and all others with cystinosis will live healthy and full lives.



By Erin Little, Olivia's mom

PORT ELGIN, ONTARIO, CANADA

## MY TMC FAMILY

# Showing Continued Support for Our Cystinosis Community

By Jen Peachman,  
VP Member Engagement at The Mortgage Collaborative and Morgan's mom  
AVON LAKE, OHIO

I've been fortunate to work for many excellent organizations in my 15-plus years in the financial services and mortgage industry. But I've never found myself feeling like I was part of something special, something that feels like family, something that makes me feel like I have the backing of an entire organization, as I have since joining The Mortgage Collaborative two and a half years ago.

After learning of Morgan's diagnosis and more about cystinosis, The Mortgage Collaborative announced that beginning this year, the golf outings at our biannual conferences would become Mulligans Fore Morgan charity golf outings, benefiting the CRF. Our vice chairman and president David G. Kittle brought me up on stage at our conferences to talk about Morgan, cystinosis and the impact it has on my family's daily life. After showing a brief video and talking about the dozens of prescriptions Morgan needs every six hours to keep her healthy and slow the progression of the disease, the donations started pouring in.

The Mortgage Collaborative's founders, board members, lender members, preferred partners and employees have shown tremendous support, and earlier this year, our family made a record-breaking donation of \$38,958 in Morgan's honor!



*“Nothing gives me more pleasure than to help Morgan in her journey to be healed. She has the full support of my partners and the entire TMC family. We have Morgan's back!”*

— David G. Kittle CMB vice chairman and president at The Mortgage Collaborative

At our Summer Conference last month in Chicago, after hitting the links for the second TMC Mulligans Fore Morgan charity golf outing with 32 golfers, I had the opportunity once more to hit the stage with David. I shared a very personal piece that I wrote called “Cystinosis Momma,” offering a very raw and real view into my take on what it's like parenting a child with an ultra-rare and terminal disease.

I'm going to be completely honest: Sharing a truthful account and my perspective in such vivid detail was terrifying. But, I think I nailed it! With many brought to tears, and our conference attendees on their feet at the end with applause, I'm humbled and overwhelmed by the support I've received. Thousands of dollars donated, crying and embracing with other parents and friends, notes and emails from so many of our members and the continued support of my TMC family makes me strong and gives me so much hope.

We'll be hitting the links again in February 2019 at our Winter Conference in Austin in Morgan's honor —all thanks to the support from the TMC Family and Team Peach!



With her signature hot-pink golf ball, Morgan kicked off the 4th annual Mulligans Fore Morgan golf tournament at Bob-O-Link Golf Course in Avon, Ohio, crushing the ceremonial first shot off the tee. With a record-breaking number of golfers looking on, her swing and spirit continues to amaze and inspire!

It takes guts for anyone — especially an 11-year-old girl with cystinosis — to hit a golf shot with more than 100 folks gazing your way. But all her practice over the summer has paid off — Morgan's swing was smooth and confident, an excellent way to kick off the day's events.

Morgan's good friend Jake, who also has cystinosis, joined us again this year and even sported Team Peach colors! And by her side every year at Morgan's lemonade stand on the course were her best friends Abbie and Marissa, along with her little sister Maddie. With terrific friends who offer continued love and support, she's one lucky girl who knows how important the special bonds she's formed are!



A total of 96 golfers hit the course on Sunday, September 16, with one mission in mind: to raise money to help find a cure for cystinosis for Morgan and everyone fighting this disease every day. And by raising over \$15,000, we're one step closer to accomplishing our goal!

Our Mulligans Fore Morgan tournament sponsors, hole sponsors, golfers, volunteers, friends and family continue to amaze us with their continued support! In the past four years, we've raised over \$90,000 in Morgan's honor, and we won't stop until we find a cure. Together, we're stronger — and the overwhelming support and generosity of our community continues to fuel our hope.



