cystinosis magazine

For friends and supporters of the Cystinosis Research Foundation

DEDICATION ♥ DEVOTION

Cystinosis Love Stories

WINTER 2017

OUR CYSTINOSIS

LOVE STORIES

ISSUE

Stéphanie Cherqui, PhD and Corinne Antignac, MD, PhD in Cherqui's lab. PAGE 8

OUR CYSTINOSIS LOVE STORIES

We all have cystinosis stories of love and persistence. Families and friends are continuously dedicated to the well-being of their loved ones with cystinosis, and researchers are devoted to their studies and making a difference. The journey of both families and researchers includes pure love and sacrifices, with the same goal of finding the cure.

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.

Art Direction and Printing: Idea Hall

CYSTINOSISRESEARCH.ORG
949 223 7610 | 18802 Bardeen Avenue, Irvine, CA 92612

WINTER 2017

cystinosis magazine

CYSTINOSIS RESEARCH FOUNDATION
RESEARCH • HOPE • CURE

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 $39 million for cystinosis research in an effort to find a cure.

WELCOME

RESEARCH FEATURES

RESEARCH HIGHLIGHTS

ANNOUNCEMENTS

CRF CHAMPIONS

FAMILY STORIES

CYSTINOSIS MAGAZINE IS A PUBLICATION OF THE CYSTINOSIS RESEARCH FOUNDATION

The Cystinosis Research Foundation is a nonprofit, tax-exempt entity pursuant of Section 501(c)3. Federal Tax ID #32-0067668.
100 percent of your donations go to support cystinosis research. All gifts are tax deductible.

DEAR FAMILY AND FRIENDS

Cystinosis is a love story. A love story between parents and their children, doctors and their patients, researchers and their work. It's a love story between the cystinosis community and you – our cherished family and friends who have never given up on finding a cure.

In 2003, Natalie made a wish for her 12th birthday: to have her disease "go away forever." Her wish was the beginning of the cystinosis love story and is now the rallying cry for others in the cystinosis community. We never could have imagined that her simple and innocent wish would result in a global effort to find better treatments and a cure for this disease.

We have made extraordinary progress because you have been at our side, supporting our efforts, encouraging us to stay focused and to never give up. Our children – those affected by cystinosis – have touched the lives of so many people in such an intimate way. Their stories of courage, determination, and resilience are inspiring and have moved many people to embrace their struggles and join our fight to end cystinosis.

What more could we as a community ask for than to have others by our side through this journey? That is love, and we are humbled and blessed by your dedication to the cystinosis cause. Without you, we simply would not be where we are today. We are closer to a cure than ever before because of your commitment to our community.

LIFE IS BETTER WITH YOU BY OUR SIDE

Cystinosis is a life of challenges and obstacles. At times, life with cystinosis might seem overwhelming and impossible to navigate. For those with cystinosis, life is often consumed by doctors' appointments, health scares, days of feeling miserable, and juggling a myriad of medications. There are days when it is hard for me, as a mother, to see Natalie in pain or in tears because she feels miserable from the medications she must take.

I am humbled by the people in our community who share their personal stories with me; I am often moved to tears. I hear stories about children and adults not tolerating their medications, waiting years for a kidney donor, losing their eyesight, having difficulty swallowing or using their hands because of muscle wasting, or the very real social issues because of the intolerable smell and effects of cysteamine.

How do our children do it every day? I am not sure, but I do know that when they have the support of others it means everything and makes life that much easier. You are our "silver lining" in this journey and we are forever grateful.

Our community is bonded by our love for our children and adults who have cystinosis. Your love and support have given our children hope, and with hope, they continue to courageously battle their disease.

This magazine issue is special. We will introduce you to four CRF-funded researchers who work every day to find better treatments and a cure. Their brilliance and commitment to our children is real and gives us hope. We know you will enjoy the stories of children and adults with cystinosis who are living their lives, feeling loved by their families, and accomplishing great things. Once again, we will introduce you to two new cystinosis champions who have, by their actions, helped us make a difference in the lives of our families.

LOSS AND GRIEF

What is impossibly hard to accept is when someone we know and love from our community dies. Many of you knew Shannon Paju. Our family met her 25 years ago when she was 5 years old. Shannon was active in the community and was a brave fighter who loved life and lived it to the fullest. She participated in several clinical trials to help find better treatments and a cure for cystinosis. She always gave back and never gave up. Shannon died in April after suffering from cystinosis for years. We celebrate her life in this issue on page 40.

Many of us also had the privilege of knowing and meeting Brian Neils at the Day of Hope family conference in April. He was an inspiration to all of us and was so enthusiastic about life and his future. He had been waiting for a kidney donor and finally received the call just days before he was killed in a tragic accident. Brian's mother, Connie Niewald-Dyson honors his memory in this issue on page 44.

We miss Shannon and Brian and the other people with cystinosis whom we have known and loved. Our community is small; we are connected, and when one of us hurts, we all hurt. We mourn the lives of those we lost. They are a reminder that we must forge ahead and continue to work every day to find a cure.

OUR UNWAVERING COMMITMENT TO RESEARCH

It is astounding what we have accomplished together. Since 2003, CRF has funded 159 multi-year research studies in 12 countries. Our science community is thriving and making discoveries that have changed the course of this disease. Our researchers have published 68 articles in prestigious journals as a result of CRF funding. CRF funded researchers have dedicated their careers to making a difference in our community. We are grateful for their commitment.

CRF is unique when it comes to funding research. It is our strategy to ensure the donations we receive are continually and wholly invested in research. Twice a year, we announce a global call for new research grants and we receive applications from scientists and researchers from around the world who want to solve the complexities of this disease. By funding research twice a year, we can accelerate the research process and expand our knowledge about cystinosis.

Cystinosis is a systemic disease that affects every cell in the body. Therefore, our research portfolio is comprehensive. We have a complete list of studies we have funded on page 16. Because our research teams work collaboratively, the work and discoveries made by one group of researchers invariably helps the work of another research lab. Our research efforts include focus on the kidneys, eyes, muscle wasting, neurological issues and endocrine complications of cystinosis.

We are forever grateful to our prestigious Scientific Review Board (SRB), whose members dedicate innumerable hours of their time twice a year to carefully analyze and evaluate all applications. Their leadership and guidance has shaped the work we do and the direction of the science. The SRB has ensured we have funded only the best and the brightest researchers in the world and by doing so, they have created a synergistic research community.

In March 2018, we will host the sixth CRF International Cystinosis Research Symposium. We will gather over 65 CRF-funded cystinosis researchers and scientists to share their work, and to foster collaborations between research labs. The symposium is co-chaired by three dedicated world-renown scientists: Corinne Antignac, MD, PhD; Stéphanie Cherqui, PhD; and Julie Ingelfinger, MD.

We honor and are thankful for the dedication of those who work every day to solve the mysteries of cystinosis and who treat our children with love and dignity. We have come so far; we have built a strong foundation for innovative research that continues to flourish and produce extraordinary results.

As our research community grows, we expect that there will be enhanced collaboration and more frequent discoveries in the future. Given our global funding efforts, we know that every minute of every day there is a cystinosis researcher in this world working on behalf of our children to save their lives.

From the beginning, all CRF operating costs have been privately underwritten so that 100 percent of your donations to CRF go toward research.

EIGHT NEW GRANTS FUNDED THIS SPRING - $1,553,414

We are pleased to announce that in July 2017 we issued eight new grants totaling over $1.5 million in research awards. The grant recipients for spring 2017 are listed on page 64 along with a lay abstract of each study. The new grants focus on stem cell research, distal myopathy, novel treatment, newborn screening and research focused on the cellular and molecular aspects of cystinosis. In December 2017, we will announce additional new grants.

CLINICAL TRIALS ON THE HORIZON

For many years CRF has supported bench research with the hope that one day that research would lead to clinical trials. We are realizing our goals and are close to announcing new clinical trials. We can now apply what has been discovered in the lab to the bedside, to our children. Your support has enabled us to translate promising scientific discoveries into potential new treatments and a cure!

STEM CELL AND GENE THERAPY

Dr. Stéphanie Cherqui at the University of California San Diego (UCSD) continues to work diligently using stem cells and gene therapy. Based on mouse studies, we are hopeful that bone marrow stem cells hold the promise of a cure for cystinosis. With a one-time treatment in mice, Dr. Cherqui reversed cystinosis including corneal cystinosis, thyroid dysfunction and kidney disease. We have a special Q&A with Dr. Cherqui on page 8 where she shares what motivates her and what keeps her going every day in the lab.

Dr. Cherqui's treatment for cystinosis involves using the patients' own blood stem cells which are gene-corrected to introduce a functional CTNS gene and then transplanted back into the patients. This approach, called autologous transplantation, is safer than using foreign stem cells. 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.

Dr. Cherqui continues to work with the FDA on the safety studies for this approach and we are optimistic that she will obtain FDA approval for a phase I clinical trial for cystinosis in 2018.

NANO TECHNOLOGY AND NOVEL TREATMENTS FOR CORNEAL CYSTINOSIS

Corneal cystinosis is the painful build-up of cystine crystals in the eyes that causes photophobia (extreme sensitivity to light) severe eye pain, damage to the eye and sometimes blindness. There is an existing treatment, but it is rigorous, often painful and requires hourly dosing of medicated eye drops. We are in desperate need of a new treatment.

After our call with the FDA in April, we are in full swing with the nanowafer project. We have an amazing and talented team working on this project. There is no doubt we will be successful. We are hopeful that we will have FDA approval in 2018. The nanowafer was developed by Dr. Ghanashyam Acharya, PhD at Baylor College of Medicine. The concept is to load the nanowafer with cysteamine and place it on the eye where the medication slowly releases, thereby treating the eye for hours with just one application.

CRF owns the license to the cysteamine-loaded wafer, which allows CRF to control the pace and direction of the research. CRF's wholly owned subsidiary, Corneal Cystinolysis Inc. (CCI), will facilitate the continued development and clinical availability of the Cysteamine Nanowafer.

THE BROAD REACH OF CYSTINOSIS RESEARCH

CRF funded stem cell and gene therapy work offers hope to other diseases and disorders. We are pleased that many discoveries made by CRF researchers are currently being applied to other more prevalent and well-known disorders and diseases including other corneal diseases, kidney diseases and genetic and systemic diseases similar to cystinosis. Your support of cystinosis research has reached far beyond the cystinosis community. A cure for cystinosis will help find cures for other diseases potentially helping millions of people.

WE REMAIN COMMITTED TO FINDING BETTER TREATMENTS AND A CURE

We remain committed and focused on funding research that will help our children and save their lives. We pray for a life without medications, without pain, without muscle weakness, without hospital visits and blood draws, and especially without worries about life expectancy.

Your steadfast support, your commitment to research and your compassion and love for our community gives us hope. Our children dream of a life free of cystinosis, a life they dare to live with determination and perseverance.

We have made extraordinary progress and with your continued support, generosity and love, we will reach new heights and find a cure for cystinosis.

Thank you for supporting cystinosis research, for standing by our side and for embracing our community. We are grateful for your partnership in our quest for the cure. We are blessed by your encouragement, your prayers and your unwavering belief that together, we will find the cure.

With heartfelt thanks and gratitude,

Nancy & Jeff

A NOTE FROM Natalie

Dear Family and Friends,

It has been six months since I started my job at Taller San Jose Hope Builders. I have already gained extensive knowledge in my field and feel much more confident in myself since the start of my career. I am excited to keep learning and reaching my full potential. Not only have I been able to grow professionally, but I have also realized how blessed I am and how important it is to give back to underserved communities.

The young adults who are part of the Hope Builders' program are low-income, basic skills deficient, have been in the juvenile justice or foster care system, and most have been affected by violence -- most commonly with gangs. These young adults come to Hope Builders because they want a second chance in life and our program brings them hope. They actually want to better their lives and are motivated to commit to the program so that they can improve their economic and life stability. Every day I grow more and more passionate about helping this population succeed. I know my role as a development manager is not direct, but it is important and is changing the lives of these young adults.

Because of committed parents, patients, doctors and researchers, the battle is almost over.

Being a part of Hope Builders has also made me realize how fortunate I am to have such an amazing life. I have a wonderful, loving family who is always there for me and I have supportive friends who always make me feel better when I need someone to brighten my day. I also have been incredibly blessed to know our cystinosis community. Every person who has been touched by those with cystinosis is determined to find a cure. They give those with cystinosis hope. Over the past few months, I have had time to reflect on all that life has given me; in spite of the existence of this terrible and chronic disease, I appreciate and embrace life.

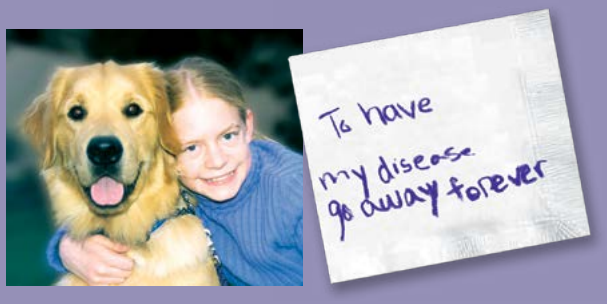
Hope is really what brings people closer together. The cystinosis community is small, but it is strong. We lean on each other when we need to, and we see every day as a gift from God. Because of committed parents, patients, doctors and researchers, the battle is almost over. Though life is hard at times and gets in the way of staying strong, it is important to remember how hopeful we are that we will find a cure in the near future.

I want to thank everyone in the cystinosis community for your dedication, support and generosity. You are making my wish come true. I am forever grateful to all of you who have not given up on me or our cystinosis community.

With Love,

Natalie

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



WHAT IS CYSTINOSIS?

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

Medication is available to control some of the symptoms of this terrible disease, but cystinosis remains incurable.

Cystinosis affects approximately 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.***

CYSTINOSIS
RESEARCH FOUNDATION
RESEARCH • HOPE • CURE

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 FUND PROVIDER OF GRANTS FOR CYSTINOSIS RESEARCH IN THE WORLD, funding more than 159 studies in 12 countries. ***CRF has raised over $39 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.

THANK YOU!

WE CELEBRATE OUR CRF COMMUNITY
AND ARE GRATEFUL EVERY DAY FOR YOUR SUPPORT!

We are on the brink of new clinical trials and closer than ever to the cure. It is because of you that CRF has been able to fund extraordinary researchers across the globe.

IN SPRING 2017, CRF FUNDED:

$1.55 million in research grants

8 scientific studies

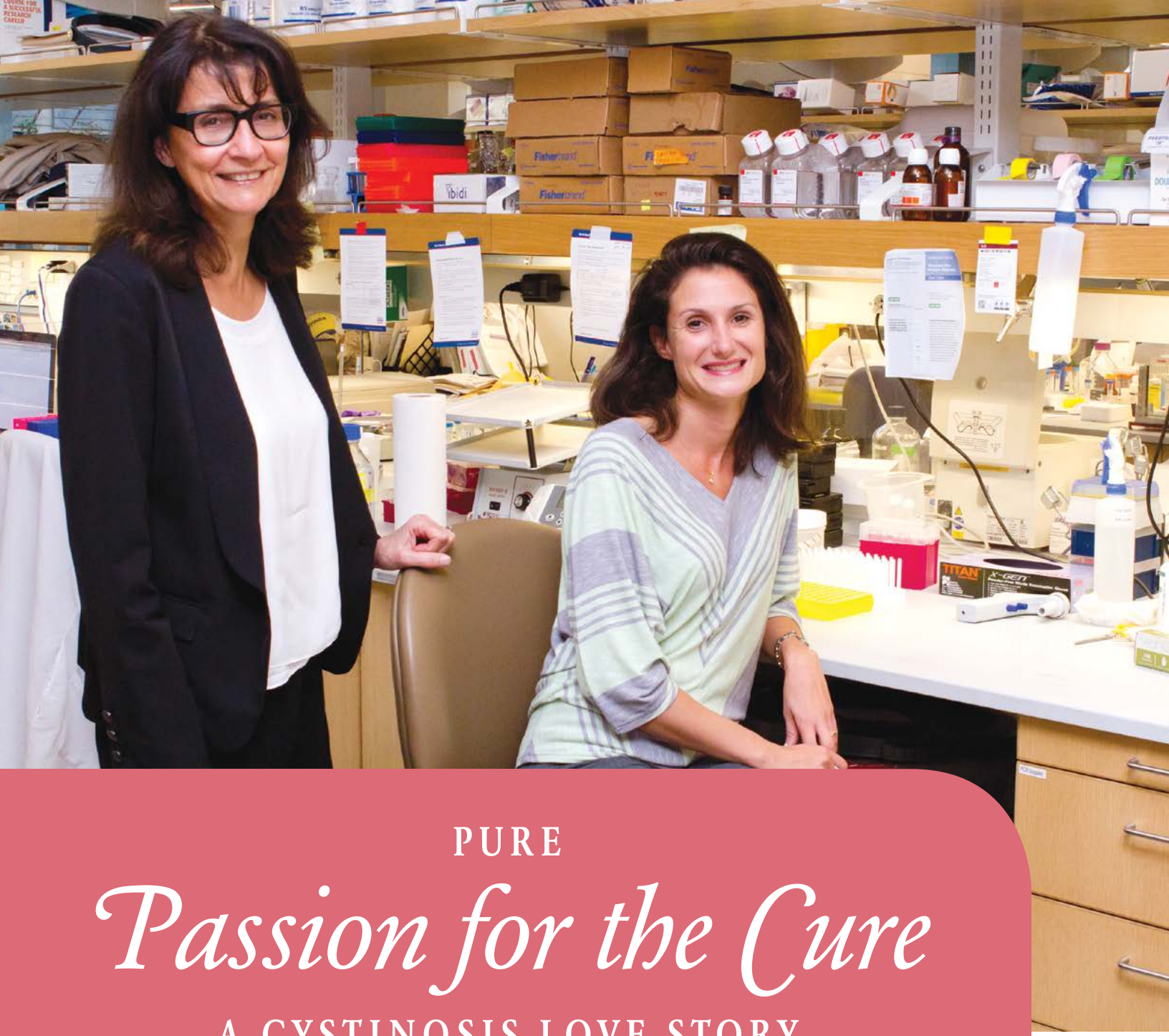
SINCE 2003, CRF HAS ISSUED:

159 cystinosis research grants in **12 countries**

bringing us **1 step closer**

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

You have changed THE COURSE OF CYSTINOSIS



PURE

Passion for the Cure

A CYSTINOSIS LOVE STORY

Q&A *with*

STÉPHANIE CHERQUI, PhD

Please share your background with us? How did you develop an interest in science?

