

cystinosis

magazine

For friends and supporters of the Cystinosis Research Foundation



FALL 2016

HOPE THROUGH
RESEARCH
ISSUE



Morgan Fedorchak, PhD, Assistant Professor of Ophthalmology
University of Pittsburgh School of Medicine and the Louis J. Fox Center for Vision Restoration



THE POWER OF ONE.

One community's international connection is bridging research with hope and is empowering one goal: to find a cure for cystinosis. One World. One Hope. One Step Closer.

CONTACT US:

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

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

The entire cost of *Cystinosis Magazine* is underwritten by friends of the Cystinosis Research Foundation.

Cover Art: Kristy Prince
Art Direction and Printing: Idea Hall

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FALL 2016

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Dear Family & Friends

The cover of this issue of Cystinosis Magazine says so much about our community: One World. One Hope. One Step Closer. We are a small disease community but we are filled with hope and united in our quest for the cure. We thank you for remaining steadfast in your support of our efforts to find better treatments and a cure for cystinosis.

We know you will enjoy this issue of the magazine. In addition to heartfelt family stories, awe-inspiring accounts about our cystinosis champions, amazing fundraising ideas and community villages that support our efforts, we have an abundance of information about the research we fund, including abstracts for the new grants and in-depth interviews with three of our most promising researchers.

We are incredibly thankful to the entire science and medical community who work every day to unravel the complexities of cystinosis and who strive to think outside the box in their search for better and novel treatments. We have come so far; we have built a strong foundation for innovative research that continues to flourish and produce extraordinary results.

The Research Expands

The cystinosis research world has changed as a direct result of your donations, which we have invested in the research community. When we began funding research, there were very few researchers and investigators studying or even interested in cystinosis primarily because of a lack of ongoing funding and resources. It has been your belief in us that we can make a difference in our children's lives by finding new treatments and a cure for cystinosis that inspires us and pushes us forward every day.

The Cystinosis Research Foundation has awarded 143 multi-year research grants in 12 countries. Our researchers have published 66 articles in prestigious journals as a result of CRF funding. You have helped us create a thriving and synergistic global research community that has advanced the field of

cystinosis study and treatment. CRF funded researchers work passionately and tirelessly on behalf of our community – they have made our quest for a cure their quest, too.

Since 2003, the Cystinosis Research Foundation (CRF) has become the largest fund provider of cystinosis research in the world, raising more than \$35 million. CRF has changed the course of cystinosis by investing donors' gifts strategically and aggressively to create a thriving research community. From the beginning, all CRF operating costs have been privately underwritten so that 100 percent of every dollar you donate goes toward research.

FROM A YOUNG COUPLE IN ISRAEL "We are thankful beyond words. The fact that we are not alone in this and were exposed to the Cystinosis Research Foundation gives us a lot of hope. The mental strength and encouragement you have just given me is priceless. We thank you from the depth of our heart."

Hope is a Universal Feeling

Every week we hear from families around the world who are seeking medical help, resources, family connections, clinician information and information about research. These families are as

far away as Sri Lanka, Syria, Israel, Saudi Arabia, Venezuela, Colombia and India and as close as Canada and the U.S. It doesn't matter where cystinosis families are from, they are always thankful to CRF for the hope we have given them through the research we fund. Your unwavering commitment to all of the children and adults with cystinosis has left a ripple effect of hope around the world.

There is nothing more important to a parent of a child with cystinosis or a person with cystinosis than to know that every minute of every day, somewhere in this world, a CRF funded researcher is working to find better treatments and a cure for cystinosis.

Accelerated Research Program

After raising a record amount of money – \$3.3 million! – at the Natalie’s Wish event on April 9, we knew we had an opportunity to fast track research. As a direct result of this successful event, we established the CRF Accelerated Research Program in an effort to increase the pace of research and to fund research that will help us move closer to clinical trials. The program allows for grants to be issued outside the bi-annual grant application process for projects that aim to accelerate the development of better treatments and a cure for cystinosis. Your generosity has allowed us to propel the research forward in a way that we could not before. Over \$208,000 was recently granted to Stephanie Cherqui, PhD, who demonstrated that additional funds would allow her to accelerate and expand the stem cell and gene therapy program which we believe will lead to the cure for cystinosis.

More than \$1.2 Million Awarded to Researchers in July

Natalie’s wish, “to have my disease go away forever,” was the reason the Cystinosis Research Foundation began and today it remains the driving force in our effort to find the cure. The last 13 years of funding research have transformed the field of cystinosis. Your support has helped us translate promising scientific discoveries into new discoveries about cystinosis. You have helped us accelerate new discoveries – there are novel treatments on the horizon.

FROM A MOTHER IN VENEZUELA

“It has been a hard experience, but he’s very good right now, thank God, and thank the foundation and all the doctors and team that have supported us. There are so many good things happening with the research, we’re so happy and grateful!”

We have targeted several areas of research including muscle wasting, neurological issues, corneal cystinosis, endocrine complications of cystinosis and stem cell and gene therapy.

We are pleased to announce that eight investigators from four countries received grants this cycle. The grant recipients are listed on page 66 along with a lay abstract of their study. We are excited to introduce three new researchers to the field of cystinosis.

- In an effort to expand our research in the area of corneal cystinosis, we recently awarded a grant to Morgan Fedorchak, PhD, and Kanwal Nischal, MD, from the University of Pittsburgh School of Medicine. They aim

FROM PARENTS OF A CHILD IN THE U.S. “We are extremely optimistic that there will be a cure in her lifetime. Thanks for everything you all have been doing.”

to establish a more direct delivery of reduced quantities of drug than traditional treatments via a gel eye drop.

- Understanding more about myopathy is a priority for CRF. We have awarded a grant to Florian Eichler, MD, from Massachusetts General Hospital, who will focus on distal myopathy in cystinosis. He will define clinical outcome measures that accurately quantify disease progression in cystinosis for use in future clinical trials.
- Our third new researcher, Patrick Jouandin, PhD, from Harvard Medical School, will focus on the effects of the CTNS mutations on cysteine balance and cellular metabolism.

In total CRF has funded \$1.47 million in 2016 through July. We hold great expectations that these newly funded researchers will help us learn more about cystinosis and how to treat it and cure it.

FROM A FATHER IN SAUDI ARABIA “On behalf of all families of patients with cystinosis, thank you for your tremendous achievement. Please keep going, a cure for cystinosis is not too far.”

Research Highlights

Nanotechnology and Corneal Cystinosis: We remain committed to funding research for novel treatments for corneal cystinosis. 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 treatment but it is rigorous, painful for many and requires hourly dosing of medicated eye drops making compliance difficult.

Two exceptional researchers, Ghanashyam Acharya, PhD, of Baylor College of Medicine, and Jennifer Simpson, MD, of the University of California Irvine, are collaborating on a novel treatment for corneal cystinosis. The nanowafer was designed by Dr. Acharya to deliver medication to the eye. The concept is to load the nanowafer with cysteamine, place it on the eye where the medication slowly releases, treating the eye for hours. CRF owns the license for the cysteamine-loaded wafer, which allows CRF to control the pace and direction of the research. Our ultimate goal is to receive FDA approval for a new treatment for corneal cystinosis.

We are excited to report that based on the progress made in laboratory studies, CRF formed a wholly owned spinoff company called Corneal Cystinoloysis Inc. (CCI) to facilitate the continued development and clinical availability of the Cysteamine Nanowafer. The immediate goals of this effort are the formalization of manufacturing procedures, as well as the completion of pre-clinical testing required for initiation of a U.S. clinical study. We are preparing the necessary documents for the FDA and we anticipate that this will result in initiation of a clinical trial in early 2017.

Stem Cell and Gene Therapy: Bone marrow stem cells hold the promise of a cure for cystinosis. Dr. Stéphanie Cherqui's work is our hope – not only has the treatment reversed cystinosis in mice, last year she successfully cured corneal cystinosis in the mouse model as well as thyroid dysfunction after a single stem cell transplantation. Dr. Cherqui, of the University of California San Diego (UCSD), continues to work with the FDA on the safety studies for this approach to obtain FDA approval for a Phase I clinical trial for cystinosis. These studies are conducted in mice but she is also using patients' stem cells. In fact, the strategy is to use patients' own stem cells and then to gene-correct them to introduce a functional CTNS gene before transplanting them back in the patients. This approach, called autologous transplantation, is safer than using foreign stem cells, but requires optimization of the gene-correction step. We are grateful to the many volunteers with cystinosis who have donated their blood for this study so that Dr. Cherqui's group can determine the most efficient protocol to obtain corrected stem cells.

This technology will soon be transferred to Dr. Donald Kohn's facility at the University of California, Los Angeles (UCLA), where patients' cells will be gene-corrected during the clinical trial. Then the next step will be for Dr. Cherqui and Dr. Kohn to conduct a FDA required "Proficiency Run" using healthy donor cells, which will allow them to go through every step that will be part of the clinical trial: isolation of the stem cells at UCSD,

shipping of the cells to UCLA, gene-correction of the cells at UCLA, and shipping the gene-corrected cells back to UCSD. The data collected from the Proficiency Run will be included in the Investigational New Drug (IND) application that will be submitted to the FDA.

We are optimistic that the FDA will authorize us to commence the first autologous stem cell and gene therapy clinical trial in 2017.

Cystinosis Research Goes Beyond Our Community

Many of the discoveries made by CRF researchers are currently being applied to other more prevalent and well-known disorders and diseases. CRF-funded stem cell research will help other corneal diseases, kidney diseases and genetic and systemic diseases similar to cystinosis. Your support of cystinosis research has extended far beyond the cystinosis community. Finding a cure for cystinosis will help find cures for other diseases potentially helping millions of people.

Our Work is Not Done

We are on the brink of new treatments and we are close to the cure – but we are not there yet. There remain more studies to fund and clinical trials to support. Clinical trials take time to plan and they are expensive to run, but with your continued help, we will fund the research that is necessary to make these new treatments a reality.

Your support has provided us with hope. It has taken each of us, working together for our common goal of finding a cure for cystinosis,

to ensure the research moves forward. CRF is the only foundation in the world funding millions of dollars in new cystinosis research grants every year. Your compassion for our children ensures that we will continue to move forward toward better treatments and a cure.

Our Extraordinary Donors – Thank You

Now more than ever, we are in a race to save our children. We pray for a life without medications, without pain, without muscle weakness, without hospital visits and blood draws, and without worries about life expectancy.

Your generosity has been the driving force behind every achievement, every milestone and every step forward. As we push forward with the research, we work as ONE community bonded by our love for our children and our determination to find a cure. Your dedication to our community guarantees that all children and adults with cystinosis will never be forgotten.

Your support has allowed all those with cystinosis to dream of a life without the disease. Working as ONE, motivated by ONE hope, we are ONE step closer to finding the cure for our children. Thank you for supporting cystinosis research, for standing by our side and for embracing our community.

*With heartfelt thanks and gratitude,
Nancy and Jeff*

H PE THROUGH RESEARCH



A Note from Natalie

Dear Family and Friends,

This past May, I graduated from the University of Southern California with a master's degree in social work. Since then, I was fortunate to take a couple of weeks and travel with my family to Japan, a country that I have always wanted to visit. We tried many interesting foods and toured all around Tokyo and Kyoto. The culture in Japan is very different from America; it was interesting and I learned a lot about the people who make that land their home. The trip was a once-in-a-lifetime opportunity. Traveling the world is a passion of mine, and I hope to visit many other countries in the future.

I have been working as a paid social-work intern at a nonprofit in South Los Angeles. The internship is with the Drew Child Development Corporation, which is an organization whose mission is to provide children with safe and stable environments so that they can succeed and help strengthen their community's future. I have been working on a legislative project which has allowed me to not only advocate on behalf of the organization but also expand my knowledge about nonprofit management, an area of particular interest to me. The Drew Child Development Corporation has given me a wonderful opportunity to continue to grow professionally. Soon, I will be working toward obtaining my LCSW (Licensed Clinical Social Worker) certification, which will help me expand my opportunities in the field of social work.

I am forever grateful to my friends and family who have stuck by my side and continue to be there for me during this transition in my life. Finishing graduate school and entering the workforce are major milestones, especially for someone who has a chronic illness. It has been a challenge for me at times but it has been a good challenge and I have learned a lot.

As I get older, I am more aware of the importance of taking my medications and taking care of myself, both mentally and physically. I know there will be obstacles along the way, but I also know that I have the unwavering support of my family, friends, and the cystinosis community. I have chosen to live my life to the fullest and cherish every moment that I am alive because you never know what might happen. I will always be optimistic about my life and future and I will never let this disease take over my life.

Words cannot express how meaningful it is to me to know how dedicated our community is to CRF and to finding a cure. It means so much to me as well as to all the others who have to overcome cystinosis on a daily basis, to know you are there for us. My parents, the doctors and most importantly, the cystinosis community have made a life free of cystinosis more plausible than ever before. I want to thank you for your generosity, compassion, and, most of all, for your determination to make my wish come true.

*Love,
Natalie Stack*



Global Research providing Hope

THANK YOU FOR YOUR
CONTINUED SUPPORT

Every patient, family and donor from all over the world has changed the course of cystinosis and has given hope to our community. There was essentially no research prior to 2003, and now look!

THE IMPACT OF CRF RESEARCH SINCE 2003

143 MULTI-YEAR STUDIES IN 12 COUNTRIES

66 ARTICLES PUBLISHED

1 FDA-APPROVED DRUG

from CRF-funded research!

1 ALLOGENEIC STEM CELL TRIAL AT UCLA

1 LICENSE FOR NOVEL DEVICE FOR CORNEAL CYSTINOSIS



FIRST CYSTINOSIS FELLOWSHIP PROGRAM



CCIR FIRST AND ONLY INTERNATIONAL PATIENT REGISTRY

BIENNIAL INTERNATIONAL RESEARCH SYMPOSIUM
for CRF-Funded Scientists

FIRST AUTOLOGOUS STEM CELL AND GENE THERAPY TRIAL

ANTICIPATED
IN 2017

WHAT IS CYSTINOSIS?

CYSTINOSIS AFFECTS
APPROXIMATELY
2,000
people worldwide

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

The Cystinosis Research Foundation is the largest fund provider of grants for cystinosis research in the world!

CRF was founded in 2003 after Natalie Stack made a wish on the eve of her 12th birthday.



Since 2003

\$35
MILLION
HAS BEEN RAISED
FROM PEOPLE
AROUND THE WORLD.

and

100%
OF ALL YOUR
DONATIONS GO
DIRECTLY TO
SUPPORT CYSTINOSIS
RESEARCH.

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.***

The Cystinosis Research Foundation was established in 2003 with the sole purpose of raising funds to find better treatments and ultimately a cure for cystinosis. Today, CRF is the largest provider of grants for cystinosis research in the world, funding more than 143 studies in 12 countries. ***CRF has raised \$35 million with 100% of all your donations going to support cystinosis research.*** CRF’s efforts have changed the course of cystinosis and given new energy to its investigators and scientists. CRF’s commitment to research has given hope and promise to the global community of cystinosis patients and their families.

The Impact of CRF Research

AREAS OF RESEARCH FOCUS *and* GRANTS SINCE 2002

CELLULAR AND/OR MOLECULAR STUDIES OF THE PATHOGENESIS OF CYSTINOSIS

35 Grants

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



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,
STANFORD, CALIFORNIA

Bruno Gasnier, PhD
PARIS DESCARTES UNIVERSITY, PARIS, FRANCE

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

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

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

STEM CELLS AND GENE THERAPY: BONE MARROW STEM CELLS, INDUCED PLURIPOTENT STEM CELLS, GENE THERAPY AND GENE EDITING

26 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
MONTREAL CHILDREN'S HOSPITAL,
QUEBEC, 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

GENETIC ANALYSES OF CYSTINOSIS

4 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



THYROID

1 Grant

Pierre Courtoy, MD, PhD
DE DUVE INSTITUTE, UNIVERSITÉ
CATHOLIQUE DE LOUVAIN,
BRUSSELS, BELGIUM



CRF-FUNDED RESEARCH
IS PROVIDING HOPE!

KIDNEY RESEARCH

17 Grants



Robert Chevalier, MD

UNIVERSITY OF VIRGINIA,
CHARLOTTESVILLE, VIRGINIA

Pierre Courtoy, MD, 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

Tara McMorrow, MD

UNIVERSITY COLLEGE DUBLIN,
BELFIELD, DUBLIN, IRELAND

Philip Newsholme, PhD

CURTIN UNIVERSITY,
PERTH, WESTERN AUSTRALIA

Daryl Okamura, MD

SEATTLE CHILDREN'S RESEARCH INSTITUTE,
SEATTLE, WASHINGTON

Mary Taub, PhD

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

SKIN, MUSCLE, BONE



6 Grants

Robert Ballotti, PhD

FACULTÉ DE MÉDECINE, NICE, FRANCE

Christine Chiaverini, MD, PhD

FACULTÉ DE MÉDECINE, NICE, FRANCE

Paul Grimm, MD

STANFORD UNIVERSITY SCHOOL OF
MEDICINE, STANFORD, CALIFORNIA

Mary Leonard, MD, MSCE

STANFORD UNIVERSITY,
STANFORD, CALIFORNIA

Robert Mak, MD, PhD

UNIVERSITY OF CALIFORNIA, SAN DIEGO,
LA JOLLA, CALIFORNIA

NEW DRUG DISCOVERY CYSTEAMINE, NEW MEDICATIONS AND DEVICES

20 Grants



Ghanashyam Acharya, PhD

BAYLOR COLLEGE OF MEDICINE,
HOUSTON, TEXAS

Pierre Courtoy, MD, PhD

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

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

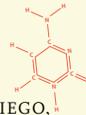
BAMBINO GESÙ CHILDREN'S HOSPITAL,
ROME, ITALY

Paul Goodyer, MD

MONTREAL CHILDREN'S HOSPITAL,
QUEBEC, CANADA

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

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

NEUROLOGICAL



12 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

EYE – CORNEAL CYSTINOSIS RESEARCH



7 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,
GAVIN HERBERT EYE INSTITUTE

Kang Zhang, MD, PhD

UNIVERSITY OF CALIFORNIA, SAN DIEGO,
SHILEY EYE INSTITUTE, LA JOLLA, CALIFORNIA

CURE CYSTINOSIS INTERNATIONAL REGISTRY (CCIR)



1 Grant

Ranjan Dohil, MD

UNIVERSITY OF CALIFORNIA, SAN DIEGO,
LA JOLLA, CALIFORNIA

66 Published Studies

by CRF-funded researchers including these since the Spring 2016 issue of Cystinosis Magazine!