INDIVIDUALIZED EDUCATION PLAN  
**THE IEP PROCESS**  
**OUR PRE-K JOURNEY WITH CYSTINOSIS**

By Jill and Clay Emerson, Brooke's Parents

Since diagnosis, we have come to understand that children with cystinosis typically require additional accommodations at school. While we knew it would be Brooke's reality as well, we anticipated it would be a bridge we would cross when she entered elementary school. But when our school district changed the Pre-K program to a mandatory full-day schedule, we decided to discuss Brooke's diagnosis with the school district's administration.

We first met with the district's social worker and provided her with a CRF pamphlet, which describes cystinosis in detail, a complete list of Brooke's medications and schedule, and a list of potential modifications and assistance Brooke may require in the classroom. A lot of what we knew was based on feedback that we had received from other parents within the community. The social worker immediately recommended an Individualized Education Plan or IEP. An IEP is a written plan, which details the IEP team's goals for the student, and the accommodations and services the school will provide in order to assist the student in reaching these goals.

Our school district (in the state of New Jersey) agreed that cystinosis qualifies as a disabling condition that can adversely affect development and/or learning and may require special education and specialized services. We brought Brooke into school to be assessed by a physical therapist, occupational therapist, child psychologist, speech therapist, a special education teacher and a general education teacher. During this

evaluation, we reviewed Brooke's complete medical history, medication schedule and medical needs. Brooke was evaluated by the therapists and teachers to determine the services for which she would be eligible. The school district then provided a proposed IEP plan, which we reviewed and executed at the final IEP meeting. We were also able to meet with the school nurses and Brooke's teacher to discuss the school year.

Brooke's IEP for Pre-K is relatively basic: She will receive physical and occupational therapy services during the school day; she is allowed a modified-length school day; she is excused from school for her quarterly doctor's appointments; she has access to water and the bathroom as needed; she will have sunglasses available; she is in an air-conditioned building in a classroom close to the nurse's office; and her teachers will monitor her food and water intake. We also have a caseworker who is always accessible, and we have direct access to the nurses and teachers as needed.

While we've heard of mixed experiences with the IEP process from other parents, our experience to date has been extremely positive. Perhaps there are things in this plan that Brooke may not need in the near future; but what we find comforting is that she is in an environment in which everyone understands her disease, her needs and our expectations. There is also a legally binding document that the school district must abide by, and we have peace of mind knowing that our child is protected and is in a position to receive the education that she deserves.





## CYSTINOSIS COMMUNITY

# CALENDAR OF EVENTS

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

Saturday, November 3, 2018

### HARTZ HALLOWEEN PARTY IN HONOR OF LANDON HARTZ

Home Economics Building, South Park, Pennsylvania  
For information contact Lauren Hartz, laurenhartz@gmail.com



Saturday, December 8, 2018

### GETTING JOLLY FOR JOSIE IN HONOR OF JOSIE KANUPKE

Fraternal Order of Eagles, Blue Island, Illinois  
For information contact Laura, lmchristophers30@gmail.com

GETTING **Jolly** FOR **Josie**

Saturday, March 23, 2019

### 2400 FT OF SCHWEITZER 24 HOURS FOR HANK, HENRY STURGIS

Schweitzer Mountain, Sandpoint, Idaho  
For information send email to information@24hoursforhank.org



Thursday-Saturday, March 28 – March 30, 2019

### CYSTINOSIS RESEARCH FOUNDATION DAY OF HOPE FAMILY CONFERENCE

Fashion Island Hotel, Newport Beach, California  
For information send email to info@cystinosisresearch.org



Saturday, March 30, 2019

### CYSTINOSIS RESEARCH FOUNDATION NATALIE'S WISH CELEBRATION

Fashion Island Hotel, Newport Beach, California  
For information contact Zoe Solsby, zsolsby@cystinosisresearch.org, 949-223-7610



