Cystinosis MAGAZINE

FALL 2012 FOR FRIENDS AND SUPPORTERS OF THE CYSTINOSIS RESEARCH FOUNDATION

Global Outreach. Global Impact.

Celebrating
10 Years and $20 Million
Raised for Cystinosis Research

Currently, there is no cure for cystinosis,

but there is hope.

Cystinosis is a rare, inherited, metabolic disease that is characterized by the abnormal accumulation of the amino acid cystine in each of the body's cells. 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 insidious disease, but cystinosis remains incurable.

Cystinosis afflicts approximately 500 people, mostly children, in North America and fewer than 2,000 worldwide. It is one of the 7,000 rare or "orphan" diseases in the United States that collectively affect 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 is 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.

Cysteamine, currently the medicine used to treat cystinosis patients, is also in clinical trials as a possible treatment for Huntington's disease and NASH (fatty liver disease), which affect millions of people worldwide.

The Cystinosis Research Foundation was established in 2003 with the sole purpose of raising funds to find better treatments and ultimately a cure for cystinosis.

Today, CRF is the largest provider of grants for cystinosis research in the world, funding more than 103 studies and fellowships in 11 countries.

CRF has raised nearly $20 million, which it has granted or committed to cystinosis research studies around the world. CRF's efforts have changed the course of cystinosis research and given new energy to its investigators and scientists.

CRF's commitment to research has given hope and promise to the global community of cystinosis patients and their families.

CYSTINOSIS
RESEARCH FOUNDATION

For more information about the Cystinosis Research Foundation, call 949-223-7610 or visit www.cystinosisresearch.org.

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Cystinosis Research Foundation website www.cystinosisresearch.org

Dear Friends and Family

It always amazes us how quickly the year passes – the seasons come and go and now the air is brisk and the days are shorter. Holidays are around the corner and with them, the traditions that are part of family gatherings. Friends and family will soon join together to celebrate each other and reflect on the blessings of the year.

All of us at the Cystinosis Research Foundation have so much to be thankful for and to celebrate. 2012 has been another year of momentous milestones and accomplishments for the foundation. It has also been a year of tremendous growth and community outreach, which has strengthened our resolve to find a cure for cystinosis.

This issue of *Cystinosis Magazine* celebrates the research progress we have made. We are pleased to share the recent successes made by our team of scientists, the announcement of the first allogeneic stem cell pilot study for cystinosis and the addition of four new members to the CRF Scientific Review Board. We are making progress every day and the results are tangible.

CYSTINOSIS RESEARCH: GLOBAL REACH, GLOBAL IMPACT

This spring we issued a record number of new grants. CRF funded 11 new research grants during the spring application cycle totaling over $1.6 million. There is a lay-version summary of each new research study in this magazine, which we hope will help you understand more about the research you fund through CRF.

Since 2003, as a direct result of your generous donations, we have issued 103 grants to scientists in 11 countries. The grants issued to date total over $17 million. Every dollar donated goes directly to research and CRF issues grants bi-annually thereby ensuring a dynamic cycle of on-going research.

The CRF makes an effort to recruit new researchers and scientists to ensure that we always have new ideas for novel treatments and new energy to move the research forward. During the spring cycle, we issued grants to two new researchers: Dr. Robert Chevalier from the University of Virginia, and Dr. Olivier Devuyst from the University of Zurich, Switzerland. We look forward to working with Dr. Chevalier and Dr. Devuyst to increase our knowledge about cystinosis and move us closer to finding the cure.

One of CRF's most important goals is to fund translational research. Bench research is the foundation of all research but we must be able to take what is learned in the lab and translate it to the patient's bedside. We have been successful in that endeavor, reaching two important milestones – a new medication and a stem cell treatment pilot study trial.

We expect that on January 31, 2013 we will celebrate FDA approval of the delayed-release medication!

Several years ago, CRF targeted research aimed at finding better treatments and we were successful. CRF funded every bench and clinical study that led to the discovery of delayed-release cysteamine. Simply put, without CRFs financial commitment to find a better treatment for cystinosis, we would not have a delayed-release medication that is now only months away from FDA approval. If the new drug is approved in January, this will be the most significant advancement in the treatment for cystinosis in decades.

The other important milestone is in the area of stem cell therapy. Dr. Cherqui's stem cell work has been translated into a patient pilot study. We are proud to announce that Dr. Stephanie Cherqui's work has resulted in the first allogeneic (donor) bone marrow stem cell transplantation pilot study for cystinosis at the Ronald Reagan UCLA Medical Center in Los Angeles, California. We await the first patient and with it, the hope that this treatment will reverse if not cure, cystinosis.

Although the allogeneic stem cell treatment is available now, Dr. Cherqui is working full-time on a future clinical trial involving stem cells and gene therapy. Autologous stem cell treatment uses the patient's own stem cells, which are harvested, then genetically modified and finally reintroduced into the patient. This procedure presents less risk, however more research must be completed in the lab. Dr. Cherqui is now working closely with the FDA to develop a clinical trial, which we hope will be a reality in the next four years.

Corneal cystinosis, a debilitating form of cystinosis and a condition that causes severe eye pain, corneal scarring and loss of vision due to the build-up of cystine crystals on the cornea, is another area of focus for CRF research. Cysteamine eye drops are available to reduce the crystals on the cornea, but the drops must be taken every waking hour of every day to be effective, making compliance virtually impossible. Dr. Jennifer Simpson, of The Gavin Herbert Eye Institute at the University of California, Irvine has been investigating the effectiveness of new therapies including stem cells, and new ways to deliver cysteamine eye drops including a timed-release lens treatment. We look forward to translating Dr. Simpson's research into a clinical trial for a novel treatment within 2–3 years.

Your donations have funded the seed money necessary to obtain large NIH grants. Dr. Cherqui and Dr. Simpson, both CRF-funded researchers, have been awarded NIH grants totaling $3.4 million as a result of CRF grants. The NIH grants have leveraged CRF grant money and helped accelerate promising research that will impact future generations of cystinosis patients.

To keep up with the increase in applications, the CRF Scientific Research Board (SRB), chaired by Dr. Corinne Antignac, has added four new members. We welcome Dr. Pierre Courtoy, Dr. William Smoyer, Dr. Lisa Guay-Woodford and Dr. Martin Konrad. (Their bios are on pages 77 and 78 of this magazine.) We are thankful for their expertise and commitment to the cystinosis community and we look forward to working with them as CRF expands its research efforts and breadth of research funded.

MORE THAN 2,000: POTENTIALLY MILLIONS

The impact CRF-funded research has had on more prevalent and well-known diseases and disorders is even more exciting than the enormous impact it has had on the cystinosis community. Because cystinosis is a metabolic disease that affects every cell in the body, research results and discoveries made by cystinosis researchers and scientists are applicable to other diseases and disorders. In fact, the delayed-release medication discovered by cystinosis researchers is now being used in clinical trials for Huntington's disease and NASH, a fatty liver disease caused by obesity.

CRF-funded stem cell research and treatment including the work of Dr. Cherqui and Dr. Simpson among others, also has the potential to reach millions of people with systemic disease like cystinosis. Your donations have significantly impacted the cystinosis community and they offer hope for better treatments for many others worldwide.

CYSTINOSIS FAMILIES: TOGETHER WE ARE STRONG

We know you will be moved by the stories of our cystinosis families written by the parents of children with cystinosis and patients with cystinosis. They have opened their hearts to share a little bit of what their life is like with cystinosis. I am certain you will feel the sense of hope each family and patient has about their future. Research ensures that there will be brighter days ahead and it allows us to dream of a life free of cystinosis.

I read an article recently that talked about kids who defy the odds because they have grit. That word resonated with me because by definition it means: bravery, tenacity, fortitude, courage and perseverance. *Grit* – the perfect word to describe our children and the adults diagnosed with cystinosis. They have moved beyond the diagnosis and prognosis of cystinosis to live life to the fullest, to experience joy and laughter, to love and to be loved.

The hope that we feel, the spirit of community and the belief that a cure is in sight is tempered by the reality that we have lost several people in our community within the last few months. We mourn the heroes who have lost their lives from complications of cystinosis. Daryl Heizingler shares the story of his brother Dean who recently lost his battle with cystinosis.

As a mother of a child with cystinosis, I can tell you that not a minute passes that I do not think of Natalie and her battle with this insidious disease. Although parents and people with cystinosis seek to and do live each day to the fullest, the reality of their daily lives is filled with numerous doctor and hospital visits, round the clock medications, learning challenges, kidney transplants, blindness and muscle wasting.

The average age of death from cystinosis has not changed in the last decade – it remains at 28 years old, however that number is what we rail against, what we seek every day to change and we are making progress. The progress we have made is measurable, it is impactful and it gives the cystinosis community the hope we so desperately seek.

All of you, our friends and family, have had a direct and positive impact on the lives of our children. You have stood by us as we have navigated this disease. You have been a source of strength for us personally and for the entire cystinosis community.

We are continually astounded and amazed by the goodness in people's hearts and your willingness to embrace our family and those with cystinosis. For Natalie and the others with cystinosis you have provided the greatest gift of all – hope.

With blessings from our family to yours.
Nancy and Jeff

A NOTE FROM NATALIE

Dear Friends and Family:

Natalie Stack with Shannon Keizer

I spent this past summer in Tours, France (a town of 200,000 near the Loire Valley) for seven weeks. I am a psychology major at Georgetown but my minor is French so traveling abroad was a way to focus on my French language skills. While studying abroad I met a lot of amazing people and learned about the French culture. Each day brought a new adventure – we toured wine caves and visited dozens of chateaus.

We even visited a less conventional site: a goat farm (to learn about chèvre). I lived with a French family of five, which allowed me to immerse myself in French culture and language. Although we had classes most weekends, I was able to travel to other cities including Paris and London. I was able to be fully independent and take care of myself without having any health issues while abroad. It was an unforgettable experience and by far, the best summer I have ever had!

This year, I am a senior at Georgetown University in Washington D.C. It is amazing how quickly college has gone by! It still feels like I arrived just yesterday! I am living in the dorms, again but this year, I have a single room. I am looking forward to what the future has in store for me, but at the same time, I am also going to be sad to leave Georgetown.

At the beginning of the school year in August, I met someone else who has cystinosis, Shannon Keizer. Shannon was visiting the NIH for her eye appointment, so the timing was perfect for us to meet. I really enjoyed meeting her and getting to know her and talking about some of our shared experiences. It was good to meet someone else who was (and is) going through the same struggles as me but who is also living life as normally as possible. We are both living our lives and pursuing our dreams every day, regardless of the reality that we both suffer from a terminal illness.

Although each day is a challenge for me physically, it does not stop me from doing my best; and, I have hope every day because I know that we are closer to a cure for cystinosis. The thought of life without cystinosis would never be possible if it was not for the incredible love and determination of my parents, our friends and family, the researchers and the entire cystinosis community who all believe that a cure is in sight.

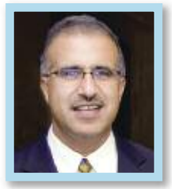
I am so thankful to be alive and although I am still afraid, I have hope.

Love, Natalie

Cystinosis Research

Holds The Potential To Help Millions Worldwide

"Cystinosis is a metabolic disease that belongs to the big family of lysosomal storage disorders. These diseases often affect children and result in progressive multiple organ dysfunction and severe clinical complications. Developing new therapies for cystinosis will provide insights to approaches that may have general applications for these diseases." STÉPHANIE CHERQUI, PHD, UNIVERSITY OF CALIFORNIA, SAN DIEGO



"Cysteamine has been available for the treatment of cystinosis for over two decades. However, it is only since the development of delayed-release cysteamine, with twice daily ingestion and hopefully fewer side-effects, that interest in the use of this drug for other conditions has arisen. Although studies are still ongoing and no results are available, delayed-release cysteamine is presently being evaluated in multi-center studies for non-alcoholic fatty liver and Huntington's Disease. Recent laboratory studies also suggest that cysteamine may play a therapeutic role in the treatment of kidney fibrosis." RANJAN DOHIL, MD, UNIVERSITY OF CALIFORNIA, SAN DIEGO

"In our recent CRF-funded research studies that were designed to provide new insights into the question of why cysteamine has been so effective in preventing chronic kidney disease in patients with cystinosis, we have discovered that it reduces kidney scarring – a universal process of kidney destruction that mediates all chronic kidney diseases. If these findings are confirmed with further studies, they would provide rationale for testing the efficacy of cysteamine as a treatment for many other forms of human kidney disease."

ALLISON A. EDDY, MD, FRCP(C), BC CHILDREN'S HOSPITAL, VANCOUVER, BC, CANADA

"Corneal cystinosis offers several advantages as a model from which therapies for more prevalent eye diseases will also benefit. "Examples of such potential cross-over benefits include the use of stem cell transplantation and long-acting drug delivery systems. While both of these approaches are being developed for corneal cystinosis, they also have tremendous potential in other ophthalmic conditions. These include, corneal chemical burns, which results in corneal scarring; corneal surface dysfunction, which causes severe dry eye; and a number of conditions that require chronic drop therapy, most notably glaucoma and uveitis. With the well-defined clinical endpoint of reduced crystals, corneal cystinosis provides valuable scientific and regulatory validation for novel therapeutic approaches to these more common conditions." JENNIFER SIMPSON, MD, UNIVERSITY OF CALIFORNIA, IRVINE

"Chronic kidney disease (CKD) is a major health problem affecting 1 in 7 people in the United States and its increasing prevalence in Europe and Asia suggest that it is quickly becoming a global health problem. Furthermore, kidney dysfunction is a recognized risk factor for poor outcome in a variety of disease states, yet there are few therapies to stop the relentless progression of CKD and alleviate the ongoing oxidative stress within the kidney. Our recent study demonstrates that cysteamine bitartrate reduces oxidative stress within the damaged kidney and attenuates the progression of fibrosis by modulating the behavior of interstitial fibroblasts, a key cell in matrix production. Our current studies are investigating the mechanisms of this effect with the hope of future clinical trials." DARYL OKAMURA, MD, UNIVERSITY OF WASHINGTON SCHOOL OF MEDICINE

By Betty L. Cabrera, CCIR Curator

CCIR BRINGS THE FIGHT AGAINST CYSTINOSIS TO THE WORLD STAGE

Cystinosis is a rare genetic disease but its reach is wide, affecting people from the coast of the United States to the coast of Africa. Access to quality medical care and cystinosis therapies often varies from region to region, with several patients and their families struggling to secure these valuable resources.

This may lead some to feel isolated and neglected. Where these resources are readily available, the disease can be fairly well managed and life prolonged, though the medical regimen can be demanding and detract from quality of life. Interestingly, recent research has shown that even with early treatment and good compliance with cysteamine therapy, kidney transplants are often still necessary [1] and other disease complications still exist. Taken altogether, it appears that there can be substantial burden to individuals with the disease and their families around the world.

Studies that attempt to capture this burden and collect vital information about cystinosis have been done on a small scale mostly among adult populations in the United States and European countries. The Cure Cystinosis International Registry (CCIR), an online patient registry established in August 2010, is the first and only database that has a global focus and that encompasses cystinosis patients of all ages. It is also the only database that allows patients to share anonymous data with research and medical professionals who have a legitimate interest in cystinosis, wherever these professionals may be.

Data centralization and free and open access by professionals are key features of the registry that CCIR believes will catalyze progress in cystinosis research. Similar to patients, clinicians and researchers who wish to study rare diseases like cystinosis may be isolated and neglected in the scientific community. Without disease burden information from patients, securing research money can be difficult; and without access to a pool of potential patient volunteers, the pursuit of novel therapies in clinical trials is almost impossible.

Cystinosis support groups throughout the world recognize what a valuable asset CCIR is and proudly help us promote it to patients and doctors in their home countries. In the past two years, CCIR has been invited to make presentations at patient conferences in Brazil, Italy and France. To date, 357 people from 34 different countries are registered.

CCIR anticipates that early next year it will participate in a registry project with a wider scope called the Global Rare Diseases Registry, which is overseen by the National Institutes of Health Office of Rare Disease Research. The idea behind the project is that research analyses and drug and therapeutics development for rare diseases may be easier and more efficiently conducted if de-identified patient data across several rare disease registries are combined in a standard way. We look forward to being part of this effort and are hopeful it will benefit our participants.

As a way of giving back to the cystinosis community, CCIR grants registered patients access to the anonymous, aggregate data. Registrants also have an opportunity to anonymously pose questions about cystinosis to experts in the field. Fifty-nine such questions have been received in various languages. A sampling of the Q&A strings are available on the website.