Synergistic Cysteamine Delivery Nanowafer as an Efficacious Treatment Modality for Corneal Cystinosis

Published September 2016 in *Molecular Pharmaceutics*
by Ghanashyam Acharya, PhD
BAYLOR COLLEGE OF MEDICINE, HOUSTON, TEXAS

The Proximal Tubule is the Primary Target of Injury and Progression of Kidney Disease: Role of the Glomerulotubular Junction

Published May 2016 in *American Journal of Physiology – Renal Physiology*
by Robert L. Chevalier, MD
UNIVERSITY OF VIRGINIA, CHARLOTTESVILLE, VIRGINIA

Carboxyl-Terminal SSLKG Motif of the Human Cystinosin-LKG Plays an Important Role in Plasma Membrane Sorting

Published May 2016 in *PLOS One Journal*
by Francesco Emma, MD
BAMBINO GESÙ CHILDREN'S HOSPITAL AND RESEARCH INSTITUTE, ROME, ITALY

CRF GRANTS ARE LEVERAGED BY MILLIONS

\$12,214,460

NEW \$5.2 MILLION GRANT AWARDED TO STÉPHANIE CHERQUI, PhD



CRF-funded researcher Stéphanie Cherqui, PhD, at the University of California San Diego was recently awarded a two-year \$5.2 million grant from CIRM (California Institute of Regenerative Medicine). The grant will allow Dr. Cherqui and her team

to do the pre-clinical work needed to demonstrate that the potential treatment is both safe and effective, paving the way for FDA approval of clinical trials in the near future.

Dr. Cherqui's goal is to take blood stem cells from people with cystinosis, genetically-modify them to remove the mutation that causes the disease, then return them to the patient. The hope is that the modified blood stem cells will create a new, healthy, blood system free of the disease.

CRF issued its first grant to Dr. Cherqui in 2007 to explore the possibility of a stem cell treatment to cure cystinosis. CRF and Dr. Cherqui have worked closely together over the years to ensure the research moved forward. "This award is the result of pivotal work funded by the Cystinosis Research Foundation," Dr. Cherqui said. "I share this success with CRF, who has always been so supportive of me since the beginning of this project." Since 2007, Dr. Cherqui has been awarded over \$10.6 million in grants from other grant institutions. Today, we are closer than ever to a cure for cystinosis. We are extraordinarily proud of Dr. Cherqui and thankful to her for her dedication to the cystinosis community.

Collectively, CRF researchers have been awarded \$12,214,460 in additional grant funds by other institutions as a result of "seed" money provided by CRF. The discoveries made by CRF researchers benefit the greater scientific community and assist other more prevalent diseases and disorders. By funding the cystinosis research community, CRF donors are effectively helping millions of people with other diseases.

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HAPPY HOLIDAYS

FROM THE CYSTINOSIS RESEARCH FOUNDATION

Dear Friends and Family,

As we enter into this holiday season, we find ourselves overwhelmed with gratitude for all the people who make the Cystinosis Research Foundation what it is today.

Each of you exemplifies the good that can come when people pull together for a common cause, and we know that because of you, we will continue to find better treatments and eventually a cure.

- We are inspired by those of you with cystinosis, who continue to teach us and bring us joy daily through your incredible courage, determination, optimism and unconditional love.*
- We are inspired by our cystinosis families, who provide enduring care and support for their loved ones even in their darkest hours.*
- We are inspired by our friends and donors, who provide ongoing support in our relentless quest for a cure.*
- Finally, we are inspired by the scientists and researchers around the world who have dedicated themselves to beating this disease.*

Each of you plays a critical role in our fight against cystinosis. Because of you, we are filled with hope and united in our journey to develop better treatments and a cure.

Your support has allowed us to come so far and we thank each and every one of you from the bottom of our hearts.

*With blessings from our family to yours,
Nancy and Jeff Stack*



**TO MAKE A YEAR-END GIFT TO THE
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New research suspends cysteamine in a liquid that turns to a gel, offering the promise of controlled release and added convenience.



Morgan Fedorchak, PhD

ASSISTANT PROFESSOR OF OPHTHALMOLOGY

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE AND
THE LOUIS J. FOX CENTER FOR VISION RESTORATION

By Dennis Arp

“Cure” ranks first, of course, but otherwise few words resonate more deeply with cystinosis patients and their loved ones than do “comfort” and “convenience.” So it’s heartening to report that researcher Morgan Fedorchak is working on a groundbreaking project that may provide more of both.

Thanks to a grant from the Cystinosis Research Foundation, Dr. Fedorchak is developing a new way to treat corneal cystinosis. If it realizes its promise, the new drug-delivery system will improve quality of life for patients and caregivers alike.

There are now multiple projects targeting the current corneal cystinosis treatment, which requires the hourly application of cysteamine eye drops to keep crystals from forming in eyes. The severe limitations of the demanding regimen inspired an ongoing research project using nanowafer technology (see the update article in this issue of *Cystinosis Magazine*). Now the same quality-of-life quest motivates Dr. Fedorchak and the CRF to explore suspending cysteamine in a gel that delivers the medication steadily and at the ideal dosage.

“We hope to decrease the likelihood of side effects through a more direct delivery of less drug than with traditional eye drops, while still maintaining a high enough concentration to be effective,” Dr. Fedorchak says.

Here’s how it works: The drug cysteamine is combined with a hydrogel, and the mixture is then applied as a liquid eye drop. Once the liquid reaches body temperature, it becomes a gel that naturally nestles below the lower eyelid, where it safely remains. Inside the gel are microspheres that break down over time,

steadily releasing the cysteamine so it can prevent crystals from forming.

Once the medication is used up, the gel is removed with a saline solution and a new drop is applied.

“Our goal is weekly application, but we’re being realistic, so we’re also developing a daily version so we increase our odds of success,” Dr. Fedorchak says.

The research project is building on the effectiveness of a similar formulation to suspend a different drug as a glaucoma treatment. That project is in its sixth year, with the formulation proving safe and effective. By minimizing systemic absorption, less drug is needed, reducing the risk of side effects. And because the number of applications is greatly reduced, compliance becomes much easier.

The corneal cystinosis investigation is just over a year old, but it’s already generating optimism.

“Any time you switch to a new drug, there is an adjustment,” says Dr. Fedorchak, assistant professor of ophthalmology, chemical engineering and clinical and translational sciences at the University of Pittsburgh School of Medicine. “Fortunately there are similarities in the treatment of glaucoma and cystinosis.

“Both are small-molecule drugs, which helps us pull from our glaucoma experience. However, the high water-solubility is unique to cysteamine, not the glaucoma drug. I’m a scientist, so these things excite me.”

Dr. Fedorchak is also an engineer, which helps drive the investigation process because “I like to break things down, get under the hood and see how things work,” she says.

That spirit of discovery energized Dr. Fedorchak when she got a call from Dr. Ken Nischal, chief of pediatric ophthalmology at Children’s Hospital of Pittsburgh. Dr. Nischal wanted to collaborate, and Dr. Fedorchak quickly learned that he is “amazing and brilliant – also an expert on corneal cystinosis,” she says.

Dr. Nischal had read about her glaucoma research and wondered if the technology could be adapted to treat cystinosis – a disease Dr. Fedorchak says “wasn’t on my radar.”

“But when he started to describe what these kids go through and what the dosing of the drug is, we saw an opportunity to use this technology to improve their lives,” she says.

The project’s next step is *in vivo* testing of the cystinosis gel formulation, using the rabbit model (for pharmacokinetic testing only). After a year of testing, “our goal is to be prepared to understand what we need to do to get to clinical trials,” Dr. Fedorchak says. Within another year, “we hope to get the green flag (from the FDA) to put it in patients’ eyes.”

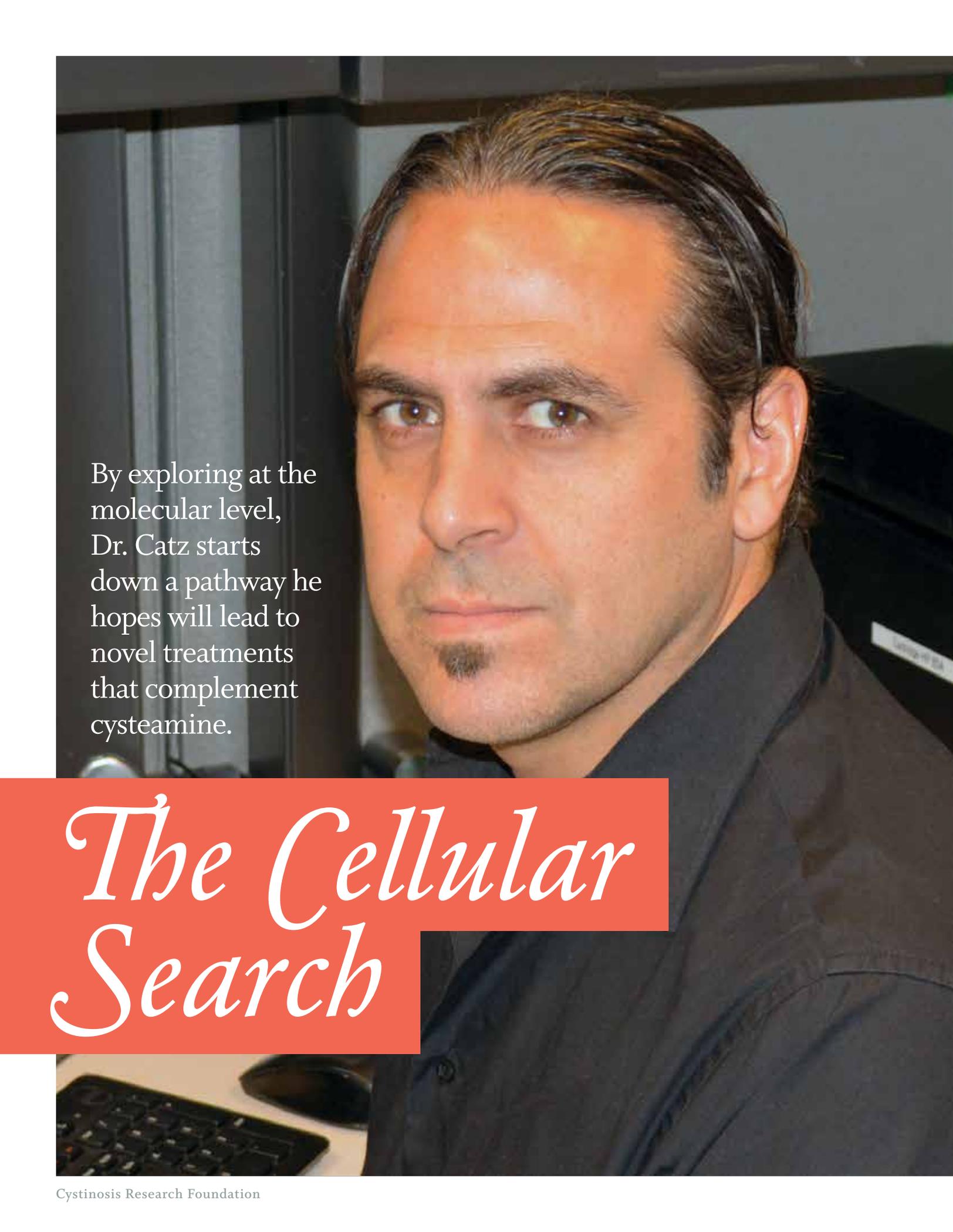
The sense of teamwork that has developed with Dr. Nischal and the CRF fuels Dr. Fedorchak’s optimism, she says.

“There’s a level of interaction with the CRF that I haven’t experienced anywhere else,” she notes. “They place trust in the investigators while still being personally invested. When we talk about this level of collaboration, colleagues can’t believe it. I’d say that we lucked out, but luck has nothing to do with it.”

Of all the projects Dr. Fedorchak has under way, “this is a favorite,” she says.

“It’s perfect for what we’re doing,” she adds. “Patients already are as compliant as they can be, and everyone in the cystinosis community is so supportive. We’re excited to see where we can go with this.”

“We’re excited to see where we can go with this.”



By exploring at the molecular level, Dr. Catz starts down a pathway he hopes will lead to novel treatments that complement cysteamine.

The Cellular Search



Sergio D. Catz, PhD

THE SCRIPPS RESEARCH INSTITUTE
LA JOLLA, CALIFORNIA

By Dennis Arp

For the growing network of cystinosis investigators, there are many avenues to better treatments. In the research realm of Dr. Sergio Catz, those pathways are at the cellular level, which takes him deep inside the disease.

Overall, the research community is well versed in the molecular mechanism of cystinosis that can be repaired by the drug cysteamine, which is the traditional therapy. But though cysteamine can effectively reduce the buildup of cystine crystals in cells and organs, many patients still suffer kidney damage.

That's why Dr. Catz and other researchers think cystinosis disrupts more than one cellular pathway.

"Cysteamine decreases the lysosomal overload, but patients still get end-stage renal disease even though they comply with treatment plans," says Dr. Catz, Associate Professor in the Department of Molecular and Experimental Medicine at The Scripps Research Institute in California. "That tells us that other mechanisms aren't being covered."

With grant support from the Cystinosis Research Foundation (CRF), Dr. Catz is exploring the defective molecular mechanisms that lead to cell dysfunction and tissue injury. It's expected that greater knowledge will lead to new treatments that correct these defects.

Maintaining, or in this case restoring, proper cell function requires the appropriate distribution of cellular components. In studying cystinosis, researchers from Dr. Catz's laboratory have identified the mislocalization of an important autophagy receptor in cystinotic cells. The trafficking of this receptor, named LAMP2A, is regulated by cystinosis, the cystine transporter that is affected in cystinosis.

"This function is critical to maintain cellular balance and survival," Dr. Catz says. "Our research has uncovered a novel pathway that will increase our understanding of the interplay between cystinosis (CTNS) and the chaperone-mediate autophagy receptor LAMP2A in cystinosis."

The researcher and his team are using state-of-the-art microscopy to determine the role of CTNS and its activity on the regulation of LAMP2A distribution and trafficking, using cells lacking CTNS or LAMP2A.

One way that Dr. Catz hopes his project will ultimately improve cellular function is by increasing LAMP2A trafficking, correcting its localization and improving autophagy.

As a system of degradation that works inside cells, autophagy basically is a waste recycling system used by cells to degrade macromolecules and

turn them into building blocks, Dr. Catz explains.

"Different types of autophagy are more active in different cells and tissues," Dr. Catz says. "Some approaches will have a high impact on certain patients and not others. We won't know just what's going on until we do more experiments."

The only way to understand the mechanisms to be corrected is to study them at the molecular level, the doctor adds.

"If you start by studying in larger organisms, say with an animal model, it's hard to determine what's actually happening," he says. "You might be able to determine the tissue malfunction, but it would be difficult to start the studies that lead to novel therapies unless you target the molecular process."

Of course, the ultimate goal is to have skilled professionals working at all levels of investigation, from molecular research to animal studies, clinical trials and ultimately the widespread use of novel therapies on patients.

When it comes to cystinosis research, this chain of collaboration begins with support from the CRF, he says. Both the International Research Symposium and the Foundation's annual Day of Hope Family Conference are tremendously beneficial, he adds.

"The interaction the CRF establishes between researchers helps take all of us to a different level of skill and activity," he says. "Plus, it's fundamental to understand the clinicians' perspective and gain from their experience."

And the cystinosis families?