As soon as I learned about genetics at school, I became passionate about this field. During the weekends, I was often working with my dad, who was doing some construction work in laboratories and hospitals, and this may be the reason why I decided at a very young age to become a researcher. I had my first internship when I was 16-years-old in a large institute in France called Genethon where the human genome was being entirely sequenced for the first time. I quickly became particularly interested in human genetic diseases and their potential treatment by gene therapy.

Thus, I entered a very specialized and selective BS/MS program focused on human genetics at the University Denis Diderot in Paris and completed my PhD on cystinosis in Dr. Corinne Antignac's lab in June 2002.

After my PhD, I moved to San Diego for a postdoctoral experience to learn about stem cell and gene therapy at The Scripps Research Institute in Dr. Daniel Salomon's lab. My goal was to apply this knowledge to develop a new treatment for cystinosis. After four years of post-doc, I became Staff Scientist and then Assistant Professor at The Scripps Research Institute. It was there that I developed the stem cell and gene therapy project for cystinosis. As the research moved us closer to a clinical trial, I joined the Department of Pediatrics at the University of California San Diego (UCSD) in 2012. They have a great Research Institute that is closely associated with a high-tech hospital and health centers. I am now Associate Professor at UCSD where my lab focuses on the development of a stem cell gene therapy strategy for cystinosis and other genetic disorders. Research has always been my passion. I love the excitement of discovering new mechanisms, new paradigms and new strategies that might help people who suffer from a genetic disease and this is what brought me to science and this profession.

Why did you become interested in the field of cystinosis?

As I was passionate about human genetic diseases and their potential treatment by gene therapy, I wanted to do my PhD in this field. However, at that time gene therapy was too risky for a PhD project. Thus, I wanted to work on a genetic disease with the goal to one day be able to treat it with gene therapy. I did my master's internship in Dr. Antignac's lab, and at the end of the internship, she proposed that I do my PhD in her lab on cystinosis.

They were looking for the gene for this disease at that time. I really enjoyed her lab and working with Corinne, and I thought this project would be perfect because this would allow me to go from the gene to, maybe one day, gene therapy for this genetic disease. This was 20 years ago, and the beginning of my adventure with cystinosis. While working in Dr. Antignac's lab in 1998, we made a very significant discovery, we identified the gene involved in cystinosis, the CTNS gene, and characterized its function as a lysosomal transporter of cystine. In another important discovery, we generated the mouse model of cystinosis, the Ctns-/- mice. I am now close to achieving my dream of using a stem cell gene therapy approach for the treatment of cystinosis. This goal is now much more than a project purpose; I know many families impacted by this disease so finding a new treatment for cystinosis is a personal fight.

CRF awarded its first grant to you in 2006. How has CRF support impacted your research goals?

The stem cell gene therapy project started because of the CRF funding. This project was controversial and risky so it would have been very difficult to find funding to support such a project. CRF trusted me and allowed me to launch these studies. The first proof of concept that wild-type HSCs could treat cystinosis in the mouse model of cystinosis, the Ctns-/- mice, was fully funded by CRF. This data then allowed us to get funding from other sponsors. Many other projects related to this novel therapy for cystinosis are also funded by major agencies such as the National Institute of Health (NIH) and the California Institute of Regenerative Medicine.

CRF is an amazing advocacy group, while helping and advising families, they also focus on research because they believe this is the way to get better treatment for cystinosis. They are so right! This is how Procysbi® was developed and many other drugs or therapies for cystinosis are currently being discovered with the support of CRF. For my part, CRF is not only providing financial support to me; the foundation has always been so supportive, with encouragement and by helping me figure out issues. If something goes wrong, I call Nancy, and our long conversations are always so helpful. Because of CRF this project could begin and evolve to a future clinical trial for cystinosis; this is a team work.

Would you briefly describe what is involved in the stem cell trial (how it works)?

The therapeutic approach we are going to use consists of using patients' own blood stem cells, which are gene corrected in the laboratory using a biological tool called lentiviral vector. A lentiviral vector is derived from the HIV virus, and the one we are using contains

The cystinosis community is eager for news about the status of the stem cell trial. When do you anticipate filing the Investigational New Drug (IND) application and getting FDA approval?

I wish I knew the answer to this question. Our goal is to file the IND in 2018. However, filing an IND is very complicated and requires many studies to complete and paperwork to be filed. We are doing everything we can to go as fast as possible but there are many aspects that do not depend on us and some that take much more time than expected. The Institutional Review Board (IRB) at UCSD who reviewed the clinical protocol for this study said that this is the most complicated study they have ever seen.

a functional CTNS gene. By infecting the stem cells, our lentiviral vector brings the CTNS gene into these cells. The corrected gene cells are then transplanted back into the patients.

Subjects who are interested will be encouraged to take their time and go over the consent form that explains the study; it is a lengthy procedure. Once the patient signs the consent form he/she can begin the screening process. The screening assessments help decide if the patient qualifies for study; this takes approximately two to four days of screening tests. After the screening assessments are evaluated by the medical team and if the patient qualifies, the patient will return to San Diego to begin the baseline assessments.

Baseline assessments gather clinical information about the current function of many organs to help us establish the state of the disease prior to the stem cell transplant. Baseline assessments, which take seven days, will help us evaluate whether or not the stem cell therapy improves the disease complications. After the baseline studies, the patient's stem cells will be collected (mobilization/apheresis procedures) which will take another five days. The patient will then return home while the collected cells will be corrected in the lab for the mutation (called transduction). This can take two to three months. Once this is completed, the patients are asked to return to San Diego to start the conditioning regimen (chemotherapy; this will take approximately six days) to prepare for transplant of the gene-corrected cells. Transplant takes one day.

After transplant, the recovery period begins. The recovery phase is approximately three months and the patient will need to stay in the San Diego area (in-hospital for one month and out-patient for two months) in order to monitor the treatment. Once the patient is able to return home, he/she will be asked to return to San Diego for follow up appointments three more times over two years.

The approach we are using is challenging because it involves the use of hematopoietic stem cells that will be genetically modified, but the disease is also challenging because most of the organs are impacted and will have to be evaluated. Therefore, the manufacturing process of the cells is complex and the involvement of many body systems require the involvement of many specialists to provide expertise in their respective area for this project. This is what makes this IND so difficult, but we have a great team who works countless hours to assemble the IND application so I am hopeful that we will be able to file it in the next few months.

CRF believes that it takes a village to get things done. Who do you collaborate with?

First, I have an amazing team who works full time on this project with great motivation and enthusiasm including Laura Hernandez, Maulik Panchal, Peter Hevezi, Carlos Castellanos, Tatiana Lobry and Thi Le. I am lucky to have the support of the Sanford Stem Cell Clinical Center at UCSD, and in particular Vickie Schekler, who is an expert in regulatory and IND. We also have the support of the UCSD CIRM Alpha Stem Cell Clinic, in particular Betty Cabrera, who is guiding us for the clinical aspect of the trial. The clinical trial will be conducted by members of the Cystinosis Stem Cell and Gene Therapy Consortium. The Consortium includes medical experts in neurology, nephrology, gastroenterology, ophthalmology, endocrinology and metabolic diseases. Finally, support from the patients and families for the development of this clinical trial has been very high. Some patients have travelled on their own expense to UCSD to donate their blood so we could optimize the protocol for the gene-correction of the cystinosis patients' stem cells.

Who or what inspires you every day to work on cystinosis?

The families impacted by cystinosis inspire me every day. I have pictures of several of the children I know on the wall of my office, and if I feel down or discouraged, I look at them and my willingness to fight and bring this treatment to patients comes back. I am amazed by the strength and courage of the patients and parents affected by cystinosis; they are my models in my everyday life. My husband, Fabien, and my kids, Matteo and Noah, also encourage me a lot. Every year, they attend the Day of Hope event and my presentation. They know all about cystinosis and what I am trying to accomplish. Often my kids ask when I will start treating the patients with cystinosis, they tell me that I have to go faster – like I don't have enough pressure! Last week Matteo had to write about his life as a homework assignment, and one of the questions was about his most important family history event, and he responded, "My mom will find the cure for cystinosis." I was amazed that he felt so strongly about finding a cure for cystinosis. This is motivating, but it is also very scary that so many people believe and count on me. I hope I will not disappoint them.

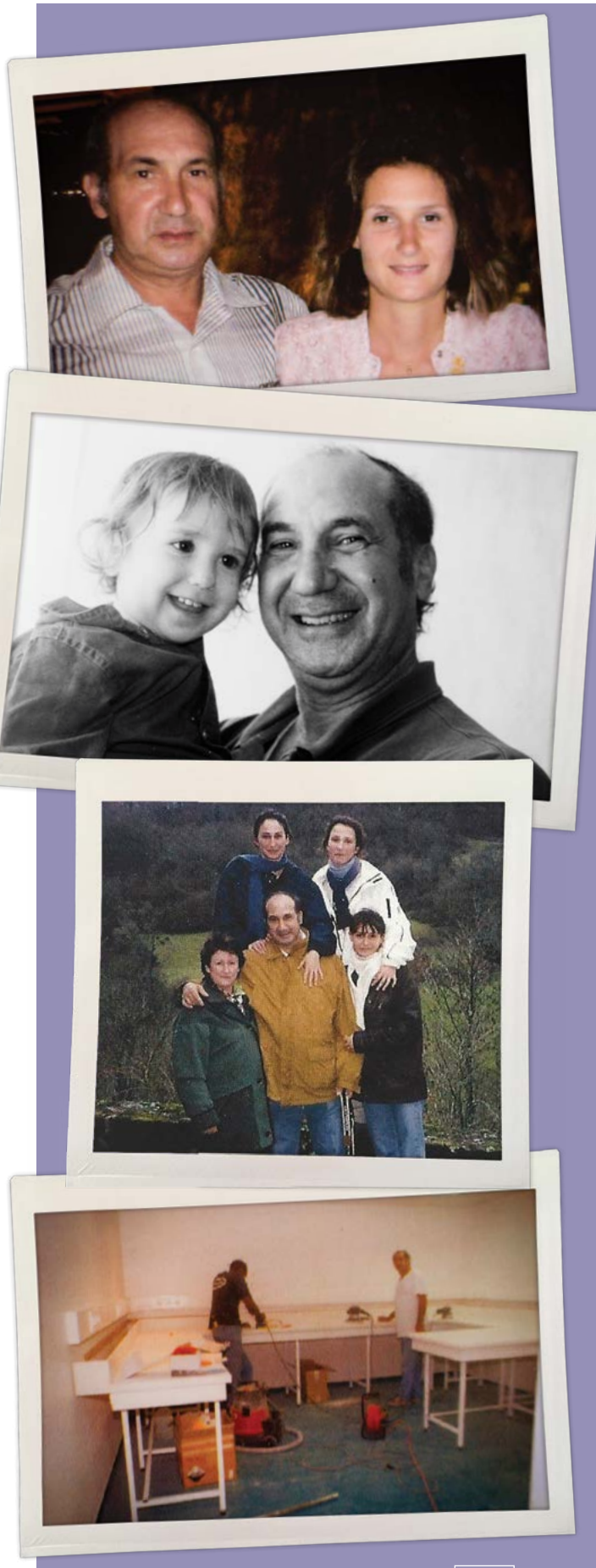
What other diseases will be helped by your work on cystinosis?

We were very surprised that the hematopoietic stem cells, which generate blood cells, worked so well to prevent tissue degeneration in the mouse model of cystinosis. We showed for the first time that the transplanted hematopoietic stem cells differentiated into macrophages (phagocytic cells) within the tissues and led to the transfer of healthy lysosomes to the adjacent deficient cells via long cellular protrusions called "tunneling nanotubes". This discovery opened new perspectives in regenerative medicine and in the application to other genetic disorders. Because mitochondria can also be transferred through the tunneling nanotubes, we tested the impact of hematopoietic stem cell transplantation on a mouse model of Friedrich's ataxia (FRDA), a neuro-muscular degenerative disorder for which there is no treatment. The neurologic, muscular and cardiac complications seen in the mice were completely prevented by this treatment.

Another disorder we are working on in collaboration with Dr. Eric Adler, cardiologist at UCSD, is Danon disease, which is due to a defective transmembrane lysosomal protein such as cystinosis. Patients generally die from heart failure by age 30. Again, hematopoietic stem cell transplantation in the mouse model, led to the rescue of the cardiac and muscular defects.

Based on our work, Dr. Olivier Devuyst in Switzerland, tried the same stem cell approach in the mouse model of Dent Disease, which also impacts the kidney and patients develop a Fanconi syndrome and chronic kidney disease. Dr. Devuyst also observed rescue of the kidney defects of the mice treated with stem cells with a similar mechanism of action involving the formation of tunneling nanotubes.

Hence our findings may deliver a completely new paradigm for the treatment of a wide assortment of diseases, and if so, the CRF, by supporting the launch of the stem cell project for cystinosis, will have helped many patients with untreatable and very debilitating diseases.



THANK YOU CANADA!

WORKING TOGETHER TO FIND THE CURE

We are forever grateful to our Canadian cystinosis families, who have worked in partnership with the Cystinosis Research Foundation (CRF) since 2009 to fund research.

Canadians can send donations directly to CRF, or they can contribute to CRF through the Canadian Aqueduct Foundation. Through the Aqueduct Foundation, Canadians have created an efficient and effective fundraising process which allows them to raise funds, ensure their donors receive a charitable tax receipt for that country, and support CRF Scientific Review Board approved research studies. The donations in the Aqueduct Foundation are funded directly through CRF to the research institution.

The Cystinosis Awareness and Research Effort (CARE) and the Liv A Little Foundation have a strong working relationship with CRF. Jody Strauss (CARE) and Erin Little (Liv A Little) are CRF Board of Trustee members which ensures Canadian donations are regularly supporting cystinosis research.

Since 2003, CRF has funded 159 studies in 12 countries, and it is the largest funder of cystinosis research in the world. CRF has a Scientific Review Board composed of world-renowned cystinosis scientists and experts who review and recommend research applications for funding. We are committed to funding the most promising and innovative research.

CRF is thankful for our close and productive relationship with Canadian families who have joined CRF in an effort to find better treatments and a cure.

A very special thank you to the following Canadian cystinosis families who have helped raise money and donated to find a cure for cystinosis:

- *Valéri Talbot and Eric Bilodeau*
- *Amanda and Dave Buck*
- *Monique and Don Carriere*
- *Sue and Pete Chatelain*
- *Karen McCullagh and Don Cunningham*
- *Kristen Murray and Nathan deBruyn*
- *Marthe and Rick Drolet*
- *Rachel and Mahlon Kuepfer*
- *Erin and Chad Little*
- *Fannie and Wayne Martin*
- *Katie and Terry Monaghan*
- *Susan and Peter Penner*
- *Marianne Sincennes and Daniel Picard*
- *Liz Ewart and Dan Roberts*
- *Jody and Trevor Strauss*
- *Diane and Elroy Wagler*
- *Crystal and Bob Walker*

Since 2016, Canadian families have directly funded grants through Aqueduct totaling $388,012.75.

The following grant payment was recently funded by donations from Canadian families:

Paul Goodyer, MD
MCGILL UNIVERSITY HEALTH CENTRE

ELX-02 therapy for cystinosis caused by CTNS nonsense mutation
$37,500
Funded by Liv A Little Foundation

If you would like to learn more about how to fundraise in Canada, please contact Erin Little (*ce.little@bmts.com*) or Nancy Stack at *(nstack@cystinosisresearch.org)*

Scientific Review Board

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.

CHAIR

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

BOARD MEMBERS

Daniel G. Bichet, MD, MSc
Professor of Secondary Affiliation (Medicine)
Department of Molecular and Integrative Physiology
Faculty of Medicine, Université de Montréal
Centre de recherche, Hôpital du Sacré-Coeur de Montréal
QUEBEC, CANADA

Sergio D. Catz, PhD
Associate Professor
Molecular and Experimental Medicine
The Scripps Research Institute
LA JOLLA, CALIFORNIA

Stéphanie Cherqui, PhD
Assistant Professor
Department of Pediatrics
Division of Genetics
University of California, San Diego
SAN DIEGO, CALIFORNIA

Pierre J. Courtoy, MD, PhD
Board Certified Internist
Professor of Cell Biology and General Pathology
Louvain University Medical School
Head of Cell Biology Unit
de Duve Institute
BRUSSELS, BELGIUM

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

Paul C. Grimm, MD
Professor of Pediatrics
Stanford University School of Medicine
Pediatric Nephrology
STANFORD, CALIFORNIA

Julie R. Ingelfinger, MD
Deputy Editor of the
New England Journal of Medicine
Professor of Pediatrics
Harvard Medical School
BOSTON, MASSACHUSETTS

Martin Konrad, MD
Department of General Pediatrics
University Children's Hospital
MUENSTER, GERMANY

Thank you for your dedication to the global cystinosis community.