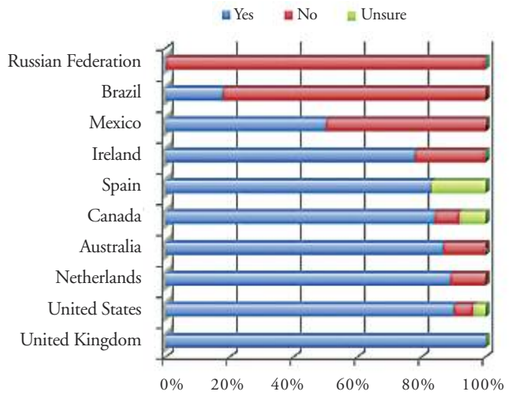
The bottom line is that CCIR is much more than a data bank. It provides a unique opportunity for voices from all corners of the earth to be heard, and the message being sent is clear: more needs to be done to improve the lives of those affected by cystinosis. We hope you find the international statistics and comparisons we share with you in this report interesting. We encourage those who have not yet registered to do so; and for those who have registered, we urge you to share with others what a great resource CCIR is.

Contact Betty Cabrera directly with any questions you may have (curator@cystinosisregistry.org).

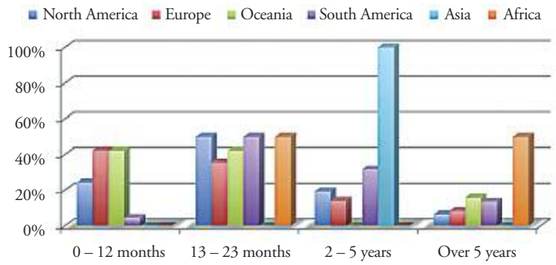
CCIR CURE CYSTINOSIS INTERNATIONAL REGISTRY

1 According to a publication by Albane Brodin-Sartorius et al., in the 2012 81st volume of Kidney International titled "Cysteamine therapy delays the progression of nephropathic cystinosis in late adolescents and adults", 91% of the cohort of patients observed developed end stage renal disease (ESRD). However, among adults who started cysteamine therapy before the age of 5, ESRD was significantly delayed (mean age 13.4 +/- 4.8 years) compared to untreated patients (mean age 9.5 +/- 2.0 years).

Regular Monitoring of White Blood Cell Cystine Levels – by Country (n=237)



Age Cysteamine Therapy First Received (n=286)



CCIR Registrants by Country

Venezuela	1	Greece	1	Spain	7
Sweden	1	New Zealand	2	Russia	7
Saudi Arabia	1	India	2	Netherlands	10
Saint Barthelemy	1	Belgium	2	Ireland	10
Portugal	1	Switzerland	3	France	14
Israel	1	South Africa	3	Australia	17
Germany	1	Scotland	3	Brazil	21
Czech Republic	1	Norway	3	Canada	28
Chile	1	Iran	3	United Kingdom	38
Bolivia	1	Italy	3	United States	141
Bahamas	1	Argentina	4		
Poland	1	Mexico	6		

Correction: In the spring 2012 issue of *Cystinosis Magazine*, the legend for the graph "Growth Hormone Use Among Registrants" had a print error. We apologize for this misprint. Please note that in the age groups 1–5 years, 6–10 years, and 11–20 years growth hormone use was 14%, 43% and 64% respectively.

Register at www.cystinosisregistry.org

"Registries are certainly a huge step forward, not only for cystinosis but also for all rare diseases, particularly their impact on research. Among others, it enables researchers to study good number of patients instead of the small cohorts with fragmentation of clinical and biological data restricting the power of clinical studies."

NEVEEN A SOLIMAN, MBBCH, MSC, PHD PROFESSOR OF PEDIATRICS AT CAIRO UNIVERSITY AND DIRECTOR OF THE EGYPTIAN GROUP FOR ORPHAN RENAL DISEASES (EGORD)

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Joshua's Journey of Hope

24 hours for Hank

Hope for Holt – Reaching For A Cure

Jenna & Patrick's Foundation of Hope

Leader in the Lab

And in directing CRF's life-changing research efforts

By Dennis Arp

Beyond her own pioneering research, Dr. Corinne Antignac sparks a collaborative spirit that bridges continents.

Corinne Antignac, MD, PhD, has every reason to revel in her role as a pioneering researcher. After all, her work brings great hope to cystinosis patients who once knew only dread and uncertainty.

But Dr. Antignac doesn't view her contributions in singular terms. Instead she chooses to herald triumphs won through teamwork and collaboration.

Speaking by phone from her lab in Paris, Dr. Antignac praises colleagues from across two continents. "I can think of at least 15 laboratories that are involved in cystinosis research – from France, Belgium, Italy, Ireland, the United States and Canada," says Dr. Antignac, who adds that the lifeblood of that research is funding support from the Cystinosis Research Foundation (CRF).

Beyond her accomplishments in the lab, Dr. Antignac helps unite this web of international researchers. She chairs the CRF Scientific Review Board and is a member of the CRF Cystinosis Gene Therapy Consortium. She also co-chaired the Third CRF International Research Symposium in March.

The doctor has served in many other critical roles and earned impressive awards during her professional life. She is a member of the International Society of Nephrology, European Society for Paediatric Nephrology, Société de Néphrologie Pédiatrique, Société de Néphrologie and American Society of Nephrology as well as many scientific boards.

So great are her contributions to science and medicine that she has been awarded the Legion d'Honneur, the highest decoration in France – a recognition of supreme service that was founded in 1802 by Napoleon Bonaparte.

And yet, the experiences Dr. Antignac treasures most have nothing to do with accolades. They are the breakthroughs in the lab and cooperation with colleagues, whose collective work makes a daily difference in the lives of cystinosis patients.

"We have a strong group who helps and learns from each other," said Dr. Antignac, section head of the Laboratory of Hereditary Kidney Diseases at Necker Hospital in Paris.

In the fight against cystinosis, few moments have been as significant as the one in which the CTNS "cystinosis" gene was identified in 1998. The discovery came in Dr. Antignac's lab and has opened doors for better treatment, including stem cell therapy and the hope for prevention of tissue injury in patients.

"Even when we cloned the gene, we were part of a collaborative group," Dr. Antignac says, "since we did it in close collaboration with Margaret Town and William van't Hoff in London.

Her protégé, Dr. Stéphanie Cherqui, turned her attentions to cystinosis at the suggestion of Dr. Antignac. Now the mouse model developed by Dr. Cherqui, when she did her PhD in Paris, is the foundation for genetic research being performed around the globe.

Though they are now separated by thousands of miles, Drs. Antignac and Cherqui still converse regularly. "It's sad for me that she is not back in Paris, but her success is absolutely wonderful," Dr. Antignac says. "I'm not at all surprised she has been successful. She has always wanted to treat children, she is an optimistic person, and she really believes in what she's doing."

Dr. Antignac is just as driven by belief, and she is never more optimistic than after attending the CRF International Research Symposium. That's when she and her colleagues get to exchange notes and insights but also talk in person and build rapport.

"It is really exciting that so many new people, who've heard about what we are doing, are coming to the field."

Dr. Antignac also enjoys attending the *CRF Day of Hope Family Conference*. The chance to meet with cystinosis families and explain what she does to those who are directly affected grounds her research in the real world of treatment, she said.

It's important to remember that what she and her colleagues are doing has the power to improve lives, she added. And she is quick to credit patients for their role in advancing research.

"The research was possible because we had patients' DNA," Dr. Antignac said. "From that, everything was deduced. Now we have a very good tool to explore the way cystinosin works."

Dr. Antignac is also grateful to those who back her research and that of her colleagues through their support of the CRF.

"What is wonderful about the CRF is its willingness to fund projects around the world and fund projects in both applied and fundamental research," she said. "To my thinking, this is the way to expand the field of research.

"We are seeing the effects of this research now and I think we will continue to see exciting breakthroughs well into the future."

For cystinosis families, the annual Day of Hope conference provides a wellspring of empowerment and possibility.

By Dennis Arp

SOURCE *of* SUSTENANCE

Marcu and Ben Alexander at the 2012 Day of Hope Conference

The shock of diagnosis was still fresh in their minds as Marcu and Ben Alexander boarded a plane at Seattle-Tacoma International Airport. If ever a couple needed a day of hope, it was the Alexanders. Just two weeks before, they had learned that their youngest daughter, Hadley, was battling cystinosis, and they were struggling to cope with the massive changes to all of their lives. Marcu had sought out the best information she could find on the disease, which led her to the Cystinosis Research Foundation (CRF) website, where she discovered the annual Day of Hope Family Conference in Newport Beach, California. The Alexanders knew they had to attend.

While they longed to learn more, they were also apprehensive about what the conference experience might hold.

"We were very emotional," Marcu Alexander recalled. "I was a little nervous that I would be a wreck."

Almost as soon as they got off the plane in Orange County, they encountered the warm embrace of the cystinosis community.

"It far surpassed our expectations," Marcu said of the April conference, which culminates with the celebratory Natalie's Wish event. "I was amazed to find that all of these kids seemed to be thriving. And everyone was so welcoming that immediately we felt this familial tie.

"We had fun and we learned a ton. I know it sounds like a cliché, but we felt like the Day of Hope truly changed our lives, and we didn't expect that."

For Erin and Chad Little from Ontario, Canada, the 2012 Day of Hope was also their first time at the conference, and the understanding they encountered was "unbelievable," Erin said.

"We were coming from a place of thinking that no one knew what we were going through, then suddenly we met others who go through the same daily regimen we do," said Erin, whose daughter, Olivia, was diagnosed with cystinosis in July 2011.

"Everyone (at the Day of Hope) was so positive and so hopeful. We learned a lot from the medical specialists, but the biggest thing we got was support from complete strangers. We felt that in this room full of people we were just meeting, we could trust them with everything that was going on in our lives.

"We are constantly reminded about the Day of Hope and the CRF. The impact is way more than three days long."

The next conference is scheduled for April 18–20, 2013, at the Balboa Bay Club in Newport Beach. There, cystinosis families from around the globe will meet to hear updates from experts at the cutting edge of research and treatment, with plenty of opportunities to get questions answered.

The young patients will get a chance to play with peers in an atmosphere of acceptance and joy, while their parents also learn the true meaning of community and support.

When Jennifer Peachman arrived at the most recent Day of Hope with her husband, Jamie, and their daughter, Morgan, she didn't expect that her 5-year-old would get as much from the experience as she and Jamie would.

"It was really good for Morgan to see that other kids have to take 'ucky' medications," said Jennifer, who traveled with her family from their home in Avon Lake, Ohio. "She gravitated to one of the teachers during day care, and it was also nice to know she was in good hands."

DAY *of* HOPE
CYSTINOSIS RESEARCH FOUNDATION
FAMILY CONFERENCE
APRIL 18–20, 2013

Gotta be there!

BALBOA BAY CLUB AND RESORT
NEWPORT BEACH, CALIFORNIA

The elder Peachmans' take-aways included information about organ donation – especially the ins and outs of the kidney donation chain. They also gained from educational sessions about research related to the eyes and general cystinosis treatment.

Then there was the "refreshing and enlightening" opportunity to meet another family with a daughter who was transitioning to kindergarten.

"I know there are a lot of private groups on Facebook, and it's great to be able to talk to people who are all around the world," Jennifer Peachman said. "But to be there in person and talk with people who are so involved in fundraising and research and just the day-to-day challenges of cystinosis, it really is a an amazing opportunity."

For the Littles, knowledge gained at the Day of Hope provides an added confidence they now take into meetings with Olivia's doctors. Erin and Chad also learned that it's important to take care of themselves and each other as they also care for Olivia.

"I now have a whole contact list of people who are happy to give advice, with no judgment attached," Erin said. "And we're eager to share any tips we can offer from our experience."

In general, the unqualified support of a sustaining community makes it easier to face the daily challenges and roll with the occasional crises that are side effects of cystinosis, Erin said.

Such is the "new normal," as the Littles describe their existence. And the Day of Hope is their new source of empowerment.

"The 2013 Day of Hope is already on our calendar," Erin noted, "and it will be every year."

Karen Kuphal, PhD
Sigma-Tau Pharmaceuticals, Inc.
Sr. Manager, Project Management

FDA APPROVES CYSTARAN™

FOR THE TREATMENT OF CORNEAL CYSTINE CRYSTAL ACCUMULATION IN PATIENTS WITH CYSTINOSIS

Sigma-Tau Pharmaceuticals, Inc. has received approval from the U.S. Food & Drug Administration (FDA) for CYSTARAN™ (cysteamine ophthalmic solution) 0.44%, a topical ophthalmic therapeutic, developed in partnership with the National Institutes of Health (NIH), for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

It has been quite a path from 1985 when Dr. Kaiser-Kupfer conducted early cellular experiments throughout the years of continued efforts from dedicated researchers such as Dr. Gahl, Dr. Schneider, Dr. Thoene, and Dr. Tsilou (to name a few). Dr. Gahl, the Clinical Director of the National Human Genome Research Institute, summarized the approval "as an important advance for children and adults who suffer from cystinosis". Dr. Gahl also indicated, "FDA approval of this drug represents the culmination of a longstanding collaboration among the National Eye Institute, the Eunice Kennedy Shriver National Institute of Child Health and Human Development, the National Human Genome Research Institute and Sigma-Tau Pharmaceuticals. It also has involved invaluable cooperation from cystinosis advocacy groups …" Sigma-Tau Pharmaceuticals appreciates the time devoted to this endeavor and recognizes the enduring support by so many individuals that made this day possible.

As mentioned, this project allowed for an opportunity to demonstrate the fruitful collaboration among the private industry (Sigma-Tau Pharmaceuticals), advocacy groups, academic institutions, and government agencies. Sigma-Tau Pharmaceuticals continues to work closely with the principal investigator, Dr. Bishop, of the active clinical trial (Protocol 86-EI-0062) at the National Eye Institute to develop a mechanism of eventually transferring access of CYSTARAN™ from NIH to a specialty pharmacy. Information will be provided to the patients as soon as it is available.

The most frequently reported ocular adverse reactions, occurring in ≥ 10% of patients, were sensitivity to light, redness, eye pain/irritation, headache and visual field defects.

For more information about CYSTARAN™ please see the full prescribing information at www.cystaran.com, or contact Lesli King, Senior Manager of Patient Affairs, at (301) 670-5450 or email Lesli.King@sigmatau.com.

sigma-tau
PHARMACEUTICALS, INC.

Grandparents SPRINKLING STARDUST

It has been said that grandparents "sprinkle stardust over the lives of little children." Ah, but if it were only that simple. This is our stardust.

Only child (Bob) marries the youngest of seven children (Liz) almost 40 years ago. Two great children and the addition of a wonderful son-in-law, and daughter-in-law take us over the moon. At one time early in our relationship we spoke of having a family of four children. We feel blessed we have those four now.

Nothing prepared us for the full joyful experience of grandchildren. One of the most powerful handclasps for Bob was that of each of his newborns, and later the grip of his new grandbabies around the finger of a grandfather. Grandma-grandchild relationships are simple. Grandmas are short on criticism and long on love. It's like getting to do parts of the early years over again except it's mostly only the fun parts. We have more "wisdom" on our side this time.

What an adventure to be the mother and father of a new mother. To see firsthand your child's early moments with her daughter … *priceless.*

Our big extended family has welcomed many grandchildren and great grandchildren into its fold. Thankfully, although we have worries over some conditions, there have been few serious health concerns in a family this size. We were all thunderstruck when our perfect little grandchild was diagnosed with cystinosis. I'm sure all families are floored with this unforeseen condition.

Bob and Liz Miller with their granddaughter Abbi

What does a family do when faced with a threat? Tears and disbelief were mingled with time spent reaching out for support from those we love. No prior practice had readied us to deal with the pain suffered by our daughter as she struggled to come to terms with the certain change in her little family. No young couple should have to ache with such a loss of innocence in their early married life. Katie and TJ as the loving parents they are, moved ahead quickly to research for the best plan for Abbi's care. They agonized as they explained to us that the present course of available treatment was slowing down the disease process but not curing it. It was time to circle the wagons. Even this terror could be broken down and dealt with. Everyone was kept abreast of the treatment.

Years before in our speeches at our childrens' weddings we voiced our belief in the saying, "it takes a village to raise a child." As grandparents along with the full force of our "tribe" of family and friends, we rally to keep Abbi well. We are in awe of the magnificent job her parents carry out every day in treating her as a well child who needs special action to keep her from getting sick. At age six she is treated as other six-year-olds with heaping helpings of love and realistic structure to nurture her growth. As grandparents we sometimes have to be gently reminded to stand aside and allow her to try things we might feel she is too fragile at times to master. Skinned knees are treatable. Living in a forced cocoon outside of the real world is not acceptable.