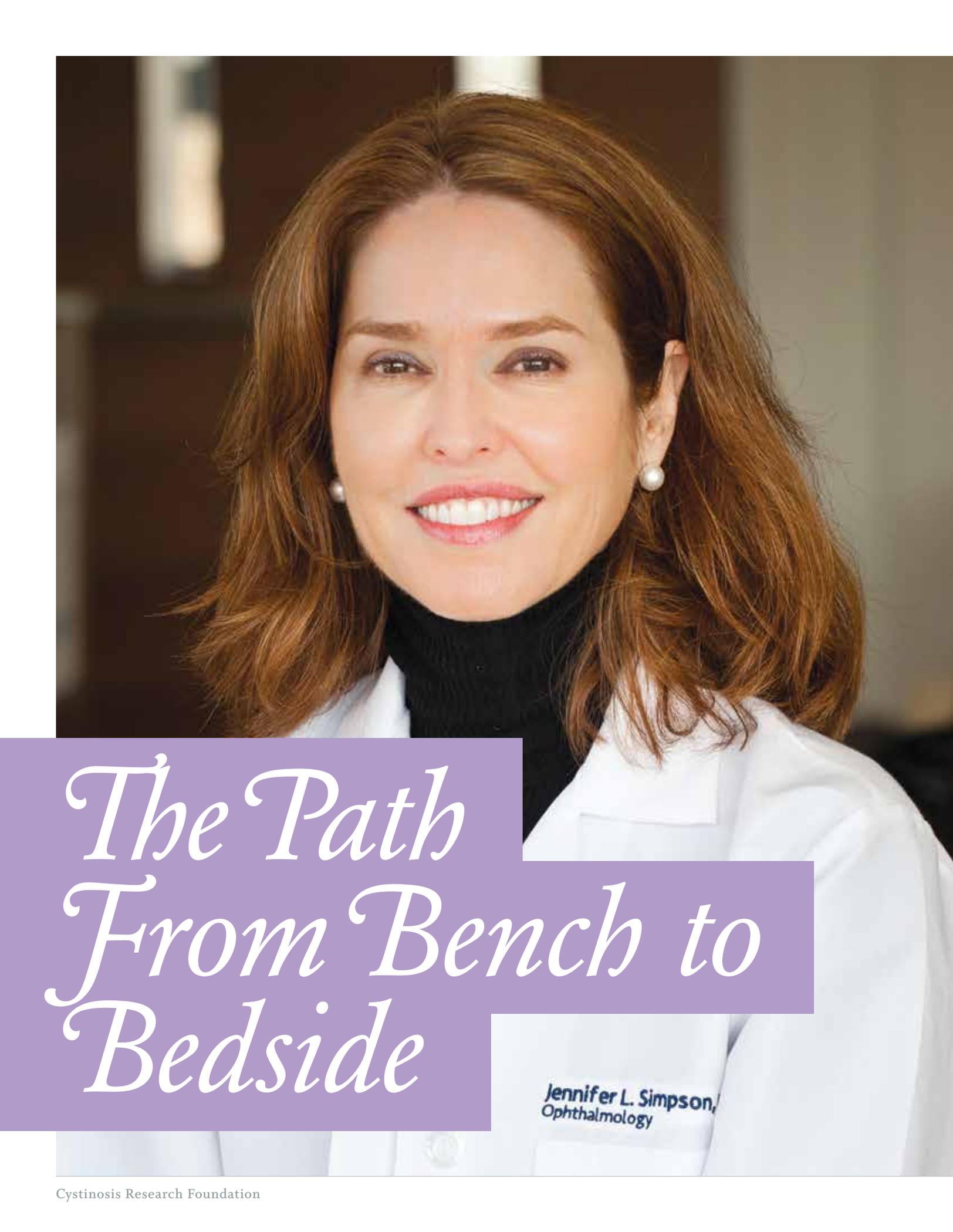
"It's hard to realize the daily obstacles they face without hearing from them directly," Dr. Catz says. "It's highly motivating."

When he hears parents describe their struggles helping their children comply with therapies, "it puts an emphasis on us to find alternatives," he adds. "Cysteamine is an effective but difficult drug. What we do may lead to better or complementary treatments. That's not a cure, but if we can delay or eliminate some of the major problems, then lives get better."

So although Dr. Catz's research may start at the molecular level, it's clear that seeing the ultimate impact doesn't require a microscope. Likewise the rewards.

"Opportunities like this to help," he says, "are why we started doing research in the first place."

"When it comes to cystinosis research, this chain of collaboration begins with support from the CRF."



*The Path
From Bench to
Bedside*

Jennifer L. Simpson,
Ophthalmology



Jennifer L. Simpson, MD

GAVIN HERBERT EYE INSTITUTE
IRVINE, CALIFORNIA

The CRF's nanowafer project makes progress to support clinical trials.

By Dennis Arp

For cystinosis families, few dangers of the disease are more ever-present than the threat to patients' sight. The need to apply hourly eye drops or risk the accumulation of cystine crystals that damage corneas creates a classic love-hate relationship.

We appreciate that an approved medication is available to treat corneal cystinosis, but the hourly drop regimen that is required to treat the disease is burdensome for everyone involved.

The good news is that a new drug-delivery system that could simplify the treatment of corneal cystinosis continues to make steady progress along the difficult path to clinical trials. As described by Dr. Jennifer Simpson, the system consists of a tiny wafer that dissolves in the eye, delivering time-released doses of the drug cysteamine. Instead of needing hourly eye drops, patients might only need to apply the wafer once a day.

"It would be wonderful to have a therapy for corneal cystinosis which is more consistent with how people really live," says Dr. Simpson, who not only conducts research but also treats cystinosis patients as a professor of pediatric ophthalmology, at the Gavin Herbert Eye Institute, University of California, Irvine. It was through Dr. Simpson's clinical practice that she witnessed the eye drop challenges that cystinosis patients faced, which leads directly to the nanowafer project. Funded by the CRF since the outset, the project unites Dr. Simpson with fellow researcher Dr. Ghanshyam Acharya, an expert in nanomedicine drug delivery at Baylor College of Medicine in Houston.

"We have progressed from proof-of-concept in a mouse model and are now making the necessary steps to evaluate the nanowafer in a U.S. clinical trial," Dr. Simpson says. "This involves standardizing the manufacturing process for the nanowafer and performing additional pre-clinical tests, both of which must be reviewed by the FDA."

To help streamline progress on the nanowafer project, a wholly CRF-owned company has been formed to efficiently advance the project through the regulatory process, Dr. Simpson says. The goal is to initiate the first trial in early to mid-2017.

"The research is very promising," Dr. Simpson says. "Support from the CRF has been instrumental. Not only financial support but also interest from families helps push us to move as quickly as we can. Knowing we are doing this to meet an acute need really motivates us."

Dr. Simpson says it's exciting to pursue the possibility of offering a new medication. Every year, Dr. Simpson looks forward to sharing progress with families at the CRF Day of Hope conference in California.

"It's a major source of inspiration for me," she says. "I feel very fortunate to be part of a team that's so focused on meeting unmet medical needs for this community."

That spirit of teamwork helped inspire her to reach out to Dr. Acharya and learn more about nanowafer technology over four years ago. The two have collaborated ever since.

"Distance has never been a barrier to our collaboration," Dr. Simpson says. "We're both aligned in our goal to see this drug-delivery system become a reality as a corneal cystinosis therapy."

At the same time, Dr. Simpson is eager to take on other vision related issues affecting cystinosis patients. Cystinosis can damage both the retina and optic nerve and lead to vision loss over time.

"Optic nerve damage related to raised intracranial pressure is not well understood in cystinosis and can be easily overlooked or misdiagnosed," she says. "We're working to better understand this problem so we can prevent optic nerve damage."

But for the time being, the nanowafer project remains her top research priority.

"The nanowafer project is a perfect example of how a novel technology can help fill an unmet need in the life of a patient," she says. "I feel privileged to be part of a project that may one day help relieve the burden of hourly eye drops."

"I feel very fortunate to be part of a team that's so focused on meeting unmet medical needs for this community."

Brooke: Cystinosis, Six Months In...



By Clay and Jill Emerson, Brooke's parents
HAMMONTON, NEW JERSEY

It has been six months since Brooke's diagnosis. There have been ups and downs, good moments and bad, victories and setbacks. We have worked tirelessly these months to get Brooke's disease in check, to speed up her weight gain and growth, to adjust to our new "normal" as parents and caregivers of a child with a chronic illness, all the while trying to give Brooke a typical toddler life.

While this isn't the life we dreamed of for ourselves or for Brooke, it is our reality, and we strive to be the best parents we can for Brooke. Brooke appears to take it all in stride, and has bounced back from all of the obstacles she has faced thus far. She always amazes us, and we have learned so much from her and how well she deals with this adversity. Oftentimes, we gain our strength from her strength.

The cystinosis community has been the biggest blessing to date. We have made some amazing friends we communicate with regularly who have become some of our closest confidants. This summer, we were fortunate enough to take a weekend vacation with another cystinosis family, Megan, Michael and Charlotte Coe. As Brooke and Charlotte are only a few weeks apart in age, they have a lot in common! The girls loved spending time together, learning from each other and developing a special bond. We have no doubt that as the girls get older, this bond will become stronger and more important as they navigate life with a rare disease. For us, it has been so comforting to have Megan and Michael as our support system, and as fellow parents of a little girl with cystinosis who understand what we are going through better than anyone else. We also have friends whom we've only met through social media, but who have been there to guide us through some dark moments and cheer us on through the bright times. Nothing feels better than knowing that as lonely as this diagnosis often feels, we are never alone because this community is strong, supportive and accessible. We owe that in large part to CRF and the Day of Hope conference, which helps unite us all and gives us a platform to meet fellow families and the experts.

We would be lying if we said we don't wish that Brooke didn't have a chronic illness, but on a daily basis we remind each other of the positives that this diagnosis has brought into our lives: our intense appreciation for every moment spent with our daughter; our admiration of all of her accomplishments and milestones reached, regardless of how small or seemingly inconsequential; our awe at her strength, tenacity, and feisty spirit; and the wonderful new friends who have come into our lives.





ALAN'S STORY:

Mending Hearts with his Infectious Spirit

By Katelyn Kerkhof, Alan's mom

WALLACEBURG, ONTARIO, CANADA

Our dream of expanding into a family of three became our reality on Aug. 25, 2013. Alan was here. Our hearts were full.

Eight months later, our struggle began. He refused his bottles, taking two hours to drink 5 ounces of formula. Food was nearly impossible, constipation an ongoing battle, and vomiting a regular occurrence. After a particularly difficult day, we agreed we'd expected parenting to be hard, but not in this way.

The result was a series of doctor visits and referrals, all prescribing that Alan would "just be small." We wanted this to be true, but we knew Alan just wasn't OK. We were feeling lost and worried, questioning everything we did.

Finally, On April 6, 2016, we brought Alan to the emergency room at our nearest children's hospital. Since it wasn't an emergency situation, we didn't know if they'd see us after the nearly two-hour drive. Alan was admitted for failure to thrive, and we were relieved to be taken seriously.

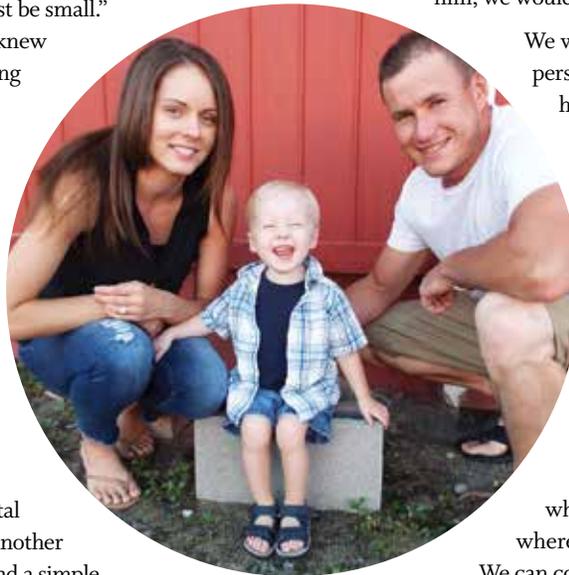
We spent one week in the hospital feeling guilty, like we were taking another child's bed. We were hoping Alan had a simple toddler problem: curable, just something we needed to change.

That's the week cystinosis went from a word we'd never heard to the center of our universe. It was as if the Earth dropped from beneath our feet, and we were left trying to hold on for Alan's life. What did this mean for Alan? For our family?

For two years all we wanted were answers and now that we had them our lives had completely changed. Having a diagnosis is so strange because you need to know, you want to know, but hearing it completely breaks your heart. We couldn't

wish it away, because that felt like wishing Alan away. You want to return to when your child didn't need medications, but that feels like a betrayal, because he is who he is, and you want to love him in his entirety.

After staying in the hospital and meeting so many great kids and families, it's hard to ask "Why us?" "Why Alan?" because, well, "Why anyone?" Alan is ours, he was always meant for us, and we for him. There is nothing we wouldn't do for him, and if traveling this journey of life with cystinosis means keeping him, we would choose cystinosis any day.



We wish we could bottle up Alan's personality – his smile, his resilience, his strength, his sense of humor – and give it to every person we meet. His spirit is infectious; he brightens up a room.

We have read that cystinosis is an orphan disease, but Alan is in no way an orphan on his journey. All the people who have touched our lives and made our new path brighter are with us, and we are grateful.

We were advised to focus on what we can control in this situation where it feels like all control is lost.

We can control our medication compliance.

We can control how we face this journey as a family: with positivity, strength and determination. We can still raise our son in a happy home and help him become a strong, kind and happy man.

Alan is growing and thriving with his treatments, and we are grateful for the good days and the hard. Alan can run in the grass, dance to his heart's content and play with his friends in a way that wasn't possible before.

The pages of our story may be different than we expected, but our hearts are fuller than we ever dreamed.

WE ARE A TINY, *but mighty* community!

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

Dear Family and Friends,

Jenna and Patrick have begun the sixth grade! The twins are already enjoying their school year. The days are long and sometimes stressful for Jenna, who still experiences knee pain and who we are working to get "patched up" as soon as possible. She will have a surgery to correct her knock-knees (typical in many children with cystinosis) before the holiday season. Jenna's procedure will have a pediatric orthopedist (at Shriners, in Sacramento) placing "guided growth implants" or staples on the growth plates of her knees. In about 18 months, after her knees have straightened, the implants will be removed. This is a surgery that Patrick will need in the coming years as well. While the idea of more medical intervention seems overwhelming at times, we are anxious to have Jenna feeling better. To see her navigate her days at school with crutches, a heavy backpack, and her awkward gait, is to know that she is carrying quite a burden each day. She takes it all in limped stride, and smiles all the time. She is a happy and joyful and caring girl.

Patrick likes to walk around with Kevin's phone or mine, playing Pokémon Go. It's almost enough to make us believe he could use his own phone... but not quite! Patrick is enjoying history lessons and math. He is a calming, spiritual and nurturing presence in our family. He is generous with his hugs and we are happy to take him up on every one.

In April, I was diagnosed with breast cancer. I'm happy to say I am almost done with my chemo treatments. By the time this article is published, I will be done with radiation and ready to get back to "normal." To learn about breast cancer, and to be treated for it, has been such a study in contrasts after being immersed in the world of cystinosis for 12 years. The depth of knowledge, the research, the data and the cure rates for breast cancer are astoundingly good. I am going to be just fine. Every nuance of my disease has had a clear medical explanation, targeted drugs to treat it, many talented local doctors, and books and countless advocates to turn to for support and reference.

The contrast is in how differently an orphan disease such as cystinosis is approached. There is much less knowledge, research and data to turn to as we seek treatment for our children. People hear of cancer each day, while most will go their whole lives without hearing of "cystinosis."



In the last 10 years, research of cystinosis has ramped up extensively, thanks to the Cystinosis Research Foundation and all who work to support it. But I am reminded every day that there is still a great amount of work to be done. There are life-altering symptoms and side effects of cystinosis that have yet to be researched.

The Cystinosis Research Foundation sent out its most recent call for research proposals just last week. There is an impressive \$1.5 million dollars available to doctors and researchers who might find their passion in the study of cystinosis. CRF's call for research proposals states:

"We are very interested in research that is aimed at the endocrine complications of cystinosis: specifically, male fertility, neurological issues and muscle wasting."

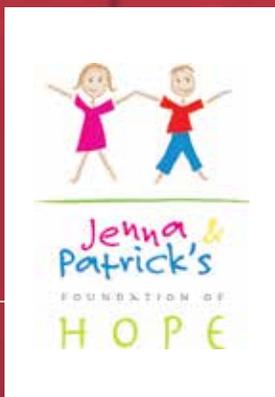
Twice a year, these research applications are emailed and sent to hundreds of institutions and researchers around the world. If you have knowledge of someone who might like to receive these calls for research, please forward their information to the CRF. A personal connection to a rare disease community can go a long way toward progress and new knowledge.

It is so easy to take our good health for granted. As I write this, I feel awful. My body and spirit are so tired. My chemo treatments have made me think, day after day: Is this what Jenna and Patrick feel like every day of their lives? I have been given a window into what our kids might be experiencing as they manage their days. The difference? I am experiencing compromised health for mere moments; I have a finish line. Jenna and Patrick's finish line depends on all of us and in a cure for cystinosis.

The study of cancer may be the most important medical task of our time in human history. The study of cystinosis will be the most important medical task of Jenna and Patrick's time. Cancer and cystinosis are two very different diseases that require tremendous resources, study, time and commitment. One is common, and one is not. Thanks to the supporters of Jenna & Patrick's Foundation of Hope and the Cystinosis Research Foundation for helping us keep the study of cystinosis moving forward. We are a tiny, but mighty community!

Teresa Partington

SEE THE
CAPITAL CUP GOLF
TOURNAMENT ON
PAGE 62!



SWING GOLF TOURNAMENT & BLING AUCTION & DINNER



Ron Thomas talks to Jenna and Patrick during a break at Catta Verdara



Jenna



Bling Auction and Dinner



Jed Risse, Jan Batt, Michael Heller

SWING & BLING SOLD OUT!



Patrick, Grandma Jan, Jenna, Grandpa Doug



Tom + Susie Jones, Darci + Karl Berger

This year's Swing & Bling fundraising events to benefit the **Jenna & Patrick's Foundation of Hope** raised an **incredible \$300,000** for cystinosis research! On March 10, the sold-out Swing golf tournament welcomed 120 golfers who played with both enthusiasm and generosity. The following day, the Bling gala fundraising dinner and auction was held at the Citizen Hotel in Sacramento and it too was a sell-out with 235 big-hearted donors. The events were organized by Teresa and Kevin Partington and their team of dedicated family and friends in honor of their twins Jenna and Patrick Partington. CRF and the cystinosis community are thankful to the Partington family for their continued partnership and commitment to help find better treatments and a cure for cystinosis.



Gary Gallelli, Kevin, Carolyn AuFranc



Tim Schaedler, Gary Gallelli



Nicole Sedleniek, Aunt Nancy Batt



Randy Dixon, Tom Walcott, Chris Zenner, Scott Bennett



Michael Ault, Dan Corfee



Three Moms, Two Countries, One Rare Disease

By Erin Little, Olivia's mom

PORT ELGIN, ONTARIO, CANADA

Have you ever had friends that you wish you had never met? Have you ever felt a strong connection with complete strangers but hate the reason that you met?