THE IMPACT OF CRF Research

CELLULAR AND/OR MOLECULAR STUDIES OF THE PATHOGENESIS OF CYSTINOSIS

41 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
Rossella Conti, PhD
PARIS DESCARTES UNIVERSITY, PARIS, FRANCE

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

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

Alessandro Luciani, PhD
UNIVERSITY OF ZURICH, SWITZERLAND

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

Norbert Perrimon, PhD
HARVARD MEDICAL SCHOOL, BOSTON, MASSACHUSETTS

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

Matias Simons, MD
IMAGINE INSTITUTE, PARIS, FRANCE

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

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

28 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

CURE CYSTINOSIS INTERNATIONAL REGISTRY (CCIR)

1 GRANT

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

GENETIC ANALYSES OF CYSTINOSIS

5 GRANTS

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

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

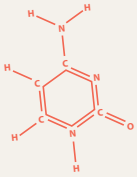
Elena Levtchenko, MD, PhD
UNIVERSITY HOSPITAL LEUVEN, BELGIUM

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

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

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 Levtchenko, MD, PhD
UNIVERSITY HOSPITAL, LEUVEN, BELGIUM

THYROID

1 GRANT

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

AREAS OF RESEARCH FOCUS *and* GRANTS
SINCE 2002

KIDNEY RESEARCH
18 GRANTS

Robert Chevalier, MD
UNIVERSITY OF VIRGINIA, CHARLOTTESVILLE, VIRGINIA

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

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

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

Elena Levtchenko, 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

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

NEW DRUG DISCOVERY CYSTEAMINE, NEW MEDICATIONS AND DEVICES
22 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
Laura Rega, PhD
BAMBINO GESÙ CHILDREN'S HOSPITAL, ROME, ITALY

Paul Goodyer, MD
MONTREAL CHILDREN'S HOSPITAL, QUEBEC, CANADA

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

SKIN, MUSCLE, BONE
7 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

NEUROLOGICAL
14 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
8 GRANTS

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

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

Morgan Fedorchak, PhD
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE, PITTSBURGH, PENNSYLVANIA

Jennifer Simpson, MD
UNIVERSITY OF CALIFORNIA, IRVINE, GAVIN HERBERT EYE INSTITUTE

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

SPRING 2017 CRF RESEARCH Grants Funded

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

Sergio Catz, PhD, ***Principal Investigator***
Jinzhong Zhang, PhD, ***Research Fellow***
The Scripps Research Institute, La Jolla, California

$75,000.00 – One-year grant (September 15, 2017 – September 14, 2018)

MECHANISM OF BONE MARROW STEM CELL-MEDIATED THERAPY IN THE MOUSE MODEL OF CYSTINOSIS

Stéphanie Cherqui, PhD, ***Principal Investigator***
University of California, San Diego, La Jolla, California

$345,829.00 – Two-year grant (September 1, 2017 – August 31, 2019)

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

Florian Eichler, MD, ***Principal Investigator***
Reza Seyedsadjadi, MD, ***Co-Principal Investigator***
Massachusetts General Hospital, Boston, Massachusetts

$177,132.00 – One-year grant (September 1, 2017 – August 31, 2018)

DEVELOPMENT OF A TOPICAL, CONTROLLED RELEASE CYSTEAMINE EYE DROP

Morgan Fedorchak, PhD, ***Principal Investigator***
Kanwal Nichal, MD, FRCO, ***Co-Principal Investigator***
University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

$163,819.00 – One-year grant (September 1, 2017 – August 31, 2018)

CYSTINOSIS RESEARCH FOUNDATION GRANTS SUPPORT SCIENTIFIC STUDIES ON

Cell Function, New Treatments and the Quest for a Cure

TOTAL SPRING 2017 GRANTS FUNDED: **$1.55 million** FUNDING 8 RESEARCH PROJECTS

ELX-02 THERAPY FOR CYSTINOSIS CAUSED BY CTNS NONSENSE MUTATIONS

Paul Goodyer, MD, ***Principal Investigator***
McGill University Health Centre, Montreal, Quebec, Canada

$150,000.00 – Two-year grant (September 1, 2017 – August 31, 2019)

NEWBORN SCREENING FOR CYSTINOSIS

Sihoun Hahn, MD, PhD, ***Principal Investigator***
Seattle Children's Research Institute, Seattle, Washington

$234,458.00 – Two-year grant (September 1, 2017 – August 31, 2019)

AUTOPHAGIC LYSOSOMAL REFORMATION AND LIPID SIGNALING IN NEPHROPATHIC CYSTINOSIS

Alessandro Luciani, PhD, ***Principal Investigator***
Olivier Devyust, MD, PhD, ***Co-Principal Investigator***
University of Zurich, Switzerland

$240,000.00 – Three-year grant (October 1, 2017 – September 30, 2020)

IMPACT OF LEPTIN SIGNALING ON SKELETAL INTEGRITY AND GROWTH IN INFANTILE NEPHROPATHIC CYSTINOSIS

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

$167,177.00 – One-year grant (September 1, 2017 – August 31, 2018)

LAY ABSTRACTS FOR SPRING 2017 RESEARCH GRANTS CAN BE FOUND ON PAGES 62-69.

RESEARCHER
PROFILE

Alan Davidson, PhD

ASSOCIATE PROFESSOR, HEAD OF MOLECULAR MEDICINE AND PATHOLOGY

Teresa Holm, MD, PhD

RESEARCH FELLOW, MOLECULAR MEDICINE AND PATHOLOGY

THE UNIVERSITY OF AUCKLAND, GRAFTON, AUCKLAND, NEW ZEALAND

Answers IN AN Organoid

By Dennis Arp

New Zealand research partners help pioneer a regenerative world of lab-grown mini kidneys, seeking breakthrough treatments and perhaps a new path to transplantation.

As a researcher, Teresa Holm travels the intracellular pathways of cystinosis, searching for clues that might lead to breakthroughs in treatment. But she's also on another journey that makes her lab work even more inspiring.

You see, Holm is training to be a transplant surgeon. So even as she and her co-investigator husband, Associate Professor Dr. Alan Davidson, convert lab-grown stem cells into kidney organoids (mini kidneys) as they seek solutions to renal problems caused by cystinosis, Holm chases a parallel dream.

"I'd like to take one of these little organoids we're creating in a dish, and I'd like to make one big enough to put in a patient," says Holm, M.D., Ph.D. "The goal is to give them a kidney made from their tissue, but with a repaired gene – give them back an organ that's fully functional."

In this 21st-century world of regenerative medicine, the promise of induced pluripotent stem cells (iPSCs) seems almost larger than life. But the truth is that while Drs. Davidson and Holm build toward a future full of brilliant opportunities, they also ground their research in the possibilities of the here and now. With funding support from the Cystinosis Research Foundation (CRF), the co-principal investigators are coaxing those cells to maturity, creating mini kidneys that can model the disease and perhaps provide insights with direct applications.

"We're looking at the very basic cell biology," says Dr. Davidson, whose research lab is in the Department of Molecular Medicine & Pathology at the University of Auckland in New Zealand. "Our first objective is to characterize these cystinotic kidney organoids and determine how well they model the renal defects of cystinosis."

By making kidney tissue in the lab, using cells directly derived from adult tissues, "we now have a renewable source of cells that carry the (cystinosis) mutation," Dr. Holm says. This provides a novel human-based platform for testing new drugs that hold potential as cystinosis treatments. In addition,

Drs. Holm and Davidson plan to examine and assess the intracellular mTOR pathway – a major metabolic signal that plays a critical role in regulating the cell cycle.

"Because we're using this human-based source of cells, any advances we make will be more relevant," Dr. Davidson says. "Rodent and cell-culture models are important, but these other models can't reproduce everything that we see in humans. Drugs and other compounds often don't act in the same way."

The researchers have been studying cystinosis since 2008, when Dr. Davidson headed his own research program at the Center for Regenerative Medicine at Massachusetts General Hospital and Harvard Medical School. The doctor is internationally known for his research in the fields of embryonic kidney formation and renal regeneration.

The iPSC technology for cell generation was pioneered at a Tokyo lab headed by Shinya Yamanaka, who was awarded the 2012 Nobel Prize for medicine along with Sir John Gurdon. Their work led to the discovery that mature cells could become pluripotent, or capable of developing into any tissue in the body.

"If you know the right cocktail of growth factors to mature iPSCs into your tissue of interest then there is tremendous potential for these cells to model human diseases in a dish," Dr. Davidson says. "These are the perfect cells for developing new treatments."

As the researchers move from collecting information to testing the effectiveness of medications and other compounds, they plan to focus on drugs already approved by the Food and Drug Administration (FDA). By repurposing drugs shown to have a rescue effect, the project could move rapidly to clinical trials, Dr. Davidson says.

"We might shave years off the process," Dr. Holm adds.

They begin this new phase of their research with expectations for a multi-year journey. There are no certainties, but they hold great hopes, and they know that none of the promise would be possible without the support of the CRF.

"The foundation is a game-changer," Dr. Davidson says. "This project would not have started without CRF funding. And one of the great things about the CRF is that there are no boundaries. We started our research in Boston and now we're back in Auckland, but that hasn't changed anything."

Drs. Davidson and Holm have also found that distance is no barrier to the warmth within the cystinosis community.

"Last year there were nine cystinosis families in New Zealand, but we have come together as a global community," Dr. Holm says. "There is one specialty Department of Pediatric Nephrology in Auckland, with a handful of pediatric nephrologists traveling all about the country. Still, it all works very well."

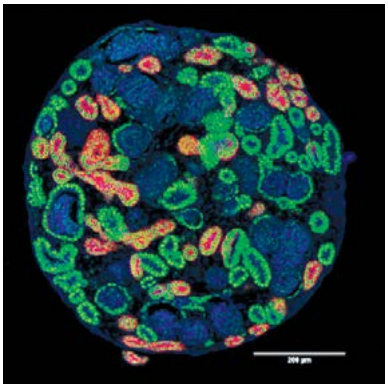


Photo: Veronika Sander. Cross section of a human kidney organoid showing kidney tubules stained in green and red.

The researchers note that they also benefit from attending the CRF International Cystinosis Research Symposium in Southern California.

"It's a unique opportunity to set up collaborations that might not happen otherwise," Dr. Holm says. "Even a conversation over lunch might lead to something bigger."

Dr. Holm also draws insights and inspiration from her work as a clinician.

"To see firsthand how research can change lives – pediatric lives – that's huge," she says. "That's motivation in itself."

The support of cystinosis families and friends "also permeates the research," Dr. Davidson adds. "There's a constant desire to produce something to help these families. It's a slow grind on the (lab) bench. There are eureka moments, but they're tempered by the reality that the real test of new discoveries is in patients, which is challenging. Through it all, we have a passion to make a difference, and that's the reality that drives our work."

"TO SEE FIRSTHAND HOW RESEARCH CAN CHANGE LIVES – PEDIATRIC LIVES – THAT'S HUGE, THAT'S MOTIVATION IN ITSELF."

As Dr. Holm continues on her path toward becoming a transplant surgeon, she says she's excited about "building a bridge between the laboratory and the operating theater, where few bridges exist." Though she knows that her dream of turning her research into transplantable organs is still years away, she pursues it because of its transformational potential.

"Time is always at the forefront," she says. "The good news about the future is that cystinosis patients will be first in line to benefit from our breakthroughs."

RESEARCHER
PROFILE

Florian Eichler, MD

DIRECTOR OF THE LEUKODYSTROPHY SERVICE, DEPARTMENT OF NEUROLOGY

MASSACHUSETTS GENERAL HOSPITAL FOR CHILDREN

A STRONGER Grasp of MUSCLE WEAKNESS

By Dennis Arp

New CRF-funded research explores distal myopathy, providing hope for patients who struggle with breathing and swallowing.

A deep commitment to patient care drives Dr. Florian Eichler to also perform groundbreaking clinical research. The life-changing potential of this work is never more profound than when it brings hope to those with cystinosis.

A neurologist at Massachusetts General Hospital and Harvard Medical School, Dr. Eichler specializes in the care of patients with genetic disorders. That's how he met Shea Hammond, who has fought through more than two decades of cystinosis treatment, including three kidney transplants. Caring for Hammond gives Dr. Eichler a firsthand view of cystinosis patient courage and perseverance.

"I can only imagine what life is like for him to go through this day by day," says Dr. Eichler, director of Harvard's Center for Rare Neurological Diseases. "But while heroic efforts have saved vital organs, the effects on his nervous system and the deterioration of his muscles are putting him in ongoing danger."

Thanks to a grant from the Cystinosis Research Foundation (CRF), Dr. Eichler and his investigative team are seeking answers about muscle weakness that could alleviate difficulties with swallowing and aspiration – problems that can be life-threatening for patients like Hammond.

"I've always had a passion for thinking about genes and how they might give us an opportunity to intervene and transform patients' lives," Dr. Eichler says. "If we can understand a genetic abnormality and then correct it, we have a chance to have a tremendous impact on quality of life."

For decades now, treatment with cysteamine has been lengthening and improving the lives of those with cystinosis. But even as therapies evolve and treatment options grow, patients often suffer muscle weakness that creates difficulties with swallowing and aspiration.

"We see patients suffering pneumonias and succumbing to this complication," Dr. Eichler says. "Clearly we need to understand more about this."

The goal is to identify and eventually implement clinical trials targeting distal myopathy, a condition in which adults experience weakness of specific muscles. Distal muscles are those farther from the center of the body, like in the throat, lower legs and forearms.

The first step of Dr. Eichler's study is to gather information about muscle changes over time, finding out how many muscles are affected and determining "the window of opportunity to intervene so we can salvage muscle performance," he says.

> "IF WE CAN UNDERSTAND A GENETIC ABNORMALITY AND THEN CORRECT IT, WE HAVE A CHANCE TO HAVE A TREMENDOUS IMPACT ON QUALITY OF LIFE."

"As cystine accumulates, clearly it's doing greater harm to distal muscles versus proximal muscles (those closer to the trunk)," Dr. Eichler adds. "There are some things that biology is telling us, such as how this occurs, but how it evolves is still a mystery."

In late spring 2017, Dr. Eichler and his research team started examining cystinosis patients and gathering data via surveys that provide a window to patient experience. The team includes two neurologists, two speech and swallow specialists and two research coordinators. The team also includes Dr. Reza Seyedsedjadi who brings new expertise to the cystinosis patients, examining strength, coordination and hand function with new devices and Stacey Sullivan who has applied knowledge from her ALS experience to the swallow exams. So far, they've seen nine of an expected 20 patients.

Among their tools are measurements on a scale specific to those with cystinosis, allowing researchers to determine the strength of cough air flow. Similar measures have recently been shown to differentiate safe versus unsafe swallowing in patients with amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease.

"In Year 2, we will bring back (cystinosis) patients for a repeat examination and an expiratory muscle strength training regimen," says Dr. Eichler, principal investigator on the CRF-funded study. "This will help assess whether physiologic measures of swallow and cough could be improved."

Researchers benefit greatly from the previous studies involving ALS patients.

"We're very lucky here to have one of the largest ALS centers in the nation, with an active trial network," Dr. Eichler says. "We're constantly trying to borrow or steal from one disease to improve the treatment of another."

Often simple steps can make a big difference. For instance, advice on changes to posture can sometimes prevent choking.

"The other thing we've noticed is that some patients have silent aspirations – ones they don't even recognize," the doctor says. "We can also tell them what foods and liquids to avoid."

After the study team gathers insights from cystinosis patients and assesses current timelines and treatments, the study will move to step three, in which researchers implement medications or other therapies to improve patient outcomes. This could involve drugs that are already FDA-approved, or it might be that current meds simply are not reaching the pertinent muscles, Dr. Eichler says.

"Gene therapy is a possibility," he adds. "A whole variety of options are out there. We're excited about the possibilities, but we're committed to doing this in a step-wise fashion so we thoroughly assess the benefits."

As the study progresses, researchers gain insights every day, including about the quality of the cystinosis community.

"I can't emphasize enough what a pleasure it is to work with such a well-organized patient community," Dr. Eichler says. "It's also critical to have the support of the CRF. Natural history studies are very rarely funded by the (National Institutes of Health); often the work of collecting outcomes is sadly neglected."

Nothing means more to Dr. Eichler and his team than to hear directly from cystinosis patients. Often the researchers can learn about an impairment just by listening to the weakness in a voice or a change in vocal tone.

"I find that quite moving," Dr. Eichler says. "It really adds a sense of urgency to this whole undertaking. As someone who's relatively new to this disorder, I appreciate that patients are so generous in teaching me about their plight. I hope I can return that generosity by providing steps that improve their lives."

HAPPY HOLIDAYS

FROM THE CYSTINOSIS RESEARCH FOUNDATION

Dear Friends and Family,

As we reflect on our *cystinosis love stories*, we find ourselves overwhelmed with gratitude for all the people who make CRF 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 Cystinosis Research Foundation, visit
www.cystinosisresearch.org/how-to-help/donate-online

2018

CRF International Cystinosis Research Symposium

SAVE THE DATE

THURSDAY, **MARCH 1** & FRIDAY, **MARCH 2, 2018**

WE ARE PROUD TO ANNOUNCE
OUR 2018 KEYNOTE SPEAKER

Benjamin Freedman, PhD

Assistant professor
University of Washington Medicine/Nephrology

"Organ-specific cell lines and organoids in hereditary kidney diseases"

2018 SYMPOSIUM CO-CHAIRS

Corinne Antignac, MD, PhD

Stéphanie Cherqui, PhD

Julie Ingelfinger, MD

LOCATION

ARNOLD AND MABEL BECKMAN CENTER OF THE NATIONAL ACADEMIES OF SCIENCE AND ENGINEERING
100 Academy, Irvine, California 92617
www.nationalacademies.org/beckman/

INFORMATION

Contact Foundation President
NANCY STACK
at 949-223-7610 or
nstack@cystinosisresearch.org

CYSTINOSIS RESEARCH FOUNDATION
RESEARCH • HOPE • CURE

BY INVITATION ONLY
CYSTINOSISRESEARCH.ORG

Humor, Advocacy, Connection and Hope

By Sue Maguire, Sinéad and Ciara's mom
MEATH, IRELAND

We first heard the word "cystinosis" 22 years ago, when our precious, smiling, loveable, blonde (first clue there!) 25-month-old daughter Sinéad was diagnosed. Four years later, our family was completed when another beautiful little blonde, Ciara arrived. She was diagnosed at birth and this time everyone was at least aware of what to expect.