As in every household, raising a family today is not for the faint of heart … parents work, meals are made, houses are kept, bills are paid, and then after a lot of effort fun happens. In this family the effort list is a little steeper … meds are given, vomit happens, pain comes and goes, hospitals and doctors are routine, fluids are always and meals are "special." This is where Grandma and Papa can ride in on the white horse or in the SUV with booster seats in the back. This is where we can help keep a lid on the "menace" cystinosis presents. Before retirement we juggled time to lend a hand. Today we pitch in more freely where we can. We are not saints. We balance life as we have in the past. Work hard and play. Try and keep well for ourselves and our family.

If the power of the love and support surrounding Abbi could be bottled, its potency would eradicate the danger to her health.

Team Abbi is made up of warriors played by her wondrous parents, her incredible little brother, her marvelous aunts, uncles and cousins, an amazing troop of friends, and her very neat grandparents.

We all have no doubt medical research will change Abbi's life for the better. Just as Abbi and her family work a day at a time to keep ahead of this genetic condition, so must the researchers and doctors work diligently to discover the cure. We count on it.

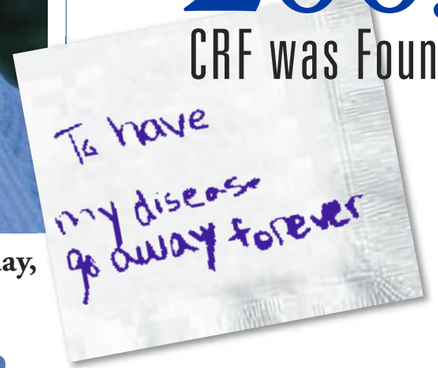
I do not seek out psychics, but a psychic found me. She stated clearly that the path I see ahead for my granddaughter will be the path she will follow. I see Abbi in the future as myself … a very proud grandma.

Bob and Liz Miller, Abbi's grandparents, St. Catharines, Ontario, Canada

CYSTINOSIS RESEARCH FOUNDATION

Miracles, Milestones & The Power of One

12 On the eve of her 12th birthday, **Natalie Stack made a wish** no child should ever have to make



In **2003** CRF was Founded

60 RENOWNED **SCIENTISTS** FROM **AROUND** THE **GLOBE** attended CRF's Third International Cystinosis Research Symposium in March 2012

AND WITH YOUR SUPPORT CRF HAS RAISED

$20 MILLION

TO BRING NATALIE'S WISH CLOSER TO REALITY

33 **articles** resulting from **CRF-funded** research have been **published**

1,000,000+

CRF-FUNDED RESEARCH ALSO OFFERS

HOPE TO MILLIONS

WHO SUFFER FROM OTHER RARE AND WELL-KNOWN DISEASES SUCH AS HUNTINGTON'S DISEASE AND NASH (FATTY LIVER DISEASE)

YOUR COMMITMENT HAS GIVEN

NEW HOPE

TO 500 CHILDREN AND YOUNG ADULTS IN THE UNITED STATES WITH CYSTINOSIS

AND 2,000 CYSTINOSIS PATIENTS THROUGHOUT THE WORLD

The Power of ONE

Thank you to everyone who has **traveled with us** on the **journey towards a cure.** Each of you has made a remarkable difference. **We appreciate you** more than words can express. Now, we hope you will **stay with us to finish** what we have so nobly started – ***to find the cure for cystinosis.***

By Dennis Arp

ONE SMALL STEP

Hopes for a giant leap from mouse model to human stem cell therapy start with a pilot study and a big concern for safety.

Dr. Theodore Moore and his UCLA colleagues will begin their pilot research project with hopes as high as those of anyone in the cystinosis community. But they also understand that there are no guarantees as, for the first time, they take the promise of genetic research using a mouse model and apply it to human cystinosis patients.

That's why they are taking extraordinary care in preparing to begin their bone marrow transplant study, which is made possible by support from the Cystinosis Research Foundation (CRF).

"This is an intermediate step, then the hope is that we will move into a cure for everyone with cystinosis," said Dr. Moore, a specialist in pediatric hematology at Ronald Reagan UCLA Medical Center. "But this study has a very limited focus, and we are doing everything to make it as safe as possible, because the risk of bone marrow transplant can be significant."

The study is to determine if blood stem cell transplants, using bone marrow from matched related donors, will slow down or prevent the progression of cystinosis.

"THIS IS AN INTERMEDIATE STEP, then the hope is that we will move into a cure for everyone with cystinosis." DR. TED MOORE

The study will also look at the risks of this treatment when measured against the potential benefit of avoiding long-term consequences of cystinosis.

Bone marrow transplant has never been used to treat cystinosis in humans. However, recent studies show that this form of therapy prevents the advance of the disease in mice, which is why everyone in the cystinosis community is excited to see the results of this next critical step.

The UCLA team is screening candidates carefully to find the initial six patient participants. To qualify, patients must have strong physical function as measured by tests of heart, lungs, kidneys, liver and other organs. They must also have a related donor who is a match on 10 of 10 identified factors.

Both adults (18 or older) and children (ages 13–17) are eligible to participate in the study, but the eligibility criteria are different for the two groups.

Adults must have stable kidney function (defined as less than 20 percent change in creatinine clearance from the prior 12 weeks), plus one or more of the following: muscle weakness, swallowing difficulties, progressive visual loss or intestinal malabsorption.

Eligible children will be those who do not tolerate or do not take cysteamine (defined by leukocyte cysteine levels greater than 5nmol half-cystine/mg protein for two consecutive time points at least three months apart during the prior six months or parental confirmation of patient intolerance). They will also have worsening clinical manifestations, as determined by a physician who is not an investigator on this study.

Because this pilot project is experimental, "we're only offering it to patients for whom oral medication is not working," Dr. Moore said. "CRF has been very supportive with getting people access (to study protocols and other information). Those who are interested should talk to their physician," he added.

Patients who meet the criteria will learn about the process in great detail so they understand the risks as well as the potential benefits, Dr. Moore said. "The process is very complex."

Although bone marrow transplant is experimental for cystinosis patients, it has been around since the 1980s as a potential therapy for those with genetic disorders.

"Some children have had wonderful results halting their disease," Dr. Moore said. "We had one little girl, 3 or 4 years old, with deteriorating neurodegenerative disease who had a wonderful response – it was a very happy ending."

However, there are also cases and diseases for which bone marrow transplant is appropriate in theory but ends up being ineffective in practice, for whatever reason, the doctor added.

In the case of cystinosis, "we have a wonderful mouse model" provided by Dr. Stéphanie Cherqui, who has done pioneering research at The Scripps Research Institute in La Jolla, California, Dr. Moore said.

And so, although there are no guarantees, "we proceed with confidence," he said.

If you are interested in participating in the pilot study, contact Zoe Solsby at 949-223-7610 or zsolsby@cystinosisresearch.org

Unearthing New Insights from STEM-CELL SUCCESS

By Dennis Arp

For genetic researcher Stéphanie Cherqui, success glows in greens, reds and yellows. Today, she is encouraged that the battle against cystinosis is yielding important advances.

The amazingly effective stem cell gene therapy explored by Dr. Cherqui features a mouse model utilizing dual fluorescence. This microscopic effect distinguishes the red host cells from the green transplanted ones, with the vibrant hues helping to illuminate the value of stem-cell-based gene therapy in treating cystinosis.

Now, in the latest leg of their research, Dr. Cherqui and her colleagues are seeking to better understand why the model has yielded such strong results. They'll be looking for host/donor-fused cells in several organs, with the cells identifiable by their bright yellow color.

Isolating the host and donor cells will help unearth the major genetic factors related to cell fusion between the stem cells and the host cells in the mouse model or other mechanisms involved in the formation of these dual color-cells.

"We're looking forward to better understanding this mechanism of stem-cell-based treatment and thus get insights to the effectiveness of the mouse model," Dr. Cherqui said. "This is an important step for stem-cell therapy as it relates to cystinosis, but it also offers exciting possibilities for regenerative medicine in general."

The investigative project, featuring Dr. Cherqui and research fellow Brian Yeagy, PhD, is supported by a grant from the Cystinosis Research Foundation (CRF).

As Dr. Cherqui launches this new phase of her investigation, she is also involved in the pilot study that will propel her groundbreaking research from mice to humans.

The study being led by Dr. Theodore Moore, a specialist in pediatric hematology at Ronald Reagan UCLA Medical Center in Los Angeles, will explore whether blood stem cell transplants can slow or prevent the progression of cystinosis in humans.

The clinical trial using bone marrow transplants from matched related donors marks a major milestone for Dr. Cherqui, but more importantly for cystinosis patients.

"THIS IS AN IMPORTANT STEP for stem-cell therapy as it relates to cystinosis, but it also offers exciting possibilities for regenerative medicine in general." DR. STÉPHANIE CHERQUI

"We know this therapy works very well in mice," the doctor said, "and now we get to answer the big question about whether it works as well in humans.

"If it works, the FDA will be more willing to go faster in the advancement of this research."

On the occasion of this pioneering moment, Dr. Cherqui praised the courage of cystinosis patients – especially those who will take part in the bone marrow transplant study.

"This is a big step," she said, "and the study participants are the ones who are making it possible."

Dr. Cherqui has recently accepted the position of Assistant Professor at the University of California, San Diego, Department of Pediatrics, Division of Genetics. She will continue her work on cystinosis in an environment that is better adapted for the clinical translation of her research projects. "This is an exciting move for me because there are several physicians/researchers in the UCSD Department of Pediatrics who work on cystinosis," Dr. Cherqui said, "I will now be working more closely with Dr. Ranjan Dohil, Dr. Robert Mak, Dr. Doris Trauner and Dr. Bruce Barshop. It will be a very stimulating environment where we will be able to combine forces which should lead to positive results for the entire cystinosis community."

Research Study of Bone Marrow Transplant

FOR PATIENTS WITH CYSTINOSIS FROM MATCHED RELATED DONOR

A research study is being done by physicians at the Ronald Reagan UCLA Medical Center in Los Angeles to determine if blood stem cell transplants, with bone marrow from matched related donors, are an effective treatment that will slow down or prevent the progression of cystinosis. The study will also look into the risks associated with this treatment and if they are acceptable considering the potential benefit of avoiding the long-term consequences of cystinosis. Bone marrow transplant has never been used to treat cystinosis in humans, but recent studies in a mouse model of cystinosis show that this form of therapy, not only helps, but prevents disease progression in mice. In this experimental study, the most successful form of bone marrow transplant, HLA-matched related donor bone marrow transplantation, will be performed.

Eligibility criteria for participating in the study includes:

1. A) Adults, ages 18 and older with nephropathic cystinosis with stable kidney function (defined as less than 20% change in creatinine clearance from prior 12 weeks) and one or more of the following: a) muscle weakness; b) swallowing difficulties; c) progressive visual loss; d) intestinal malabsorption.

   or

   B) Children ages 13-17 years who do not tolerate or do not take cysteamine (defined by leukocyte cystine levels greater than 5 nmol half-cystine/mg protein for 2 consecutive time points at least 3 months apart during the prior 6 months or parental confirmation of patient intolerance) and worsening clinical manifestations as determined by a physician who is not an investigator on this study.

2. Patients must have a related bone marrow donor who is HLA-matched on 10 of 10 alleles.

3. Patients with adequate physical function as measured by:

   Pre-transplant tests of heart, lungs, kidneys, liver, and other organs and must not have a serious infection, be pregnant, or have undergone a prior stem cell transplant.

New Clinical Research Study
At Ronald Reagan UCLA Medical Center

Ucla

Research Study of Bone Marrow Transplant for Cystinosis Patients From Matched Related Donor >

Interested subjects should ask their physician to contact Zoe Solsby at the Cystinosis Research Foundation for additional information. Telephone: 949-223-7610 or email: zsolsby@cystinosisresearch.org.

Making the Case for GROWTH HORMONE

By Dennis Arp

For Dr. Robert Mak and many cystinosis patients, it's a double whammy they know all too well.

Not only does cystinosis and the chronic kidney disease that often comes with it cause patients to lose their appetite, but it also forces them to expend energy more rapidly. Less energy in and more energy out can lead to severe muscle wasting and growth retardation.

"Growth is very much a problem with cystinosis patients, even before the onset of chronic kidney disease," said Mak, MD, PhD, Professor and Chief of Pediatric Nephrology at UC San Diego. "For a number of reasons, children with cystinosis experience much more severe growth retardation compared with those whose kidney impairment comes from other causes."

Patients have to drink a lot of water to keep their fluid balance up, and then they tend to lose nutrients in their urine from the Fanconi syndrome often associated with cystinosis. The common complication of hypothyroidism and the accumulation of cystine in muscles and bones can also impede growth.

Dr. Mak is studying the causes and effects of muscle wasting in cystinosis patients, thanks to a grant from the Cystinosis Research Foundation. He is also an expert on the use of growth hormone by those with cystinosis.

Dr. Mak argues for the use of growth hormone because he has seen it make a significant difference. In fact, its use has been shown to improve a child's height standard deviation score by as much as two points, he said. cystinosis patients who are often minus-4 on the scale (with zero being average height for someone in the general population) might see the score improve to minus-2 on growth hormone treatment. That would put him or her inside the average range (minus-1.5 to minus-2) for someone with chronic kidney disease.

It's important to identify muscle-wasting and height retardation early because they can have a profound effect on well-being, Dr. Mak said. In addition to psychological effects such as lower self-esteem, growth failure can correlate with reduced survival rates.

There is no "one-size-fits-all" age at which to begin growth hormone therapy, the doctor said. It often depends on when cystinosis is diagnosed, how growth-retarded the child is and what other treatment protocols are in place.

"There has been some controversy about starting growth hormone in the first year," Dr. Mak said. "But beyond the first year, if you are providing sufficient nutrients to the child, have corrected metabolic problems, are using vitamin D supplements and the child still isn't growing, then there's an indication for growth hormone therapy."

Dr. Mak says that no major side effects to growth hormone have been observed. Concerns about a faster onset of puberty and an increased risk of diabetes and bone disease are unfounded, he added.

Though the use of growth hormones is approved by the FDA for chronic kidney disease patients, health insurance companies sometimes are reluctant to cover it because the once-daily injection can cost as much as $10,000 to $20,000 a year per patient, the doctor said.

Physicians often "have to jump through hoops to get patients approved," he added, which is why he encourages parents to be well-informed and prepared to take on an advocacy role for their children with cystinosis.

In fact, Dr. Mak counsels all members of the cystinosis community "of the need to raise awareness" that growth hormone can be a strong tool to improve outcomes for patients.

"It's very safe, and it can be very effective," he said.

Shannon Keizer

Out There. Adventurous. Defying the Odds.

My name is Shannon Keizer. I live in Caledonia, Michigan.

My parents often call me Shaniqua.

To my brother, I am known as Merle.

To my cousins, I'm Shani Shana Shanik Shani.

I have many aliases, but "girl with weird disease" is not one of them.

I am just me.

I am a 23-year-old with cystinosis, not yet transplanted. In one week, I enter my final year of college, student teaching at an elementary school in West Michigan. Second semester I am super excited to complete my student teaching on a military base in Heidelberg, Germany.

I'm a bit obsessed with traveling and adventure. I view each day as a gift, as if it were my last.

I am writing from a waiting room at the NIH. Yup, the annual, dreaded visit to the eye clinic. And, my first solo visit. I'm proud to say, even with my enhanced cystinosis-induced spatial reasoning skills, I managed to get lost only twice, with two stops to ask for directions. After meandering around campus for nearly a half-hour I arrived at my appointment with five minutes to spare. Such is the life of a cystinotic. It's definitely not boring. Each day is almost like a mini scavenger hunt.

I try to find the positive in every situation, but I'm not gonna lie. This disease seriously sucks. Feeling ill multiple mornings a week, the pungent odor and other cysteamine side affects, 'round the clock meds, (supposedly) hourly eye drops, the inability to throw up but frequently feeling the need to do so, low energy, potential muscle wasting, and kidney damage/ failure … just to name a few.

At the time of my diagnosis in 1990, cysteamine was still experimental. Without meds, as my parents read, I would not live past ten years old. Thanks to the generations of cystinotics who paved the way before me, the tenacious doctors who dedicate their lives to the disease, the research, and those who have invested time and money, prayers, and my parents who loved me enough to force feed meds through any means possible, I AM able to live a full life and love every minute of it (Well … almost).

If you have browsed my Facebook page, you'll notice I'm a bit obsessed with traveling and adventure. I view each day as a gift, as if it were my last. Life is a blessing. It's a concept I like to call "living in dog years." My most recent extravaganzas occurred this past summer while nannying for cousins in the small, mountain village of Telluride, Colorado. With my cousins I was able to horseback through miles of open country, hike nearby peaks,

dangle from 2,000 foot cliffs by a wire, run a 5k at 9,000 feet elevation, right seat a private plane to Vegas, and explore Michigan and Wisconsin via plane, train, ferry and automobile. Incredible as all of these experiences were, the adventures were secondary to quality time spent with friends and relatives.