Saturday, April 13, 2019

### 3RD ANNUAL CURL FOR A CURE TOURNAMENT IN HONOR OF LOLA LONG

Chaska, Minnesota  
For information contact Melissa Long, melismahan@yahoo.com



Spring 2019

### HOPES & WISHES IN HONOR OF JAKE KRAHE

Weymouth Country Club, Medina, Ohio  
For information contact Amy Krahe, ajkrahe@gmail.com



SAVE THE DATE

# day of HOPE

## CYSTINOSIS RESEARCH FOUNDATION

Learn, share, laugh and celebrate for three inspiring days with fellow members of the cystinosis community. CRF-funded researchers and clinicians will lead discussions on stem cell and gene therapy, treatments for corneal cystinosis, muscle wasting and myopathy, kidney disease and more.

The conference will include important sessions led by CRF-funded researchers and clinicians. A partial list of confirmed speakers:

- **Stéphanie Cherqui, PhD**  
Stem Cell and Gene Therapy
- **Ranjan Dohil, MD**  
GI Issues in Cystinosis
- **Morgan Fedorchak, PhD**  
Novel Gel Sphere for Corneal Cystinosis
- **Paul Grimm, MD**  
Kidney Disease and Cystinosis
- **Stephen Jenkins, MD**  
All About Cystinosis
- **Julian Midgley, MD**  
Adults and Cystinosis
- **Kathleen D. Rickert, MD**  
Bone Deformities and Cystinosis
- **Patrice Rioux, MD, PhD**  
Novel Treatment for Cystinosis

### WHEN

Thursday, March 28 to  
Saturday, March 30, 2019

### WHERE

**Fashion Island Hotel**  
690 Newport Center Dr,  
Newport Beach, CA 92660

For more information on the conference or the Family Assistance Fund contact:

[info@cystinosisresearch.org](mailto:info@cystinosisresearch.org)  
949.223.7610

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

**TOGETHER,  
WE ARE  
one**

**1 PURPOSE. 1 JOURNEY. 1 CURE.**

# TOGETHER, WE ARE **One**

Denis Lillard — Tolvsrød, Norway

## LOCAL BUSINESSES STANDING TOGETHER FOR A GOOD CAUSE - THE CYSTINOSIS COMMUNITY



Earlier this year, Maria Lillard was contacted by a company wishing to help with fundraising in honor of her son, Denis. What was initially a couple of companies; Kepler Bilservice and Tønsberg Antirust, wanting to help, turned into a community of local businesses standing together to help Denis and others living with cystinosis. A fundraising event took place while Maria and Denis were at the CRF Day of Hope family conference in April this year. The event lasted three days with businesses donating a portion of their revenues and contributions to the Cystinosis Research Foundation. In addition, a fundraiser on Facebook generated donations from all over the country. The combined fundraising efforts raised more than \$11,723 to help find better treatments and a cure for cystinosis.

The Lillard family is grateful to family and friends and the business community for their love and support of Denis and those living with cystinosis.

Lillyanna Suetta — Etna, California

## LEMONADE STAND AND BAKE SALE

Miss Lillyanna Suetta, 7 years old, recently organized and promoted another very successful lemonade stand and bake sale in honor of her sister, Emma Grace. The Etna, California, community displayed its support and generosity by helping to raise \$2,000 for cystinosis research. On behalf of the cystinosis community, thank you!



# 1 PURPOSE. 1 JOURNEY. 1 CURE.

Katie Roy — Franklin, Tennessee



## CRAWFISH BOIL

Jenni and Rick Kloete hosted their fifth neighborhood Crawfish Boil on April 28th in Franklin, Tennessee. The event is a fundraiser for cystinosis research in honor of their daughter, Katie Roy and in memory of Jenni's siblings, Jeff, Jan and Hope Rouse. Live crawfish were flown in from the Louisiana Bayous for guests to enjoy with jambalaya and duck fat fries. Musicians gathered on the front porch and performed to entertain the community during the afternoon. It was a beautiful sunny day and a fun way to raise money for cystinosis research! This year's event raised over \$4,500 bringing the Crawfish events combined totals to \$5,600.