Our story since that point is very similar to all of yours. We have faced the same numerous challenges which you have all faced: We have rejoiced in the small victories, ("She ate 10 pieces of pasta today!); we have felt so low and desperate that we wondered if we would ever laugh and find joy again. At times, we felt hopeless. However, as we got stronger and minor battles were won, Andy and I decided (maybe naively!) that cystinosis was going to have to fit around our lives and not the other way around. Obviously, we had to concede a little with the rigorous medications schedule, night feeds, vomit clean-ups, and hospital appointments; but once we got into a routine we did everything we could to have a "normal" life. A sense of humor has always helped us get through, even though some days it was nearly impossible to see the light side of the situation! Also, whenever help was offered I always accepted it.

Being proactive and doing something to try and make a difference to our daughters' lives also helped. We were two of the founding members of Cystinosis Ireland in 2003. Our main aim from the start was to fundraise to support research and it still is. Since then, our small but determined group has helped to contribute almost €2million to cystinosis research, an achievement we are extremely proud of. At the start, we felt the research was very much aspirational and privately we wondered if we would ever see results that would have an impact on Sinéad and Ciara's lives. We kept on fundraising and kept telling our story anyway. So, don't give up!

This year, we not only fundraised for research, but our daughters also took part in it. We flew to Boston in August for them to participate in Dr. Eichler's study, "Clinical Trial Readiness for Distal Myopathy in Nephropathic Cystinosis," funded by CRF. This was a significant moment for us, becoming an actual part of research – that thing we were always talking about when raising money.

Another first this year was in spring. Sinead: "Mum and I attended our first Day of Hope. I had been feeling very down, was out of work and finding it hard to motivate myself to do anything. However, meeting other adults with cystinosis had given me such a lift. Before that I felt very alone, that it was just me and Ciara. My confidence has grown and I'm ready for new challenges now! Everyone can notice a difference in me. Since April, I have joined a gym, completed a mini marathon and…. got a new job!"

Along the way, we have met many people. Since the explosion of social media, we have encountered and made friends with many more. The means to connect with several others all over the world instantly and to get an answer to a question nobody locally can give you is amazing. Meeting other like-minded people has been the best thing about joining this club that none of us want to join. Also remember, you won't gel with everyone, but nurture the connections you make that work for you.

In conclusion, the one thing I can and do say to newly diagnosed families is that today's picture for their child is so different from 1995 when Sinéad was diagnosed. The long years of research are now yielding such exciting and promising results. Treatments that will have a positive and permanent impact on their lives, (something we only dared hope about), now have a real chance of becoming reality.

Thank you to the Stack family and everyone at CRF for all you are doing for the worldwide cystinosis community.


BOSTON TEA PARTY
SHIPS & MUSEUM ★★★★★ DECEMBER 16, 1773
A REVOLUTIONARY EXPERIENCE℠

SETH DEBRUYN

GRANDPARENTS' REFLECTIONS

DAY OF HOPE BRINGS ENLIGHTENMENT, LOVE AND HOPE

By Mark deBruyn and Carol Thatcher
ALBERTA, CANADA

It was with excitement and anticipation that my partner, Carol, and I decided it was time to attend this year's Cystinosis Research Foundation's Day of Hope Conference with my son's family. Nathan and Kristen and the boys had been to two of these annual events before, and we were amazed at how deeply they had been affected by these experiences when they returned home. It was time to find out why!

Nathan and Kristen have 5-year-old twins, Seth and Leif. Seth deals with cystinosis, and Carol and I were wanting to learn more about this disease and the amazing network of CRF families and researchers that Nathan and Kristen had been telling us about for several years. We were also curious to find out who were these mysterious "California friends" that the boys kept talking about.

We boarded our flight in Vancouver, British Columbia, and a few hours later we met Seth and Leif and their parents in the lobby of the luxurious Island Hotel in Newport Beach. The boys were so excited about being there, they could scarcely contain themselves as Carol and I staggered around overwhelmed by the instant open-hearted acceptance and welcome we felt from everyone we were meeting. We had not anticipated this deep sense of connection!

Shortly after meeting up, we took the boys to the childcare center that had been set up inside the hotel so that parents could choose to attend events and presentations without the need to look after their kids. As we passed through the door, we were met with the electric buzz of a lively crowd of 4- to 12-year-olds lounging on the floor in groups of various sizes, excitedly engrossed with each other and with all manner of games and activities. Most were oblivious to their anxious parents hovering about to be sure their child felt comfortable, welcome and safe before leaving them with the expert caregivers hired by the conference. Our boys were met with "Hi Seth! Hi Leif!" and "Hey, look! Leif and Seth are here!" and "Hey, great to see you – we missed you last year!" from several of the other children already there.

It was like watching two fish being released back into the water: The boys just dove in and instantly were absorbed into the pulsing body of youngsters. These must be their "California friends," I realized. This was a part of their life Carol and I had known nothing about.

Our very first session as adults was an unforgettable family roundtable where all the families met each other. Many had been to previous conferences, but for others like Carol and me it was a first. Each family took its turn to stand before all the others and briefly tell of their cystinosis journey, how they discovered the CRF family and ended up at this conference. We were also introduced to a number of adults with cystinosis who had been learning to manage this disease for their entire lifetime. Hearing the very personal story of each one – unique but all having common threads of heartbreak, courage, resilience, and acceptance – was extremely moving. I had seldom witnessed such humble and candid sharing from the heart as these folks were doing and I noticed tears, including some of our own, all around the room.

This was far more than a support group – it was family! All these people were bonded into one caring, collective group of individuals who could fully feel and understand the unique hardships and joys of dealing with this condition we call cystinosis. And weaving it all together was the subtle but constant love and presence of Nancy and Jeff Stack. Without their vision of possibility and their unwavering belief in achieving it, this entire extended family might never have been born. It was a privilege to have been invited into this experience.

The feeling of family, bound by a special kind of love, continued throughout the rest of the conference. We listened to numerous technical presentations from the powerful and creative team of researchers from all over the world who are seeking better ways to manage this disease and to ultimately find a way to cure it. Each project was unique, but bound like the rest of us by a profound sensitivity to the particular challenges presented by this disease and a deep respect for those who suffer from it. There were many opportunities between sessions, over meals, and even in the pool to personally mingle with the scientists and ask questions and share stories. I have been to many scientific conferences in my life, but never to one like this where the pursuit of science never eclipsed the humanity and delicacy of the subject of their research: the cystinosis children and their families.

Because it is such a rare disorder, families with this disease seldom meet other families struggling with the same fears, anxiety and crises that cystinosis brings. Isolation and feelings of helplessness can debilitate a family's ability to keep love foremost. Through the unwavering vision, courage and incredible generosity of the Stacks and those they have drawn around them, the Cystinosis Research Foundation has attracted and funded world-class researchers into its fold – people whose passion for making a difference with this disease is palpable. Perhaps most important, the foundation continues to be a beacon of hope for cystinosis people around the world, helping them learn from each other how to navigate their lives and keep their love flourishing.

For Carol and me, the honor of attending the 2017 conference introduced us to this remarkable organization and the people that had given my son and his family so much hope and encouragement when the shock and despair of discovering their son had cystinosis nearly overwhelmed them. We came to understand far more deeply why these people – their "California friends" – hold such a special place in their hearts. And, we ourselves gained an expanded understanding and compassion for our son and his family as well as the other families we had met in California.

We are immensely grateful to the Stack family and CRF for all they've done for our loved ones, and for so many others around the world. We came away as more than just cystinosis grandparents; we, too, are a part of this larger family of hope and promise. We will be back to California for more!

FINDING COMFORT THROUGH ACTION

By Annica Schröder, Karolis' mom
STOCKHOLM, SWEDEN

Karolis is like most 9-year-old boys. He goes to school, plays football, struggles with homework, love/hates his 3-year-old little brother and loves to play video games. But when you start to look into his routines you realize that his life is different – he swallows over 70 pills daily, takes eyedrops and gets growth hormone injections every single day.

Five years have passed since he received the diagnosis of cystinosis, and our world changed. At the time, we thought that we never would be able to cope with the diagnosis and now it is our life and it works just fine. Of course we have our ups and downs, but we have found ways to manage.

Karolis is the bravest, coolest boy I know. Most days he takes his meds without complaining even though he really hates them. We have seen him get more and more secure with all the doctors, tests and blood samples – from being deathly scared of needles to taking his growth hormone shots himself and letting the nurse take the blood samples from his arm without numbing creme while he is looking at what they are doing.

He now understands more and more about cystinosis and knows that without research he will never get cured. One day when he was really upset about this, we talked and I came up with the suggestion that we should raise money for research. He lit up and started to think about how. Together we decided to make bracelets with the words, "FIND A CURE."

We are now selling a lot of bracelets to spread information about cystinosis and to raise money. It feels good to know that we are doing what we can to find the cure for Karolis and everyone else with cystinosis.

Karolis loves the feeling of doing what he can to find a cure.


SVERIGE

Our daily cystinosis love story

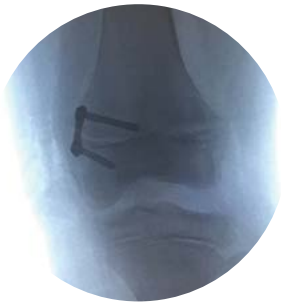
Doug Batt, Teresa's father, with Jenna and Patrick.

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

Dear Supporters:

The Partington Family and the Board of Directors of Jenna & Patrick's Foundation of Hope just celebrated the 2017 Swing & Bling Event in October.

Jenna and Patrick have started seventh grade. Patrick had both of his knees and both of his ankles operated on a week before school started, and he bravely began his junior high experience in a wheelchair. After two weeks of taking it easy he is moving about just fine, and the wheelchair has been retired. We are excited for both kids to continue to grow in height, which will make the guided growth implants in their knees and ankles "activate." Over the course of a couple years, the kids will be watched closely with regular x-rays and follow up visits to Shriners Hospital. Once their knock-knees (a symptom of cystinosis) are straightened, the kids will have another outpatient surgery to have the growth implants removed. To the right is a photo of the implant in one of Patrick's knees.



We have so many to thank for their support and dedication to the cystinosis cause. We would like to give special kudos to Maggie Melarkey, who chose cystinosis and our local charity as her eighth-grade exit project topic. She wrote a wonderful, well-researched paper, and presented what she learned to her teachers and class. There are many ways to create awareness of a rare disease such as cystinosis. We appreciate Maggie's interest and sharing.

Jenna and Patrick will turn 13-years-old this December. Time moves quickly, and there is much to be done to ensure Jenna and Patrick might live long, healthy lives. Thank you for your part in helping us discover treatments for our children and so many others who live with cystinosis and similar diseases.

With Love and Gratitude,

Teresa, Kevin, Patrick and Jenna Partington

JENNA & PATRICK'S FOUNDATION OF HOPE
SWING AND BLING 7
OCTOBER 13 & 14, 2017

We are pleased to share that this year's Swing & Bling event to benefit Jenna & Patrick's Foundation Hope was a great success! We raised over $300,000, which will be passed along to the Cystinosis Research Foundation. Guests enjoyed a fabulous day at Catta Verdara Golf Club for the Swing event. The Bling dinner event was held at a special new location: the beautiful Sacramento Railyards Paintshop. We are grateful to all who showed up and supported this event once again. We have an amazing community.

Love, Teresa and Kevin

FEELING BLESSED IN UTAH

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

So far, 2017 has been a year of big changes for our family. I completed my residency training at the University of Utah in internal medicine, and I got a job as a clinical instructor and hospitalist at the University of Utah. I love my new job and all the time off I get to spend with my family. Our family has always loved exploring the beautiful state of Utah, but this past summer we were able to go to a lot of new places. Our favorites were Calf Creek Falls in the Grand Staircase Escalante National Monument and Kanarraville Falls just north of Zion National Park.

We also bought a new house! Fortunately, it's just a few streets west of where we were living previously, so Sam gets to go to the same elementary school, this year as a third-grader! Lars turned five in July and has started kindergarten. Both of them love being back in school, except for the homework! Ashton loves owning her place; she can finally unleash all her creative energy on fixing it up!

Despite all the changes and business, we knew we wanted to do something to help the Cystinosis Research Foundation in our effort to find a cure for Sam and Lars and everyone else affected by cystinosis. In the past, we've had the most success with silent auctions. Ashton emailed and contacted hundreds of businesses in the area to get auction items, and we ended up with more than 100 items for people to bid on. Ashton posted everything on Instagram on her account, @samshopeforacure. On September 8 and 9, people left bids in the comments. The most popular items were the many restaurant gift cards we had received, as well as gift cards for Altra running shoes. There was also an unexpected bidding war on some hair bows for little girls. One person paid $100 for five bows! Other popular items included personal art donated by our friends Missy Wallace and Zach Proctor. At the time of this writing, we raised over $7,000 from our Instagram auction! We will also be teaming up with our friends, the Waldron and Luke families, to do a 5K and carnival in October.

This year I've also been blessed by the fundraising endeavors of my siblings. My twin sister, Lauren, who lives in Alabama, did a cupcake sale with her children Abby, Claire, Ben and Hannah. They raised over $150 in one morning!

My little sister Maryn was taking a manufacturing class at Brigham Young University, and her assignment was to create an original product with her group, sell it, and donate half the profit to a charity. There was a competition in the class for who could make the most money. Her group designed a triangular shelf, called Trelf, and they dominated the competition. They raised over $450 and donated it to our nonprofit, Sam's Hope for a Cure. Not too shabby for a college project!

When we said we were doing a fall fundraiser, my older sister, Sarah, decided to have a concurrent fundraiser selling cake bites online. She's an attorney, but she could make it as a professional cake bite chef. In one week, she sold 35 dozen cake bites, raising $700 for cystinosis research!

We feel so blessed by the love and support of our family and friends. We are excited about the future and all the amazing research the Cystinosis Research Foundation is funding. We have hope that our boys Sam and Lars will have long and healthy lives!

GABRIELLE STRAUSS

Built for a Purpose

By Jody Strauss, Gabbie's mom
ONTARIO, CANADA

Trust, believe, and all is well.

These words were written on an envelope from our neighbor's nanny with a donation toward the lemonade stand fundraiser for cystinosis that she missed. We were touched by her kindness. I could feel the faith and hope behind her words. I thought to myself, this is how I must continue to live in the face of cystinosis. I must trust, believe, and all will be well.

Gabbie is now 10 years old and in grade 5. With age comes a greater understanding and comprehension of cystinosis. Gone are the days when she wouldn't ask or know the reality of the disease. Now we are educating her on the importance of supplements and medication and how critical it is to take them on time. There have been times when I have found a syringe on the kitchen table 30 minutes after my request because I had to attend to our baby or toddler. This is very frustrating. We are encouraging Gabbie to make her health a priority and it is a process that we are working on daily.

When asked to share a little about herself for school this year, Gabbie wrote the following:

My name is Gabrielle Strauss. I have green eyes. I have three sisters: Chloe, Hannah and Eliana. Eliana cries a lot. I have a disease called cystinosis which I hate.

Reading the last sentence broke my heart and made me feel sad. I laughed about the baby crying a lot. Eliana did cry a lot this year, but we are thankful for her. Babies have a way of making all the other children big helpers. Each of us has had to think of ourselves less and others more and we are all better off as a result. My girls are most joyful when they are loving, giving and serving others.

Gabbie had some great moments this past year. She placed in the top 1/3 of the regional cross country meet and ran a strong race. She won five third-place ribbons at her school track and field meet and then advanced to the regional race for the 200-meter. These victories for any child are worthy of celebration, but for a child fighting cystinosis they are miraculous. Gabbie is also developing a passion for music. She will play the piano when she is happy, sad or angry, which means she plays a lot and is developing her gift. She was one of two students selected from her school to play in a special concert. One of her favorite summer camp songs was, "Made for This."

I was made for this, I live for this,

God has a reason, a reason for my life,

I'm gonna shout it out, without a doubt,

I was born for this, built for a purpose.

He is with me, He is for me, I am not alone.

I love to hear her sing these words and I usually have to hold back tears. I believe with all my heart that God has a purpose for her life and that He will continue to give her the strength that she needs.

Gabbie celebrated great victories this year, but she also encountered great challenges. Gabbie wasn't a child that threw up ever and suddenly she had episodes of sickness. She threw up on the bus to the track and field meet and then again in her teacher's van on the way to a Bible trivia competition. We thought it was because of nerves or excitement, but then she progressed to develop anxiety and a once-confident girl faded away. She had difficulty functioning in school and staying focused. We prayed night and day and became desperate and exhausted. Finally, we took her to Sick Kids Hospital for a full assessment only to be sent home with no answers.

Eventually, we realized that her Cystagon® dose was too high and we were overloading her body almost to toxicity. In an effort to keep cystine levels very low, the dose became too high and as one doctor put it, she went "over the cliff." We dropped the dose and immediately saw an improvement in her behavior, appetite and skin. It was a huge relief and hard to believe that the solution to such erratic behaviour was so simple. Gabbie finished the school year strong and received a good report card.