I am proud to say that I am one of those lucky women with a 1 in 200,000 chance of having not one but two beautiful friendships that I wish I didn't have. Our friendship is all because of a disease called cystinosis. Lauren Hartz and Nicole Manz are the friends I wish I had never met and we wouldn't have met if our children had been born healthy.

The friendship that has blossomed among the three of us is absolute magic. When Lauren, Nicole and I first met, we made the usual small talk about cystinosis; what time do you do meds? What meds does your child take? Do you miss sleep as much as I do? You can imagine the endless things we could talk about when it comes to cystinosis. I'd be lying if I said our friendship didn't include conversations about cystinosis in fact, this is where our friendship has deepened.

We often talk about the dark days that not everyone understands but the best part about sharing our dark days is that we push each other back up. We are there to support each

other, not push each other down or give the oh-so-loved advice that, "Tomorrow is a new day." We send each other random texts about our favorite books, quotes, movies, our fears, our truths, our dreams and our goals. We talk about our children's future and what we want for each of them. We talk about how we can become better mothers, wives, teachers and friends. We ask each other for advice and encourage each other to grow. We can cry when things are tough and not just cystinosis tough but life tough, all of the other stuff we moms and women go through. There is never judgement, only love and kindness.

We started off being Facebook friends and then we had a couple of random phone calls. Then we met at the CRF Day of Hope and in September we are off to an "I Can Do It Conference" where we will have a girl's weekend. My guess is we will spend the weekend learning together, laughing, crying and sleeping through the night. The three of us took a chance on each other and that's because we took a chance with the Cystinosis Research Foundation.

I wanted to share this story of our friendship because it's rare just like cystinosis

and like the Cystinosis Research Foundation. When Chad and I attended our first Day of Hope in 2011 we were curious about everything: the families, the research and the organization itself. We got involved in fundraising and working with the CRF because they were doing the work and moving mountains. We wanted a better future for Olivia and all of those with cystinosis. I never would have thought that I would form lifelong friendships with other families. I never would have thought I would love their children as much as I love my own. I never would have thought I would have found true friends.

As important as the research for a cure and better treatments is, so are the personal connections that are formed because of the Cystinosis Research Foundation – they are priceless. I can't thank everyone enough for bringing this foundation together: the Stack Family and everyone who gives and fights for our children and our families. Hope comes in many forms – better treatments, a cure and lifelong friendships.

Together, we can move mountains.

Finding Inspiration in the Bravest of Smiles

By Maria Lilland, Denis' mom
TOLVSROD, NORWAY

The first day of February this year, I took my son, Denis, to our doctor. Nothing was really wrong with him except that he was drinking loads of water and I had been told that I was encouraging a bad habit by allowing him to have water whenever he wanted it, including throughout the night. After hours of Googling symptoms, I was certain he had diabetes. However, the doctor told me it was not diabetes, which felt like 20 kilos lifted off my shoulders. My motherly instinct, however, told me something was still wrong. The doctor must have sensed this because he asked me to collect a urine sample from Denis and deliver it the next day.

The doctor called me the very next day, but before I picked up the phone I felt a wind of grief come over me. I knew this call would change everything, and it did. We were told to pack a suitcase and leave for the hospital immediately. After a night in the hospital, while we waited for the diagnosis, Denis took his first real steps in the hallway of the hospital. He learned to walk! He learned to walk when I was at my lowest point: when I was scared and angry. This moment was not as I had pictured it would be. It was not the idyllic moment I had imagined in my head.

The first results of the blood draws and tests were uplifting. My mother was with me at the hospital – she has been a steady pillar for me in all of this. The nurse told us that Denis had Fanconi Syndrome. She said, “It’s an easily managed disease. You are actually lucky it wasn’t diabetes like you expected. Fanconi Syndrome is easy to treat with some tablets of bicarbonate.” My mum and I high-fived each other with relief as we followed the nurse out of the room.

Although we had a diagnosis, they wanted to find out the cause of the Fanconi Syndrome. I Googled Fanconi Syndrome and after reading through a jungle of articles I found the word, “cystinosis.” As I read about the disease, I realized this would be the real diagnosis. I knew my son had cystinosis. There were little signs that I had never thought were health related that now made perfect sense. One was that my son is completely blonde and there is no reason for him to be and the other was his thirst for water.

When I finally got the call that confirmed cystinosis, I answered politely saying, “OK, thanks for calling.” I hung up and then I cried. I cried out all of my tears. I am both the mother and the father of my son, and I had never felt as alone as I did at that time.

Since the diagnosis we have been in and out of the hospital constantly. I understood quickly that I needed to learn everything about everything in order to give my son the proper care. Being informed was the way I picked myself up. There was no chance I would give up on him, or the disease. There are fewer than 10 cases

of cystinosis in Norway. My son is the youngest with cystinosis. I have learned a lot about myself since the diagnosis. I am stronger than I had believed I was.

I found my support and information from parents of children with cystinosis. The feeling I had of being all alone in the world, changed to a feeling of our life having a higher meaning. We were going to beat this!

They say that hard obstacles only come to the people who are strong enough to tackle them. My son is a champ. In six months he has gone from four people holding him down for blood draws to looking forward to the blood draws and even asking for more!



At the age of 2, he has learned that when he feels sick or throws up, it is time for the hospital. Now after only a few months, he takes all of his medication orally and by himself. He is proud as can be every time. He is my hero. Although I am constantly telling Denis to eat, try new foods and drink, he doesn’t complain.

When we go outside he squints, asking for his sunglasses. You can clearly see he is in agony, though he doesn’t complain. We have days when he is not feeling well and wants his mommy by his side in bed. When I am with him, he strokes my hair giving me his bravest smile like he’s telling me that everything is going to be fine. That says something about how strong he is, and how much love this little boy has in his heart. He is truly my inspiration in life.

We have learned to live with cystinosis thanks to other cystinosis families, as well as doctors and the Cystinosis Research Foundation. I now believe that I need to, and want to, give back to all the people who have helped me. It is so easy to think someone else will do things for you, but now it is my time to do something of high importance besides caring for Denis at home. It is in my hands to spread the word “cystinosis” and bring awareness to a disease that is almost unheard of.

We have raised over \$4,600 for CRF in just a couple of months and that makes me happy. Raising funds soothes me emotionally because I know I am doing something that counts, and I am helping get us one step closer to the cure and medical improvements. I am sure we will see the cure because we are working all together. If we stand together we can do anything. I really believe that!

I want to thank everybody who has taken the time to answer me, guide me, and listen to me at my most desperate moments. I want to thank you for giving me the tools to improve my son’s quality of life. I am forever grateful for this, and I want to tell you all that you are superhumans.



SEE THE GO-FUND-ME
RESULTS ON PAGE 6o!



CHARLOTTE COE:

Love Helps Break Through the Heartbreak

By Megan and Michael Coe, Charlotte's parents
WEBSTER, NEW HAMPSHIRE

Has it almost been a year already? It feels like yesterday we received the call from our doctor that put a name to all of the medical anomalies Charlotte was facing. "Your daughter has cystinosis." They said. How could it be true? This cannot be happening. Why her? What does this mean? It was like a dark cloud hanging over us that would not go away. We knew so little about this disease, making the time before and just after Charlotte's diagnosis an extremely dark time in our happy lives.

Shortly after her diagnosis we received another call, this time from Nancy Stack. She shared Natalie's story with us and a few months later we were on a plane to California for the Natalie's Wish event. Our family has had the highest highs and lowest lows over this past year; doctor's visits, G.I. surgery to place a feeding tube, multiple medicine adjustments, so many challenges to Charlotte's health and our family's well-being. However, the highs always lift us out of the mud that cystinosis tries to stick us in.

We feel fortunate to have had the chance to visit California, just two weeks after Charlotte's surgery, and to meet the amazing doctors that are working around the clock to find better treatments and a cure. We were floored by their compassion and dedication to their work and to the patients and families affected by cystinosis. We also made wonderful connections with the other families who share in the same challenges and learned a lot about love, strength and bravery from everyone there. Charlotte loves her new friends and, now that she is talking up a storm, we hear her

saying their names from time to time and assigning them to her stuffed animals and to the stars on the ceiling of her bedroom. It's amazing how something so challenging and often heartbreaking can bring about the most love and connection in people.

In June we met with the Emerson family in Woodstock, New York, for a weekend getaway. Charlotte had a blast with her friend Brooke and they learned so much from one another while enjoying a nearby creek and having cookouts. Charlotte took her first steps just a couple weeks before the trip and it was the most joyful thing as parents to finally see her moving about on her own and chasing after Brooke! The girls got to see each other taking and we parents were able to share tips, stories and just be there for one another. If Charlotte has to grow up with this disease, we are truly grateful that she will not be alone.

We feel so close to all of the families in the cystinosis community; the Stacks and the Cystinosis Research Foundation have truly created one big family dedicated to not only finding a cure but to supporting one another, and celebrating the love and the highs that come from fighting this disease. Each day we fight, and each day that Charlotte has success over cystinosis, we can see that dark cloud dissipate a little more. Through the education, research and support of this community we are feeling a lot more positive about Charlotte's future. Charlotte is thriving and we are living, loving and fighting for each day.

May love be with you in all that you do,

The Coe family



‘DEFYning’ Cystinosis



Jake (left) and his twin brother, Austin

By Jeremy Krahe, Jake's dad

MEDINA, OHIO

This is the big year that my twins, Jake and Austin, reach the decade mark! They are now 10 years old and as a father I find myself asking the age old question of, "Where does the time go?" It has been eight and a half years since Jake was diagnosed with cystinosis. The day we received the diagnosis will forever seem like just yesterday; however, time continues on and they are growing up fast. Like every other proud parent, we cried at the first steps, laughed at the first words, applauded at the first concert and cheered at every baseball game. Every day is a blessing and provides us a constant reminder of the strength of our children.

As the father of a bright fourth grader that reads everything he can get a hold of, I know that Jake will read this magazine cover to cover like he always does! It is for that reason I'm going to take this opportunity to write a note for my son, Jake.



To Jake ("My Little Buddy"),

Over the past several months you have come to Mom and me with lots of questions about cystinosis. You've asked us hard questions that NO ten year old should have to ask and you listened intently as we try to define cystinosis. Mom and I always knew that one day you would want to learn more about your disease and we will continue to always be there to help answer any and all of your questions. We are amazed at your ability to comprehend and proud of the strength and attitude that you approach our discussions.

Jake, I used to ask myself how cystinosis would define your life. Your Mother and I hoped and prayed that God would give YOU the courage and strength to achieve everything in life you want. We promised that we would do whatever we can to help you achieve all your dreams. We never want your life to be defined by cystinosis. What you have showed us is that you have NEVER allowed cystinosis define you, instead you continue to "defyn" cystinosis.

I know you'll be reading this little buddy, and I want you to know that Mom and I are so VERY PROUD OF YOU! We are proud of you in everything you do! We are proud of the way you sit up tall and point out to the nurse the best location for a needle at your blood draws. We are proud of the way you take all 54 of your pills every day without once complaining about taking them. We are proud of you when we pull you from your game with friends to give you eye drops without a fuss. When you get sick in the mornings before school and come out with a smile on your face you show us what real strength and courage is.

Recently, you stood up in front of a room full of strangers at a Rotary Club meeting and helped an audience full of adults understand cystinosis. You answered questions and showed everyone in that room just how incredible you are. You taught a room full of strangers what Mom and I already knew, that you are an amazing young man with the ability to teach others about courage and achieving things beyond expectations. As I watched you answering questions, I once again realized that you, my son, are not defined by cystinosis, rather YOU are "defyning" the disease.

You have never asked, "What can't I do?" To the contrary, I find myself once again at the start of school sorting through a pile of permission slips for sports, scouts and instruments. Every club and every activity that your school presents, you bring home wanting to join. There isn't a sport you haven't played nor a challenge you have backed away from. You have never feared failure and you work hard to be the best you can be in everything you do! You're an inspiration to Mom and me, and you're an inspiration to all those around you.

My promise to you, Jake, is that I will always love you and always support you in everything that you do. Your positive attitude, strength and courage will open every closed door life throws at you. Never let anyone or anything define you or keep you from pursuing your dreams. I'm confident that you are going to accomplish so many incredible things throughout your life and NOTHING is going to hold you back. Cystinosis will never define you... you instead have chosen to "defyn" cystinosis!

Mom and I are so very proud of you and love you!

Love, Dad



SHATTERED EXPECTATIONS; *Abundant Joy*



By Ann Abele,
Keegan's great aunt

When my niece, Elizabeth Nicole Abele Manz (Nicky to family), asked me to write an article about her son Keegan for the next CRF magazine, it was surprisingly challenging to put my emotions and thoughts about him into words. My wise mother tells me that is because it is difficult to describe unconditional love. That's what comes when a cystinosis diagnosis shatters all expectations.

Keegan was born in the spring of 2013, two months after my husband was tragically killed. Because my niece and her family lived 500 miles away, I didn't meet Keegan immediately. But his healthy birth was a bright light at a very dark time for me.

When he was 6 months old, Keegan became seriously ill. Thankfully, his mother persisted in seeking repeated medical help as he became more and more lethargic. During that first hospitalization, he almost died because of his critically low potassium level. His survival was the first indication of his resilience and ability to endure life-threatening circumstances. Because I am a pharmacist, I tend to be the family's patient advocate and medical interpreter for health care. Thankfully, Nicky was educated as a nurse (divine plan) so we speak the same language in that regard.

I was the one who was there when Nicky received the devastating call from the geneticist confirming Keegan had cystinosis. Like other cystinosis families, they have learned how to deal with an overwhelming amount of medications and lots of doctor visits; use and maintain first a feeding tube, then later the present gastric tube; function with disrupted and never enough sleep; and expect at any time that they may need to clean up unexpected projectile vomiting – to name but a few of their common, everyday realities due to this disease.

Staying with them for extended periods of time, I found my first glimmer of hope for surviving my own grief when I was rocking Keegan in the early hours of one of his restless, pain-filled, sleepless nights.



With all expectations gone for both our futures, the only things that could be done were to be present in the moment with love and earnestly pray for his well-being. He was and still is a happy, determined child with a naturally sweet disposition.

Nicky, my oldest niece, makes living with cystinosis normal for Keegan by letting him help administer the plethora of his around the clock “vitamins,” showing him how

to give eye drops to his stuffed animals, and envisaging his new orthopedic foot/ankle braces as “construction shoes like daddy wears.” Her “blending” diet for nutrition to supplement oral intake has helped battle the failure to thrive tendency and has also drastically reduced Keegan’s electrolyte and metabolic imbalances and side effects. Sharing networking tips like this with other cystinosis families is part of the mutual support of the small though strong community of which she is an active participant.

She is not battling alone: Nicky’s husband, Brad, changes diapers, cleans up vomit, gives baths, alternates/shares night duty on the many nights that Keegan does not sleep soundly, and has dressed in only a speedo and cowboy boots to raise money for cystinosis research. I love the shouts of joy from his two boys when he gets home from work in the evening; his steady, calming presence especially in crisis situations; and his obvious devotion to his wife and sons.

Despite full schedules and huge responsibilities, they Nicky and Brad actively raise funds for CRF because of their belief in the goals and the management of the organization. With the determination and financial resources to fund promising, ongoing research, there is not only hope but confidence that a cure will be found ... hopefully in Keegan’s lifetime.

Keegan’s brother Shane is an exceptional 7-year-old who has become Keegan’s hero and



protector. At the 2015 Day of Hope conference, he was very protective, warning everyone to be careful around his little brother who had cystinosis – and was surprised to meet so many other active children around him retorting “I have cystinosis!”

Keegan’s cystinosis has impacted his grandparents, great-grandparents, uncles and aunts, cousins, and other family and friends. The diagnosis was a bombshell. We felt helpless with the reality of what is necessary to keep this precious child alive. We grieved that our “normal healthy child” assumption was snatched away by a rare, recessive gene combination that was unknown to everyone in the family tree. However, out of the ashes of expectations and dreams, we are pleasantly surprised at the joy and blessings that have been received.

I have neither the wisdom nor the eternal perspective to understand why the Lord leads people down a road of pain and hardship except there is abundance to be found along His pathway. Keegan is truly a treasured gift in our family. Our life is so much richer with him in it!

BECAUSE OF KEEGAN, WE ARE:

REPLACING SHATTERED EXPECTATIONS
WITH SIMPLE CELEBRATIONS.

LIVING WITH THE AWARENESS THAT EACH
NEW DAY IS A GIFT, NOT A GUARANTEE.

OPENING OUR EYES AND OUR HEARTS TO
WHAT IS UNFAMILIAR.

DISCOVERING A BEAUTY THAT IS FELT
DEEP WITHIN OUR SOULS AND RELEASING
IT IN THE FORMS OF LOVE, KINDNESS,
COMPASSION AND GENEROSITY.

Keegan is fortunate that his parents encourage his playfulness and development. His life is always going to be more difficult than other children without special needs, but he is not going to be allowed to use cystinosis as an excuse. It is just his normal – until the cure is found.

Celebrating a Summer of Adventure

By Brian and Tricia Sturgis, Henry's parents
SANDPOINT, IDAHO

This was a great summer for Henry – a season filled with lots of fun, play and adventure.

He has a great group of friends that he loves to hang out with, and they enjoyed spending their days playing and riding bikes in the neighborhood. In August, he attended a weeklong adventure camp at Schweitzer Mountain Resort in Idaho, where he and other kids spent the days hiking, swimming, playing games, and riding the chair lift to the top of the mountain to pick huckleberries. Schweitzer has been a big supporter of our cause, hosting several events to raise funds for cystinosis research.