So how do I manage the affects of cystinosis and live a normal, adult life? Simple. I know nothing else. Actually, it's so much a part of my life that I usually forget about the disorder, and rarely do other people even know about it. If they ask, I'll openly share. But cystinosis does not define me. It has helped shape who I am, my zest for life, and compassion toward others. For this I am grateful.

Having this disease has been more difficult on my parents than on me. Granted, I don't remember the diagnosis and years of torturous procedures at the start of the journey. When they retell the stories of my decrepit Ethiopian-looking body, rickets, nonstop screaming for water, stuffing tubes down my nose, and force feeding meds to the point that I nearly chose to drown, I get teary eyed and think, "poor child." As if it were some other kid.

Well, now that my thumbs are sore from typing on an iPhone, and my saucer-sized, dilated pupils can no longer make out the words on the screen, I'd like to leave you with this final thought; **don't let cystinosis define you. Embrace it.** We are trailblazers on a difficult path. However, new developments and milestones are being made every year! So let's get out there, be adventurous and continue defying the odds. **And to the parents of those who are just beginning the journey – hang in there, it gets better. Hope is no longer a dream of the future. It is reality, and it's here now.**

Gabbie's Family and Friends CONTINUE TO SHOW THEIR LOVING SUPPORT







Gabbie Strauss may have cystinosis but she is a lucky girl in many ways. Her family and friends continue to find new ways to show their steadfast love and support. Each event is planned from the heart with one goal in mind – a cure for cystinosis.


Gabbie, Trevor, Jody and Chloe Strauss

1. **NCR Spirit Committee's Pancake Breakfast**
   This workplace fundraiser came as an unexpected and pleasant surprise. Gabbie's grandma worked at NCR for many years. Their pancakes flipped in $355 towards cystinosis research.

2. **3rd Annual 'Uncle' John's Pig & Poker**
   Two of Gabbie's biggest supporters are 'Uncle' John and Robyn Beresford. Not only do they come to every event, but they host their own! This roast has raised over $3,200 in the last three years.

3. **Treat Yourself Spring Fashion Show**
   Four amazing women – Gloria Deutschlander, Carole Stacey, Phyllis Wagner and Gabbie's grandma Dianne Strauss – planned a beautiful event complete with live musical entertainment, fashion, food, door prizes, gift bags and chef demonstrations. 230 women attended and raised $11,420.

4. **3rd Annual Paper Shredding Party**
   Family friend and realtor, Lance Roberts, held a document shredding and computer hardware recycling fundraiser on June 3. Local small- and medium-sized businesses were invited to make a donation to cystinosis in exchange for shredding any unwanted documents. The event was complete with coffee, treats and a raffle. Over the last three years, $1,000 has been raised.

5. **Street Impressions 3rd Annual Charity Car Show**
   Trevor's cousin, Jeff Moser, loves cars. He races them, has a car club and is in the tire business. He also has a big heart for Gabbie. Jeff has helped us race towards a cure by raising over $6,500 in three years.

Gabbie continues to amaze everyone around her. At 4 years old, she learned to ride a bike on her own, refusing any help. She rides with such zeal that within six months her tires were completely bald and one tire popped on the way to school.

Gabbie lives each day to the fullest. She loves being outside biking, scooting, swimming or jumping on the trampoline. This summer she expanded her outdoor hobbies to include snorkeling, fishing and frog catching.

Gabbie is now a senior kindergarten student. She and her younger sister Chloe love taking piano lessons and gymnastics class together. With winter upon us, Gabbie is starting ice skating again. She is so determined to improve that she will stay on the ice and practice without any breaks until the zamboni driver tells her to clear the ice.

Gabbie never complains. She wakes in the middle of the night for medication and takes 22 syringes a day without any objections. She has an infectious laugh and a passion for life that inspire many around her. She is courageous, brave and joyful. Our family continues to take one day at a time, hoping and praying for a cure. We live by faith that one day Gabbie will walk in perfect health.

Thank you to everyone who is making Natalie and Gabbie's wish come true.

"to have my disease go away forever."

By Alexis Allison, QMI Agency

Kente Kiwanis Continue Cystinosis Support

It isn't the first time the Kente Kiwanis have supported the Strauss family, and it doesn't look to be the last.

Kiwanis president Derek Shaver presented Jody Strauss and daughter Gabbie with a cheque for $500 to be donated to the Cystinosis Research Foundation (CRF), adding to their previous donations raised through fund raising events and other campaigns.

At four years of age, Gabbie has been living with cystinosis for almost three years, a disease which attacks and slowly destroys all the body's organs, starting with the kidneys and eyes.

But Strauss is the bright-eyed picture of optimism as she discusses Gabbie's battle with the disease and the impressive progress the CRF has made in just three, short years.

"Everything is going well right now in terms of health," said Strauss. "The achievements they [the CRF] have made in research have been outstanding. Usually there's a setback or something, but right now everyone is just driving forward."

Strauss describes a stem cell treatment researchers are currently working on that is delivered to the eye via laser technology. This treatment would only need to be delivered one or two times over the course of the lifetime of the patient, a huge improvement from the 22 syringes that Gabbie needs daily in order to keep the disease at bay.

But the small group of cystinosis sufferers – an estimated 50 in Canada and 2,000 worldwide – can cause problems for funding research.

"The number of affected people is so small that we don't receive government funding," said Strauss.

Alexis Allison/Trentonian Kente Kiwanis president Derek Shaver hands a check for $500 to Jody Strauss and her four-year-old daughter Gabbie Strauss, who was diagnosed with cystinosis when she was 15 months old. The donation will go to the Cystinosis Research Foundation to help fund research to find a cure.

"All the money raised for research comes from private funding, but that also means that every single dollar raised goes to the research. It's not going to salaries or anything else, every dollar is helping find a viable cure."

And a cure is the goal for the pair who haven't slept through the night since Gabbie's diagnosis, waking up at 1 a.m. every day to deliver and take the medication.

"It's just part of the process, something that needs to be done, you learn to adjust," said Strauss.

Residents of Waterloo, much of the Strauss's extended family lives in the Quinte West region. When Shaver and Kiwanis member Terry Broderick first heard their story they wanted to do everything they could to help and continue to provide an extended support network.

"Three years of medical research is really just a drop in the bucket," said Broderick. "It's remarkable how much they've achieved since we first connected with the Strauss family."

Right now, the FDA is currently in the approval stages for a similar drug to the one Gabbie is currently taking, but that only needs to be delivered once every 12 hours.

"It shows what happens when everyone comes together and works towards one final goal," said Strauss. "While they're working on one thing, they're working on something better."

The Strauss family founded the Cystinosis Awareness and Research Effort (CARE) shortly after Gabbie's diagnosis, the only non-profit organization devoted to the cystinosis cause in Canada. In just two years, CARE has contributed over $230,000 to the CRF thanks to donations from organizations like the Kente Kiwanis.

Story originally published on the trentonian.ca website.

It takes a village

Patrick, Jenna and Tucker

Dear friends of CRF,

We are writing this update following a great fundraising celebration here in Sacramento! On Friday, October 5, Jenna & Patrick's Foundation of Hope (JPFH) hosted *Swing & Bling #3,* which included a day of golf for more than 150 participants and a sold-out dinner with 230 guests.

Jenna & Patrick's Foundation of Hope raised more than $195,000 during this year's event. We are proud to pass along 100 percent of the proceeds to the Cystinosis Research Foundation.

Kevin and I are so grateful to the JPFH board of directors and *Swing & Bling* committee for making this such a great event year after year. We have an amazing community of supporters – "a village" – here in Sacramento and beyond, who give so much of themselves to this event and to our family. We are very humbled. We are exceedingly blessed!

"A picture is worth a thousand words," and we have plenty to share from the day. We hope you will get a feel for the fun-filled day. Golfers gathered at 8:30 a.m. at Teal Bend Golf Club for an 18-hole golf scramble. A "Paris" theme was great fun to work with as we planned the dinner event.

The generous donation of airfare and accommodations for a spring-time trip to Paris added to the auction excitement. A delicious French-themed menu and Parisian street market-style floral arrangements and macaroon cookies gave the evening an authentic aura.

However, the beauty and excitement of all of these luxuries couldn't stand up to the great energy that emanated from the room full of people gathered in the name of a special cause. A highlight of the dinner program was hearing from special guest Dr. Stéphanie Cherqui, who told guests about some of the exciting research their contributions are funding. Kevin shared personal stories of his fatherly experiences raising two kids with cystinosis, making for an emotional but starkly honest moment in the evening.

As we wrap up this year's event we are excited to return to our focus – home. We treasure the moments with our kids as they grow and change, and are more able to forget cystinosis for a while when we aren't in the throes of planning an event to fund the research of it. As you read through this magazine you realize that this community of supporters is but one of many, who have all become woven together as a greater community because of the tremendous efforts of the Cystinosis Research Foundation.

There has never been more hope!

Love, Teresa, Kevin, Patrick and Jenna Partington

Jenna and Tucker are welcomed into Neiman Marcus during a visit to pick up a Chanel Handbag, which was raffled off during the Bling event on October 5.

From the heart

KEVIN PARTINGTON'S TALK AT SWING AND BLING

Before I get started, I would like to thank our Board of Directors and the Swing and Bling Committee members, including Pete and Jen Demello and the State Street Volunteers, for all their hard work in putting this day together.

I would also like to thank the Citizen Hotel and Chef Oliver, Harmony, Brent Larkin, Craig Zarro, Pete Thompson and Kipp Blewitt for working so closely with our foundation and providing this exquisite venue for the past three events.

There is a saying that, "It takes a village to raise a family." As I look around the room this evening, I see Jenna and Patrick's extended family, as well as their kindergarten, first and second grade teachers, their school principal and their priest, Father Looney. I see their UC Davis nephrology doctor, Dr. Butani, who oversees their cystinosis treatment, as well as their neighborhood pharmacist.

There are families from Holy Spirit School and from all around Sacramento showing incredible support. And once again, I see a Real Estate Community that has embraced this cause and given generously over the years.

We live in a very special "village."

I have been asked to speak to you this evening from a father's perspective about how it feels to raise children with cystinosis. And while I feel qualified to do this – considering Teresa and I are raising our twins, Patrick and Jenna, who both have cystinosis – I want to be clear that we are not the people with this frightening illness. I don't want to pretend that I know what it is to have cystinosis and minimize the fight that the adult, young adult, teenage and child patients deal with every minute of every day.

They are the true champions and deserve all of our admiration for the relentless fight they endure daily.

With that in mind, allow me to discuss how our journey to date has been with Jenna and Patrick, our seven-year-olds who are in second grade at Holy Spirit School in Sacramento.

Patrick and Jenna were both diagnosed with the genetic disease cystinosis when they were 15 months old. At that time we had no idea what cystinosis was or what was in store for us over the coming years. By nature, I believe my wife and I are optimistic and positive people. I mention this only because I believe that cystinosis has forced us to differentiate between being optimistic and positive role models for our kids, while battling the harsh realities of the disease they are affected by. In fact, this has become our daily dilemma. I would like to offer a few examples of what I mean.

School

Like many parents, we struggle to get our kids to do their homework. We wonder during some difficult teaching moments if they are struggling for "normal" reasons or because of cognitive reasons caused by cystinosis? Do we push them to "get it done" or are they truly hitting a roadblock that Teresa and I can't see because of cystinosis? We are not educated or trained to manage the education process or understand the learning disabilities associated with cystinosis. So, we do our best to differentiate between what is normal second grade behavior and what is a "cystinosis roadblock."

We are truly encouraged by young adults with cystinosis who have had successful school and college careers. We hope Jenna and Patrick will be motivated toward – and capable of – similar achievement.

Thank you to Holy Spirit, Mrs. Rogina and Mrs. Glenn for your incredible patience and understanding.

Sports

This has been very difficult for me because I grew up around sports. My dad was a basketball and tennis coach, my sisters were swimmers, my brother and I played college basketball. I am the guy who "winds down" to ESPN *Sports Center* at the end of the day, and I look forward to every big sports moment I can see, either live or on TV. Sports is quite simply a big part of my life. My children, it seems, may not share this passion!

Soccer is very popular in Sacramento, but Sacramento reaches 100 degree temperatures on a regular basis during the summer months. Even golf camp last summer proved too hot. I would like to see the kids exposed to all the positive life lessons that team sports provide: teamwork, sportsmanship and exercise – all are very important. At the same time, we aren't willing and the kids aren't interested in being exposed to the dehydration,

A glowing Teresa Partington

Kevin Partington, Dr. Stéphanie Cherqui, Patrick Reichenberger, Teresa with Sacramento Assemblyman Dr. Richard Pan. Dr. Pan, who is a member of the California State Health committee, presented a State Resolution to Dr. Cherqui for her exceptional and tireless work on behalf of the cystinosis community.

Dr. Stéphanie Cherqui presenting some of her findings to a spellbound audience at the Bling event.

exhaustion and literal "wilting" that is a result of exercising outdoors in the heat. We encourage them to participate in sports where they can: swimming is good (it keeps them cool) and they are showing some interest in baseball, but their passion doesn't match mine. Of course, there are limitless possibilities for our children to be successful at other things they will enjoy and that will bring them peace throughout their entire lives. It may even be a sport they discover along the way, but for now I've had to adjust my thinking.

I even took piano lessons for a couple of years, so I could be an example of something artful and nonaerobic – something other than basketball or golf. Unfortunately, I am a terrible piano player. We are trying to help our children discover sports or other hobbies that take place in a cooler environment and provide the same life-lessons.

Social Situations

Like all kids with cystinosis, Patrick and Jenna drink a lot of water – about two gallons a day, each! Naturally, what goes in must come out and they pee about every 45 minutes or so around the clock. As a result, our nightly routine consists of pull-ups, changing sheets and water refills. This routine has made it difficult to know when sleep-overs with their friends will be appropriate. How will this affect their confidence? Does it open them up to ridicule? Do we try to hide it, or do we just lay it on the table and trust that Jenna's and Patrick's peers will handle the facts kindly?

As parents, so far, we have chosen to confront issues about medications and the symptoms of cystinosis up-front and head-on. This is a reality of the disease and

could be for years. The kids have already had a few fun and successful overnighters at friend's homes, thanks to parents in this "village" (you know who you are) who have assisted in stealth midnight operations to keep it all on the "down low."

Fortunately or unfortunately, cystinosis is a very rare disease that forces the family to carve out a niche within the community that doesn't fully understand what cystinosis is. Cystinosis only affects internal organs, so it makes it difficult for those around us to understand what the kids are actually going through and the severity of the disease. The prevailing thought is, "They look healthy, so what's the problem?" Even as well-informed parents, we sometimes succumb to the rather normal outer appearance of our children – thankfully forgetting for a time that they suffer from a terminal illness.

It is a blessing to have these "normal" moments, but we can't relax too much, or "forget it" for too long, because the clock keeps on ticking and there is always a daily reminder to jolt you back to reality. Education, research and awareness are critical parts of dealing with cystinosis and finding a cure.

As fathers, we love our kids more than words can express. In many ways cystinosis has brought me closer to my family and it has provided life-lessons that may not have otherwise presented themselves in a quote "normal" situation: things like cherishing each moment we have together; knowing what is truly most important in your life; realizing the value of family, friends and schoolmates; and developing a deeper sense of community.

These things being said, I don't pretend to have all the answers and frankly at times, realize we are living day to day and just doing the best we can in the best ways we know how. Jenna and Patrick and all the kids, young adults and adults with cystinosis are the real champions as they fight this disease day to day and they teach us all how precious life is and how fragile it can be.

I think about a cure for cystinosis daily, and for the sake of our older patients it can't come soon enough. I am amazed by and in awe of our cystinosis researchers and scientists and what they have accomplished to date. I only ask them to continue their search for better treatments and the cure, while we commit to providing the funds they require to do so.

On behalf of my family, I would like to thank each of you for coming tonight and I hope that you enjoy this celebration of all the progress **WE** have made during the past ten years.

To my wife, thanks for leading our family down the right path every day and doing all the heavy lifting. I love you.

To my family, my dear friends, my colleagues and my community, thank you for coming.

Normal is what you make of it

Nicole Hall

Angie and Nicole Hall

August 16, 2007… that was the date we received news that our daughter Nicole suffers from a disease called cystinosis. We had never heard of this disease, so we did not know what to expect.

In a way, it was a relief to finally get a diagnosis after over a year of doctor's appointments trying to determine why she was struggling to grow. However, with this answer, a new round of questions were being asked since the weight of this diagnosis seemed astronomical at the time – how would this change our lives and would our little girl ever get to lead a "normal" life?

It is hard to believe that we received that news just over five years ago. Nicole turned seven in October and is now in first grade. She is beginning to understand that she is different from her friends, and has started to realize that she doesn't need to be embarrassed by it.