Looking back I don't think we would have survived the past year without our faith in Jesus. He is the anchor that holds our family through the storms and challenges of life. With cystinosis, you don't always know what the next day will bring. We trust and believe that God has a perfect plan for Gabbie. We believe in Nancy and Jeff Stack. We believe in CRF. We are grateful for Natalie Stack's courageous wish and the sacrifices that she and her family have made. We believe in all the dedicated doctors and researchers and the cystinosis families and communities that support them. We believe in a cure and we trust that CRF will get us there. Until then, it is well with my soul.

"A true friend is the greatest of all blessings."

-Francois de La Rochefoucauld

By Tricia Simms, Hank's mom

SANDPOINT, IDAHO

Our family first met the Flerchinger family at Christmas time in December of 2007, right after our son Henry was diagnosed with cystinosis.

Henry was 17-months-old at the time, and Tina, (Mark and Denice's daughter), was four years and three months. We drove down to Clarkston, Washington, and had dinner with them. Henry and Tina met and played late into the night and again the next day. I remember Henry chasing Tina around the house with her baby stroller, it was so funny.

Mark, Denice, Brian and I talked about what life with cystinosis would be like. We tried to soak up all the information they could give us and learn everything we could from this amazing family we had just met a few hours before. We had an instant bond. Unfortunately, I don't have any pictures of this first meeting, but I have pictures of almost all of our visits that followed.

In January of 2009, we had our first 24 Hours for Hank ski event at Schweitzer Mountain in Sandpoint, Idaho, where we live. It is about a three hour drive from the Flerchingers' house in Clarkston. The Flerchingers made the drive up and attended our fundraiser. Schweitzer thought it would be fun to have the Mountain Fire Truck bring Henry and Tina into the parking lot where all the event participants were waiting to kick off the first ever 24-hour ski challenge. I rode in the front with Henry on my lap and Denice road in the back with Tina in her lap. Tina came up on stage with us and it was so great to share this memory with the Flerchingers.

In the Spring of 2009, we attended the Flerchingers' first fundraiser in Clarkston. It was a great time, getting to meet lots of their huge extended family and friends. Tina's sisters have also been an instrumental part in helping Tina and Henry grow their friendship. They are wonderful big sisters to Tina and Henry! In the summer of 2009, the Flerchingers made their way up to our house in Sandpoint and we enjoyed time on the beach and playing "tools."

In the winter of 2010, the Flerchingers attended our ski event again. This time Tina and I had matching blue coats! I could see in just one year how much Henry and Tina had both grown. That has become the trend each year.

Easter has been one of the holidays we have spent at the Flerchingers' house a few different times. They have always been so gracious in inviting us to be part of their family. We shared Easter with them in 2011 and 2013. Tina is always such a good sport and that's one of the qualities that make her such a good friend. I remember Denice and Mark had an Easter egg hunt and Henry ended up with three times as many eggs as Tina because she was a good sport and let Henry get the eggs when she could have easily have tipped him over and grabbed them first. Henry loved every minute of it: from dying the eggs the day before to the actual hunt and the wonderful brunch afterward. It has always been one of my favorite memories with the Flerchingers.

In 2014, we went to Tina's fundraiser and Henry was so excited to try every dessert that was served and felt so much pride sitting with Tina at one of the tables and wearing her sticker on his shirt. Knowing someone else has a fundraiser helps make him feel like he is not the only one.

Again in 2015, we attended Tina's fundraiser and you could see that Henry might be starting to get a crush on this

beautiful little lady! At that event, Henry also watched the CRF video for the first time, and was very taken-back by the statements in the video and had some questions for me afterward. Questions about cystinosis are never easy to answer as a parent; however, what better place to watch a video on cystinosis than at your friend's cystinosis fundraiser?

The special times these two friends share at each CRF Day of Hope just keep on getting better! The 2017 photo was from this spring's Day of Hope in April 2017 right before we had to leave for the airport to fly home. At this conference, I had mentioned to Denice that I would love to get the kids together this summer, so we made it happen. Henry went down to Tina's house and shared a few days with the Flerchingers. He had a great time, learned lots of new things and had a lot of fun playing games and swimming. Of course, I didn't have to worry about the meds, the med schedule, bed pads, being a picky eater, dehydration, getting tired, or anything else we cystinosis moms worry about because Denice had it covered. She was ready to combat any of the above and I knew Henry would be in good hands.

There is an angel statue in the Flerchingers' yard right next to their front door, it is just as welcoming and helpful as the Flerchinger family. It is one of my favorite statues I have ever seen and has always had a special place in my heart. It is a symbol to me that Tina is an angel to Henry and everyone she meets. She has taught Henry so many things like how to eat chocolate chip cookies with your Subway turkey sandwich, how to try ethnic foods like egg-flower soup at PF Changs, how to tackle more challenging things like swimming, how to have a good sense of humor and most of all: How to be a good friend.

Tina, you are an angel and you help so many people! Thank you from the bottom of my heart for being such a wonderful friend to Henry, and a wonderful person!

Some of my best friends are moms I have met through CRF and have become very close to. Even though I only get to see them in person usually once a year at the Day of Hope, we connect in other ways throughout the year and these friendships are very special to me. I'm sure many of you reading this article have similar stories of families you've met through CRF and there was an instant bond and a lifelong friendship has been made. That is the beauty of our cystinosis community at CRF and one of the silver linings of having to go through life with this disease. I hope this inspires you to continue to reach out and take chances connecting with others. You never know who may become a true friend forever.

A SUCCESSFUL 24 HOURS OF SCHWEITZER TO BE TRANSFORMED IN 2018

By Brian Sturgis, Hank's dad
SANDPOINT, IDAHO

March 24, 2017 was the ninth annual 24 Hours of Schweitzer. This year's theme, "Hunting for a Cure," had 77 participants ranging from eight to 76 years old and included hourly challenges where teams competed for the overall victory. The challenges ranged from paint gun target shooting, ski relay races, slack lining in ski boots, and golfing with skis on. Following the skiing event was an awards dinner and auction in Schweitzer Mountain Resort's Lakeview Lodge. Dinner featured Schweitzer's chefs at their best: preparing beef, duck, venison, buffalo and game hen. Desserts included hazelnut eggrolls with strawberry coulis, chocolate donuts with crème anglaise.

More than 100 live and silent auction items were available including a Slope-Side Condo for one week at Breckenridge, Colorado, and a seven-night stay at Waipouli Beach Resort & Spa on Kauai. The top two fundraising teams raised over $72,000 and when the event was all done over $200,000 was raised for cystinosis research.

We have already started the planning for next year's event that will be held on March 24, 2018. We have huge plans for 2018 as 24 Hours of Schweitzer is retired, and 2,400 Feet of Schweitzer makes its debut!

This new format will allow even more people to get involved, as participants will no longer need to take a day off from school or work to participate. The event will begin before sunrise on Saturday morning, as participants load the chair two hours before the resort opens. The initial run down will be the first unique concept of this new event: a giant slalom course from the Sky House Summit lodge to the Outback base lodge! The route drops 2,400 vertical feet in 2.4 miles and will take even the fastest skier over three minutes to finish. Fundraising efforts will determine the start order with top fundraisers running first on a smooth fresh track. After finishing the grueling run, participants will be treated to an exclusive breakfast at the Outback lodge, the second unique concept. They will then complete several challenges over the course of the day. At the conclusion of the ski day, we will have an awards dinner/auction followed by an after party in the Schweitzer Mountain Resort Lakeview lodge.


Hank's Minions
WHISKEY
JACK
CREW
Hank's Minions
schweitzer


24 Hours for Hank


Schweitzer

IN MEMORY OF

Shannon Paju

SHANNON'S MOM REMEMBERS

I Have Loved You Your Whole Life…I Will Miss You the Rest of Mine

By Bonnie Paju, Shannon's mom
ANAHEIM, CALIFORNIA

Dear Shannon,

I have never known anyone who loved life more than you. You have taught me many things, none the least of which is the love that I hold for you, my wonderful daughter. No one could have fought harder than you did to live.

You were so into helping find a cure for cystinosis that you donated your organs to cystinosis research. You participated in lots of clinical trials over your lifetime. You spoke at conferences, fundraisers and to people you would meet to raise awareness of cystinosis. I am so proud of you.

To know you was to love you. Your beauty both inside and out will never be forgotten. You cared more about others than yourself. You were a true giver.

You inspired so many people, and gave them hope by your example. Doing dialysis six days a week, blood transfusions every two to three weeks, platelets every month or two, endless doctor appointments every week – you showed the patients at the unit what real bravery is. You never complained, they would ask how you do it and you responded with, "I wake up every morning, ready to meet each day and praying for a cure, this is what I do."

I know you had to go, I know you were ready. I have loved you your whole life; I will miss you the rest of mine. I thank you for your strength and courage to fight the fight for as long as you did. You showed such great bravery and resilience. You were always so amazing.

I will never forget your last words to me:

"I love you Mommy; thank you for always being with me and taking care of me. Is this the hospital where my friend Erica died?" (I nodded yes.) "OK."

My darling daughter, I will always love you and miss you,

Mommy

A SISTER'S TRIBUTE TO 'THAT GIRL'

By Jaclyn Ann Suri, Shannon's sister in spirit

I remember as if it were yesterday… a chilly Wednesday night. I remember the sound of the sliding glass door as it "wooshed" open and close. Smokers outside standing too close… fearful if they moved further away they'd miss the doctor who would give them an update on their loved one in surgery.

I sat in my wheelchair wondering if perhaps I stayed home would I start to feel better on my own? After all, I did just get out of the hospital. Maybe I did not give it enough time? Was I truly sick enough? Would I be taking the spot of someone who needed it more? In my mind, I set a timer. "If nothing happened in the next 20 minutes, I'd go home."

Not five minutes later, it happened! It was as if God was giving me a sign. The front door "wooshed" open. A redheaded lady, obviously exhausted from the trials and tribulations of the day, was wheeling in what seemed to be her daughter. Or, as I knew her, "That Girl."

"That Girl" that was there during my last five stays at the hospital. "That Girl" was sitting on her bed, in the room next to me, after my nine-hour surgery. "That Girl" was who I waited behind for an x-ray. "That Girl" was the girl that the nurses said was probably in the hospital more than me. WOW! Who is "That Girl?"

She was beautiful. She looked like a movie star. She wore big dark glasses, and had platinum blonde hair. Her frame was tiny but her raspy voice was so big it demanded attention.

At that moment, I didn't know what ailed her, but it didn't take a genius to know from the look on her mother's face that it wasn't good. You could tell from the look in her mom's eyes that this "blonde bombshell" was her lifeline.

Selfishly, I wheeled myself over to them. "Hi! You don't know me but I feel like I know you. Every time I'm in this hospital I see you. If I'm in the ER… you're in the ER. If I'm staying in the hospital… you are in the room next to me. I know I probably look as crazy as a loon. You don't have to say a word, but I feel it would be remiss if I didn't at the very least introduce myself. My name is Jackie!" As we shook hands she said, "Shannon, my name is Shannon. This is my mom Bonnie."

This was the start of something so big, so awesome, and so special that my words could not possibly give it the justice it deserves. We both had so much to say, to compare, to talk about. As quickly as we could, we were talking about our ills. Talking about what brought us here, the rareness of our illnesses, and how much time we spent in hospitals not really living but coping.

What she said next brought a tear to my eye. "Would you be my big sister? Like a mentor?" Normally, one would think this odd. But, if you were there in the moment, you would know it was oddly natural.

I told her yes, under one condition. Even though we suffer with different but oddly similar diseases, we can never give up! We can lean on each other, but under no circumstances can we give up the fight. She agreed. We exchanged numbers.

Everyday Shannon and I spoke. Every day, good or bad, we learned something new about each other. It didn't take long for me to see that Shannon had a beautiful soul. She had so many hopes and dreams. She never took it for granted and always did what she could to fulfill those dreams.

She was a loving daughter to Bonnie and Hillar. She was a girlfriend to fellow "cystinosis warrior" Freek from the Netherlands. She was a published poet, an actress, a singer, a musician, and of course she was a warrior.

She touched the lives of so many and will continue to do so for many years to come. To me, she was a friend, sister, and a sounding board, and a gift from God.

I will always remember Shannon as "That Girl." However, later I learned I was not the only one who called her this. For so many she became "That Girl." At thirteen months, her battle began. Doctors worked nonstop on her for over nine hours in one day. To the amazement of her doctors, that very next day, "That Girl" not only pulled through, but made it look as though nothing ever happened.

At 15 Shannon traveled, was acting professionally, and learned to play many instruments. She faced her fears head on and underwent transplant surgery. At the time, they believed it to be a total success. "That Girl" did it again!

At 17 the new kidney died. She was strong but feared the world was slowly going to come crashing down around her. All she ever wanted was to be "normal!" Shannon told me more than once… "In God's eyes we are all perfect! After all, He created us," a mantra I now choose to live by. Not everyone can go through all of this and come out on top. "That Girl" did! Shannon is now my hero!

Cystinosis not only takes a physical toll but also takes a mental toll. Shannon was on dialysis four days a week. She took 66 pills a day and 12 shots a week. I remember when the doctors at the hospital wanted to put her on hospice. Shannon, with her mother in tow, would not have it. Shannon worked her magic. Yes, "That Girl" pulled through yet again. As a matter of fact, she lived close to four more years.

Yes, cystinosis is rare but so is Shannon. All the odds said she wouldn't make it to adulthood. "That Girl" did! She made it past 30. Shannon always looked at the glass as half full. She never took her life for granted. She spoke openly about giving the gift of life via organ donation. Shannon always reminded me… "Have faith and believe!" If not for yourself, do it for "That Girl."

SELFLESS LOVE

By Andrew Hofstetter, Shannon's friend

I wish I could put into words what Shannon was to all of us, but that would be impossible. The best I can do is try and tell you who she was to me. She was my person, the one you call when all is good and the one you call when all hell breaks loose.

Even though she was living with cystinosis, she was one of the bravest people I knew. She never seemed afraid. She took each day on with a smile and didn't let her disease navigate her life; she navigated it for herself. With everything she had been through in her life, she never worried about what would happen to her. Instead, she worried about what would happen to us when she was gone. She would always ask what I would do when she left, and worry if Mom and Dad would be all right. Nothing else mattered.

Shannon was there for me even my own worst moments. I will always remember the day I had to call and tell Shannon how I was rushed into emergency surgery the night before. I was living in Idaho at the time, so I had no one with me to help me through a very scary experience. Regardless of her health and her inability to travel, she was ready to fly up to Idaho and be with me. It was the first and only time I can recall Shannon being scared.

She knew she wasn't long for this world, but during her short time with us she made a long-lasting impression. The one thing that will always haunt me is that one day, if I have kids of my own, they will never get to meet their Aunt Shannon. They will know of her and what she did for all of us, but they'll never get to experience her love. I love you Shannon. See you on the other side.

IN MEMORY OF

BRIAN NEILS

By Connie Niewald-Dyson, Brian's mom

ROCKLIN, CALIFORNIA

I named him Brian, meaning "strong." How ironic because that's exactly what he was! Through all of the hospital stays, cancer, failed transplant, 15 years on dialysis and he still stayed positive. He had a great sense of humor. Most people didn't see it too often, but I did. He was meant to be MY SON. We made a great team through all those hospital stays. He cheated death for 37 years and he loved more that anyone I have ever known. I will miss him forever but I was blessed to have him for those years. He was my best friend and I will stay strong to honor him.
He was asked many times, "Aren't you afraid to die?" Brian's answer, "NO! we are all gonna die someday." That was my beautiful boy.

Love you honey, Mom xoxoxo

Connie (Brian's mother) and Brian

Brian, Patrick (Brian's father) and Jason (Brian's brother)

Save the Date

CRF Day of Hope

2018 FAMILY CONFERENCE

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

when

Thursday – Saturday

APRIL 19TH – APRIL 21ST

where

The

ISLAND HOTEL

690 Newport Center Dr,
Newport Beach, CA 92660

CYSTINOSIS COMMUNITY CHAMPIONS

A CUT ABOVE

SALON OWNER SHANNON CLEMENTS STEPS OUTSIDE HER COMFORT ZONE TO STYLE A SPECIAL ARRAY OF SUPPORT FOR PRESTON LUKE AND HIS FAMILY.

By Dennis Arp

Shannon Clements has long been a powerful advocate for her family, her friends and her thriving business, Elements Salon in the Water Street District of downtown Henderson, Nevada. But some things don't come naturally, and one of them is pitching to scores of strangers.

"I was deathly afraid," Clements says of going door to door in the downtown business district, seeking support for cystinosis research. "That sort of thing is definitely not comfortable for me."

It's amazing what you can do and where you can go when inspired by a child. For Clements, that inspiring youngster is Preston Luke, who at two years old was diagnosed with cystinosis, a rare genetic disease that attacks every organ of the body.

"Seeing his beautiful face, thinking of his courage – that he's able to do things I can't – how could I not do things for him and for others with cystinosis?" Clements explains.

Clements worked to help Preston even before she had met him. The Luke family lives in Utah, but Preston's mom, Ciara, grew up in Henderson, and her parents and sister, Tessa Adams, still live there. In fact, Adams works as a stylist at Clements' salon. One day, Tessa and Ciara's dad, Tim Hartman, came into Elements spreading the word about an upcoming golf tournament to support Preston and the Cystinosis Research Foundation (CRF).

"At the time, I didn't know anything about cystinosis," Clements recalls. "We talked about its effects, and then I did a Google search. The more I learned about the disease, well, I would hate for any child to go through what Preston does. These children don't have a chance unless an adult steps up to help."

Clements not only stepped up but stepped out. Beyond walking the downtown district handing out fliers and sharing information about the golf tournament and the effects of cystinosis, Clements started organizing her own fundraisers. She knew that the 16 stylists in her salon and all of their devoted clients would be moved to help pitch in.