Henry keeps active and participates in weekly water therapy where they are focusing on core strength in addition to his weekly physical therapy. In late June, we had orthotics made to help with flat feet and ankle pronation. The pronation has caused his leg muscles to work overtime which affects his balance and causes fatigue. The orthotics make his feet sore and sometimes cause blisters on the arches of his foot, because he puts so much pressure on that area. We are hoping that they will work out, if not we will try leg braces.

The highlight of Henry's summer was a weeklong houseboat trip to Shuswap Lake in Canada to celebrate his grandma and grandpa's 50th wedding anniversary. Henry's 10th birthday happened to be during the trip, and he thought it was pretty cool to celebrate his special day on a boat.

SEE 24 HOURS OF
SCHWEITZER
ON PAGE 60!



International Relationships Abound

By international cystinosis partners and mother-daughter duo, Karen McCullagh and Kelsey Cunningham
LANGDON, ALBERTA, CANADA

As many of you know our daughter Kelsey made the brave and adventurous move to Ireland in December 2015. We will skip over the impact that her leaving had on our family, suffice it to say she is missed every day.



She hit the ground running, making Cystinosis Ireland her first point of contact. After a few meetings, long discussions and recognition for what she could bring to the table, the board took a chance and hired her to manage some of the day-to-day business of the society.

In July of this year, Andrew and I flew over to visit Kelsey and were honored to meet some of the champions of her board. We had a wonderful dinner at the Pig's Ear with Mick Swift, chairman of the board and Liam McFadden their treasurer. What was so inspiring is that neither one had a family member affected by cystinosis, yet their passion for our cause was abundantly evident. Our second dinner was at a great spot called Saba with Sue Maguire, assistant secretary at Cystinosis Ireland and her husband, Andy, who sits as a member on the board. They have two adult daughters with cystinosis. What started out as cautious inquiry soon turned into an evening where conversation, food, passion and a wee bit of wine flowed. We left feeling like we had been lifelong friends.

After meeting and breaking bread with these wonderful folks, the world of cystinosis feels a whole lot smaller. We all want the same thing – a cure – but we are willing to invest in research that will result in a greater understanding and bring better treatments for cystinosis to the forefront. We are looking forward to seeing how we can span the geographical distance to find more ways to work together in our efforts.

What follows is an account of Kelsey's experience since she left Canada and headed to Ireland. As an advocate for a unified international cystinosis community, I couldn't have said it better myself. As a mother, I simply could not be more proud.

I've had the unique privilege to experience firsthand the intricate relationships of the international cystinosis community; first as a family member, and now as a professional working for Cystinosis Ireland. From this experience, I have grown to better understand how incredibly fortunate we are to be involved with a rare disease community that looks at other national and global cystinosis groups as companions instead of competitors.

As a charitable community, we have identified that the sharing of information, research and resources will be the fastest and most efficient means for us to find a cure. Something that the international groups have been actively working on has been to check in and update one another, be that through phone calls or emails, or by attending conferences or scientific symposiums. Collaboration allows us to "throw a wider net" to ensure that our research is diverse; it enables us to fund research we otherwise would not be able to subsidize, and encourages us to work together to and to learn from one another.

It would be very easy to develop an us-versus-them mentality toward each of our individual charities, but that is not the nature of our greater cystinosis family. Instead, we look beyond borders and boundaries to support and better one another. A great woman once wrote, "We are only as strong as we are united," and I believe that our community grows stronger every single day.

My Wish For You

By Jessica DeDio, Bailey's mom
FULLERTON, CALIFORNIA

Bay turned 18 on November 26 of last year. It was a beautiful day. We made it even though the doctors thought we would not. Although Bailey spent most of his high school career on home or hospital school instruction, Bailey graduated from high school on May 25 of this year. What a beautiful day it was for me, his mom, to see him walk across the stage with his diploma. Although I was happy, I was also sad because I had a feeling that something was severely wrong with his health. He was pale, lethargic and all skin-and-bones. But he did it, he graduated! His graduation day remains a picture in my head that I will carry with me forever.

A week after the graduation, Bay was hospitalized. He was lifeless and almost died. He lost 30 pounds, could not eat or hold down food and had high fevers. Bay spent the next nine days in the hospital being poked and prodded – they did every test known to man. He was diagnosed with cytomegalovirus (CMV) virus which attacked his body and almost took his life. His intestines were like raw meat. Bailey had to get a PICC line inserted, was stabilized and then finally released after a torturous, emotionally traumatizing hospital stay. We left the hospital still needing to administer heavy antibiotics for a month and we are still not out of the woods.

Right now things are better, but living with cystinosis is a struggle every day and it takes a toll on the whole family. We are so grateful and humbled by all of our supporters – Bailey Believers – and the Cystinosis Research Foundation, which is our family. It takes a village to live with cystinosis.

I dedicate the lyrics from the song “My Wish” by Rascal Flatts to my son Bay:

*My wish, for you, is that this life becomes all that you want it to,
Your dreams stay big, your worries stay small,
You never need to carry more than you can hold,
And while you're out there getting where you're getting to,
I hope you know somebody loves you, and wants the same things too,
Yeah, this, is my wish.*

Love Always & Forever, Mom





A Grandparent's Joy

By Steve and Monica Gielarowski, Kaleb's grandparents

LORTON, VIRGINIA

When our daughter Kate and her husband, Mike, told us they were expecting their first baby, we were thrilled but a little nervous at the thought of becoming grandparents. That is until Kaleb Michael Lawshe arrived early in the morning on August 27, 2013. At 6 pounds 14 ounces, he was beautiful and we fell in love immediately.

By 9 months, Kaleb started showing signs of failure to thrive. No answers from the doctors, only lectures that he needed to gain weight to grow. Months went by with no change, only more worry. When our son-in-law's company announced that they were switching insurance plans requiring employees to find new doctors, we were elated.

They found their new pediatrician through a referral and met with him the following week. Less than two days later, Kaleb was admitted to the University of Virginia (UVA) Children's Hospital in Charlottesville, Virginia. After two weeks of intensive treatment and numerous tests, they finally had answers. At the age of 21 months, Kaleb was diagnosed with cystinosis. As one of the UVA doctors told them, "...his new pediatrician saved his life."

As a parent, you want the best for your children. You see to their needs and protect

them from all harm. It's different as a grandparent; we felt helpless watching them go through everything and not being able to fix any of it. We were not only worried about Kaleb but worried about Kate and Mike and how they were coping with it all. All we could do was to be there for them and pray. Their little boy, our beautiful grandson, was sick with an incurable rare disease.

So much has changed since and life has a new normal. Kaleb is now 3 years old and doing well. Because of the late diagnosis his doctor says he will definitely need a kidney transplant much sooner than initially thought by UVA. We continue to have faith and hope. We know so much more about cystinosis now and while we still worry, we aren't afraid for the future.

Kate, Mike and Kaleb now live in Charleston, South Carolina, and love being near the beach. Kaleb receives care through the Medical University of South Carolina (MUSC) Children's Hospital Nephrology Department. He is a playful and fun-loving little boy who doesn't know life as any different and we love going to visit as often as we can.

We are especially thankful and comforted knowing that they are part of the Cystinosis

Research Foundation (CRF) family and online support community. Most importantly, they aren't alone anymore in this journey and we hope one day soon they will share their story so others will be inspired. Their strength and courage throughout has been amazing and we know without a doubt that our precious grandson is cared for by the best mom and dad heavenly possible.

There is still so much to be done in raising awareness and educating the medical world so children like Kaleb don't have to wait so long to be diagnosed, and so parents like Kate and Mike don't have to endure the worry and gut-wrenching fear of not knowing what's happening to their child. Most of all, we find great hope in knowing that CRF is passionately working on research to find a cure. We can all be a part of their journey whether it's parents, grandparents, extended family or friends. Whether we live close by or far away, we can all make a difference!

Our greatest joy...this beautiful little boy named Kaleb Michael Lawshe.



SAM AND LARS JENKINS



Ob La Di, Ob La Da, Life Goes On!

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



Samuel and Lars have been really into the Beatles lately. Their favorite songs are “Yellow Submarine,” “Hey Jude” and “Let It Be.” The song “Ob La Di, Ob La Da” comes to mind when I think about our current journey with cystinosis. While we still have daily struggles and frequently ask ourselves why we have to deal with this disease, we try to keep an optimistic spirit and enjoy the ride as, “Life goes on!”

Samuel has come a long way since he was diagnosed with cystinosis six years ago. I remember days when I thought he would never eat food, and now he eats just about everything we put in front of him (except fruit). He definitely still has his preferences: cheese, nuts, French fries, Brussels sprouts, Zuppa Toscana Wedding soup, cheeseburgers and pizza. He is growing taller but hasn’t gained weight for a while, so we are still supplementing with tube feeds at night.

I remember days when I thought Sam would never walk (he didn’t until he was almost 2 years old). Now I see him running around with the neighborhood kids, riding his scooter, and climbing trees like a hooligan. We go hiking a lot as a family and he always keeps up. We’re still working on riding a bike.

I remember days when I thought Sam would never talk. He was a late talker and for a long time most of what he said was unintelligible. Now he and I have conversations about topics ranging from wild animals to World War II. He still goes to speech therapy at school, but other kids can understand him now. He did just lose his two front teeth, which has resulted in an adorable lisp.

He just started second grade and loves going to school. His favorite things to learn about are history and science. He loves to read, especially books about Star Wars or anything military. Of course, school comes with its challenges, too. Math and writing seem to require extra work. He has to go to the office every day to get potassium through his G-tube, and sometimes it makes him nauseous. The smell of cysteamine is also a

problem, even with Procysbi®. Not all kids are very tactful about that.

Overall Samuel is doing remarkably well. Like all kids with cystinosis, he takes an impressive list of medications, but he does it without arguing (most of the time).

Lars is basically a normal 4-year-old kid; he just has to take cystagon every 6 hours. He’s never had problems with any milestones. He’s big for his age and makes friends with everyone he meets. He loves playing with bigger kids, especially teenagers. He loves to eat, especially sweet things. He would be happy to subsist on ice cream and fruit for the rest of his life. He loves dogs and has picked up a love of stuffed animals from his older brother. His favorite show to watch is Octonauts. Right now he is obsessed with pill bugs, or as he calls them “roly polies.” He spends hours looking for them in the yard and building “roly poly” kingdoms. He just had a check-up with the nephrologist, and aside from some mild protein in his urine, he has no evidence of cystinosis from the kidney end of things. We will probably switch him to Procysbi® soon, now that he is ready for pre-school. He has started picking up more crystals in the cornea so we’ve doubled down on giving him his eye drops. He doesn’t tolerate them as well as Samuel and frequently tells us his eyes hurt after getting drops. I’m looking forward to the nanowafer trial coming up!

We are so grateful for everything the Cystinosis Research Foundation is doing to help our boys. Every dollar of research holds the potential for improving their quality of life. There are so many great things in the pipeline. Hopefully Dr. Emma will be able to share the results of his drug library screening soon, so that other drugs may become available to treat the disease. We are especially excited about the work Dr. Cherqui is doing with gene therapy and stem cells. I used to hesitate to say the word “cure,” but now I pray for it every night. Our boys have never known a life without cystinosis, but we are hopeful that one day they will.



Camella & Bill Helbling



Heart for cystinosis

Our beloved friend and long-term supporter William (Bill) Helbling passed away on Monday, February 29, 2016. Bill was a devoted husband, father, grandfather and great-grandfather with a heart of gold and known for his firm handshake. He is survived by his loving wife Carmella, of more than 63 years, who resides in Moscow, Idaho. In the early years, he and Carmella spent many hours dealing with cystinosis, which took the lives of five of their ten children.

(They) spent many hours dealing with cystinosis, which took the lives of five of their 10 children.

The Helbling family have been avid supporters of cystinosis research. At the family's request memorials were made to Tina's Hope for a Cure in the amount of \$5,370. Bill will be missed by all who knew him, but he is now at peace with his five celestial angels—David, Steve, John, Mary Ellen and Brian.

The Rally Behind Tina!

By Denice Flerchinger, Tina's mom
CLARKSTON, WASHINGTON

Letter-Writing Campaign

Navigating a rare disease for 12 years has proven to be extremely challenging, and this year is no exception. Tina has had a challenging year. Although she is sometimes frustrated by the daily obstacles of her disease, she is courageous in her daily fight. She is the typical 13-year-old, but on the inside her body is fighting its own battle.

Tina's kidney function is rapidly declining. We have added a daily growth hormone injection to her already daunting daily regimen of medications (54 pills and hourly eye drops). Although Tina rarely complains, the added growth hormone injection has been extremely difficult for her.

Tina's specialists are hoping this addition will not only help reverse growth retardation, but will also help preserve muscle mass.

It is with heavy hearts that we did not hold our annual Wine, Stein & Dine event last May. We need this time to care for Tina and her emotional and physical needs. However, realizing the importance of funding research is more critical now than ever we sent a letter to family, friends and past supporters asking for their continued support. The campaign letter raised an astounding \$85,000.

We continue to be humbled and our hearts are overflowing with thanksgiving for the continued support that we receive from our community. Along with money to help continue research we receive daily notes of encouragement and prayer – we are inspired by each one! Together we will find a cure!

SEE ROGERS TOYOTA'S
"CHOOSE YOUR CHARITY"
CAMPAIGN ON PAGE 61!

The campaign letter raised an astounding

\$85,000





FINDING INSPIRATION IN A JOYFUL SPIRIT

My name is Ellie Watson, and I am a junior at Summit Academy in Cottonwood, Idaho. I first came to know Tina and the Flerchinger family when her older sisters, Nichole and Catherine, and I went to the same school in Lewiston, Idaho. Sometimes, I would go over to their home, because my own sister was very sick with a severe heart condition and often spent a lot of time in the hospital. Even though Tina didn't often feel well, she always seemed joyful. Her joy was an example to people like me about how to offer up our little sufferings every day. I knew that if Tina could do it, I could do it.

Her family was loving and kind, always trying to look at things in a positive light. Nichole and Catherine were so helpful getting syringes and medications ready for Tina. They would do whatever they could do to help out. I knew it had to be hard for them to see their sister so sick. Tina and her family have always been an inspiration to me.

Growing up with my own little sister having many medical conditions, my heart has always gone out to the Flerchinger family. Seeing their example of selfless love was moving. Tina is such a beautiful girl. She always has a smile and looks so happy. It is truly amazing how the Flerchinger family started Tina's Hope for a Cure and is doing their part to find a cure for Cystinosis.

I have been participating in 4-H for several years, and every year I choose a good organization to donate 10 percent of the profit from the sale of my market animal. This past year I donated 10 percent from the sale of my lamb to Tina's Hope for a Cure. I hope that Tina and all those who suffer from this disease may one day be cured and that Tina's hope may one day be a reality. May God bless you all on your journey to find a cure for cystinosis!





Thank you for your support on "Pink Out with Nicole" Day!





CLASS ACTS

From students and teachers to parents and administrators, a school community rallies to provide uncommon support for Nicole.

By Dennis Arp

Nicole Hall wanted nothing more than to be a typical student at Saint Paul the Apostle Catholic School in Richardson, Texas. But that hope disappeared every time her classmates went to lunch in the cafeteria while she trudged to the nurse's office to take her sustenance through a feeding tube.

"I think we can all understand the feeling of not being part of the group," says Darbie Safford, principal at Saint Paul.

To combat that isolation, Nicole and school officials turned to information. With support from school nurse Kim Gump, Nicole visited every class in the school to share about cystinosis and explain why she has a G-button on her abdomen. For someone as naturally shy as Nicole, the talks took substantial courage. It was a great help to know that wherever she went, she was among friends.

"It was a really big thing that Kim was able to get her to go around and be more comfortable talking about it," says Aaron Hall, Nicole's father. "Now Nicole can walk around school with her pole, including sometimes to lunch with her friends. She can let people know, 'This is my normal.'"

"Without the help of the school, I guarantee that would not have happened."

The support felt by Nicole and her parents, Aaron and Stephanie, takes many forms. In addition to administrators and nurses, teachers understand that Nicole has specialized needs, including medication, lots of water and rest during particularly taxing days.

Because cystinosis irritates Nicole's eyes, sometimes teachers lower the room lights to ease her pain. When fatigue sets in,

there's a class beanbag chair that allows her to relax and recharge.

"Not once have the other kids complained that Nicole gets special treatment," Aaron says. "It's all part of the love shown to Nicole."

In fact, classmates actually look forward to helping Nicole. They share the role of accompanying her to the drinking fountain, nurse's office or other campus destinations. Particularly fun are the "movie lunches" they all share in the classroom because Nicole can't always join them on the playground.

"I think all of our kids benefit from in their relationship with Nicole," Safford says. "They learn that everyone is different and everyone is an important part of our community."

Stephanie Hall says that other parents tell her their children are learning to be better people because of their friendship with Nicole.

"They see their kids learning a higher level of compassion," Stephanie says. "Everyone is giving back to everyone. That's something all parents can hope for, and we're blessed that we get to experience it."

Stephanie emphasizes that the support extends well past the typical school day. During summer, Gump has hosted Nicole for "play dates" that include tea parties and movie watching. She and her husband once welcomed Nicole for a weekend stay so Aaron and Stephanie could travel to an event.

"Nicole and I have a great time," Gump says. "It's a relationship that goes beyond patient and nurse."

Parents of Saint Paul students also regularly pitch in. In particular, Annie Clark, Teri Glover and Mary Keddy

organized "Race for Nicole Day" to raise funds to help defray the costs of Nicole's anticipated kidney transplant. The three moms joined Stephanie Hall on a committee to plan the school's fundraising auction and learned that they worked well together.