# TOGETHER, WE ARE One

Andrew Cunningham — Langdon, Alberta, Canada

## A BRRRRRILLIANT DAY HAD BY ALL

September 15th marked the 7th annual JCFG Memorial Golf Tournament hosted by the ForeFathers. Despite freezing rain, cold northern winds and low temperatures, our dedicated sponsors, golfers and volunteers made their way out to the Boulder Creek Golf Course in support of Andrew Cunningham. Andrew was diagnosed at 17 months of age, and recently transitioned to grade 10 as a healthy, happy teenager.

Andrew's uncles Alan and Neil, once again donned alter ego costumes and made their way around the course, with music blaring and shenanigans to spare, much to the delight of the players. The rest of the McCullagh-Cunningham Clan, along with a multitude of amazing volunteers, kept the tournament, the laughs (and a few Irish whiskeys) flowing.

The tournament was started in 2012 as tribute to four fathers, John McCullagh, Conway Cameron, Frank Halluk & Gordon Cunningham (JCFG) who lost their lives to heart disease. John and Gordon were Andrew's granddads, so it always feels fitting that in addition to raising funds for heart disease, 60% of the proceeds from the event are directed in support of cystinosis research. We are so proud of the partnership we have with the CRF, and will continue to drive the funds we raise, in support of the incredible efforts of the doctors and researchers dedicated to battling this disease alongside our families. We have full faith, that one day, the tournament will be held in celebration of the cure of cystinosis!



Kenzie Lawatsch — Marinette, Wisconsin

## KENZIE'S DRIVING "FORE" A CURE

The Lawatsch family held their 2nd Annual Kenzie's Driving Fore a Cure Golf Tournament in honor of their daughter Kenzie, on August 12, 2018. Family and friends, along with their community of supporters, came together to honor Kenzie and to raise money to help fund research and find a cure for cystinosis.



Kenzie had a blast on the golf course with the golfers and made sure everyone had a great time. Guests joined the golfers at the end of the tournament to enjoy good food and beverages, and to participate in an opportunity drawing and silent auction.

Overall, it was a perfect day and an absolutely amazing event!



# 1 PURPOSE. 1 JOURNEY. 1 CURE.



Brookfield, Missouri

## 2018 WESTON TSCHANNEN MEMORIAL GOLF TOURNAMENT

The 2018 Weston Tschannen Memorial Golf Tournament was another wonderful success with additional sponsors and more participants raising over \$20,000. The proceeds were divided in support of CRF for cystinosis research, and the local wrestling and golf teams, two sports that Weston was very committed to. The family decided to support the school wrestling program that started a scholarship for a graduating senior in Weston's memory. One of the highlights of the live auction was a donation from the local animal shelter of an adorable puppy, which brought in \$2,300, and to make it extra special the new owners named him "Wes."



# TOGETHER, WE ARE One



Landon Hartz — Pittsburgh, Pennsylvania

## LOTS OF LOVE FOR LANDON CHARITY GOLF OUTING

On behalf of Landon and the rest of our family, we wanted to thank you for participating in the 7th Annual Lots of Love for Landon Charity Golf Outing. Having a child that is born with a disease is difficult for any family to endure. Organizing charitable events gives the parents and family of the child the opportunity to feel like they are doing as much as they can to contribute to the child's quality of life.

We're extremely excited to announce that we were able to raise over \$20,500 this year, bringing the total raised from our golf tournament to more than \$120,000! Thank you to those that have been with us since the first year and to the newcomers for allowing us to continue to grow every year. Every dollar that was raised goes directly to the Cystinosis Research Foundation to help fund studies that will result in better medical care — and we hope ultimately a cure!

Abbi Monaghan — St. Catharines, Ontario, Canada

## 2018 "SHOOT FOR ABBI" CHARITY SHOOT

DECEW GUN CLUB - FONTHILL, ONTARIO

The Decew Gun Club hosted its third annual charity shoot in honor of 12-year-old Abbi Monaghan. Abbi is the only known case of cystinosis in the Niagara Region of Canada.