"We get about 50 clients coming in each day, and a lot of them know Tessa. When they hear about a child in need, their hearts open a little bit more. If you know someone special, it matters a little bit more," Clements says.

Her first fundraiser was a painting party, which Clements hosted at her home. About

Merideth Hartman, Sherrie Parry, Tessa Adams, and Shannon Clements

Tessa Adams (Ciara's sister), Shannon Clements, Kim Chaffin (paint instructor and family friend), Ciara's mom, Merideth Hartman.

PRESTON LUKE
Herriman, Utah

30 attendees, including Adams and her mom, Merideth, got a lesson from an art instructor, then they turned blank canvases into paintings of sunflowers.

"She taught us step by step, and because none of us are painters, it was fun rather than intimidating," Clements says. "There was food and drink, we told jokes and painted pictures. It was a good time. It was the best time because it was all for an important cause."

The painting party raised close to $1,000, the total ballooning thanks to a Facebook page, Instagram posts, word of mouth promotion and a jar for donations strategically placed at the Elements salon so people who couldn't make it to the party could donate anyway.

It felt good to make a difference, Clements notes, but it certainly felt more like a beginning than a culmination. Almost immediately, she pondered: Now what shall we do next?

Easter was just around the corner, so Clements approached a local florist and asked if she could make unsold flowers available to salon clients for a donation. The blooms brightened the salon, and the idea took off. Then more funds were raised thanks to a Fourth of July gift basket Clements put together and auctioned off, featuring all kinds of picnic items based on a theme of Americana.

"From the start, Shannon has been all about 'whatever it takes' – she has been continuously amazing," Ciara Luke says. "I'm from Henderson, but I don't even live there anymore. For Shannon and her family to respond means so much to all of us."

The Lukes have received nothing but responsive support from the CRF and the cystinosis community since they got their diagnosis a year and a half ago, Ciara notes. The same day she and her husband, Shane, learned that Preston had cystinosis, Ciara found online a TV news story about Ashton and Stephen Jenkins, who also live in Utah and whose sons, Lars and Samuel, have cystinosis. In less than a week, the Jenkinses were visiting the Lukes to answer questions and deliver a gift bag with things like a water bottle for Preston's thirst and protective coverings for his bedding.

Sam Jenkins, then younger than seven, also brought a dry-erase board to help explain his and Lars' cystinosis.

"For him to understand at that age what he has and what it means was amazing," Ciara Luke says. "I felt comforted. It just made me feel like we would be OK, and that we were not in this alone."

The Lukes also heard almost immediately from Nancy Stack and other members of the CRF family.

"Nancy made sure we felt connected," Ciara says. "It was clear that this was more than an organization that funds research. It's made up of people who care."

But even amid a community of caring people, Shannon Clements stands out as a champion for Preston Luke and his family.

"Preston is doing remarkably well – you'd never know that he's sick, even though he takes 18 doses of medication a day," Ciara says. "He's very courageous, and it definitely helps that we have so much support."

For Clements, Preston's courage is at the heart of her commitment to give all that she has to make his life better.

"He inspires me every day to push beyond my comfort zone," Clements says. "I've gained confidence and I've put my own insecurities aside. I've found that there's nothing to be insecure about when you're working for a cause that really matters."

CYSTINOSIS COMMUNITY CHAMPIONS

BUILDING A TRIBUTE OUT OF LOVE

TO HONOR A FRIEND, REDI-ROCK COLLEAGUES AND CUSTOMERS RALLY SUPERSIZED SUPPORT FOR CYSTINOSIS RESEARCH.

By Dennis Arp

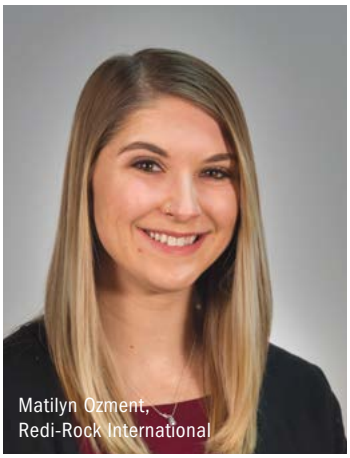
Mike O'Leary was retiring, and everyone at Redi-Rock International in Charlevoix, Michigan, wanted to do something super special for their exceptional friend. The company makes and markets retaining-wall systems, and O'Leary's 15 years of oversized impact had made him a cornerstone of Redi-Rock's success.

As the retirement date approached, there was talk of getting O'Leary a really nice watch, but that seemed way too impersonal for someone so kindhearted and generous.

"When we really thought about how to honor Mike, we knew the most meaningful gift we could give him would be to rally together and raise money for a charity near and dear to him," says Matilyn Ozment, a colleague of O'Leary at Redi-Rock. "Mike deeply loves his family, especially his grandson Aidan, which everyone comes to know once they spend more than five minutes with Mike."

Recently, 1-1/2-year-old Aidan O'Leary was diagnosed with cystinosis.

"Mike has made a huge impact on my life, and I'm certain many of your lives, too," Ozment wrote in a message to the broad community of Redi-Rock employees, customers and manufacturers. "Let's work together to raise money to help


Matilyn Ozment, Redi-Rock International

"We are forever grateful to Matilyn and RediRock for their generous support to help us raise money for Aidan's Army and cystinosis research in honor of my father's retirement. Our family was brought to tears by their thoughtfulness. Thanks to the individual contributions of people like Matilyn, and the tireless efforts of the Cystinosis Research Foundation, we are very hopeful for a bright future."

find a cure for cystinosis to help Aidan and the other children who are affected by this terrible disease."

One call to action was all it took to mobilize Redi-Rock friends and colleagues, who became eager enlistees in "Aidan's Army." Ozment embraced her leadership role in rallying support, but she says her job was a joy because everywhere she looked she found champions of the cause.

"I'm the lucky one who was tasked with sending out messages and keeping track of the money coming in, but it was totally a team effort," Ozment says. "Those who came together to donate – they're the ones who made this special."

The fund drive celebrating O'Leary's retirement launched with the wholehearted support of Redi-Rock and its owners, the Manthei family. In fact, they pledged to match donations supporting Aidan and Cystinosis Research Foundation (CRF) up to $5,000.

As the word went out, support poured in. Inside the Redi-Rock offices in Charlevoix, O'Leary is described as "hardworking, driven, passionate, loving and giving," so a case for support didn't even need to be made. But O'Leary also works directly with retail partners who contract to manufacture and sell Redi-Rock products. Turns out their respect and appreciation for O'Leary is just as strong.

"Mike is kind of the link between the manufacturers and headquarters," Ozment says. "If they have a request for something, Mike will fight for them. We want their businesses to be successful, and no one exemplifies that more than Mike. It's easy to connect to him and respect him."

Piece by piece, the campaign came together with the precision of a Redi-Rock wall system. The first step was to set up a "Donate for Aidan O'Leary" page on the CRF website. Then the effort was promoted on the Redi-Rock site as well, and Ozment crafted emails that went out to manufacturers and others.

In addition, the opportunity for support was announced at Redi-Rock's annual meeting in Charlevoix called The Summit, at which manufacturers are invited to provide feedback, network and learn about new products. There's a closing dinner in the Party Barn, where announcements are made and awards handed out.

During the event, Ozment talked about Aidan and the hurdles he and other cystinosis patients face, as well as the courage they exhibit.

"Some diseases require you to take medications now and then," Ozment says. "This is all the time."

In many ways, the gathering is more like a family party than a company annual meeting.

"We have an organizational value that says 'Make time to care,' because we truly care about each other," Ozment says. "There are no boundaries, especially when someone is in need."

The depth of the concern for Aidan and the appreciation for O'Leary really hit home when one of Redi-Rock's customers donated $10,000.

"That blew us all away," Ozment says. "When they called to tell me the amount, I didn't have any words. I have been so moved by the generosity of our customers."

All told, the "Donate for Aidan O'Leary" campaign raised $24,000 for the CRF and cystinosis research. Mike O'Leary knew about the campaign his retirement had inspired, but he didn't know just how much support it was generating. So during the party, when he was presented with a giant check that revealed the figure, "you could see on his face just how overwhelmed he was," Ozment says. "His wife Denise was there too, and she teared up. It was an incredible moment when we knew we had been able to help, and that Mike was so grateful."

These days, it's a bit different in the Redi-Rock offices without O'Leary around day to day. But he still visits and calls, usually with an update about Aidan.

"He talks about how Aidan loves his dog, or about anything new Aidan is doing," Ozment says. "He's so proud to share stories, as he should be. Aidan is such an adorable kid."

O'Leary also sends links to cystinosis videos and provides news about research.

"His passion in life is to find a cure," Ozment says. "We have so much confidence in that happening as Mike leads the way for us. There's a deep connection now, and we will be ready to help in any way we can."

CYSTINOSIS RESEARCH FOUNDATION ★ NATALIE'S WISH

TENTH ANNUAL - NATALIE'S WISH

Fore a Cure

GOLF TOURNAMENT

CYSTINOSIS RESEARCH FOUNDATION

WE ARE GRATEFUL FOR YOUR PARTNERSHIP AND YOUR GENEROSITY, BECAUSE OF YOU WE RAISED MORE THAN $445,000 FOR CYSTINOSIS RESEARCH. ON BEHALF OF THE CYSTINOSIS COMMUNITY...

Thank You

MONDAY, OCTOBER 16, 2017 | PELICAN HILL GOLF CLUB | NEWPORT BEACH

MASTERS/PRESENTING SPONSOR

Oltmans Construction Co.

HOLE-IN-ONE SPONSOR

Sares Regis Group

FORECADDIE SPONSORSHIP

Lincoln Property Company
a company for people, a company about people.

COCKTAIL RECEPTION SPONSOR

CBRE
Bret Quinlan & John Schumacher

EAGLE SPONSORS

Contract | EAGLE | Horizon Pharma | JLL | Silverline Construction Inc.

BIRDIE SPONSORS

Allen Matkins | Bank of America Merrill Lynch | Bank of the West | BNP Paribas Group | Ben's Asphalt Inc. | berkeley point

CBRE
Brad Bierbaum, Brian DeRevere & Ryan Peterson

Commercial Roof Management Incorporated | Fashion Furniture Rental | First American Title™ National Commercial Services | General Underground Fire Protection, Inc.

GB&A | Gorman Roofing Services, Inc. | Howard Roofing Company, Inc. | J.P.Morgan Asset Management | J-Squared | Lee & Associates® Commercial Real Estate Services

Millie and Severson General Contractors | Miner Your Facility Expert | Moran & Company | Dave & Bianca Mossman | NWS Norm Wilson & Sons Inc. General Contractors

RGA Office of Architectural Design | SCM SullivanCurtisMonroe Insurance Services, LLC | S&W Painting & Waterproofing, Caulking & Waterproofing, Floor Coatings www.swpainting.com | TCA Architects | Ticor Title | villa park landscape

AWARD PRIZES

GuardTop

BAG TAGS

berkeley point

BEVERAGE CART SPONSOR

ALABOUT FIRE INC

CIGARS

MSF Manly Stewart Finaldi Lawyers

CLOSEST TO PIN

berkeley point

GOLF CARTS SIGNAGE

Colliers International
Steve Bellitti & Tom Taylor

GOLF BALLS

PARTNER Engineering and Science, Inc.
www.PARTNEResi.com

GOLF CLUBS

MAC Mechanical Air Control, Inc.
Mechanical Contractors

HATS

CommerceWest Bank
Bank on The Difference

LONGEST DRIVE

BRISTOL GROUP

PIN FLAGS

J-Squared

PUTTING CONTEST

BRISTOL GROUP

RAFFLE PRIZES

CBRE
Val Achtemeier, Barbara Emmons & Darla Longo

COURSE SIGNAGE

THEDOT
THEDOTCORP.COM

CYSTINOSIS RESEARCH FOUNDATION 18802 Bardeen Avenue ★ Irvine, CA 92612-1521 ★ 949.223.7610 ★ cystinosisresearch.org

The Cystinosis Research Foundation is a non-profit entity pursuant to Section 501(c)3 of the Federal Tax Code. Tax I.D. number 320067668

TOGETHER, WE ARE one

1 PURPOSE. 1 JOURNEY. 1 CURE.

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

TOGETHER, WE ARE one

Franklin, Tennessee

KLOETE FAMILY RAISES FUNDS WITH CRAWFISH BOIL

Rick and Jenni Kloete hosted their neighborhood Crawfish Boil gathering at their home in Franklin, Tennessee. Live crawfish, flown in from Louisiana, were prepared along with jambalaya and truffle fries. Musicians performed during the festivities and neighbors brought side dishes and desserts for all to enjoy. The event raised more than $1,100 in honor of their daughter, Katie Roy, 25. Thank you Kloete Family!

Brookfield, Missouri

TSCHANNEN FAMILY OVERWHELMED WITH SUPPORT AT GOLF TOURNAMENT

William Tschannen, his parents Barb and Terry, along with William's close friends, organized a golf tournament on May 13 in memory of his twin brother, Weston, who passed away August 28, 2016. A full roster of golfers enjoyed the perfect weather and a day of golf with friends. The exciting live auction raised $5,000 and at the end of the evening a total of $19,000 was raised in memory of Weston. The Tschannen family was overwhelmed with the support and love of those in attendance. On behalf of the cystinosis community thank you Tschannen family!

1 PURPOSE. 1 JOURNEY. 1 CURE.

Chaska, Minnesota

CURL FOR A CURE RAISES $70,000

Melissa and Jim Long hosted Lola's Curl for a Cure on March 4, in honor of their daughter Lola. The community of Chaska, Minnesota, enthusiastically supported the event with 96 curlers participating in two separate curling sessions. Special thanks to the businesses that sponsored the ice for curling: Bridal Accents Couture, Sprung, and Simon Construction. More than 250 people enjoyed dinner, music, and a special silent auction. Lola's sister, Ava, shared a video she created that provided a glimpse of what Lola's life is like living with cystinosis. At the end of an extraordinary day and exciting evening, everyone showed their commitment to Lola by raising more than $70,000 for cystinosis research! Thank you Long family for your commitment and support!

TOGETHER, WE ARE one

Green Bay, Wisconsin

KENZIE'S DRIVING FOR A CURE HITS THE MAJORS

Katie and Shawn Lawatsch hosted their first annual Kenzie's Driving Fore a Cure Golf Tournament in honor of their daughter Kenzie, on August 20. The golf tournament scored a double eagle for all those that participated. The camaraderie and fun was evident at every turn and the weather was perfect. Guests joined the golfers at the end of the round to enjoy food, beverages and to participate in the auction and raffle.

We are grateful to the Lawatsch family and to everyone who attended, and would like to extend a special thank you to their sponsors and raffle donors for helping to raise more than $10,500 for cystinosis research! Kenzie even had her debut on the local news station (ABC2): Clearly, a star in the making.

Chippewa Lake, Ohio

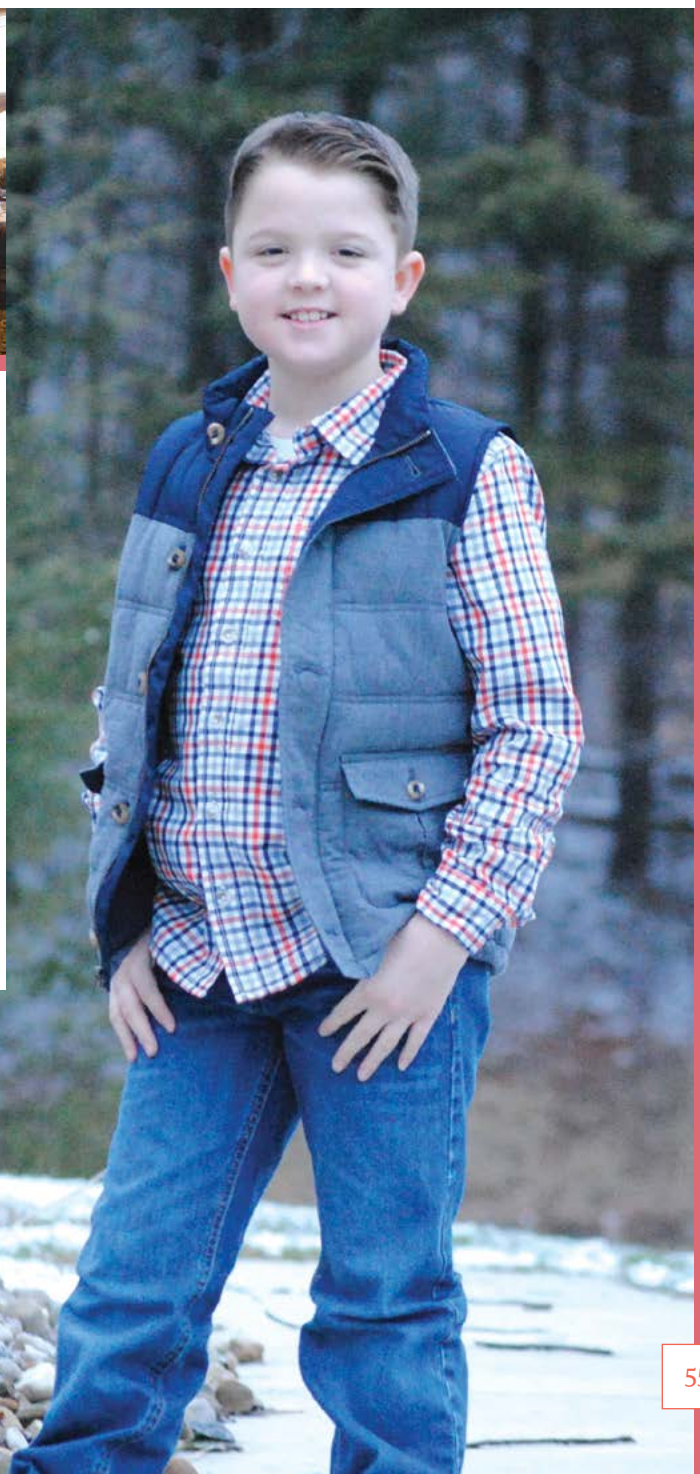
THE POWER OF FRIENDS HELPING FRIENDS

Ten-year-old Abigail Chirdon hosted her fourth annual Charity Yard Sale and Lemonade Stand July 27-30. Abigail, a kind-hearted and thoughtful friend of Jake Krahe, hosts the Yard Sale and Lemonade Stand each year and donates the proceeds to an organization of her choice. This summer, family, friends and neighbors in the community enjoyed doughnuts, lemonade and shopping to support Abigail's campaign and help raise an incredible $1,050 for the Cystinosis Research Foundation.