"That auction was a huge success, so we knew we could pull this off with the help of everyone around us," Keddy says.

For Nicole Day, they combined a carnival atmosphere with a one-mile fun run – held at Saint Paul, of course. As participants covered the course, they were showered with Silly String and squirt gun fire. More than 250 people attended, and \$13,000 was raised.

"We put it together in less than a month, but then we have this awesome school and community, so we knew everyone would help these wonderful people," Keddy says.

The Saint Paul community also responded when Nicole had to spend most of April in the hospital. Teachers offered to make lunch each school day for Nicole's sister, Angie, and parents took turns running errands to ease the Hall family's burden. Then there was the all-school Rosary organized for Nicole, accompanied by a "pink out" in which everyone wore her favorite color.

It all added up to an outpouring of affection that reinforces what the Halls already knew.

"This entire community is a champion for Nicole," Aaron says.





'HOW DID HE DO THAT?'

Inspired by 6-year-old Landon, Brad Hamilton flexes his unique talent for persuasion, inviting in new supporters of cystinosis research.

By Dennis Arp

The boxes were made of *papier-mache*, and they were just fine – totally acceptable. But not to Brad Hamilton, they weren't.

"Let's see what else we can do," he said, and he started searching for a better option to display the array of items up for bid in the Hartz family's annual auction to support cystinosis research.

It didn't take Hamilton long. With a few phone calls he found a company in a nearby town that makes beautiful display containers. He framed the need, described the cause, and suddenly he had a pledge to donate two dozen baskets that typically retail for \$50. The Hartz's annual Halloween fundraiser became that much better, and was that much more successful.

"That's Brad," says Lauren Hartz, whose son, Landon, has cystinosis and whose family hosts the fundraiser. "Brad's a 'go big or go home' kind of guy. He's like that with everything in his life. He's all in."

For the Hartz family, Hamilton is a friend, an advocate, a hero. He sees a need and meets it; finds a role and fills it. In a word, he is a champion.

"Brad has a way – a gift of connecting with people," Hartz says. "We're always saying, 'How did he do that?'"

Hamilton has been a friend of Jimmy and Lauren Hartz since before they had children. When Landon was born in 2010 and then diagnosed with cystinosis a year later, Hamilton became part of the South Park, Pennsylvania, love and support squad for the Hartz family as they dealt with the daily challenges of caring for their son.

So when the family decided to launch a Halloween fundraiser – Lots of Love for Landon – to aid the Cystinosis Research Foundation, it's no surprise that Hamilton stepped up.

At one point Hamilton literally kept the event alive.

"I was seven months pregnant with Jordan (Landon's little brother), and I was saying, 'I don't know if this is a good idea this year.' Brad said, 'Oh, you have to do it. How about if I organize it?' He coaxed us back into it, and we're so glad he did."

But Hamilton's contributions of time and talent really became integral when the family decided to add an annual golf tournament as a second fundraising opportunity. Hamilton became one of the primary organizers, and his role has grown every year since.

"This past year, he spent hours and days and weeks, and we had great prizes for our raffle," Hartz says. "I think he reached out to more than 300 companies."

Actually, it was more like 400.

"When I counted it up, I realized it was a little ridiculous," Hamilton says with a chuckle.

But all that work ensured that the day was not just a fundraising success, with \$20,000 raised; it was a fun time for the golfers, who spread the word and invited others to participate. This year, entries jumped from 104 to 132.

Hamilton has found that by targeting young companies in the golf industry, he can provide a chance to get their products known and appreciated. And they respond. From high-end golf bags to putting trainers, the gift items roll in.

"Often I'll say, 'If you can contribute one item, that's fine, we're just excited to have you involved.' Then they'll come through with five or six," Hamilton says. "Once they hear about Landon and the chance to help children with cystinosis, they want to help."

In one case, Hamilton thought he was getting a gift of five golf umbrellas. Then a box arrived weighing 84 pounds. There were 60 umbrellas inside. Another time, Hamilton saw a unique belt being pitched on the TV show "Shark Tank," so he reached out to the company.

"Now when you look at the golfers in our event, you see Mission belt, Mission belt, Mission belt," Hartz says. "Brad is amazing"

Recently Hamilton and his wife welcomed their first child, and he says that brings new perspective to his work on behalf of Landon, the Hartz family and the Cystinosis Research Foundation.

"I'll talk with Jimmy about issues of caring for a newborn, and he'll say, 'Trust me, I know,'" Hamilton says. "Lauren and Jimmy are great people, and they're doing all they can so that Landon will be healthy and happy. No one looks at him as having a disease. He's just Landon – one of the funniest and happiest kids I know."

To ensure that Landon and other cystinosis patients have a chance for better treatments and a cure, Hamilton also will continue to give all that he can to the cause.

"Brad always finds the time," Lauren Hartz says. "He's always the one who's saying, 'Let's do this right.' He's passionate and energetic, but he also brings a lot of love."

"He's all in, and his heart is all in, too."

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Dr. Stéphanie Cherqui's Lab Associates *Receive Prestigious Awards*

The American Society of Gene and Cell Therapy (ASGCT) is the primary professional organization for gene and cell therapy. The mission of the ASGCT is to advance knowledge, awareness, and education leading to the discovery and clinical application of gene and cell therapies to alleviate human disease. This prestigious organization recognized Tatiana Lobry and Spencer Goodman from Dr. Stéphanie Cherqui's lab at UCSD with awards for their excellent work.



TATIANA LOBRY
PhD STUDENT

"I am very grateful for this opportunity to talk about my experience at the 2016 ASGCT conference in Washington DC. I submitted an abstract titled "Towards a phase I clinical trial for cystinosis." I was fortunate enough that my abstract was selected for an oral communication. Therefore, I presented the in vitro and in vivo preclinical toxicology studies for autologous stem cell transplantation in cystinosis.

Many scientists from all over the world submitted abstracts for this conference. After submission, abstracts are reviewed and scored by a committee. I received a Meritorious Abstract Travel Award for my presentation and the work we are doing on cystinosis. In addition to the distinction of this award, it also funded my attendance to the conference. This was the second year in a row I received this prestigious award. The conference was a great opportunity to share our progress in cystinosis and to learn about the progress that has been made in the field of gene and cell therapy."



SPENCER GOODMAN
PhD STUDENT

"Thank you very much for the opportunity to describe my experience at the recent ASGCT conference in *Cystinosis Magazine*. At the meeting, I presented a poster on our work titled "Delivery Highways: Tunneling Nanotubes Facilitate Transfer of Therapeutic Molecules for Gene Therapy Treatment of cystinosis." This poster described our research into the mechanism of how transplanted stem cells differentiate cystinosis protein to diseased tissue via cellular projections called tunneling nanotubes.

There were several hundred other posters, and I was fortunate enough that our lab's research impressed the judges to receive an Outstanding Poster Presentation Award. The conference was a wonderful opportunity to understand the broader field of gene therapy and how new insights may relate to our work on cystinosis."

Cystinosis Research Foundation and the Canadian Cystinosis Community Unite for a Cure

Oh Canada!

We are forever grateful to our Canadian cystinosis families who have worked in partnership with the Cystinosis Research Foundation (CRF) since 2009. Now, it is easier than ever to fundraise in Canada to cure cystinosis.

Canadians can now create their own fundraising campaigns that directly support the Cystinosis Research Foundation (CRF) and help cure cystinosis. Over the course of the last year the Cystinosis Awareness and Research Effort has worked to create a fundraising process which allows Canadians to fundraise, receive charitable tax receipts and fund CRF Scientific Review Board approved research studies through the Aqueduct Foundation.

The Cystinosis Awareness and Research Effort has a strong working relationship with CRF. The Cystinosis Research Foundation is the largest fund provider of cystinosis research in the world. CRF has created a world renowned scientific review board composed of leading cystinosis scientists and experts who review and recommend research studies for funding. CRF is committed to funding the most promising and innovative research. We are thankful for the Canadian families who have joined CRF in an effort to fund the most brilliant scientists in the world.



For six years, raising funds in Canada to support CRF research studies has been excruciatingly painful due to Canadian government regulation. We are excited to announce that there is a new process which meets all stakeholders' needs and ensures that funds raised in Canada are granted to Canada Revenue Agency approved and CRF approved researchers. All Canadians have to do is create a campaign to get started.

EASY AS 1, 2, 3

- 1 Create account at www.canadahelps.org
- 2 Create a fundraiser, ensure you search for and choose Aqueduct as the Charity and Canadian Cystinosis Research Foundation
- 3 Money raised from your fundraiser will be directed by Cystinosis Awareness and Research Effort to CRF

Canada Funds \$201,929 in Cystinosis Research Foundation Grants in 2016

The following grant payments were made by donations raised by Canadian families.

Liam Feng, PhD, Stanford University, California
"Molecular Mechanism of Cystinosis" \$37,500 – March 2016

Alan Davidson, PhD, University of Auckland
"Cystinotic iPSCs: Generation of proximal tubule cells and role of the malate-aspartate shuttle" \$51,939.25 – March 2016

Robert Mak, MD, PhD, University of California San Diego
"Leptin Signaling In Infantile Nephropathic Cystinosis" \$74,989.75 – August 2016

Liang Feng, PhD, Stanford University, California
"Molecular Mechanisms of Cystinosis" \$37,500 - September 2016

The Traveling Handbag of Hope



STELLA & HADLEY ALEXANDER
Boise, Idaho

We were excited when we received the news that Neiman Marcus in Fashion Island would be donating a gorgeous Prada handbag valued at \$2,100 to the CRF Natalie's Wish event held in April at the Island Hotel in Newport Beach, California. We were thrilled with the donation and added a \$1,000 Neiman Marcus gift card to complete the auction package.

The Natalie's Wish event was a sold-out evening featuring singer and songwriter Rachel Platten. As the live auction began, the energy in the room was palpable. The beautiful Prada handbag was presented on stage for auction, and the bidding began. The auctioneer opened the bidding at \$500, but it was quickly bid up

to \$1,000, then \$2,000, then \$4,000, \$6,000, \$7,000 and finally \$9,500! The room was ecstatic and the guests were cheering, but the room exploded with shouts when the "buyer" of the handbag yelled out, "I don't need the purse – put it back in the auction and sell it again!" The room erupted with applause and the auctioneer asked the audience if anyone wanted to match the \$9,500 bid. To everyone's surprise and collective amazement, another guest shouted, "Yes!" The handbag sold twice at \$9,500 for a total amount of \$19,000!

But, the story did not end there. The final buyer of the handbag was leaving the event carrying the handbag when she was approached by a woman who happened to be a mother of a child with cystinosis. That mom, Marcu Alexander, stopped the donor and thanked her for her generosity and admired the beautiful handbag. Without missing a beat and to Marcu's complete surprise, the donor who only moments before purchased the handbag for \$9,500 gave Marcu the purse and told her to enjoy it!

Marcu called CRF the next day and shared the story with us. Although she was incredibly moved by the donor's generosity, she said she could not accept the handbag but that she had a great idea! Marcu and her husband, Ben, were planning their own fundraiser to benefit CRF. Their event, Hearts for Hadley (named after their daughter, Hadley), was held on September 24 in their hometown of Boise, Idaho. Marcu auctioned off the handbag at their event and raised an additional \$2,700. The winner announced she would donate the bag to the Boys and Girls Club in Boise for their auction. The total raised for the Handbag of Hope so far is \$21,700 and counting. We are touched by the extraordinarily generous people who are dedicated to CRF and finding a cure for our children. This traveling handbag of hope brings smiles, tears, and lots of love to all those who hear the story.



Neiman Marcus

Your voice matters. Register at the CCIR website today:
WWW.CYSTINOSISREGISTRY.ORG



HELP THE RESEARCH COMMUNITY LEARN MORE ABOUT CYSTINOSIS AND ITS COMPLICATIONS.

The development of new treatments can be a lengthy process, and there are two steps that patients can help accelerate: the collection of valuable disease information and recruitment of volunteers to clinical trials. Your participation in a patient registry can achieve this acceleration.

The Cure Cystinosis International Registry (CCIR) is the most far-reaching cystinosis patient registry in the world, with 562 registrants from 44 different countries. Thanks to those who have completed the online CCIR medical survey, the impact of cystinosis is becoming more apparent, and researchers can better understand the concerns of patients and their families. Earlier

this year, an expanded CCIR medical survey was introduced. The expanded survey is intended to capture richer, more detailed information about cystinosis that experts say is lacking in the medical literature and is necessary for advancing therapies.

To date, 55 new surveys have been completed, representing new and established registrants alike. If you have not yet had the opportunity to take the expanded survey, please take it now. It only takes a few minutes.

Your feedback on current care and treatments for cystinosis is critical for the identification of research areas to focus on in the future.

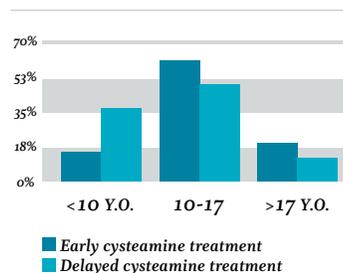
RECENT RESULTS



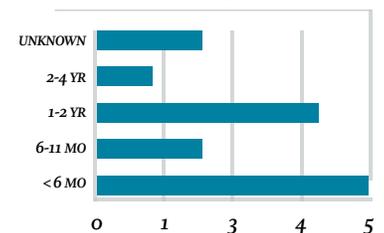
RENAL

Kidney transplants in the less than 10 year age bracket were high for those treated after age 5 years compared to those treated before 5, but the advantage of early treatment diminished in the older age groups. Wait times for kidney transplant varied, with the majority of people waiting less than one year.

AGE AT FIRST KIDNEY TRANSPLANT (n=144)



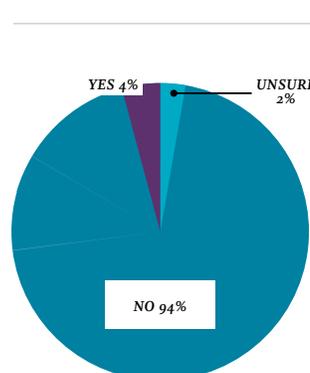
WAIT TIME UNTIL FIRST KIDNEY TRANSPLANT (n=14)



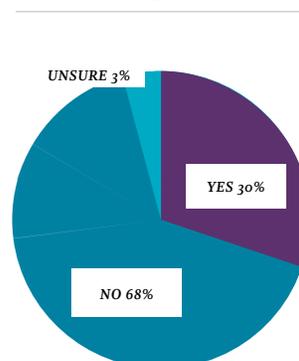
ENDOCRINOLOGY

There is a high rate of hypothyroidism and thyroid replacement therapy use (33% & 29%) even among young registrants, while only 4% have developed diabetes. Approximately one-third of patients report ever having used hormone therapy.

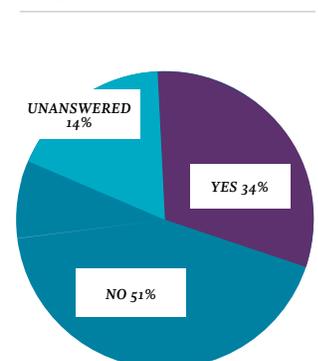
DIABETES (n=421)



THYROID REPLACEMENT THERAPY (n=413)



GROWTH HORMONE USE (n=472)





SWING, SHOOT & LIV GOLF CLASSIC

YIELDS BIG REWARDS



An Interview with Erin and Chad Little, Olivia's parents



It started to rain right before this year's "Swing, Shoot & Liv Golf Classic," but the skies cleared long enough for Olivia Little, 6,

and her sister, Harper, 3, to tee off and formally kick off the annual event, which this year raised a record-breaking \$110,000 for cystinosis research.

Fundraising wasn't always a part of the Little family's life; neither was cystinosis. But ever since Olivia was diagnosed with the disease, her parents Erin and Chad have found comfort, inspiration and hope in their work to help Cystinosis Research Foundation. They draw strength from the community of support they have found not only in their Port Elgin, Ontario neighborhood, but in the far-reaching network of cystinosis families they

have come to know through the organization.



Olivia and her sister Harper

"Being a small town, it's very emotional to receive the support we do from our community," said Erin. "It's like Chad said during the tournament. There are a lot of causes out there and everyone at the tournament chose us.

It means a lot because there is no other funding available to do the type of work we are doing through CRF."

The September 10 golf classic, held at the Saugeen Golf Club, featured an 18 hole tournament that included several activities on the holes centered around daily life with cystinosis. The event also included a barbecue lunch, dinner, live and silent auctions, raffles and a "Fund a Cure" pledge drive. Golfers managed to play almost the entire course without getting wet. The total raised over the past four years including the \$110,000 from this year's tournament is an incredible \$335,000 for cystinosis research.

The Liv-A-Little Foundation hosts two other events throughout the year including a community Easter egg hunt and a "Paint the Two Purple" awareness campaign. A variety of other groups, organizations, businesses and individuals have hosted different events in honor of Olivia including, barbecues, bake sales, pizza cook-offs – even the local skating club hosts a "Battle of the Blade" event, where hockey players are paired up with figure skaters to perform their intricate routines.

THIS YEAR, SWING, SHOOT & LIV GOLF CLASSIC RAISED A RECORD-BREAKING \$110,000 FOR CYSTINOSIS RESEARCH.

Events like these have become a family affair, drawing benefits that go beyond fundraising.

"The silver lining for Erin and me is that as much as we hate cystinosis we would never have met the amazing people we have met and gone to the places we have gone without the diagnosis of cystinosis," Chad said. "It's made our family tighter."

Chad said a new family recently diagnosed with cystinosis joined them at this year's golf tournament. "They were blown away by the support of our community," he said. Erin shared that it took them a year and a half to adjust to their "new normal" before they started getting involved in fundraising and becoming active in their new community of friends. When speaking to the new family the Littles said, "Relax. Get everything sorted. Get used to your new normal before you start to fundraise."