The shoot was open to everyone in the community (adults and children), and no shooting experience was necessary. Enthusiastic volunteers manning the firing lines provided professional guidance and took the time to help all the youngsters enjoy their first shooting experience.

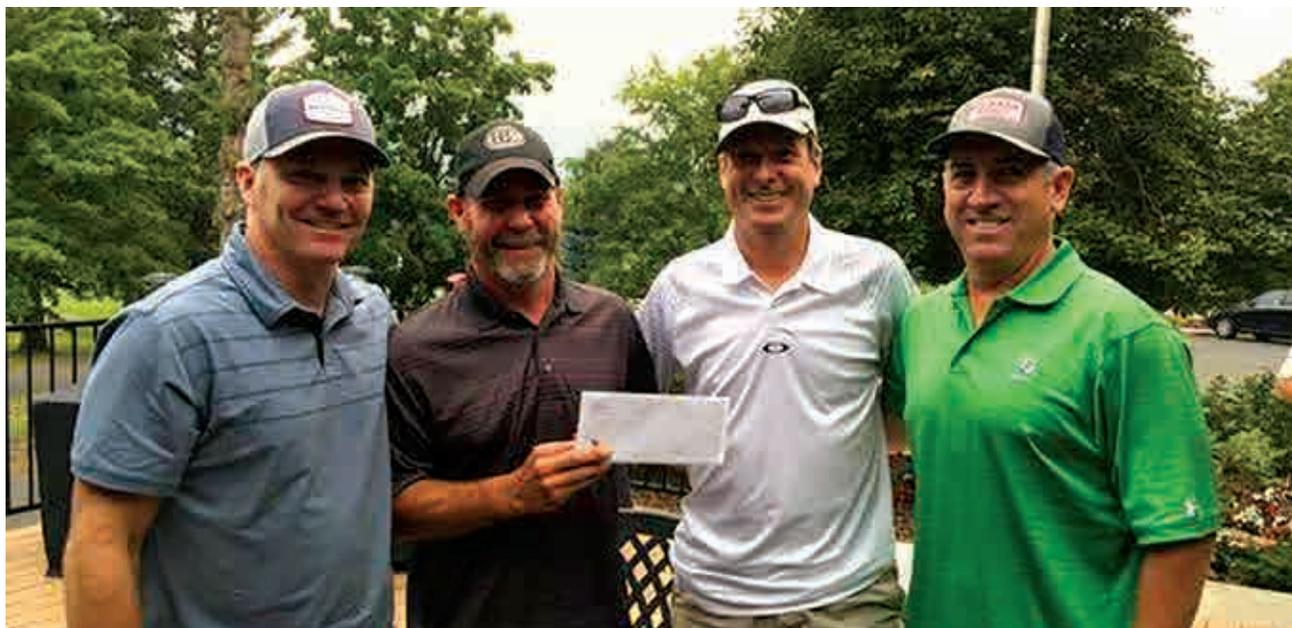
Once again, we want to express our appreciation and a huge THANK YOU to John Rakick and his family, the volunteers and everyone from the community who came out to support Abbi.

We are especially grateful to the Decew Gun Club and Destination Church for all their hard work! More than \$11,320 was raised to fund cystinosis research in support of the Cystinosis Research Foundation's mission for better treatments and a cure. Thank you!