"We had tons of donations from our family, friends and neighbors," Abigail said. "My friends and family helped, and I am glad I could help raise money to help my friend, Jake."

1 PURPOSE. 1 JOURNEY. 1 CURE.

hopes & wishes foundation



Medina, Ohio

KRAHE FAMILY'S HOPES & WISHES EVENT DRAWS 300

On May 20, Amy and Jeremy Krahe, and their family and friends gathered to celebrate A Night of Hopes & Wishes, in honor of their son Jake. Over 300 guests enjoyed dinner and music while bidding on exciting silent and live auction items. Together, the community raised over $118,000 for cystinosis research! Thank you to the Krahe Family for your dedication to CRF and the cystinosis community!

TOGETHER, WE ARE one

Etna, California

LEMONADE BY LILLYANNA

By Shelly Suetta

Lillyanna Grace has one of the biggest hearts I have ever seen, she always wants to help everyone. Earlier this year, she hosted her first-ever lemonade stand at home in our front yard, and she had several visitors and made a few dollars. She was so happy and wanted to do a stand every day!

Lillyanna also decided that all the money she raised would be donated to help fund research into her sister Emma's disease. After some discussion, we decided it would be best to do one big stand on our local annual Valley-wide Yard Sale weekend. We planned poorly and ended up having all of our doctors' appointments the Thursday and Friday before our Saturday yard sale day. All of our specialists are a long seven-hour drive away from home. That didn't slow Lillyanna. She came right home from our medical appointments and started squeezing lemons and baking. With the help of our Facebook friends and family, we were able to get some other baked goods donations that morning, too! We posted in as many places as we could think of to announce our plan, and it paid off. We had people come from 40 miles away just to visit Lillyanna's lemonade stand! Her total raised funds from our very small town equaled $600! We are so proud of her and the money she raised for the Cystinosis Research Foundation in Emma's name. She plans to make Lemonade by Lillyanna an annual event!

St. Catharines, Ontario, Canada

SHOOT FOR ABBI ON TARGET FOR CRF

The Second Annual Shoot for Abbi was a great success, raising $8,344.80 for the Cystinosis Research Foundation (donated through Canada Helps/Abbi's Road). It was a beautiful day with the sun shining, burgers and hot dogs grilling, kids laughing, playing and people coming together to support Abbi Monaghan and her fight against cystinosis.

Shoot for Abbi is a unique event with the main goal to raise awareness and funds for cystinosis research; but it also gives people the opportunity to try something they might never try. At Shoot for Abbi, attendees are given the opportunity to learn how to shoot a target with a great emphasis on safety.

There was a huge selection of donated prizes and many excited kids gathered around the head table eagerly waiting for their raffle numbers to be called. A big thank you goes out to John Rakich and family (Destination Church), volunteers, and Abbi's Nana and Bubba (Danielle and Terry) for organizing this event.

We can't wait for next year as this event continues to grow. The Third Annual Shoot for Abbi will take place July 7, 2018.

1 PURPOSE. 1 JOURNEY. 1 CURE.

Québec City, Québec, Canada

PEOPLE GET MOVING FOR CRF

By Valérie Talbot

ZUMBA FOR EVA

On June 3, I organized my first fundraising event. It was a mini Zumba-thon, held in a school on our street. Some of my colleagues went to dance and support me, and my family helped me in selling some maple-sugar fudge and passing out cups of DAVIDsTEA iced tea. A massage therapist was on site too, and donated her tips to the Cystinosis Research Foundation. Eva and her sister Eliane's daycare instructors came with some friends, so we were a small but energetic group! This two-hour event raised $625 in Canadian dollars for CRF.

QUÉBEC CITY FUN RUN

The Council of Engineering and Scientific Society Executives (CESSE) puts on a Fun Run to help a local cause at each of its annual conferences. This year's conference, ACCESSE17, took place in Québec City. I'm working at the Québec City Convention Centre and thanks to my fabulous colleague Marie-Elaine, this year CESSE, in collaboration with Travel Portland and the Oregon Convention Center, chose us. They chose CRF for the Québec City Fun Run!

So, on July 26, we were around 25 people running at 6 a.m. in the historic neighborhood of Old Québec for Eva and for every cystinosis patient. I didn't want to wake Eva at 4:30 a.m. so I went alone. Some people chose to "sleep in" so their money went directly into donations, without sweating! They also sold some beautiful hand-made sunglasses to raise money. I'm proud to say that the Fun Run raised $1,600 USD for CRF.

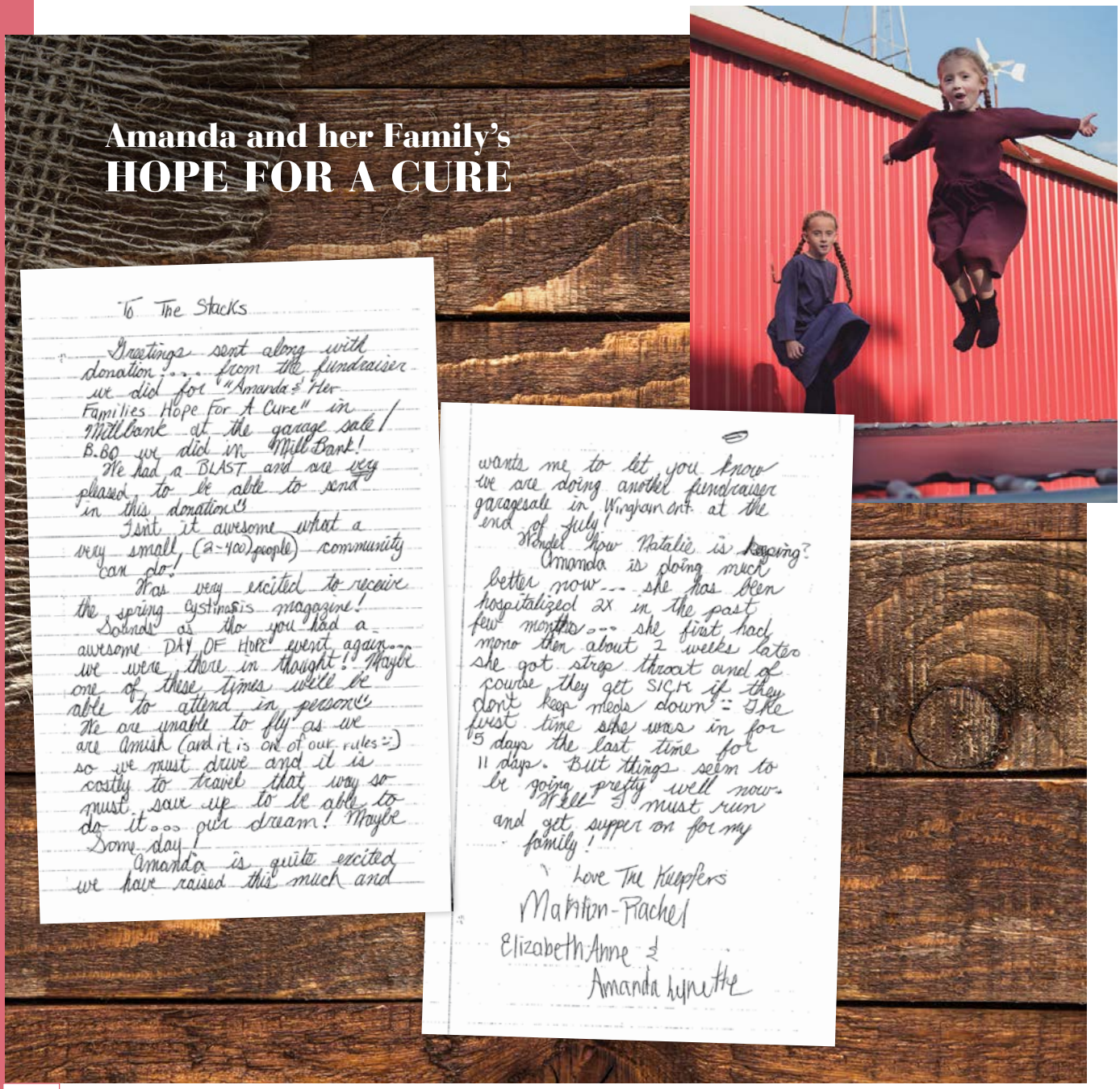
Cara Tobias from Travel Portland, Valérie Talbot (Eva's mom), and Julie DeWeese from Oregon Convention Center.

TOGETHER, WE ARE one

Ontario, Canada

SMALL, BUT COMMITTED GROUP YIELDS BIG RESULTS

The Kuepfer family of Ontario, Canada, hosted its annual barbecue and garage sale this spring in honor of their daughter Amanda. Their community of family and friends celebrated Amanda's Hope for a Cure by raising more than $4,230 to support cystinosis research. It is amazing what a small group of committed individuals can accomplish! On behalf of CRF and the cystinosis community, thank you!



1 PURPOSE. 1 JOURNEY. 1 CURE.

Garden Grove, California

GIRL SCOUTS DEMONSTRATE THAT CHARITY IS COOL

A photo from a TV spot on "Wear Your Sunglasses" day. Shown here, from left to right, are Joshua Clarke, Dominique Marchaund, Julia Clarke, Mia Bruckler, and Principal Janice Callender.

Every month, Julia Clarke and her Girl Scout Troop 2495 select a cause and a charity to support. In May, Julia made a presentation on CRF's mission to fund research for cystinosis, the rare disease that affects her brother, Joshua. As service project leaders Julia, Mia Bruckler, and Dominque Marchaund organized a "Wear Your Sunglasses" to school day in honor of Joshua.

The girls received approval for the sunglasses day from the principal, Mrs. Janice Callender of St. Bonaventure Catholic School, Huntington Beach.

Each student donated at least $1 to CRF and wore sunglasses to support the cause, raising $233. Thank you Troop 2495 for supporting Joshua Clarke!

girl scouts of orange county

Harriman, Utah

PRESTON TOURNAMENT A 'HOLE-IN-ONE'

Ciara and Shane Luke along with Ciara's parents Merideth and Tim Hartman, their extended family and very close friends, helped organize the first Pars Fore Preston Golf Tournament on May 19. With the support of their community and friends the golf outing was a "hole-in-one," raising $11,000 for cystinosis research! The players enjoyed a special day of golf, and following the round, showed their support for Preston by participating in the silent auction and fundraising activities to help fund research and to bring us even closer to the cure. Thank you Luke Family!

PARS FORE Preston

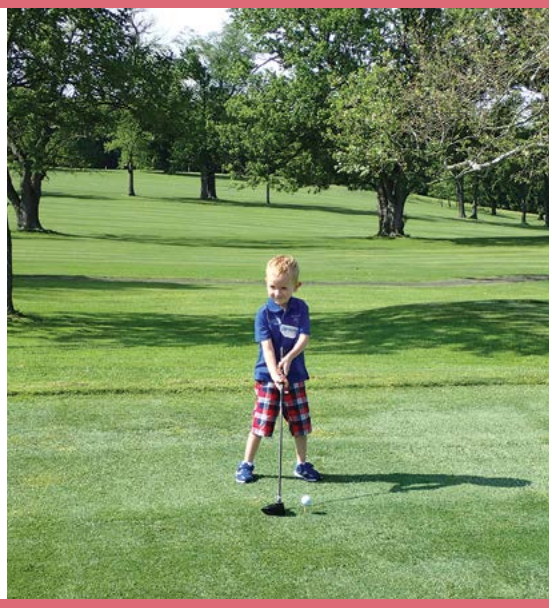
TOGETHER, WE ARE one

1 PURPOSE.
1 JOURNEY.
1 CURE.

Pittsburgh, Pennsylvania

HARTZ FAMILY SCORES WITH ANNUAL GOLF EVENTS

Lauren and Jimmy Hartz, along with their family and friends, organized the Sixth Annual Lots of Love for Landon Golf Outing held in honor of their son Landon on June 2 in Beaver Falls, Pennsylvania. The kindness and generosity of their friends and the community helped raise more than $23,000, which brings their golf event cumulative total to over $100,000 for cystinosis research. We are grateful to Landon's supporters, and to the Hartz family, for their commitment to help find the cure!



Ruth Ann achieved her goal and $3,000 was raised for cystinosis research!

Pewaukee, Wisconsin

CLIMBING MOUNT RAINIER FOR CRF

My beautiful daughter Katie was born with the rare genetic disease cystinosis, a genetic metabolic disease that causes an amino acid, cystine, to accumulate in various organs of the body. Cystine crystals accumulate in the kidneys, eyes, liver, muscles, pancreas, brain, and white blood cells. Without specific treatment, children with cystinosis develop end stage kidney failure at approximately age nine.

Because of cystinosis, Katie has had to overcome many health issues related to the disease. These include ulcerative colitis as a youngster and kidney failure and a kidney transplant at the age of 17. She and her dad were a perfect match. Despite the health difficulties, Katie has thrived and graduated from college. She works as a phlebotomist at a regional hospital. Her health had been very stable until earlier this year when she was diagnosed with lymphoma and skin cancer: one of the possible side effects from her anti-rejection meds she takes for her transplant. Katie is just 26-years-old. I am in awe at how Katie has handled her health challenges. It has been very hard to see her go through chemo, the side effects and handling the overwhelming diagnoses the way she has. We have cried many tears together. Katie is a fighter and I want to do something for her and others who live with cystinosis every single day. All of Katie's health issues have stemmed from her cystinosis diagnosis. I am climbing Mt. Rainier to raise money for the Cystinosis Research Foundation, which donates 100 percent of money raised to research for a cure. They are getting closer and have been able to advance research in many other diseases as well.

Today, we are thankful for the miracle of remission from her lymphoma. Her fight is not over as she is still affected by the side effects of treatment. We want this disease cured! It takes money and our community is small. This climb is dedicated to Katie and all of the children and families affected by cystinosis. I would also like to dedicate it to Nancy and Jeff Stack who started CRF to find a cure for their daughter, Natalie, and who donate their time and resources to all of us. Thank you. Together we can all make a difference!

Thank you,
Ruth Ann Ahnen (Katie's Mom)

It Takes A Village

ACTIVITIES CALENDAR

We would like to acknowledge all families for their support of cystinosis research. Some events may have happened by the time this issue has gone to press.

Sunday, February 11, 2018

MORTGAGE COLLABORATIVE CONFERENCE SAN DIEGO
MULLIGANS FOR MORGAN TOURNAMENT
For information contact Jennifer Peachman - jennifer.peachman@gmail.com

Saturday, February 24, 2018

MUSIC FOR MARY, IN HONOR OF MARY HEAD
Centralia Square Grand Ballroom and Hotel
Centralia, Washington
For information contact Melissa Head - mhead997@gmail.com

Thursday-Friday, March 1-2, 2018

CYSTINOSIS RESEARCH FOUNDATION
SIXTH INTERNATIONAL RESEARCH SYMPOSIUM
Beckman Center, Irvine, California

Saturday, March 24, 2018

2400 FEET OF SCHWEITZER IN HONOR OF HENRY STURGIS
For information contact Brian Sturgis - bsturgis@simulstat.com

Spring 2018

2nd ANNUAL CURL FOR A CURE TOURNAMENT IN HONOR OF LOLA LONG
Chaska, Minnesota
For information contact Melissa Long - melismahan@yahoo.com

Thursday-Saturday, April 19-21, 2018

CYSTINOSIS RESEARCH FOUNDATION
DAY OF HOPE FAMILY CONFERENCE & NATALIE'S WISH GALA
Island Hotel, Newport Beach, California

Sunday, August 12, 2018

KENZIE'S DRIVING FOR A CURE IN HONOR OF KENZIE LAWATSCH
The Woods Golf Club, Green Bay, Wisconsin
For information contact Shawn Lawatsch - 715-587-4317

Sunday, September 16, 2018

4th ANNUAL MULLIGANS FORE MORGAN,
IN HONOR OF MORGAN PEACHMAN
Bob-O-Link Golf Course, Avon, Ohio | The Woods Golf Club, Green Bay, Wisconsin
For information contact Jennifer Peachman - jennifer.peachman@gmail.com

Clinical trial readiness for distal myopathy in nephropathic cystinosis

Florian Eichler, MD, *Principal Investigator*
Reza Seyedsadjadi, MD, *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:

We are conducting retrospective and prospective studies to define sequence and timing of dysphagia symptoms and assess for modifiers of progression. Currently in Year 1 of the study, we are gathering data from patient examinations and patient reported outcome surveys. In addition to our disease specific distal myopathy function scale (DMFS), we are collecting 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. In Year 2, we will be bringing patients back for a repeat examination and an expiratory muscle strength training regimen. 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 span of these prospective studies we may not gain knowledge on prolonged 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*
Ken 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 the 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.