This year she gave a presentation to her entire school about cystinosis and why she gets her nourishment through her "button" – the feeding tube that was inserted into her stomach when she was nine months old. The school has done a great job catering to her special needs by administering her midday medication, giving her eye drops, and feeding her during the day. She now wheels her pole down to the cafeteria and "eats" with all of the other students at lunchtime, which makes her enjoy school that much more. Her class recognizes that she is different from them, but they deeply care for her and surround her with love. We feel so blessed that she is in such a great environment.

Nicole receives over 17 doses of medicine each day to keep her system regulated. This requires attention to detail when planning on leaving the house for the day – we need to be sure that we bring medicine and eye drops with us in the event we are away from home when her medicine is needed (the 11:00s and 5:00s have forever been changed in our family). Nicole has encountered some "speed bumps" when her medication needs to be adjusted, however, she takes them in stride, which shows her amazing strength of character. She teaches us each day to live life for both the big AND small things, and that every issue thrown at you can be overcome.

Nicole is beginning to understand that she is different from her friends, and has started to realize that she doesn't need to be embarrassed by it.

Nicole's sister, Angie, is now 5½ and is in kindergarten at the same school. Although Angie is 17 months younger than Nicole, she has her responsibilities in helping care for her older sister. She enjoys being a part of Nicole's daily routine – whether it is helping prepare Nicole's medicine or filling up bottles for Nicole to drink during the night, she happily participates. Angie has accepted that Nicole isn't physically capable of doing everything she can do, but makes an extra effort to find activities that they can do together.

We will hold our 5th annual *Race for Nicole* event in early December. This year we hope to have four or five teams compete in the Dallas Marathon Relay. Every year, we are overwhelmed by the support we receive from family and friends. We are deeply grateful for everyone who donates their time, effort and financial support to find a cure for cystinosis. We are confident that the funds provided by supporters of *Race for Nicole* and other organizations supporting cystinosis research will lead to advancements in containing this disease, and one day a cure. It is this support that gives us hope for Nicole and the other children suffering from cystinosis.

Over the last five years, our definition of a "normal" life has been altered from what we used to think it means. But as we have adjusted to a family member with cystinosis, we have learned that we are, in fact, living a "normal" life – we may have a different routine than other families that requires additional attention, but at the end of the day, "normal" is what you make of it.

All our love and bottomless thanks,
Aaron, Stephanie, Nicole and Angie

CRF and Raptor: Working to Support Cystinosis Families

Earlier this year, Raptor Therapeutics held a workshop at the Day of Hope to brainstorm how the company could help the cystinosis community. Many families participated, and with their insight and other input, Raptor will be launching a program to support those living with cystinosis.

To help us get up to speed on this program, Jessica Dedio (mom of Bailey, age 14) posed a few questions to Raptor's head of commercial operations, Patrick Reichenberger, about the company's plans for the next few months and a program called RaptorCares that will support the cystinosis community.

Q What is RaptorCares?

A RaptorCares is an education and support program designed for the cystinosis community, by the cystinosis community, and sponsored by Raptor. Our goal has always been to provide resources and information based on feedback from those affected by cystinosis.

In the next few months, we will be rolling out educational information that can be shared with others (such as school personnel) and materials that can help improve the care of cystinosis patients (for example, helping the transition to an adult nephrologist). Soon we'll be mailing out results of the cystinosis patient and caregiver survey conducted last year. More than 70 families from the CRF completed the survey and we look forward to sharing what we learned.

We also look forward to creating more resources through RaptorCares — in addition to helpful support the CRF continues to provide — to show our commitment to those living with cystinosis. Over the past few years the cystinosis community has welcomed Raptor with open arms, and we want to show our appreciation and let you know we've listened to feedback.

We would also like to thank the CRF for graciously supporting us in generating awareness of RaptorCares among the families they serve.

Q How will RaptorCares assist families?

A RaptorCares aims to provide education and support to families living with cystinosis. Eventually, Raptor would like to provide reimbursement and access support to those in the U.S.

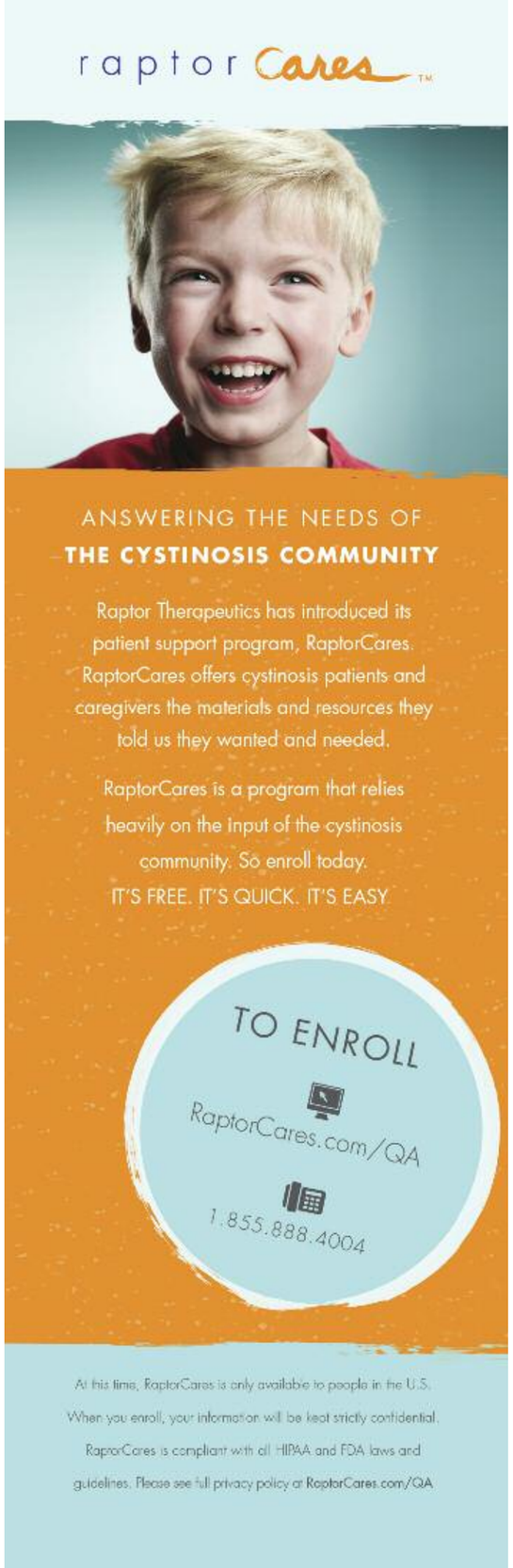
Q How can people enroll for RaptorCares?

A People can enroll for RaptorCares by visiting www.RaptorCares.com, or calling 1-855-888-4004. At this time, RaptorCares is only available to people in the U.S.

It is important to note that the information provided will be kept strictly confidential. Patient privacy is very important to us. The full privacy policy is available at www.RaptorCares.com.

Q What about those who already enrolled in RaptorCares?

A People who have already enrolled in RaptorCares should look for information in their email and mail. In the meantime, tell a friend who you think may appreciate the information!




Katie's mom, Ruth Ann Ahnen and friend Mary on their recent climb.

Trekking Up Everest for CRF

By Ruth Ann Ahnen, Katie's mom

My name is Ruth Ann Ahnen and my 21-year-old daughter Katie has cystinosis. She was diagnosed at about four and a half years old. Although she had many trips to the emergency room and numerous hospitalizations over the years, she is doing very well now.

Four years ago her kidneys gave out and she received a kidney transplant from her dad. This dramatically improved her health while also improving her self-confidence immeasurably. For the past several years we've followed the Cystinosis Research Foundation (CRF) and their honorable quest to find a cure for cystinosis.

About a year ago, well ahead of my 50th birthday, my friend Kathy, who had recently turned 50, and I decided to do something big. There was something we both shared on our bucket lists – trekking to Mount Everest's base camp. Shortly after we made our decision to go, we thought this would be a great opportunity to raise money for the CRF. Months of physical training and lots of planning ensued before our trip half-way around the world. I received much encouragement from my family, friends and even strangers.


Katie Ahnen

The purpose of our trek was to elevate awareness of cystinosis, raise money and celebrate our 50th birthdays all at the same time.

Our trip began on April 26 with a drive to O'Hare International Airport from southeastern Wisconsin. From there we flew to Munich, Germany where we celebrated my 50th birthday en route to Nepal. We arrived in Kathmandu, Nepal a day later and stayed in a comfortable hotel for a couple of days to acclimatize and meet our guide. Next, we traveled by helicopter to Lukla, Nepal, a small airport/village in the Himalayan Mountains with an elevation of about 9,300 feet. From there we started our weeklong journey up to the base camp of Mount Everest.

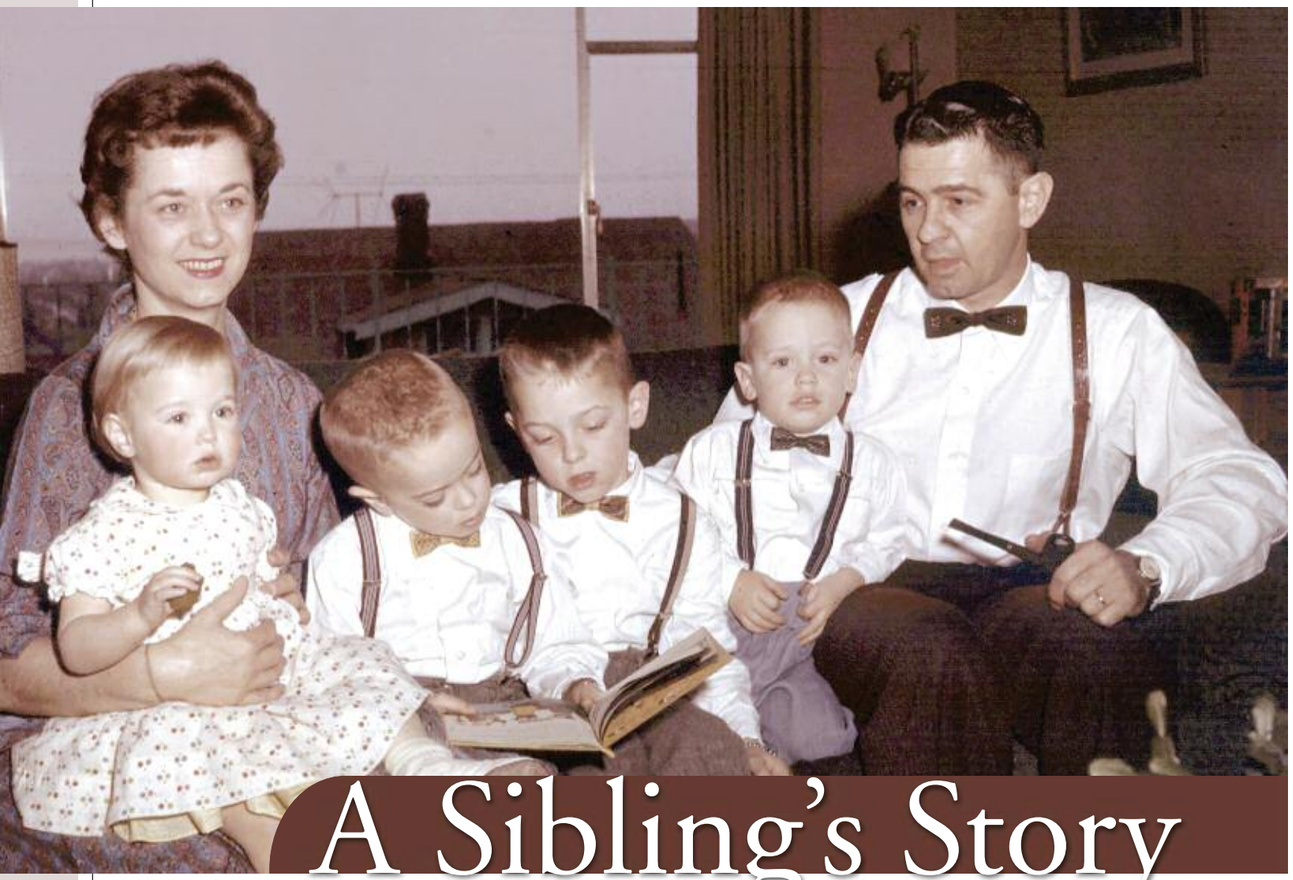
I frequently thought of my Katie and others with cystinosis and their daily battle with the dreaded disease and it carried me through the tough times on the trail. The word "warrior" often came to mind.

The climb was grueling and the altitude wreaked havoc on our bodies as we climbed higher into the thinning air.

We stayed in "tea houses" in the evenings after some very tough days of trekking along the yak trails leading to base camp. These were mainly stone structures with little to no heat and the little heat available was provided by burning dried piles of yak dung from the trails. The tea houses were merely a place to get out of the elements and get some rest. Due to the lack of oxygen at night, we'd often wake up gasping for air as if we were suffocating. It was very scary until we remembered where we were and why it was so hard to breathe. The views along the trail were breathtakingly beautiful and except for the cold, the weather was almost perfect. Living was primitive with few western conveniences. Life takes on a whole new meaning above 15,000 feet.

On May 8, we finally reached our goal of trekking to Everest Base Camp for CRF and the Children's Hospital of Wisconsin. The entire trip from Lukla to base camp lasted eight days – covering 48 miles while ascending from 9,300 to 17,600 feet in elevation. It was an extremely difficult journey replete with altitude sickness and bouts of dysentery. We challenged what we thought was physically possible.

When we returned home from the trek I was invited to speak at local elementary schools and a newspaper article was published about our adventure. I shared basic information about cystinosis, and the importance of dreaming big, because your dreams can make a difference. We accomplished our goals and in the process raised over $7,000 for two important organizations.



A Sibling's Story

By Daryl Heinzerling (center), brother to cystinotics: Wade, Dean and Heidi; and "the luckiest guy in the world, to have grown up in this family." (photo, 1962)

Do you, or does someone in your family have cystinosis?

Do you sometimes wonder why?

Do you ever wish that you could just wake up to learn that is was only a bad dream – so you could get on with living? But then you realize that it's not going away… maybe ever.

Is cystinosis a death sentence?

How does one grapple with such questions?

Where do you go for answers to the BIG questions?

Where can you find the strength and courage to go on, to keep finding new ways to live life to the fullest in the midst of a possibly dire prognosis?

How can you maintain hope and balance and love?

Allow me to introduce the Heinzerling family. We have been living with cystinosis for 60 years, 1952 – 2012. Along the way we found answers to the hard questions posed when a family is stricken by this insidious disease. And yes, it is the whole family that must cope, not just the children diagnosed with cystinosis.

Our story begins when World War II veteran Melvin Heinzerling met Jean Crook in 1950. He was dashing, intelligent and a great dancer. She was beautiful, soon to be a University of Washington graduate and also a great dancer. They soon fell in love and married in July 1951. A jack-of-all-trades, Mel could build or fix almost anything. He had already built a boat and the house where they would live. They soon settled down to the business of raising a family.

Their first child, Wade, born in December 1952, was every bit the delight that his parents had longed for – light blond hair, brown eyes and apparently normal in every way. But delight turned to concern eight months later when he began drinking more than normal. The true diagnosis came after several months of searching and researching. In 1953, very few doctors had ever heard of cystinosis. Eventually, doctors learned the truth and relayed to my parents that Wade wouldn't live beyond 7 to 10 year of age.

> **"Dean had a remarkable gift of never complaining no matter what he was going through."** JEAN HEINZERLING, DEAN'S MOM

I am Daryl, their second child, born in 1954. As hoped and expected, I did not have cystinosis. Convinced that I needed siblings, my parents had Dean in 1958 and Heidi in 1960. But they were devastated to learn that both Dean and Heidi also had cystinosis. These were crushing blows to our young family who anticipated living the American Dream.

My mom began searching for hope and answers. In February 1961 she got a call from a mother whose son God had healed of hemophilia, a supposedly incurable disease. This was the first real sign of hope for Wade, who was now eight years old and succumbing to the ravages of cystinosis with cystine crystals blocking his kidneys. The mother attended St. Luke's Episcopal Church near us in Seattle.

We were members of another church, and had never seen these miracles. Each member of our family gave our heart and life to Jesus, and committed to following Him and allowing His direction in our lives. When we started trusting that He loved us and had a plan for our lives, we were freed from worry about the future.

WHAT FREEDOM! WHAT JOY!

Amidst all the sickness, hospital visits and dire prognoses, we found real, abundant life. My dad worked long hours to keep our family afloat financially, while Mom stayed home to care for us kids. Mom began holding a "Good News Club" for neighborhood children. More than 50 kids became Christians in those clubs, and the news kept spreading, almost like wildfire.