Today, Erin and Chad feel inspired to be a part of something much bigger.

"What I think people forget, is that you can't raise \$100 without a dollar. You can't get to \$1,000 without a hundred dollars.

"Collectively," she said, "all these thousands turn into millions and that's when you realize that even the smallest donation makes a real difference."

SAVE THE DATE

Thursday, March 30, 2017 — *thru* — Saturday, April 1, 2017

The Island Hotel, Newport Beach, California

day of

HOPE

CYSTINOSIS
RESEARCH
FOUNDATION
FAMILY
CONFERENCE

Cystinosis families from around the world are united in their quest for a cure and have funded 143 multi-year research studies which have led to a new FDA approved drug and new discoveries about cystinosis. We will celebrate our community at the Day of Hope conference and will renew our efforts to work together in our quest for the cure.

learn | share | laugh | celebrate

Learn, share, laugh and celebrate for three exciting days at the 2017 Cystinosis Research Foundation Day of Hope Family Conference and Natalie's Wish celebration at The Island Hotel in Newport Beach, California.

The Day of Hope conference will include sessions led by CRF funded researchers and clinicians. Topics include:

- Updates on stem cell and gene therapy
- Novel eye treatments for corneal cystinosis
- Kidney disease and transition to adult care
- Updates on muscle wasting and myopathy
- Bone and muscle clinical trial update
- Day to Day Living with cystinosis



A partial list of confirmed speakers include:

- Ghanashyam Acharya, PhD
- Sergio Catz, PhD
- Stéphanie Cherqui, PhD
- Paul Grimm, MD
- Morgan Fedorchak, PhD
- Robert Mak, MD, PhD



For information contact Zoe Solsby at (949) 223-7610 or zsolsby@cystinosisresearch.org

THANK YOU!

We are extremely grateful to our business leaders for their support in joining our quest to find a cure for cystinosis.



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TOGETHER, WE ARE **One**

DENIS LILLAND

A MOTHER'S QUEST FOR THE CURE

Maria Elin Lilland's 2-year-old son Denis was diagnosed with cystinosis in February 2016. Denis is one of eight known cases of cystinosis in Norway. Maria Elin knew that she wanted to contribute in any way she could so she immediately set up a Go Fund Me page to help raise money for research to find a cure for Denis. Thanks to her family and friends, **she has raised over \$4,600** for research!



HADLEY ALEXANDER

KEGS4KAUSE BENEFITS HEARTS FOR HADLEY AND CRF

Payette Brewing Co. is a local business located in Boise, Idaho that is well known for giving back to the community. They have a program called Payette Forward which provides support to local nonprofits. Kegs4Kause is one event Payette Brewing created as way to raise money for various causes. Every Monday evening, 50% of proceeds from beer sales are donated to a featured nonprofit. Hearts for Hadley was selected as a recipient in July.

Friends, family, co-workers and acquaintances filled up the newly expanded location along the Boise River. Adults enjoyed some cold brews while the kids enjoyed fun in the garden area coloring, blowing bubbles and drawing on the chalk wall. **The event raised \$572** for Hearts for Hadley and the Cystinosis Research Foundation!

24 HOURS OF SCHWEITZER

The 2016 24 Hours of Schweitzer was a great success! **Raising over \$170,000** for cystinosis research in honor of Henry Sturgis! New categories were added to the ski event allowing skiers and snowboarders to ski and ride all over the mountain and score team points as they completed hourly challenges throughout the 24-hour event. These new categories have become very popular and there are big plans to increase the fun meter of the challenges for 2017. The tentative date for the next ski event is March 24-25, 2017, save the date for the ski marathon!

HENRY STURGIS



1 PURPOSE. 1 JOURNEY. 1 CURE.

TINA'S HOPE FOR A CURE: CHOSEN!

teamed up with the Toyota corporate match program and committed to awarding a total of \$20,000 to four charities.

Rogers Toyota asked for the community's involvement in nominating organizations who they thought were worthy of the **\$5,000 donation**. Tina's Hope for a Cure was one of 27 charities up for vote. Voting was then done through social media and their website. THFAC rallied with many other wonderful charities to the very end, Tina's Hope for a Cure was in the final four and received one of the four \$5,000 donations. We are thankful to Rogers Toyota for their continued support.

This past spring Rogers Toyota ran a campaign which was titled "CHOOSE YOUR CHARITY." Rogers Toyota of Lewiston, Idaho

TINA FLERCHINGER

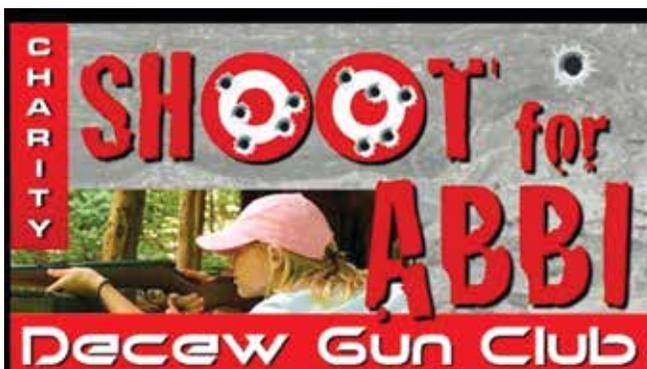


LONDON HARTZ

LOTS OF LOVE 5TH ANNUAL

The Hartz Family hosted their 5th Annual Lots of Love for Landon Charity Golf Outing in honor of their son Landon, on June 3, 2016. A record breaking 130 golfers came together to support the family and cystinosis research. The volunteers worked hard and the golfers played hard and the result...**\$25,000 was raised!** Jimmy, Lauren, Landon and Jordan Hartz are so grateful for the hard work of Jason Hartz, Jason Whitfield, Brad Hamilton and Derek Evan who helped make this tournament the most successful to date. Since 2012, more than \$90,000 has been donated to CRF to support critical cystinosis research. Thank you to all who participated and have joined our quest for the cure.

ABBI MONAGHAN



SHOOT FOR ABBI

The "Shoot for Abbi" event, held August 6 was a completely new idea presented to Katie and Terry Monaghan to raise money for cystinosis research in honor of their daughter Abbi. The journey leading up to the event introduced them to some very generous and genuine people. On behalf of the Monaghan family CRF would like to thank the Decew Gun Club, John Rakich and family, Scott Little and Destination Church for organizing and coordinating the exciting and successful fundraising event. With support from the St. Catharines community of friends and family, **more than \$6,025 was raised** for CRF. On behalf of the entire cystinosis community, thank you!

OLIVIA LITTLE



PAINT THE TOWN PURPLE

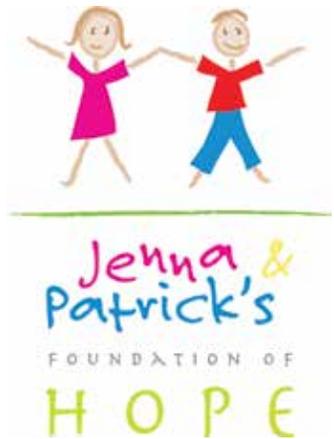
The “Paint the Town Purple” campaign in support of the Liv-A-Little Foundation and in honor of Olivia Little, was enthusiastically embraced by the entire Saugeen Shores community and the results were nothing short of amazing! Purple bows popped up on local businesses, light posts and front doors of houses around town in part thanks to Chris Swain, owner of Keepsakes & Memories in Port Elgin, who made and sold many of the bows decorating the town. The campaign to raise awareness of cystinosis, generated interest from locals and tourists alike who, after hearing Olivia’s story, donated to help find the cure.

Scott Rowland, the owner of Your Independent Grocer, proudly displayed the purple bows, and invited shoppers to make a donation to cystinosis research at checkout. On July 30, the Little family and members of the Saugeen Shores Winterhawks hockey team – dad Chad Little is a former Hawk – bagged groceries to give back to those who were giving to cystinosis. Olivia has a wonderful time helping and continues to say that when she grows up, she wants to work for Mr. Scott! This year’s campaign **raised more than \$10,000** for research to help Olivia and all those affected by cystinosis.

JENNA AND PATRICK PARTINGTON

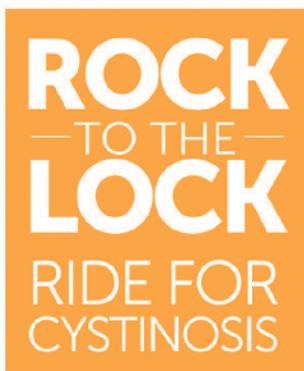
SHANNON BELL TAKES JENNA & PATRICK’S FOUNDATION OF HOPE TO CAPITAL CUP GOLF TOURNAMENT

Supporters of Jenna & Patrick’s Foundation of Hope were excited to learn that good friend Shannon Bell, President and CEO of Nor-Cal Beverage, selected JPFH as her charity of choice to play in the Capital Cup Golf Tournament held in September. Shannon expressed her thoughts about supporting Jenna and Patrick, “I am excited to be playing for the Jenna and Patrick’s Foundation of Hope. The foundation was started by Jenna & Patrick’s parents, Kevin and Teresa Partington and their friends in order to raise funds and awareness of cystinosis, a rare metabolic disease. Jenna and Patrick are beautiful 11-year-old twins that are beating the odds, but their battle takes a terrible toll on their young bodies.” Shannon set up a Crowdrise Fundraising page and **raised more than \$10,000** to support cystinosis research.



ABBI MONAGHAN

ROCK TO THE LOCK



When people come forward wanting to help raise awareness and money for cystinosis you jump in with both feet and work out the details later because finding better treatments and a cure for cystinosis is on our minds every day. Because of the support of our friends, family and community, Dan Giancola and the “Rock to the Lock Committee” **raised \$36,280** for the Cystinosis

Research Foundation. There were multiple events, fundraisers and awareness campaigns carried out by many and because of this, supports within our community have grown and our drive to continue fundraising has only become stronger. We are extremely grateful and feel the future for Abbi and others with cystinosis is bright! We thank all who continue to support and fight along with us.

ACTIVITIES



CALENDAR



Friday, December 16, 2016

STAR WARS PRIVATE SCREENING OF ROGUE ONE

Sam & Lars Hope for a Cure, Sam and Lars Jenkins
Sugar House Cinemark, Salt Lake City, Utah



Friday, February 10, 2017

MUSIC FOR MARY

Mary Head, Tacoma Sportsman's Club, Puyallup, Washington
www.cystinosisresearch.org/donate-for-Mary



Friday, March 24 – Saturday, March 25, 2017

24 HOURS OF SCHWEITZER SKI EVENT

Henry Sturgis, Schweitzer Mountain, Sand Point, Idaho
www.24hoursforhank.org



Thursday, March 30 – Saturday, April 1, 2017

CYSTINOSIS RESEARCH FOUNDATION DAY OF HOPE FAMILY CONFERENCE

Island Hotel, Newport Beach, California
For information contact Nancy Stack, nstack@cystinosisresearch.org



Saturday, April 1, 2017

NATALIE'S WISH CELEBRATION

Island Hotel, Newport Beach, California
For information contact Zoe Solsby, zsolsby@cystinosisresearch.org



June 2017

6TH ANNUAL LOTS OF LOVE FOR LANDON GOLF OUTING

For information email Jimmy Hartz, hartz24@gmail.com

LEADERSHIP. GUIDANCE. COMMITMENT.

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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Professor

Laboratory of Hereditary Kidney Diseases

Imagine Institute (Inserm U1163)

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

CYSTINOSIS RESEARCH FOUNDATION WELCOMES A NEW SCIENTIFIC REVIEW BOARD MEMBER

Sergio D. Catz, PhD, is Associate Professor of Molecular and Experimental Medicine at The Scripps Research Institute in La Jolla, California. He received his PhD at the University of Buenos Aires, Argentina in 1997. During his doctoral studies, Dr. Catz obtained additional training in innate immunity, immunology and inflammation at INSERM 297, Paris, France. In 1998, he was recruited by The Scripps Research Institute, where he was awarded a postdoctoral fellowship from the American Heart Association and completed post-doctoral studies in cell biology and immunology. In 2004 he was promoted to the position of Assistant Professor and in 2010 to his current position of Associate Professor also at The Scripps Research Institute.



Dr. Catz has authored more than 40 peer-reviewed publications, and has received numerous honors, awards and research grants, including numerous grants from the National Institute of Health (NIH) and a Certificate of Excellence for Outstanding Performance by the American Society for Cell Biology. He has served as reviewer for many national and international review boards including the NIH; the U.S. Department of Veterans Affairs; The Medical Research Council, U.K.; the Netherlands Organization for Scientific Research (NWO), the University of Buenos Aires, Argentina; Mitacs, Canada and the American Heart Association, U.S.A.

Dr. Catz is a member of the Editorial Board of the Journal of Biological Chemistry and a member of the International Scientific Advisory Board of the biennial symposium of Neutrophil in Immunity. He is an internationally recognized scientist in the fields of cellular biology and immunology. Dr. Catz's research includes the study of the cellular biology of innate immune and non-immune cells and the implementation of state-of-the-art cell biology techniques, including super-resolution microscopy, for the understanding of lysosomal trafficking and function in health and disease.

TOTAL MID-YEAR GRANTS FUNDED:

\$1,472,117

SPRING GRANTS FUNDED: **\$1,263,453.78**

IMPROVEMENT OF CELLULAR FUNCTION THROUGH CHAPERONE-MEDIATED AUTOPHAGY AND CELLULAR TRAFFICKING IN CYSTINOSIS

Sergio Catz, PhD, Mentor

Jinzhong Zhang, PhD, Research Fellow

The Scripps Research Institute, La Jolla, California

\$75,000 – 1-year grant

(September 15, 2016 – September 14, 2017)

KIDNEY ORGANIDS: A NEW MODEL TO STUDY CYSTINOSIS

Alan Davidson, PhD, Principal Investigator

Teresa Holm, MD, PhD, Co-Principal Investigator

The University of Auckland, New Zealand

\$145,852 – 2-year grant

(September 1, 2016 – August 31, 2018)

CLINICAL TRIAL READINESS FOR DISTAL MYOPATHY IN NEPHROPATHIC CYSTINOSIS (DMNC)

Florian Eichler, MD, Principal Investigator

Sherman Alexander, MSc, Co-Principal Investigator

Massachusetts General Hospital, Boston, Massachusetts

\$96,128.78 – 1-year grant

(September 1, 2016 – August 31, 2017)

DEVELOPMENT OF A TOPICAL, CONTROLLED RELEASE CYSTEAMINE EYE DROP

Morgan Fedorchak, PhD, Principal Investigator

Kanwal Nischal, MD, FRCO, Co-Principal Investigator

University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

\$155,484 – 1-year grant

(September 1, 2016 – August 31, 2017)

MECHANISM AND PATHOPHYSIOLOGICAL SIGNIFICANCES OF A GENETIC INTERACTION OF CYSTINOSIN

Bruno Gasnier, PhD, Mentor

Yann Terres, MSc, Research Fellow

Paris Descartes University, France

\$225,000 – 3-year grant

(September 1, 2016 – August 31, 2019)

ELUCIDATION OF ALTERED METABOLISM AND BIOMARKERS IN CYSTINOSIS USING LARGE-SCALE METABOLOMICS APPROACHES

Ilya Gertsman, PhD, Principal Investigator

Bruce Barshop, MD, PhD, Co-Principal Investigator

University of California, San Diego, California

\$160,589 – 2-year grant

(September 1, 2016 – August 31, 2018)



Cystinosis Research Foundation
**ACCELERATED RESEARCH
 GRANT PROGRAM :**

\$208,663.90

CRF has established the Accelerated Research Grant Program in an effort to hasten the research process. The program's ultimate goal is to provide grant money for projects that aim to accelerate the development of better treatments and a cure for cystinosis. ARGP grant awards are issued outside the bi-annual CRF funding cycle. ARGP awards are issued to currently funded CRF researchers who have proven through research publications and research progress that their work will ultimately translate into a clinical trial.

**PROFILING METABOLIC DYSFUNCTION
 CAUSED BY CYSTINOSIS**

Norbert Perrimon, PhD, Mentor
Patrick Jouandin, PhD, Research Fellow
 Harvard Medical School, Boston, Massachusetts

\$225,000 – 3-year grant
 (September 1, 2016 – August 31, 2019)

NLRP2 IN THE PATHOGENESIS OF CYSTINOSIS

Giusi Prencipe, PhD, Principal Investigator
Fabrizio De Benedetti, MD, PhD
Co-Principal Investigator
 Bambino Gesù Children's Hospital, Rome, Italy

\$180,400 – 2-year grant
 (January 1, 2017 – December 31, 2018)

**ONE YEAR STEM CELL RESEARCH
 ASSOCIATE SUPPORT**

Stéphanie Cherqui, PhD
Principal Investigator
 University of California, San Diego

\$67,582.30 - 1-year grant
 (July 18, 2016 – July 17, 2017)

EQUIPMENT AND SERVICES :

\$88,148.90
 QX200 Droplet Digital PCR System

\$5,810
 Cellometer Auto T4 Plus SK-150

\$3,222.70
 Two Macintosh computers

\$43,900
 Transgenic mouse model to advance stem cell research

Improvement of cellular function through chaperone-mediated autophagy and cellular trafficking in cystinosis

Sergio D. Catz, PhD, Mentor

Jinzhong Zhang, PhD, Research Fellow

THE SCRIPPS RESEARCH INSTITUTE, LA JOLLA, CALIFORNIA

OBJECTIVE/RATIONALE:

Cysteamine is efficient in retarding the rate of glomerular deterioration and improvement of linear growth in children with cystinosis. However, cell malfunction, tissue failure and progressive renal injury still occurs, suggesting that cystine accumulation is not the only cause for all the defects observed in cystinosis. In order to improve treatment of cystinosis, it is crucial to understand the defective molecular mechanisms that lead to cell dysfunction and tissue injury. We propose to improve cellular function through chaperone-mediated autophagy and cellular trafficking in cystinosis.