# 1 PURPOSE. 1 JOURNEY. 1 CURE.

Henry Sturgis — Sandpoint, Idaho



## SWING FORE A CURE RAISES FUNDS FOR CYSTINOSIS

On Saturday, August 25, 2018, 24 Hours for Hank held their second golf tournament at Stoneridge Golf Course in Blanchard, Idaho. Pictured from left to right are Team Sturgis (Brian Sturgis, Brian McCrumb, Scott Barksdale and Alex Wohllaib), the winners of the Swing Fore A Cure Golf Tournament. The annual tournament raised more than \$8,000 for 24 Hours for Hank and cystinosis research. The longest drive went to Lara Wohllaib and the longest putt was sunk by Stephanie Allen, at a lengthy 32 feet. Event organizers wish to thank sponsors Alpine Motors, SimulStat, TraskBrit, Sandcreek Custom Wear, Saylor Owen Kerr, Friends of 24 Hours, Trinity at City Beach and the 219 Lounge, as well as all of the teams and volunteers.

## FACEBOOK FUNDERS FURTHER THE QUEST FOR A CURE.

A huge thank you to our dedicated Facebook fundraiser event organizers and donors around the world. As of October 15, 2018, Facebook fundraising events have raised \$37,945 to help us fund extraordinary research across the globe. Facebook has made it easy for people everywhere to raise money for cystinosis research through their Facebook platform and at no cost to you or CRF. Every small donation adds up! We encourage you to create a fundraiser of your own through Facebook. We are deeply grateful to our community and our donors for their commitment to fundraising for CRF and joining our quest for a cure!



# TOGETHER, WE ARE **One**

Kaleb Lawshe — Charleston, South Carolina



## THANK YOU, BRYCE, STACY AND CRF!

Our son Kaleb Michael Lawshe was diagnosed with cystinosis at the age of 21 months. Up to that point, we were filled with so much worry about what was happening to our baby, and the loneliness and guilt were almost unbearable. Once Kaleb was diagnosed, our world changed — and while we finally had answers, we still felt so alone in many ways until getting involved with the Cystinosis Research Foundation (CRF). The CRF has indeed changed our lives and has given us hope for the future through its community support and amazing commitment to funding research for better treatment and ultimately a cure.

Fundraising is all about reaching out to others and asking for their financial support in helping with a particular cause. In our case, Kaleb and all the other children and adults living with cystinosis are the reason, and CRF is the cause. When we chose to relocate from Northern Virginia to Charleston, South Carolina, we knew our network of family and friends would change. We have been fortunate to have the continued support of family and friends, no matter how far away we are from each other. We have many cousins across the United States — from the West Coast to the East Coast — and have been very blessed to have their support in so many ways.

This past August, our cousin Bryce Watson set up a Facebook fundraiser for CRF in honor of his 29th birthday. Busy with his career, buying his first house and taking care of his beautiful sidekick Harper, he didn't give up. He continued with his outreach to others, asking for their support. Bryce surpassed his goal of \$200 and reached a final amount of \$565. Later in the same month, our cousin Stacy McCauley, also set up a fundraising event for her late August birthday, asking for donations in support of the CRF.

No matter how small or large these fundraisers turn out to be, it's the support shown by family and friends in raising awareness, in raising funds for research and treatment ... and reminding us that we aren't alone in our battle to beat cystinosis. Thank you, CRF — and thank you, Bryce and Stacy, for your love and support. It means the world to us!





# 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 \$45 million with 100% of all your donations going to support cystinosis research.

## EDUCATION

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



SAVE THE DATE

Natalie's  
**W WISH**

CELEBRATION

**SATURDAY**  
**MARCH 30, 2019**

6:00 pm Cocktail Reception  
7:15 pm Program and Dinner

FEATURING  
**MATT MAUSER**  
his Sinatra Big Band and  
The Tijuana Dogs

*Fashion*  
**ISLAND HOTEL**  
NEWPORT BEACH

690 Newport Center Dr,  
Newport Beach, CA 92660

For sponsorship opportunities  
or tickets, contact Zoe Solsby:  
[zsolsby@cystinosisresearch.org](mailto:zsolsby@cystinosisresearch.org)  
949.223.7610

**HONORING** the children and adults who  
are affected by cystinosis and the cystinosis research  
community for its commitment to our children.

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RESEARCH FOUNDATION | HOPE  
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[cystinosisresearch.org](http://cystinosisresearch.org)