When Wade turned 10, his kidneys started shutting down. Artificial kidney machines were rare in 1963, so as a test, doctors connected Wade to one to see if it could help. They learned that they could prolong his life, but the disease would still take his life. But God was now in control. We didn't have to worry. If God wanted to restore Wade's life, He could. Or if He wanted to take him to Heaven, that would be okay too. We would miss him terribly until our eventual reunion, but God would give us everything we needed for our abundant life until then.

When Wade died, many people couldn't understand our joy in this time of sorrow. They thought that Mom was either going to crash when the reality of her son's death finally sunk in, or that she had lost her mind. We had all learned the freedom that comes from trusting God, believing that He loved each of us, and whatever happened would turn out for our good.

Dean and his wife Ruth, a fellow cystinotic

There are many amazing stories to be told but for now let me tell just a few that will open a window into a family who lived with cystinosis.

In 1970, Dean got a kidney transplant from dad, and Heidi got one from mom. Dean's lasted a couple of difficult years, but Heidi's was rejected after only a few months. Heidi went on the artificial kidney machine, and two years later Dean joined her. They trained mom to do home dialysis in our dining room, which had been converted to a hospital room with two kidney machines and other equipment including large water purifying deionization tanks. The machines bore little resemblance to today's high-tech variety. We had to take the machines apart and clean them regularly (that became my job).

Unfortunately, formaldehyde leaked from Heidi's machine to Dean's while he was being dialyzed. No one realized it even though Dean was getting really sick. Tough guy that he was, he kept going to school and managing the symptoms. When he started having fainting spells, we rushed him to the Emergency Room, where the doctor could not find a pulse. Immediately they called a Code Blue. Mom called dad who flew to the hospital praying all the way. When he got there Dean had been "dead" for over 15 minutes. Dad and mom knelt and prayed outside the room.

The nurse explained why they were giving him shots directly into his heart. They could see the long rolls of paper coming off the electrocardiograph with a flat line – no heartbeat. The nurse was honest – people don't usually come back after 20 minutes without a heartbeat; and if they do, it can mean brain damage. Mom reached her hands through the bars at the foot of the bed and talked to God, "Lord, if you want to take him home to Heaven, you know that's okay with me. But if you bring him back here, please don't let him have brain damage. Let him be fully whole again." At that instant Dean took a breath! The heart graph showed a very irregular heartbeat, but there was life and a chance.

His heart only beat for a few short minutes then stopped again – this time for about 10 minutes. But after lots of prayers and a total of 35 minutes with no heartbeat, Dean's heart came back strong and steady. The next few days were a roller coaster ride. We were thankful that he had survived the ordeal and that it had not affected his brain. But now, he had a story to tell of a trip to Heaven's door. He remembered the angels and the peaceful feeling. He was so close to Heaven, and he felt so good, only to be sent back to a sick, painful body. He would always say that he had no fear of death because he had been to heaven and saw how good it was.

The Heinzerlings in 1976 – Jean (Mom), Heidi, Daryl, Dean and Melvin (Dad)

Heidi went through many difficult years – lots of operations, infections, complications, including partial paralysis. In 1974, an infection almost took her life; strong antibiotics helped, but the hospital accidentally overdosed her and she lost all her hearing.

The next year I finally got my chance to help Dean. I gave him my left kidney. For the next 30 years he would joke that I gave him my best kidney because his readings were so good.

By the summer of 1975, we had been through so much, and had been tied down to the house for dialysis for years. Now that Dean had his transplant and only Heidi was on dialysis, my dad decided that we needed to go on a family vacation. At the time, the only option for a dialysis patient who was traveling was to schedule appointments at hospitals along the trip route. This was not an option for us.

AN INVENTOR OF SORTS

As I said before, my dad could make or fix almost anything. He was even an inventor of sorts. He started asking why kidney machines could not be taken on the road. He learned the biggest problem was that the big deionization tanks could not be moved once they had water in them. I worked for a company that built Reverse Osmosis water purification systems (ROs) and learned that an RO could be the water source we needed. With that knowledge we worked on power supplies, flow and purity tests to establish the viability of the system. After testing to make sure everything worked, we out fitted a trailer as a hospital and left on vacation.

When we returned to Seattle the hospital was shocked to hear what we had done. The doctor called the public relations department who interviewed us. They then called the media to let the world know that the Heinzerling family had figured out a way to make a kidney machine mobile. Soon, all the major news networks were at our door. We were on the front page of the *Seattle Times,* and even the *National Enquirer* and *Midnight Sun* sent reporters and photographers to our home.

My dad worked hard to provide a normal life and as much fun as possible. So it was no surprise when we went on a seven-state tour to the Grand Canyon and traveled up the California coast the next summer.

A SPIRIT FULLY ALIVE AND WELL

Heidi had the most difficult life I know. By the time she was 30 she could not walk or see much, and had been deaf since she was 14. She had undergone countless operations, four kidney transplants and innumerable complications. But her spirit was fully alive and well. She cared deeply for everyone and was the smartest person in our family. Dad taught us all how to play poker, but when Heidi played she usually ended up with the biggest pile of chips. She died in 1992 at the age of 32. She lived an amazing life with the cards she was dealt.

In 1990 and 1991, Dean was making regular trips to the National Institutes of Health in Maryland. Besides getting the latest treatments, he also made another life-changing discovery – Ruth. Ruth Fenstermacher was a fellow cystinotic who was nine years younger than Dean, but they made a great pair. They were married in 1991 and settled in Washington. Ruth was the sweetest angel to ever grace our family. Although, she had three kidney transplants, she died in 2004, at 37 years old.

Losing Ruth was rough on Dean, but he was tough. He got a loan and opened coffee stand at the clinic where Ruth had worked as a medical technician. He grew his own fruits and vegetables, which he used in the baked goods he sold.

In 2008, the kidney I had given him in 1975 started to fail. By December 2009 he had the first of many strokes and had to start dialysis. It was difficult, but Dean never gave in and he never gave up. Strokes were making conversation difficult, but God was working on his spirit. Mom was Dean's full-time caregiver again, which was hard for him, but as they spent countless hours together Dean opened up. By the summer of 2012, they were reading the Bible and other books about Heaven in anticipation of both their journeys. (Mom, who is still alive, was almost 88 at the time.)

We were all aware that Dean was living out his final days here on earth. After another set of strokes, the doctors said that there was no way to stop the bleeding in his brain, so we made the difficult decision to stop dialysis and let him go. On the morning of August 16, 2012, Dean got up, took a shower, ate a good breakfast and sat down to talk with mom.

> **"Dean never gave in and he never gave up … God was working on his spirit."**

I had written an email to Nancy Stack about my mom: "She continues to inspire everyone she meets, leaving a trail of healed lives, mended hearts and saved souls in her wake. She is so excited for her son to enjoy the freedoms of heaven and greet other family members there. Dean is especially looking forward to seeing his wife, Ruth again." After Mom read the message out loud to Dean, she said, "Oh Dean, won't it be wonderful?" At that exact moment Dean's eyes got wider, a little smile came across his face, his arms went up in the air, and he was gone!

"LOOK, HE'S SMILING!"

Mom called me at work, and I started the half-hour drive to their home. Mom later recalled telling the caregiver who was helping out, "Look, he's smiling!" "You're right, I see it," the caregiver said in amazement. Dean's smile lasted 10 minutes, but by the time I arrived it was gone.

Can you imagine a better homecoming? Is there a better way to leave this troubled world? God has been so good to us. We are ever thankful for the grace He has shown us over the years and the countless blessings we have received.

In going through Dean's home this last month, I found a little leather holder with an old roll of electrocardiograph paper with a flat line that goes on for yards. Occasionally the line bounces off the paper (when they tried to stimulate his heart) but then returns to flat line. That's my brother! I don't remember how many times he was at death's door, but Dean lived and loved and gave for almost 40 years after his first trip to Heaven.

HERE'S WHAT JEAN HEINZERLING WROTE ABOUT DEAN THE MONTH AFTER HIS FINAL JOURNEY TO HEAVEN

My son, Dean – what a character! He is and was very unique. In all things there is a right way and a wrong way … and, then there's Dean's way. His way was usually a shortcut to the end result. This got him into a lot of trouble in life, but he would work his way through it with a wonderful sense of humor.

Dean had a remarkable gift of never complaining no matter what he was going through. He had a lot to complain about, but took his bumps in life rather matter-of-factly. When he was losing his kidneys at the age of 10, he would surround himself with music that fed his soul and mood. He loved a Herb Alpert and the Tijuana Brass album and would play it over and over again.

When Dean was in grade school, the photographer for the school picture wanted him to smile, so he asked Dean, "What do you want to be when you grow up?"

With a big smile he said, "I want to be a farmer!" And that's exactly what he struck out to do. When he married Ruth, the two of them bought property away from city life, in the country, close to Snohomish, Washington. There he planted an orchard. He had the strength because he was living on his brother Daryl's kidney, which he had received in a transplant.

He lived 35 years on that kidney before it started to reject three years ago. Now that he is in Heaven, there's no more concern about kidney function.

Right after that transplant, he was up and doing things; going places and building a life. For Dean, life goes on with a few bumps along the way.

What a guy! What a character! I love him with his different ways, and I always will.

To learn more about the Heinzerling family's experiences with cystinosis, contact Daryl at dwheinzerling@msn.com.

A Weekend of Healing and Hope

The Peachman Family

By Jennifer Peachman, Morgan's mom
Avon Lake, Ohio

My husband, Jamie, my then-four-year-old daughter, Morgan and I attended our first Cystinosis Research Foundation Day of Hope Conference in April of this year. Since her diagnosis Morgan's health has been good and we've been navigating the waters of having a child with cystinosis pretty well.

The waters grew rougher when we were preparing to send Morgan to kindergarten. For insurance reasons, we made an appointment with a new ophthalmologist for Morgan's biannual eye check up. We were shocked by the doctor's lack of bedside manner with our daughter and family.

Our beautiful daughter, Morgan Peachman, modeling a sweater made from one of the kits being sold in *Morgan's Corner.*

Morgan doesn't know what she has, let alone the severity of her condition – and in strides an arrogant doctor, a man we'd never met before, discussing the rarity of cystinosis, eye pain, sensitivity to light, hourly drops, and preventing blindness, all in front of our innocent little girl. To make matters worse, he was followed by five medical students to see the girl with crystals in her eyes – a case they'd most likely never see again. He wrote a prescription for hourly eye drops, told us to make an appointment for three months and left the room.

That was all I had to hear. I would never let Morgan see this doctor again and immediately called our previous ophthalmologist to make an appointment, to get her opinion. We knew the hourly eye drops were coming eventually, but we were hoping to hold off until kindergarten. Much to our relief, our old ophthalmologist agreed, saying, "If Morgan was my little girl, I'd hold off. Let's get her into kindergarten before starting the eye drops." We would follow up and check her eyes again in six months and in the meantime the doctor contacted the National Institute of Health to discuss obtaining the drops when the time comes.

I've only left three of Morgan's doctors appointments crying: the first when the geneticist told us about cystinosis and that she believed Morgan had the disease; the day she was actually diagnosed; and the one with the arrogant ophthalmologist and his interns. My husband and I had no clue how to manage hourly eye drops. Our current every six hours medication regimen, and daily growth hormone injections was hard enough. How could we manage hourly eye drops, too? As I was telling my father about the ophthalmologist, he offered to buy us plane tickets to CRF's Day of Hope conference in California. After returning home and thanking him many times for his generosity, he said, "It was just the right thing to do at the right time."

At the Day of Hope conference, we met another family from Northeast Ohio with a son, Jake, our daughter's age; a family from West Virginia with a girl, Kennedy, Morgan's age; and a mother of a young girl who once lived near us in Avon Lake, Ohio. A neighbor told us that he thought a girl that used to live next to him might have had the same disease Morgan has. The girl's family had a water fountain installed for the girl's unquenchable thirst. When I heard this story, I shrugged it off, thinking it couldn't be cystinosis … it's too rare. After meeting this mother at the conference, I realized it was true! The world was suddenly so much smaller after attending the conference.

Another mother shared lessons she's learned along the way, including how to prepare our children to attend school. I've borrowed a lot of ideas and it's made my husband and me more comfortable transitioning Morgan into kindergarten this fall. We learned to have hope. We asked questions of the panel of doctors who've done so much for the disease – medication and research. As we shared tips and tricks with other parents we realized that we weren't alone. And our daughter learned that she isn't alone either. Other kids have to take yucky medications to stay healthy, just like she does.

But most of all, at the conference we learned that as parents, we know our children better than anyone; that we need to educate ourselves and the doctors who care for them; and that in any situation concerning our children, we know "just the right thing to do at the right time."

Morgan's Corner

Donna Nye, owner of Calla Lily Yarn & Gifts in Wooster, Ohio was a stranger to our family, but she is now one of Morgan's biggest supporters. Donna heard Morgan's story and began fundraising activities in her shop. In *Morgan's Corner*, Donna sells kits that contain patterns and yarn to knit children's clothing. A percentage of the proceeds from the sale of the kits is being sent to the Cystinosis Research Foundation. Morgan's great-grandmother, Grace Saari, of Ishpeming, Michigan has also donated handmade knitted items for sale in Donna's shop and all proceeds will be directed to the Cystinosis Research Foundation.

Thank you to Donna Nye, for her support, creativity and generosity!

If interested in purchasing a kit from *Morgan's Corner,* please contact:

Calla Lily Yarn & Gifts
119 E. Liberty Street
Wooster, Ohio 44691
330-264-3000
www.callalilyyarn.com

Morgan on her first day of kindergarten. She has "star sunglasses" on because her future is so bright. We are full of hope!

A Night of Hopes & Wishes

Honoring Jake Krahe Raises Over $105,000 for Cystinosis Research

A happy Jake Krahe with his mom and dad, Amy and Jeremy

On Friday, September 28, 2012 our family and friends hosted ***A Night of Hopes & Wishes*** to benefit the Cystinosis Research Foundation.

More than 350 guests joined us at our first fundraising event. There were cocktails, dinner and live entertainment by the band Shout!

A Night of Hopes & Wishes was a tremendous success and exceeded our greatest dreams. We are truly grateful and swept away by the overwhelming kindness and generosity our community has shown. I would love to share with you the many kind and heartwarming stories about how Jake's Story spread from the barbershop to the supermarket.

- ***How families shared with friends and friends invited neighbors.***
- ***How one guest's birthday wish brought donations in from Maine to California.***
- ***How our small planning committee grew an idea into an amazing success.***
- ***And how together, one community raised over $105,000 for cystinosis research.***

There are so many stories I cannot fit them on this page. Truly. What an amazing experience. We are so touched and thank each of the many people who shared Jake's Story and the many, many people who made this an incredible success.

Thank you,
Amy and Jeremy Krahe
Broadview Heights, Ohio

Jeff and Rochelle Masternak with Allyson and Ted Wright

Sam Rutigliano, former Cleveland Browns head coach with Jake (right) and his twin brother Austin at the Hopes & Wishes *event.*

The math was simple. **We knew if we tried for another child, we had a 25 percent chance that the baby would have cystinosis. But there was a 75 percent chance the child wouldn't have cystinosis! We wanted our three-year-old, Sam, who has cystinosis, to have a brother or a sister. Seeing how strong and happy Sam is, we rolled the dice. Lars Andrew Jenkins was born on July 30, 2012, six days after Sam's birthday and just a day shy of our fourth anniversary. He was a hefty 8 pounds 1 oz and 20 inches long. He was beautiful, with a nice round head and a slightly smooshed nose. But that blond hair – that was a little concerning. Sam had that same head of blond hair.**

1+1 = Infinite Love + Hope

By Ashton and Stephen Jenkins,
Sam and Lars' mom and dad,
Salt Lake City, Utah

We were ready though. We coughed up the 350 bucks to do the genetic test for the 57kb mutation, the most common cystinosis mutation. Sure, it wasn't a definitive test since we didn't know Sam's mutation, and it's not even incredibly accurate. But our nephrologist wanted to wait till Lars was about four weeks old to draw blood for the WBC cystine test, and we thought we'd burst if we had to wait that long for some kind of answer. We just wanted to buy ourselves some time.

We got the results back when Lars was about a week old. He tested negative for the 57kb mutation. We were pretty relieved. We didn't start broadcasting the good news, however, because we knew there was still a small but significant chance Lars had cystinosis. But we breathed a little easier.

Lars was a good baby and a healthy eater from the start. From all appearances he was a normal newborn. He was gaining weight. He took decent naps. But by the second and third weeks that all started to change. He started wanting to eat more often. He was colicky and hard to console. He started sleeping less. He was acting a whole lot like Sam as a baby.