PROJECT DESCRIPTION:

Correct cellular function requires the appropriate distribution of cellular components. One important receptor that mediates the degradation of macromolecules in the lysosomal lumen, named LAMP2A, is mislocalized in cystinosis. We have presented data that Cystinosin, the cystine transporter that is affected in cystinosis, regulates the trafficking of LAMP2A to the lysosome. This function is important to maintain cellular homeostasis and survival. Our proposed research will increase our understanding of the interplay between cystinosin (CTNS) and the chaperone-mediated autophagy (CMA) receptor LAMP2A in cystinosis. We will utilize state-of-the-art microscopy technologies to determine the role of CTNS and CTNS activity on the regulation of LAMP2A distribution and trafficking using cells lacking CTNS, reconstituted with either wild type CTNS or with mutants associated with the development of cystinosis in humans. In addition, we will determine the function of a lysosomal regulatory protein, Munc13-4, in the regulation of LAMP2A trafficking and function in cystinosis.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Current therapies are effective in reducing lysosomal overload but in the long term tissue degeneration and malfunction occur despite the efficiency of these current therapies. Our research is highly relevant because it identifies in cystinosin a previously unrevealed function that affects a cellular process associated with human pathologies but is independent of lysosomal overload. Elucidating these mechanisms will help develop new therapies for cystinosis that will be beneficial for both children and young adults, as they will target a different mechanism from those existing therapies.

ANTICIPATED OUTCOME:

We expect to discover a role for CTNS in LAMP2A trafficking independent of its role as a cystine transporter. We also expect that Munc13-4 upregulation will improve cellular function in cystinosis by a dual mechanism: a) increasing exocytosis (and thus reducing lysosomal overload) and b) by increasing LAMP2A trafficking, correcting LAMP2A localization and improving autophagy. The completion of this proposal will elucidate the roles of CTNS and Munc13-4 in the regulation of important cellular processes and will likely lead to new paths to correct cellular defects in cystinosis.

Kidney organoids: a new model to study cystinosis

Alan Davidson, PhD, *Principal Investigator*
Teresa Holm, MD, PhD, *Co-Principal Investigator*
UNIVERSITY OF AUCKLAND, NEW ZEALAND

OBJECTIVE/RATIONALE:

Being able to model cystinosis in cells grown in the laboratory is critical to gaining a better understanding of the cause of the disease and for finding new treatments. We have generated cystinotic stem cells that can be matured into any tissue in the body. We have developed a method to convert these cells into kidney organoids (mini-kidneys). The objective of the current proposal is to characterize these cystinotic kidney organoids and to determine how well they model the renal defects of cystinosis.

PROJECT DESCRIPTION:

Human stem cells from a nephropathic cystinotic patient will be induced to mature into kidney organoids and grown in the laboratory for several weeks. This tissue will be closely examined in tissue sections and at the molecular and protein levels for signs of cystinotic injury (swan neck lesion, oxidative stress, enlarged lysosomes, abnormal mitochondria and defects in protein uptake and degradation). In addition, the mTOR pathway, a central regulator of cell metabolism, growth, and proliferation will be examined as this pathway has been linked to cystinosis but its exact involvement remains unclear. Inhibitors of the mTOR pathway will be tested on the kidney organoids to assess whether these have the potential to ameliorate some of the cellular defects of cystinosis.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Cystinosis has a major effect on kidney function making this tissue a key target to study. At present, the analysis of human cystinotic kidney cells is limited to individual cell types grown in petri dishes and the production of more complex multi-cellular cystinotic tissue has not been achieved but is likely to be a more physiologically relevant model to study.

ANTICIPATED OUTCOME:

The proposed research will establish stem cell-derived kidney organoids as a novel model to study the cellular defects in cystinosis and as a human-based platform for testing new drugs to treat cystinosis. The involvement of the mTOR pathway will be examined and assessed as a potential therapeutic target.

Clinical trial readiness for distal myopathy in nephropathic cystinosis

Florian Eichler, MD, *Principal Investigator*

Sherman Alexander, MSc, *Co-Principal Investigator*

MASSACHUSETTS GENERAL HOSPITAL, BOSTON

OBJECTIVE/RATIONALE:

A major obstacle to implementing trials in distal myopathy in cystinosis (DMNC) is the lack of information on evolution of symptoms as well as the absence of harmonized outcome measures that are sensitive to change in this patient population. Despite cysteamine therapy many patients succumb to muscle weakness, swallowing difficulties and aspirations. In preparation for trials, we now need to define clinical outcome measures that accurately quantify disease progression in patients with distal myopathy.

PROJECT DESCRIPTION:

Our proposal will conduct retrospective and prospective studies to define sequence and timing of dysphagia symptoms and assess for modifiers of progression. In the first year we will analyze patient reported outcome surveys and introduce voluntary cough airflow measures that have recently been shown to differentiate safe versus unsafe swallowing in ALS patients. We will correlate these measures with the degree of aspiration present in patients with cystinosis. Based on our findings we will then design an expiratory muscle strength training regimen for the second year. This will help assess whether physiologic measures of swallow and cough could be impacted.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

The voluntary cough airflow measures are thought to identify patients at higher risk for penetration/aspiration, representing a valuable screening tool with high clinical utility. Defining cough effectiveness in DMNC patients may not only facilitate screening for dysphagic patients at risk for aspiration but may also represent a target for intervention. Studies in ALS patients have shown Expiratory Muscle Strength Training was feasible and well tolerated and led to improvements in expiratory force-generating pressures and swallow kinematics.

ANTICIPATED OUTCOME:

Over the short prospective studies we may not gain knowledge on decline in muscle strength over time. However, the retrospective surveys will help define sequence and timing of symptoms. Further the cross-sectional correlations of cough air flow and degree of aspiration could help design clinical trials in the future. Ultimately our exercise regimen may not improve pharyngeal strength but could benefit laryngeal muscle power to compensate and improve cough airflow thereby decreasing aspiration risk in DMNC patients.

Development of a topical, controlled release cysteamine eye drop

Morgan Fedorchak, PhD, *Principal Investigator*

Kanwal Nischal, MD, FRCO, *Co-Principal Investigator*

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE

OBJECTIVE/RATIONALE:

Our goal is to adapt our team's ocular drug delivery system for use with cysteamine to provide therapeutic levels of drug from a single dose for up to one week. The cysteamine microsphere (CMS) formulation will be suspended in a thermoresponsive hydrogel, which we have demonstrated can be administered similarly to a traditional eye drop and then retained beneath the lower eyelid for the duration of drug release. We hypothesize that the localized and less frequent administration will result in significantly enhanced tolerance and bioavailability.

PROJECT DESCRIPTION:

We will use our established design and characterization methods and in vivo testing expertise to optimize the formulation. This includes choice of polymer for the CMS synthesis and a full characterization of the resulting material properties such as particle diameter, cysteamine loading, and drug release kinetics. Further, stability of cysteamine in the lyophilized CMS will be investigated for a variety of relevant external conditions. Candidate formulations will be loaded into the hydrogel-based eye drop and analyzed for pharmacokinetic properties and preliminary safety information. The biodistribution of cysteamine will be of particular importance in assessing the likelihood of success in maintaining sufficient drug levels in the cornea.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

The goal is to address the inability for many cystinosis patients to receive the required amount of ocular cysteamine to prevent corneal crystal formation. We aim to do this by decreasing the likelihood of side effects through a more direct delivery of less drug than traditional eye drops, while still maintaining a high enough concentration to be effective. This is possible through the use of biodegradable controlled release technology that sustains therapeutic drug levels over long time periods and our unique gel eye drop that allows for topical retention of the drug delivery system.

ANTICIPATED OUTCOME:

We anticipate that the result of these studies will be an optimized controlled release cysteamine formulation that can be administered via our unique gel eye drop, providing up to one week of clinically relevant levels of drug. We will also anticipate that we will obtain a preliminary evaluation of the safety and pharmacokinetic profile of the cysteamine delivery system.

Mechanism and clinical significance of a genetic interaction of cystinosin

Bruno Gasnier, PhD, *Mentor*

Yann Terres, MSc, *Research Fellow*

PARIS DESCARTES UNIVERSITY, FRANCE

OBJECTIVE/RATIONALE:

Cystinosis is caused by accumulation of the amino acid cystine in an intracellular organelle, the lysosome. This accumulation results from genetic mutations affecting cystinosin, a membrane protein which exports cystine across the lysosomal membrane. Despite intensive studies, the link(s) between this primary lysosomal defect and the defective function of multiple organs remains unclear. Moreover, these links may differ across distinct affected organs or cell types. In this project, we aim to characterize a novel physiological role of cystinosin revealed by its unanticipated genetic interaction with another intracellular protein.

PROJECT DESCRIPTION:

In preliminary experiments using the mouse model of cystinosis, we discovered a genetic interaction between cystinosin and another intracellular protein. Mice carrying mutations in both genes die early, in contrast with the progressive (cystinosin mutations) or apparently normal phenotype of mice mutated in either one or the other gene. Such rare, strong interaction between two genes is termed “synthetic lethality.”

Our goal is to characterize the biochemical mechanism underlying this synthetic lethality and to identify the cause of death using biochemical, molecular and cellular techniques applied to cellular and mouse models. Research will develop along two main lines aimed, on one hand, at dissecting out further the cause of death and, on the other hand, at recapitulating the presumed underlying mechanism in cellular and in vivo models more amenable to experimental manipulation. Finally, we will explore the consequences of our working model on the pathology and treatment of cystinosis.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

If our working model for the genetic interaction of cystinosin proves true, our research should improve our understanding of cystinosis and its current treatment by reorienting pathological and therapeutic studies towards a specific aspect of cell defense mechanisms. Testing which cystinosis-affected organs depend on this mechanism and identifying ways to rescue it should help us to delineate the pathological cascade of cystinosis and discover novel therapeutic agents.

ANTICIPATED OUTCOME:

In this study, we expect to decipher the molecular and cellular basis for an unexpected, severe genetic interaction of cystinosin with another protein discovered in preliminary studies. The presumed underlying mechanism suggests a novel physiological role of cystinosin in cellular defense mechanisms, which may shed a new light on the cause and progression of the disease. This study might also tell us whether the current drug treatment of cystinosis rescues or, on the contrary, exacerbates the cellular defense defect predicted by our working hypothesis.

Elucidation of altered metabolism and biomarkers in cystinosis using large-scale metabolomics approaches

Ilya Gertsman, PhD, *Principal Investigator*
Bruce Barshop, MD, PhD, *Co-Principal Investigator*
UNIVERSITY OF CALIFORNIA, SAN DIEGO

OBJECTIVE/RATIONALE:

Changes in compounds related to energy have been documented in various studies of cystinosis, yet not fully described in the context of how the metabolic pathways they pertain to are altered. We believe that a thorough investigation of metabolic intermediates that span the various pathways that appear altered will help clarify unanswered questions about cellular and metabolic regulation in cystinosis. Additionally, we believe that our ability to measure many potentially altered compounds in cystinosis may lead to improved assays for monitoring patient health in response to therapy.

PROJECT DESCRIPTION:

We have monitored significant alterations of metabolic pathways critical to energy production and cell function in cystinotic cells. We will use advanced instrumentation to measure these, and thousands of other metabolites simultaneously, to improve our understanding of the cause of metabolic alterations in cystinosis. We also plan to evaluate a variety of compound types for their potential as serving as biomarkers for disease progression or as indicators of the patients' response to cysteamine treatment. Current methods used for monitoring patients' response to treatment are useful, but have weaknesses that warrant the further investigation of alternate biomarkers. We will investigate candidate compounds that we believe are getting chemically altered in cystinotic cells, which will hopefully serve to more accurately evaluate cystinotic patient health and guide clinical management.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

We believe that the comprehensive metabolic pathway analysis we will perform will elucidate critical aspects of cell health and function that are affected in cystinosis. We hope these factors can be targeted in future treatments. We also believe our biomarker(s) search will help lead to an improved clinical assay that will guide clinical management of cystinosis.

ANTICIPATED OUTCOME:

We anticipate that we will be able to precisely quantify the changes in critical metabolic pathways specific to cystinosis, and reveal the regulatory mechanisms relating to these changes. We believe that we will also find a more suited biomarker than granulocyte/mixed leukocyte cystine for monitoring disease progression and therapeutic response.

Profiling metabolic dysfunction caused by cystinosis

Norbert Perrimon, PhD, *Mentor*

Patrick Jouandin, PhD, *Research Fellow*

HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS

OBJECTIVE/RATIONALE:

Cystinosis is a metabolic disorder caused by mutations in a lysosomal cystine transporter, CTNS. Despite the known link between lysosomal cystine accumulation and cystinosis, the mechanisms that connect this cellular phenotype to the disease remain unclear. Previous studies have shown that cystine and cysteine metabolism are tightly linked, and recently I found that cysteine acts as a central regulator of general metabolism. Therefore, I propose to investigate in-depth the effect of CTNS mutations on cysteine balance and cellular metabolism according to variations in diet.

PROJECT DESCRIPTION:

I will first analyze how CTNS mutation and subsequent cystine accumulation affects cysteine balance *in vivo* using a *Drosophila* model of cystinosis. Then, I will analyze how alterations of cysteine levels affect general metabolism in the context of the disease with respect to diet. I have previously shown that diet can dramatically modify the effects triggered by cysteine. Next, as metabolism is known to be a highly dynamic process to maintain cellular homeostasis, I will analyze whether such metabolic adaptations could trigger secondary disorders in addition to cysteine imbalance. Since this process is likely to involve consumption of metabolites to compensate for the loss of other ones, I will assess whether dietary supplementation with metabolites depleted from the cells can restore the metabolic defects of cystinotic animals.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

My goal is to shed light on the fundamental biology of CTNS function and cysteine balance in the context of the disease in order to highlight alternative approaches that could be combined with existing but insufficient treatments to alleviate symptoms of the disease. Furthermore, I propose to investigate the effect of diet on each process analyzed, and to try to correct cystinotic defects by food supplementation. These studies may also help establish dietary guidelines or food supplementation approaches to improve patient fitness, bringing long-term value to cystinosis research.

ANTICIPATED OUTCOME:

The focus of my studies is to link the symptoms of cystinosis with impaired cysteine metabolism. First, I expect that my findings will provide insights into how cystine accumulation in the lysosome affects intracellular cysteine levels. I also expect to uncover the metabolic pathways affected by cysteine imbalance, and to identify secondary metabolic defects as a result of metabolic compensations in cystinotic cells. Finally, I expect to identify specific metabolites depleted from cystinotic cells that could be replenished by dietary supplementation to alleviate symptoms of the disease.

NLRP2 in the pathogenesis of cystinosis

Giusi Prencipe, PhD, *Principal Investigator*

Fabrizio De Benedetti, MD, PhD, *Co-Principal Investigator*

BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

OBJECTIVE/RATIONALE:

Indirect observations in the literature and our previous results point to a possible relation, in cystinosis, of progressive renal tubular damage and interstitial fibrosis with activation of inflammasomes. Inflammasomes are multiprotein complexes that sense microorganisms and sterile stressors and, consequently, activate pro-inflammatory processes. In preliminary study, we found that Nod Like Receptor Protein 2 (NLRP2), part of the inflammasome pathways, was markedly up-regulated in proximal tubular epithelial cells (PTEC) of cystinotic patients. Data on the murine model of cystinosis (Ctns *-/-* mice) confirmed that NLRP2 protein levels were significantly higher in the kidney. NLRP2 had a role in regulating processes of cellular death and inflammation.

PROJECT DESCRIPTION:

Based on these results, we hypothesize that, in the cystinotic kidney, up-regulation of NLRP2 may contribute to the development of interstitial inflammation and fibrosis leading to the end-stage renal disease. In this project we propose to:

- a) study, both in human and animal models, the molecular mechanisms involved in the NLRP2 up-regulation observed in cystinotic PTEC and to investigate the functional role of NLRP2;
- b) elucidate the role of NLRP2 *in vivo* by the generation of mice Ctns *-/-* that do not express NLRP2 specifically in PTEC and
- c) study other tubulopathies in order to investigate whether the up-regulation of NLRP2 is restricted to cystinotic PTEC or a more generalized phenomenon involved in the pathogenesis of several tubulopathies.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

This project will shed light on the pathogenic role played by the extremely high levels of NLRP2 present in cystinotic kidney and will provide the rationale for novel therapeutic strategies that may complement presently available conventional therapies.

ANTICIPATED OUTCOME:

We expect that our studies will lead to a better understanding of molecular pathways involved in the pathogenesis of cystinosis. Indeed, emerging data demonstrated that several mechanisms, including inflammation processes, contribute to the pathogenesis of the disease.

LOOKING AHEAD

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 13 short years. Since its inception, CRF has raised more than \$35 million with every dollar donated going directly to 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 \$1.5 million was available for the 2016 fall call for research proposals and fellowship grants. The grant awards will be announced in December 2016. Details and guidelines for applications are available online at the CRF website: www.cystinosisresearch.org/research/for-researchers.

In July, CRF issued nine new grants in four countries totaling \$1.47 million that bring 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 leading international experts in the field of cystinosis (See page 64). 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 494 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.



www.cystinosisresearch.org/research/for-researchers

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

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MISSION

The mission of the Cystinosis Research Foundation is to find better treatments and a cure for cystinosis by supporting bench, clinical and translational research. Since 2003, CRF has raised \$35 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.

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