Impact of leptin signaling on skeletal integrity and growth in infantile nephropathic cystinosis

Rober Mak, MD, PhD, *Principal Investigator*
UNIVERSITY OF CALIFORNIA, SAN DIEGO

OBJECTIVE/RATIONALE:

Patients with infantile nephropathic cystinosis (INC) exhibit severe skeletal lesions. Leptin signaling is an important regulator of skeletal integrity as leptin regulates bone mass via signaling through a melanocortin receptor. Hyperleptinemia and bone disease is evident in cystinosis mice (INC mouse model). We hypothesize that aberrant leptin signaling, through a melanocortin receptor, may contribute to progressive bone abnormality in cystinosis mice. Our proposal, if proven, may lead to novel therapeutic approaches to ameliorate the bone abnormalities in patients with INS.

PROJECT DESCRIPTION:

We will use the mouse model of INC, Ctns-/- mice, in our study. We propose to perform the following three specific aims. 1) We will characterize the bone phenotype in the Ctns-/- cystinosis mice life cycle. Bone defects were evident in 12-month-old Ctns-/- cystinosis mice. Hence, we will characterize the onset and time course of bone defects in cystinosis mice at 1 month, 4 months, 9 months and 12 months of age. 2) Leptin signals through a hypothalamic melanocortin receptor and regulates bone metabolism. Blockade of melanocortin receptor signaling improves bone phenotype in mice with chronic kidney disease. Thus, we will investigate the impact of blockade of melanocortin receptor signaling on bone phenotype in the Ctns-/- cystinosis mice lifecycle via genetic deletion of melanocortin receptor in Ctns-/- cystinosis mice. 3) Blockade of leptin signaling could ameliorate bone disease. We will investigate the impact of the blockade of leptin signaling on bone phenotype in the Ctns-/- mice via pharmacological inhibition of leptin receptor signaling.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Detailed information on the skeletal abnormalities in patients with INC is lacking. Our preliminary results suggest that cystinosis mice have elevated leptin levels and bone disease. Leptin signaling may have direct effects on skeletal integrity in cystinosis mice. We test whether blockade of leptin signaling via both pharmacological and genetic approaches could ameliorate bone abnormality in cystinosis mice. Findings of this proposal may lead to novel therapeutic approaches for bone abnormalities in patients with INS.

ANTICIPATED OUTCOME:

Using both genetic and pharmacological approaches, we intend to block leptin signaling in the mouse model of INC. We expect to observe a significant improvement in bone phenotype in cystinosis mice. Results of this proposal may pave the way for novel therapy for INC-associated bone abnormalities for which there are no effective treatments.

Newborn screening for cystinosis

Sihoun Hahn, MD, PhD, *Principal Investigator*
SEATTLE CHILDREN'S RESEARCH INSTITUTE

OBJECTIVE/RATIONALE:

Newborn screening (NBS) has proven to be highly effective at reducing healthcare costs, improving outcomes, and avoiding long-term disability in affected children. It is unfortunate that there are currently no cost-effective population screening methods available for early detection of cystinosis while it can be effectively treated with an excellent outcome if diagnosed early. This project is intended to develop a high-throughput and multiplexed assay using tandem mass spectrometry to quickly screen cystinosis using dried blood spots for potential application of NBS.

PROJECT DESCRIPTION:

We have explored an immuno-SRM assay based on one target peptide from each CTNS and SHPK. We will enhance the sensitivity of the assay by adding additional peptides of CTNS and SHPK. The SRM-MS assay by coupling with peptide immunoaffinity enrichment (immuno-SRM) for CTNS and SHPK will be tested for the ability to correctly identify the patients with cystinosis. Most mutations causing cystinosis in CTNS gene result in absent or reduced CTNS protein; thus CTNS protein itself has an enormous potential as a biomarker for the screening of cystinosis. In addition, SHPK is an additional valuable marker for patients with homozygous 57-kb deletion. We will assess the ability of a multiplexed immuno-SRM assay to correctly identify patients with cystinosis in a large set of clinical samples and proven carriers from a broad spectrum of mutations.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

Our proposal to develop an immuno-SRM assay to identify and quantify a panel of signature peptides for CTNS and SHPK in DBS would create an innovative tool to screen cystinosis in newborns. Early detection of cystinosis soon after birth, before developing any serious complications, would offer the best chance for successful and effective treatment. The translation into nationwide newborn screening will drastically change the clinical course of cystinosis and help develop more therapeutic options in the future.

ANTICIPATED OUTCOME:

The established quantitative immuno-SRM-MS assay will analyze CTNS and SHPK as potential marker proteins for cystinosis screening for the first time in a large set of patient samples from a broad spectrum of mutations. Such results will provide a testing methodology that is viable both for NBS and for rapid diagnosis for older individuals. In addition, it may be applicable to many other congenital disorders providing the opportunities for early intervention thereby increasing survival and decreasing morbidity.

Mechanism of bone marrow stem cell-mediated therapy in the mouse model of cystinosis

Stéphanie Cherqui, PhD, *Principal Investigator*
UNIVERSITY OF CALIFORNIA, SAN DIEGO

OBJECTIVE/RATIONALE:

The extent of efficacy of hematopoietic stem cells (HSCs) to rescue cystinosis was surprising especially considering that cystinosin is a transmembrane lysosomal protein expressed in every tissue. The objective of this project is to investigate the mechanism by which HSC transplantation can lead to long-term tissue repair in cystinosis.

PROJECT DESCRIPTION:

We showed that HSCs differentiate into macrophages that generate long tubular protusion called tunneling nanotubes (TNTs) that mediate the transfer of "healthy" lysosomes to the adjacent disease cells. We showed that these TNTs could cross the membrane of the proximal tubules to deliver functional lysosomes in vivo as to explain the long-term rescue of the kidney in the mouse model of cystinosis.

We made advances in the determination of the phenotype of the macrophages responsible for tissue preservation in this context and showed that they belong to the M1-sub population. The maintenance of homeostasis and immune function, macrophages have emerged as important therapeutic targets in many human diseases. Using advance high-throughput sequencing technology, we will study the expression profile and regulation of the key genes expressed in the macrophages capable of generating TNTs and involved in the tissue preservation. We also propose to identify key proteins involved in the formation of these TNTs. We are also investigating a key protein involved in the formation of the TNTs and showed so far that this protein interacts with the cell cytoskeleton.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

This work will allow the understanding of the mechanism by which HSC transplantation rescues cystinosis. This knowledge will be important for the future stem cell gene therapy clinical trial for cystinosis.

ANTICIPATED OUTCOME:

This work also already opened new perspectives in regenerative medicine that spurred the development of novel stem cell-based therapy for other disorders.

ELX-02 therapy for cystinosis caused by CTNS nonsense mutations

Paul Goodyer, MD, *Principal Investigator*
MONTREAL CHILDREN'S HOSPITAL
RESEARCH INSTITUTE, CANADA

OBJECTIVE/RATIONALE:

Cystinosis is caused by mutations in the CTNS gene. In about 10-20% of cystinosis patients, a subtle change in the DNA code (a Nonsense Mutation) tricks the cell into stopping production of CTNS protein before it is complete. Eloxx Pharmaceuticals has produced a new non-toxic version (ELX-02) of a well-known antibiotic (gentamicin) that overcomes this type of mutation. Here, we will test whether ELX-02 can overcome CTNS nonsense mutations in cystinotic mice.

PROJECT DESCRIPTION:

If ELX-02 can overcome CTNS nonsense mutations, it should repair the cystine channel in lysosomes but should also rescue other functions of CTNS proteins in the cell. We will test this idea in cultured cells with an engineered CTNS nonsense mutation. We will then study our novel CTNS nonsense mutant mouse to ascertain whether ELX-02 lowers kidney cystine levels and prevents deterioration of kidney function.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

The experiments above will provide crucial evidence to convince health regulatory authorities that a clinical trial of ELX-02 is warranted in cystinosis. Eloxx Pharmaceuticals is currently working toward a Phase IIA trial based in Montreal.

ANTICIPATED OUTCOME:

Based on preliminary studies, we anticipate that ELX-02 overcomes CTNS nonsense mutations sufficiently to bring tissue cystine levels into the therapeutic range (<20% of untreated baseline) achieved by cysteamine. We also expect that ELX-02 will restore other CTNS functions in the cell, suggesting that it may be curative.

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 in cystinosis through increased activity of the protein named Rab11, a regulator of vesicular trafficking.

PROJECT DESCRIPTION:

Correct cellular function requires the appropriate distribution of cellular components. One important trafficking regulator is the protein named Rab11, which regulates receptor expression in proximal tubule cells. We have presented data that Rab11 regulates the trafficking of LAMP2A to the lysosome. This function is important to maintain cellular homeostasis and survival. We have also shown downregulation (low expression) of RAB11 in cystinotic cells. We will test the hypothesis that the rescue of Rab11 function and CMA activity improves the function of cystinotic proximal tubule cells. We will test the hypothesis that the rescue of Rab11-associated defects improves the trafficking of megalin, an important receptor necessary for proper function of proximal tubule cells. We will extend our studies to determine the role of Rab11 as well as another protein, Munc13-4, on the regulation of LAMP2A distribution and trafficking using *Ctns-/-* cells reconstituted with either wild type CTNS or with mutants associated with the development of cystinosis in humans.

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 Rab11 a previously unrevealed regulator that is defective in cystinosis. Elucidating mechanisms to restore Rab11 function will help develop new therapies for cystinosis that will be beneficial for both children and young adults.

ANTICIPATED OUTCOME:

We expect to discover a role for the protein named Rab11 in the regulation of the trafficking and function of Megalin in cystinosis. We also expect that Munc13-4 upregulation will improve cellular function in cystinosis by increasing LAMP2A trafficking, correcting LAMP2A localization and improving autophagy. The completion of this proposal will elucidate the roles of Rab11 and Munc13-4 in the regulation of important cellular processes and will likely lead to new paths to correct cellular defects in cystinosis.

Autophagic lysosomal reformation and lipid signaling in cystinosis

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

OBJECTIVE/RATIONALE:

Cystinosis is a lysosomal storage disorder caused by inactivating mutations in the CTNS gene that encodes the lysosomal cystine transporter cystinosin (CTNS). The CTNS loss-of-function leads to storage of cystine, affecting the lysosome-autophagy functions and causing dedifferentiation of the proximal tubule (PT) cells. Functional lysosomes can be generated from existing autolysosomes: This evolutionary conserved process (termed autophagic lysosome reformation, ALR) is regulated by the membrane lipids called phosphoinositides (PIs). The functional interactions between cystinosin function, ALR and PIs signaling in PT cells remain incompletely characterized.

PROJECT DESCRIPTION:

Based on recent insights supporting a key role of distinct PIs to ensure endolysosome identity, we will explore (i) *whether alterations in PIs homeostasis impact lysosomal dynamics and functions*, with ensuing defects in autophagy and mitochondrial function that could, in turn, break the reabsorptive capacity of PT cells and phenocopy the epithelial dysfunction associated with cystinosis. Because the lysosomal network plays an essential role in maintaining PT transport functions, we will investigate (ii) *whether the loss of cystinosin compromises PIs homeostasis*, perturbing autophagic lysosomal reformation and, ultimately, the lysosome-based cellular degradative capacity in PT cells. Finally, we will evaluate (iii) *whether targeting distinct PIs to lysosomes restores the lysosome function and autophagy flux*, rescuing the transport capacity in cystinosis PT cells.

RELEVANCE TO THE UNDERSTANDING AND/OR TREATMENT OF CYSTINOSIS:

These studies should evaluate whether rebalancing PIs homeostasis may improve the lysosome-autophagy deficits and transport defects in cystinosis cells. In turn, these insights should define new therapeutic strategies that could reverse clinically relevant outcomes of nephropathic cystinosis.

ANTICIPATED OUTCOME:

These translational investigations will allow us to gain critical insights in the mechanisms sustaining PT dysfunction in the early stage of cystinosis, and may point to cellular pathways that could be targeted (or monitored) before any structural, irreversible damage of the kidney. The mechanisms identified in cystinosis may also be relevant for other forms of tubular disorders, helping us to better understand the link between proximal tubule dysfunction and renal disease progression.

cystaran™
(cysteamine ophthalmic solution) 0.44%

Order, Store, & Use

1. ***To order**, please call:*
Walgreens Specialty Pharmacy
1-877-534-9627
Mon–Fri, 8AM–8PM EST

2. 
Ships directly to your home

3. 
Store unopened bottles in the freezer

4. 

Every 7 days remove 1 bottle from freezer and thaw for 24 hours before use*

***ONCE THAWED, NO REFRIGERATION IS NECESSARY AND DO NOT REFREEZE**

5. 
Discard bottle after 7 days

Leadiant Biosciences

*You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch or call 1-800-FDA-1088***

HORIZON PHARMA

To those living with cystinosis, their family and friends,

On behalf of the more than 1,000 employees at Horizon Pharma, I want to thank the Cystinosis Research Foundation and everybody in the cystinosis community for providing us with the opportunity to meet with many of you and learn about your challenges, triumphs and goals for the future. It has been one year since Horizon began working with the cystinosis community, and we have been humbled and inspired by the stories we've heard from so many of you. With this in mind, Horizon is very proud to support the research, resources and events made available by the Cystinosis Research Foundation.

Horizon is a biopharmaceutical company focused on improving patients' lives, particularly among those with rare diseases. In our effort to learn from you so that we can create resources that best address your needs, we are supporting and attending events across the country, and we look forward to getting to know you. Meanwhile, if you have any input or feedback you would like to provide, please send us an e-mail at Connect@HorizonPharma.com.

For me, rare diseases are my passion. I couldn't be more thrilled to have the opportunity to support the cystinosis community on behalf of Horizon, a company deeply committed to rare diseases. The picture below is from Horizon's RAREis™ campaign, an effort to elevate the faces and stories of the rare disease community. You can see more pictures and stories by searching the #RAREis hashtag on Instagram, Facebook and Twitter, and I encourage you to post your own picture to your favorite social media channel with the hashtag #RAREis.

Again, thank you for welcoming us into your community. We are thrilled to support the Cystinosis Research Foundation.

Be well,

Tricia Mullins
Senior Director, Patient Advocacy
Horizon Pharma plc

Learn more about Horizon at **www.HorizonPharma.com**. You can also find us on Twitter, Facebook, LinkedIn and YouTube.

2018 Call for Research Proposals

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 14 short years. Since its inception, CRF has raised more than $39 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 $2.5 million was available for the 2017 fall call for research proposals and fellowship grants. The grant awards will be announced in December 2017. Details and guidelines for applications are available online at the CRF website: w*ww.cystinosisresearch.org/research/for-researchers*.

In the Spring, CRF issued eight new grants in three countries totaling $1.55 million that brings us closer to better treatments and a cure. All research applications received by CRF are evaluated by CRF's Scientific Review Board (SRB) comprised of leading international experts in the field of cystinosis, on page 13. The SRB provides independent, objective reviews and recommendations for each research proposal submitted based on the NIH scale of standards. Additionally, the SRB follows grant review guidelines established by the CRF and advises the foundation on the scientific merits of each proposal.

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

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.

CYSTINOSIS RESEARCH FOUNDATION
RESEARCH • HOPE • CURE

Leadership. Guidance. Commitment.

BOARD OF TRUSTEES

CHAIR

Nancy J. Stack
Cystinosis Research Foundation

VICE CHAIR

Geoffrey L. Stack
SARES•REGIS Group

TREASURER

Donald L. Solsby
Capital Bank

BOARD MEMBERS

Marcu Alexander
Hearts for Hadley

Stéphanie Cherqui, PhD
University of California, San Diego

Bruce Crair, CEO
Boingo Wireless

Denice Flerchinger
Tina's Hope For A Cure

Thomas A. Gendron
Woodward, Inc.

Traci Gendron
Tanner's Time for a Cure

John S. Hagestad
SARES•REGIS Group

Michael K. Hayde
Western National Group

Stephen L. Jenkins, MD
Sam's Hope for a Cure

Erin Little
Liv-A-Little Foundation

John C. Manly, Esq.
Manly Stewart Finaldi Lawyers

David W. Mossman
Donahue Schriber Realty Group, L.P.

Robert D. Olson
RD Olson Development

Kevin Partington
Cushman & Wakefield

Teresa Partington
Jenna & Patrick's Foundation of Hope

Jody Strauss
Cystinosis Awareness & Research Effort

Brian Sturgis
SimulStat Incorporated, 24 Hours for Hank

MEDICAL AND SCIENTIFIC ADVISORY BOARD

Stéphanie Cherqui, PhD
University of California, San Diego
San Diego, CA

Ranjan Dohil, MD
University of California, San Diego
San Diego, CA

Allison Eddy, MD
British Columbia Children's Hospital
Vancouver, BC, Canada

Paul C. Grimm, MD
Lucile Packard Children's Hospital,
Stanford University School of Medicine
Stanford, CA

Robert Mak, MD, PhD
University of California, San Diego
San Diego, CA

Jerry Schneider, MD
Dean for Academic Affairs Emeritus
University of California, San Diego
San Diego, CA

Jennifer Simpson, MD
Gavin Herbert Eye Institute
Irvine, CA

Doris Trauner, MD
University of California, San Diego
San Diego, CA

CYSTINOSIS RESEARCH FOUNDATION
RESEARCH • HOPE • CURE

Zoe R. Solsby
Vice President

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 $39 million with 100% of all your donations going to support cystinosis research.

EDUCATION

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

Save the Date

Cystinosis Research Foundation Presents

BECAUSE WE DARED TO

dream

2018 NATALIE'S WISH CELEBRATION

the celebration grows bigger and brighter every year

SATURDAY APRIL 21, 2018

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

THE ISLAND HOTEL
690 Newport Center Dr.
Newport Beach, CA 92660

HONORING

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

our kiddos play sports and plan careers

compassion blooms over and over again

lifelong friendships have formed