At three weeks we couldn't wait any longer and we got the blood drawn for the WBC cystine test. We waited an agonizing eight days for the definitive answer. The results came on a Tuesday, four weeks and one day after Lars was born. He tested positive for cystinosis.

We hoped and prayed Lars would be healthy. We also prayed that we would have energy and optimism if God had a different plan for our family. We'd never have imagined four years ago when we got married that we would one day have two children with a rare disease. Although it's not the future we had planned on, we feel incredibly grateful to be the parents of two special boys who mean the world to us.

We were able to start Lars on Cystagon® immediately. He tolerates it surprisingly well, and despite the grimaces he makes when we squirt the malodorous mixture in his mouth, sometimes he gives us a smile, as if to say, "Thanks, Mom!"

After Lars's first dose of Cystagon®, Sam hugged him and said, "Good job, Baby Lars! You took your medicine!"

As soon as we started the drug he started nursing at more normal intervals and sleeping a little longer. We don't know if the drug is just killing his appetite or sedating him, but it has been a welcome change! We're hopeful that the FDA will approve RP103 early next year, when Lars will be moving on to solid foods. Hopefully he'll like applesauce! He's also on the mandatory proton-pump inhibitor, as well as some vitamin D supplement. We're hoping that since he was diagnosed so early we will be able to avoid the kidney damage that Sam had already sustained at diagnosis. Our nephrologist told us to feed Lars whenever he wants, and he is certainly putting on the pounds. At eight weeks old he was nearly 14 pounds. Sam was still 14 pounds at one year. We don't plan on losing any ground.

Sam loves having a baby brother. He is so sweet with Lars and constantly tells us how "koot" Lars is. He refers to him as "Baby Larziroo," and wants to be at his side all the time. After Lars' first dose of Cystagon®, Sam hugged him and said, "Good job, Baby Lars! You took your medicine!" Lars doesn't even mind when Sam pokes and prods him or plays a little rough. Lars even smiles during such behavior. You can tell these two are going to be best friends.

Sam is doing very well on RP103. He throws up much less often and has boundless energy. He can come across as timid and serious when you first meet him, but he doesn't have to be around other children for long before he becomes the loudest and most mischievous. He is a truly happy kid.

He loves to make up jokes and laughs hysterically after telling each one. He likes to imagine there are trolls under every bridge, or that he is Simba from Lion King, and there are always "bad guys to fight off" wherever we play. We love to go on family hikes and Sam won't let us take resting breaks because he's too excited to get to the top. He has become adept at building with duplos, assembling train tracks and racing Hot Wheels. He's learning his alphabet and numbers, too. He loves flying on airplanes and going to Stanford University every three months for the RP103 trial.

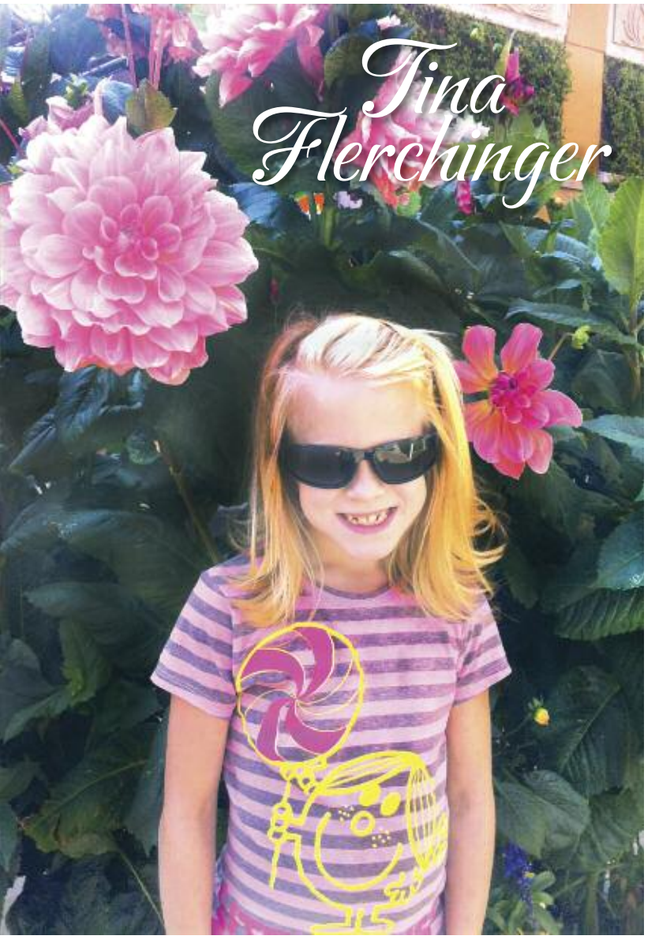
The future for our children is bright! We have so much hope for a cure. Our two sons will lead wonderful lives and have such a positive influence on those around them. Their sweet young spirits have already added so much joy to our family.

We are in the middle of a letter-writing campaign for our first fundraiser for *Sam's Hope For a Cure*. We have been overwhelmed by the generosity, kindness and support of our friends and family. We have raised over $4,000 so far. We will be giving all the donations to the Cystinosis Research Foundation to further the research and development of new and improved treatments and eventually a cure for cystinosis.

For updates on Lars and Sam, visit http://littlebravesambo.blogspot.com/

Spring in Her Step and Joy in Her Heart

By Denice Flerchinger, Tina's mom, Clarkston, Washington



Tina is now nine years old, entering the third grade, and has a big personality. A teacher who knows her once described her perfectly when she said 'Tina has a spring in her step and joy in her heart.'

It feels like this year has definitely been a transition for Tina. She is very aware that she has cystinosis, and as of lately asks a lot of questions. We try to talk about it freely with her. She tells us she worries about things, so we always try to keep it positive. It is heart-wrenching to hear her pray every night for God to cure her.

In the seven years since Tina's diagnosis we've seen a lot of progress take place. Although we do not know what tomorrow will bring, God has definitely helped us see the light at the end of the tunnel! We've celebrated all the little milestones along the way. It is truly amazing how every day holds its own surprise. Last spring, Tina suffered with daily headaches and stomach pain. In July, we appeared in the Emergency Room for dehydration and low potassium. She has since turned the corner and today is thriving!

Every day brings its own challenges, but we are confident that a cure will come in Tina's lifetime.

Until then, we will celebrate each and every day. Just watching her run through the front doors of school each morning gives me a thankful heart.

Tina is doing well on the new cysteamine treatment. We will continue travel to Stanford University until the RP103 is approved by the FDA. This "miracle drug" has changed Tina's quality-of-life. The difference has been truly amazing! We hope that one day soon every patient will be able to experience the same success.

Our next challenge is treating the cystine buildup in her eyes. I can't imagine adding another medication to Tina's already daunting regimen but the only current treatment is an eye drop that needs to be taken every waking hour. The drops must remain refrigerated and sting, which makes compliance very difficult but they will keep Tina from going blind.

The research being funded by the CRF is bringing new eye treatments and we see a cure on the horizon. We hope it will come sooner rather than later. Until then, we will continue to embrace this little girl, who is our little miracle, and thank God for each day we have with her!

Tina finally loves to eat.

Tina and her sister Nichole.

Tina at Stanford University.

4th Annual Wine, Stein, & Dine

Benefiting Tina's Hope for a Cure

Tina's Hope for a Cure held its 4th Annual Wine, Stein & Dine on Saturday, May 12 in our small town of Lewiston, Idaho. Mark and I watched as nearly 300 family members, friends and strangers filled the open showroom at Rogers Toyota Scion in honor of our daughter, Tina.

Local musicians, Duet Riendeau, played while international cuisine, Basalt Cellar wines, and Riverport Brewery beers were served. The auction of over 132 items warranted something for everyone – from a private helicopter trip, to artwork, concert tickets, and even an exclusive cooking class for six.

For me, the highlight of the evening was looking out at the sea of faces there to support not only us, but cystinosis research and being able to share the incredible and progressive treatments we have made over the past year. Rarely are you able to go to a medical fundraiser and see how each dollar raised is directly creating results, and the CRF video production built on this. The excitement and hope was palpable in the room. Our middle daughter, Catherine, spoke about the incredible highs and difficult lows of having a sister with cystinosis. It was definitely emotional for everyone in the room, as evident by the hands reaching up to brush tears from cheeks.

The energy in the room for the Fund-A-Cure was awe-inspiring, as $35,000 was raised! The momentum continued the entire evening. A total of $95,000 was raised for cystinosis research that night. It is overwhelming to think of all the people who helped make this event happen – from the board of directors, to the many volunteers, event sponsors, donors, and attendees. Truly amazing!

Save the Date

May 18 for our 2013 Wine, Stein, & Dine

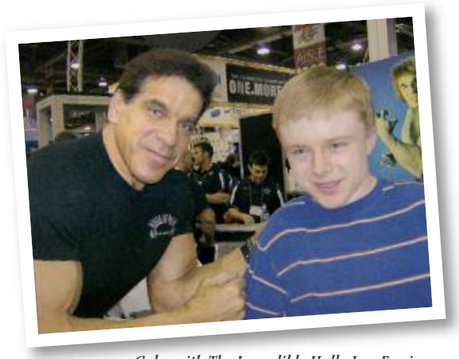
Mark and I are humbled by the generosity of our entire community. We feel encouraged, optimistic and blessed to be a part of the Cystinosis Research Foundation, as it is changing the history of cystinosis, and we are overjoyed that one day soon our precious daughter, Tina, will be cured.

By Tammy Stephenson, Gabe's mom, Dry Ridge, Kentucky

GABE STEPHENSON'S

STRONG RESPONSE

To Living With Cystinosis



Gabe with The Incredible Hulk, Lou Ferrigno.

Gabe, known as "the runner" at the April 2012 Natalie's Wish Event, did not start out running. In fact, he was 18 months old before he even walked. Eating was almost nonexistent and when he did eat, it came back in the form of projectile vomiting. Many of you noticed that Gabe looks and is very healthy. He wants to encourage other cystinotics to live life to the fullest.

Gabe is homeschooled through ABeka Academy. We believe this is one of the reasons he is so healthy and doing so well in school. When he was younger, mornings were his worst time with nausea. With homeschooling, he could get up at six for morning meds, which he took with milk, and then went back to bed for about 30–60 minutes. Then he got up for breakfast and began his school day. Today, thanks to RP103, he's up and eating at 6:30 and beginning school by 7:30.

He is in his junior year and is taking English 11, Spanish 2, Precalculus, Life Management, Chemistry, and U.S. History 11. Academically, Gabe is doing very well. Besides evening homework, Gabe helps with the farm, which includes raising produce, sheep, rabbits and honeybees. Needless to say, there is always something to do. Through 4-H, he also has his own business, Gabe's Beeswax where he sells honey, candles and lip balm.

Our family is involved in church activities as well. We also try to go to the local gym two to three days a week through the summer and four days a week through the winter.

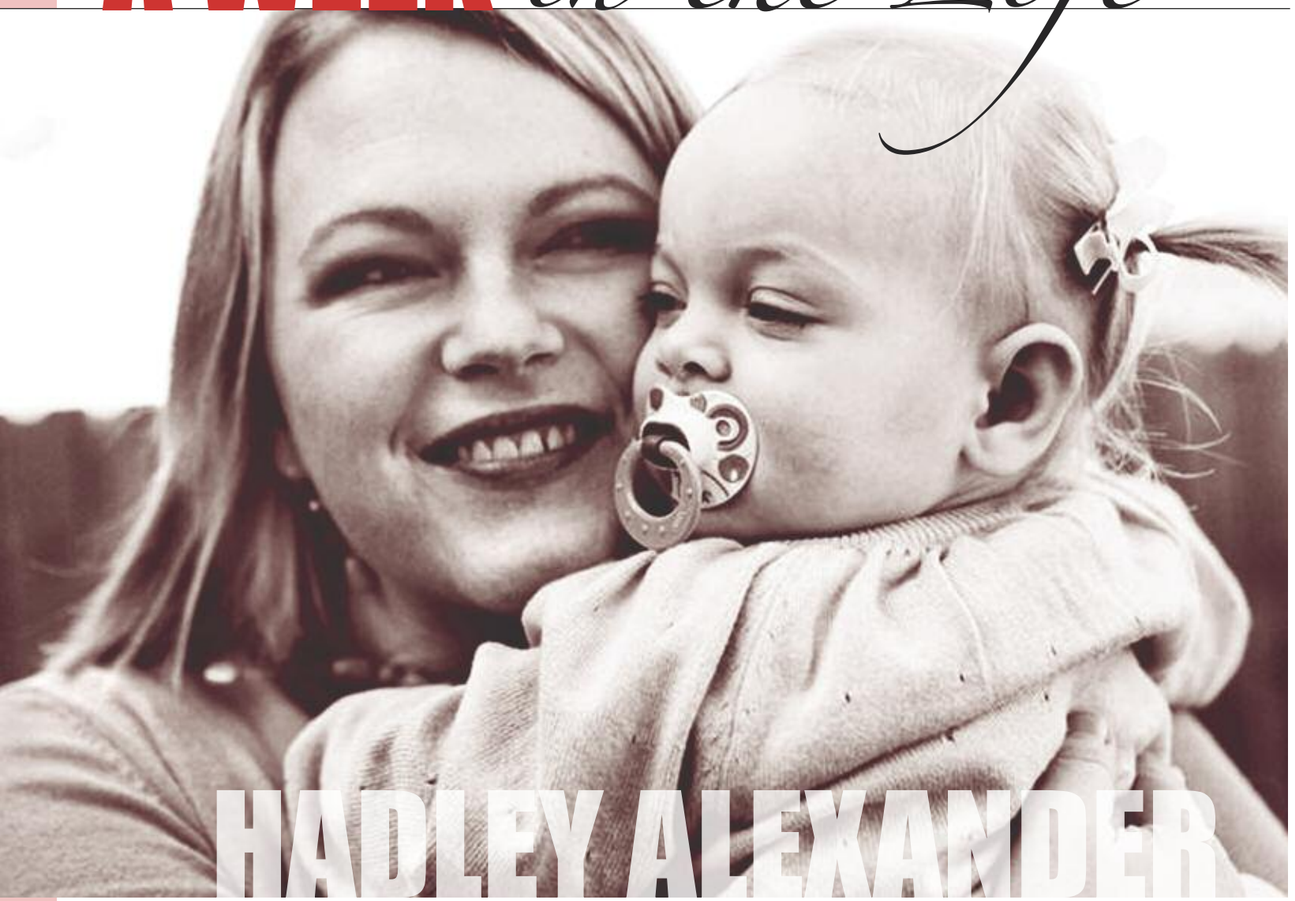
Gabe continues to enjoy keeping physically fit. In September 2011, Gabe broke his own Kentucky record for bench pressing. Weighing in at 114 pounds, he successfully pressed 130 pounds!

Although he ran on a sore ankle, Gabe was able to complete another 5K in May 2012. He finished in just over 27 minutes. He was chosen to be the race starter because the committee in charge saw the article about him in the fall 2011 issue of *Cystinosis Magazine!* What a blessing!

This summer, Gabe was enrolled in a welding course at a local vocational school. Not only will this be useful, it also means that if cystinotics take care of their bodies and take their medicine and eye drops in the correct amount and timing, there is no limit to what they can accomplish.

We were extremely encouraged by the 2012 CRF Day of Hope Family Conference. We can't wait to attend next year's conference in April. There were so many people we never got to meet. We want to share our story with other cystinotic families, especially those recently diagnosed – to give hope to them after having just received a heartbreaking diagnosis.

A WEEK *in the Life*



By Marcu Alexander, Hadley's mom
Burien, Washington

Hadley was diagnosed with cystinosis on April 4, 2012. That day will be forever ingrained in my mind as one of the most significant dates in my life. It was devastating news, yet it was a relief to finally learn what we're dealing with and it opened the door to getting her the necessary treatment.

The medicine schedule was quite daunting at first and I was concerned we'd have to alter our lifestyle to accommodate Hadley's medical needs. Thankfully, I couldn't have been more wrong. Our family has adapted well to our new "normal" and we try not to let anything get in the way of living our lives to the fullest! Hadley is a typical toddler and loves trying to keep up with her big sister, Stella. There may be bumps along the way, but we pick ourselves back up and keep on going.

A week in the life of our family looks a bit like this:

SUNDAY, AUGUST 19, 2012

6 am – My alarm goes off and I sneak in to give Hadley her morning meds. Fortunately, she stays asleep and I am able to go back to bed! Hadley gets all of her medication through a G-tube, which has provided so much relief to us. Prior to the G-tube, she didn't tolerate taking her medications orally too well and would throw up everything we gave her. Now we have peace of mind knowing she is getting each and every dose!

8:20 am – We all wake up for the day. This is a first! Our girls are usually up and ready to go by 6 am. An unusual and welcome treat!

10 am – We head out to breakfast with friends visiting from out of town. Mealtimes are always difficult for Hadley. She sits and tries to enjoy a decent meal, but she often just picks at her food and eats very little – mostly chewing her food and then spitting it out. She is making progress and fortunately we've avoided having to tube feed her. She is gaining weight and growing and that's all we can hope for!

12:30 pm – Costco trip with the family. We never plan well and always end up at Costco on weekends. This time we are able to get in and out without the girls crying or fighting. Success!

3 pm – I clean all the syringes from the prior week and prepare meds for the upcoming week. I prepare a week's worth of Cytra-K and Potassium Phosphorus each Sunday. This frees up some of my time each evening and I'm only left to prepare the daily Cystagon® doses. Three times a week, I add a dose of Vitamin D and Calcitriol.

5 pm – We take the girls to grandma and grandpa's for an overnighter so Ben and I can enjoy a much-needed date and full night's sleep!

6 pm – Ben and I head to one of our favorite local spots for dinner. I enjoy an entire meal without a child on my lap or food spilling on the floor! After dinner we head to a movie for the first time in months. It's wonderful to spend time as a couple!

10 pm – We head to bed knowing we'll sleep through the night since the kids are at my mom's and she's in charge of the midnight meds.

MONDAY, AUGUST 20, 2012

3 am – I wake up in a panic thinking I slept through Hadley's midnight meds. I wake up Ben in the process, but he kindly reminds me that the girls are at grandma's and we sink back to sleep.

5:50 am – My alarms sounds and reminds me Monday has arrived. Time to get ready for work and start the week.

7 am – Ben and I arrive at work and hit the ground running. Monday is always our busiest day. We met at work eight years ago and the rest is history!

4 pm – End of the work day! We head to my mom's to pick up the girls who I am excited to see.

5 pm – We head to Michael's craft store to pickup supplies for the girls' joint birthday party on September 1. Since the girls are only a year and two days apart, they share a party each year.

6 pm – We arrive home in time for medication and dinner. Hadley decides she doesn't want to eat and boycotts dinner. The issues around eating are one of the most stressful parts of cystinosis. I always worry when she refuses food. Luckily she drinks a ton of whole milk each day. We bolster the milk with two scoops of Duocal powder, which ensures she gets enough calories and fat each day.

7 pm – I prepare Hadley's Cystagon® for the next day and set up the rest of her medications. I use cups labeled 6 am/12 pm/6 pm/12 am to organize her daily syringes. It makes keeping track of each dose much easier!

7:30 pm – Bedtime for the girls and downtime for Ben and me. We catch up on *MasterChef* on TV and work on decorations for the girls' party.

2:30 am – Hadley wakes up crying for milk. Since Ben was on duty for midnight meds tonight, I get out of bed to tend to Hadley. She drinks at least 32 oz. of whole milk during the night. Sometimes she asks for water but milk is her drink of choice. We've been able to avoid tube feeding since she consumes so many calories throughout the night from milk. We put her to bed with two full sippy cups and have to refill them at least once during the night.

TUESDAY, AUGUST 21, 2012

6 am – Time for morning meds and to get ready for work. Hadley soaked through her diaper and her sheets need changing. I pull up her bedding and toss them in the washing machine. We use a nighttime diaper lined with a Poise pad to help combat the massive amount of urine Hadley produces each night. Unfortunately, the combo doesn't always offer enough protection so I wind up doing a ton of laundry!

6:30 am – My mom arrives to watch the girls while Ben and I go to work. She takes care of Stella and Hadley every Monday and Tuesday. She offers huge support and I'm not sure what we'd do without her!

6 pm – Finish dinner and the girls assist with Hadley's evening meds. They take turns pushing the syringes into the tube. Stella always claims the pink one (Cytra-K) and Hadley always obliges.

6:30 pm – We usher the girls to the bathtub. They're filthy from playing outside with grandma and grandpa all day. Then it's pajama time and they get to watch a show in our room before bed. The girls bicker about what to watch. Stella insists on *Go Diego Go,* Hadley demands *Yo Gabba Gabba.* Big sister wins this time!

7:30 pm – The girls are in bed after some coaxing and I'm ready to crash myself. Unfortunately, I have to finish chores so I peel myself out of Stella's bed and get to work.

8 pm – I attack a pile of laundry and wind down with Ben while watching TV. A brief moment of peace and quiet before it all starts over again!

12 am – My alarm goes off and I get out of bed to give Hadley her midnight meds. Ben and I take turns getting up to administer her meds. I am anxiously awaiting the approval of RP103 so we can all get more rest. Fortunately, Hadley sleeps through meds most of the time but the break in sleep is hard on Ben and me.

WEDNESDAY, AUGUST 22, 2012

5:30 am – Ugh! The girls woke up early today and hit the ground running. I turn on Hadley's choice, *Yo Gabba Gabba,* while we get ready for work.

6:50 am – We drop the girls off at day care, which they absolutely love attending twice a week. The center is amazing and takes such great care of my kids. Hadley's teacher administers her noon meds through her G-tube. I trust them completely and know my girls are in good hands while we are at work.

5:30 pm – My girlfriend and her daughter arrive for dinner and an evening play date. The girls have a blast while I get to enjoy a glass of wine with a friend. It's a win for everyone!

7 pm – Ben heads to the clinic for an overnight sleep study for suspected sleep apnea. He gets hooked up and monitored, but at least he gets to sleep through the night!

8:30 pm – The girls are tuckered out after playing with their friend and go to bed without much of a fight.

THURSDAY, AUGUST 23, 2012

6 am – My alarm was supposed to go off at 5:30 this morning. Instead, I sprang awake when the alarm for Hadley's meds went off at 6 am. Hadley and I were supposed to leave for the hospital at 6:20 am. Guess who didn't get a shower?

6:15 am – Ben arrives home from his sleep study in time to see Hadley and me head out after scrambling to get ready.

7 am – Hadley and I arrive at Swedish Medical Center for a VCUG (voiding cystourethrogram) test. The VCUG is being done to see if Hadley's urine is refluxing into her kidneys. She was diagnosed with pyleonephritis, a UTI and kidney infection, last month.

7:30 am – Ben arrives at the hospital after dropping Stella off at day care. I can handle most of Hadley's appointments by myself, but sometimes I need Ben's support to get through them.

9 am – We are taken to the treatment room for a blood draw, which typically does not go well for Hadley. In addition to the VCUG, it's time to check her labs and WBC cystine level. This will be the first follow-up cystine level check since diagnosis. She is a hard poke and her blood draws are usually a major ordeal. Hadley is given nitrous gas so the blood draw goes smoothly this time. The nurse then places the catheter into her bladder and we are transferred to Radiology for the test.

11:30 am – We arrive home from the hospital. Hadley doesn't have reflux and is sleeping soundly after a marathon crying session. Poor girl doesn't like getting poked and prodded! The great news is Hadley has gained weight and we're instructed to increase her Cystagon® dose to 175mg every 6 hours.

1 pm – Hadley awakes from her nap and we take advantage of our day off from work. We head to the local farmer's market and pick up a beautiful bouquet of flowers along with fresh pasta and produce for dinner.

5 pm – Hadley's nephrologist calls to inform me of Hadley's labs. Her bicarb level is low again so we were instructed to increase her Cytra-K to 5ml every 6 hours. On the positive side, her Vitamin D level is normal and we are told to reduce the amount from daily to only three times per week.

6 pm – We meet some friends at a park to watch a free Caspar Babypants concert. We enjoy a picnic as the girls dance and play with their friends.

7 pm – After the concert we head for a frozen yogurt treat at Menchies! Nothing like getting the kids wired right before bedtime. Oh well, it's good to break the rules every so often.

9 pm – Late night to bed for the girls! Ben and I follow shortly behind them.

FRIDAY, AUGUST 24, 2012

6 am – TGIF! Up for the day and give Hadley her morning meds. I get ready for work while Ben tends to the girls. Since we work together, we were able to negotiate our schedules after having children. We now work four nine-hour shifts and one four-hour shift. On Fridays, I work 7 am–11 am and Ben works 12 pm–4 pm. It gives us extra time with the girls and saves money on day care.

12 pm – The girls and I meet a friend and her two daughters for a pizza. After lunch we walk to a nearby park where the girls play and we can catch up.

1 pm – As promised, I take the girls to Build-a-Bear for being good all day. A friend gave the girls a Build-a-Bear gift card shortly after Hadley's diagnosis. She wanted the girls to have something to remind them of each other when they have to spend time apart. The girls took the bear-building experience very seriously. Stella took the liberty of naming both bears. Susie and Audrey Ted are now proud members of our family!

2 pm – Stella, Hadley and I all take a nap after our afternoon fun. It's a rare event for me to sneak in a nap and I cherish the days when they occur.

4:30 pm – The girls and I pick Ben up from work on the way to a BBQ hosted by our day care. We enjoy dinner while the girls play with their friends and we become better acquainted with the parents. Parents chatter about the overnighter at the day care later that evening. Our day care offers parents' night out once a month where you can drop your kids off overnight for a reasonable price. We decide to sign the girls up for their first overnighter. Hadley's teacher is in charge, so I feel comfortable leaving Hadley. Amy knows how to do the meds and will be able to accommodate the midnight and 6 am doses.

7 pm – We drop the girls off at day care for their big slumber party. I am a little anxious about leaving Hadley but I know the experience will be good for both of us. She is very attached to me and time away from me will help foster some independence for her.

7:30 pm – Ben and I arrive at a favorite spot for appetizers and drinks. We talk about how lucky we are to score two date nights in one week. That hasn't happened since we had children.

9 pm – We arrive home and are ready for bed! I quickly fall asleep and enjoy a full night of much-needed rest.

SATURDAY, AUGUST 25, 2012

7 am – Rise and shine! I was hoping I'd be able to sleep a bit longer but my internal clock wakes me up early even when I have the chance to sleep in.

8 am – We arrive at day care to pick the girls up from the overnighter. I'm anxious to see them and hear how it went. The kids were just waking up and it was obvious everyone had a great time. Stella fills us in on the evening's events while Hadley talks non-stop about Bunny Foo-Foo, the rabbit. She is mildly obsessed with all living creatures!

9 am – We ask the girls what they want to do and Stella insists we find some yard sales. We grab breakfast and cruise around the neighborhood looking for yard sale treasures.

10 am – In between yard sale stops, we have to pull over because Hadley has thrown up all over herself. We don't have a spare outfit so I put her in Stella's pajama top from the sleep over. It usually takes a few weeks for Hadley to adjust to increases of Cystagon®. She throws up most days but is used to it by now and bounces right back.

12 pm – We return home for Hadley's noon meds. The girls take turns pushing in the syringes and then sit down to eat lunch. Hadley is uninterested in her meal and barely takes a bite.

1 pm – I kiss the girls good-bye and head to a friend's house for a baby shower.

4 pm – We arrive at our friends' house for their annual BBQ fundraiser for Children's Hospital. Sadly, their first child passed away at Children's at only eight weeks old. Our friends host a fundraiser each year in honor of their sweet baby boy and we have gone every year to offer our support and love for their family.

6:30 pm – Hadley throws up her meds all over our friends' deck. I get a couple of looks from guests who don't know about Hadley and her condition. It's hard to explain to strangers that my child isn't contagious; she just has trouble tolerating her medication.

8 pm – Home again after the BBQ with tired and dirty kids! The fundraiser was a success and our girls had fun playing with all of the kids at the party. We put the girls to bed without baths and head to the couch for a movie.

10:30 pm – We head to bed after finishing another busy and exciting week! I think about our friends who lost their baby boy and think how fortunate we are to have our two girls here with us. Times like these make me realize that things could be so much worse. Cystinosis is a terrible disease and one I wish didn't exist, but we are facing it head on and doing everything we can to make sure Hadley has the best treatment possible. We want both of our girls to live fully and we will do everything in our power to make that happen!

To keep up with Hadley and the rest of our family, visit our family blog www.bencu.wordpress.com.

WHITNEY GLAIZE SHARES

ANOTHER JOURNEY IN HER LIFE WITH CYSTINOSIS

Sandy, Whitney's mom with Whitney

> *I hope future generations of cystinosis patients never need a transplant because the cure will alleviate the need.*

On October 26, 2011, I began yet another journey in my life with cystinosis. It was a day that I knew would eventually come and for patients with cystinosis it is an inevitable part of the disease. On October 26, I underwent a kidney transplant. I was fortunate enough to receive a kidney from my mom.

I believe that the past year of my life, since the transplant, has been one of the most challenging, medically speaking. I think that my "post transplant" life has been more stressful than the entirety of all my pre-transplant years. I was blessed to be able to put off the necessity of a kidney transplant for such a long time, something that, to date, no other patient with cystinosis has been able to do. When I was diagnosed with cystinosis in 1980 it was predicted that I would require a kidney transplant by age 10. However, I was 33 by the time my native kidneys failed.

I knew that having a transplant would not cure cystinosis but somehow I thought my life would become easier after I got a new kidney. This has been the farthest thing from the truth. Since transplant my creatinine has fluctuated more than ever before. I have had more blood drawn than one can conceive, on average three times a week, far more than the once every two months blood draw I had before transplant.

My medications have caused severe side effects, including nephrotoxicity, which means literally "toxic" to my kidney, one of the reasons my creatinine was fluctuating. Because I am super sensitive to the anti-rejection medications I take I have a very low white count (white blood cells), which means I am at even a higher risk of infection than the "typical" post-transplant patient. In fact, I have had four colds in the last 11 months; pre-transplant I averaged one a year. One of the anti-rejection medications made my hair fall out. Because my kidneys were so preserved by my compliant use of cysteamine I also preserved my Fanconi syndrome and continue to require electrolyte supplements. Because I was never on dialysis and had a relatively low creatinine (4.9) at time of transplant, my native kidneys are still working and need lots of water, sodium and potassium. In hindsight I would have had my old kidneys removed at the time of my transplant, which I discussed with my nephrologist. He was positive they would not be problematic post-transplant but he has never had another cystinosis patient. Twelve hours after transplant my creatinine had fallen to 0.8 from 4.9. I have more issues now than pre-transplant with low Hemoglobin, partly because my blood is drawn so often. My mom's kidney works beautifully for me, but there are still many factors with a kidney transplant that I was clueless about.

The surgery itself was a piece of cake for both my mom and me. Five months after donating a kidney to me, my mom had a hip replacement and she said that it was far worse pain and recovery then giving me a kidney. I was working out in the gym six weeks after my transplant. I gained about 25 pounds of water weight, which scared me to death, since none of my clothes fit. Thankfully the pounds came off and just a month after my surgery I was back down to my pre-transplant weight of 100 pounds. I had the most amazing surgeon who did an outstanding job. My scar is barely visible.

On the bright side, 11 (long) months after my transplant my creatinine is stable and for the time being we have figured out the right anti-rejection cocktail. My creatinine hovers around 1.1, which frustrates me because it was originally 0.8. I strongly believe that is due to the medications I take to prevent rejection.

I got a fabulous report from Dr. Gahl and his team earlier this month and although my compliance with cysteamine has caused some post-transplant issues, it has spared my body from any muscle atrophy and I have no signs of weakness or loss of muscle function. I still hold my breath every time I get my blood drawn and I say a little prayer that my creatinine comes back below 1.2, the highest normal value. The lab techs who draw my blood have become Facebook friends and they also say a prayer as they put the tubes of blood in the plastic bag that couriers them to the lab.

I was able to return to work four months after my transplant and continue to be able to work full time teaching special needs preschoolers. I have more energy, although I am disappointed that it is not nearly as much as I had hoped for.

I pray that I will never need another kidney transplant and that future generations of cystinosis patients will not need one either because the cure for cystinosis will alleviate the need. I would never wish this on anybody. A kidney transplant is merely a band-aid for cystinosis. My new kidney does not have cystinosis but the rest of my body still does.

OVER THE HILL
AND THROUGH THE WOODS TOWARDS A CURE

Henry and his dad Brian Sturgis

By Tricia and Brian Sturgis, Henry's mom and dad, Sandpoint, Idaho

Henry (aka Hank) Sturgis turned six on July 19. He started kindergarten in the first week of September and lost his first tooth in the same week! We have seen a lot of positive growth and progress with Henry this year. He is happy, outgoing and eager to learn. Right now Henry is enrolled in morning kindergarten five days a week and the school has been wonderful in helping us make his first public school experience positive. He has Occupational Therapy (OT) and Physical Therapy through the school and one private OT per week.

Henry loves to roughhouse and play super heroes. Henry still takes cold water and Chocolate Boost Plus almost everywhere we go. He loves to eat corn with extra butter and salt, along with chocolate chip cookies or pickles. He recently was fitted for orthotics and is wearing them in his shoes to help improve his balance.

We are continually challenged by tremendous amounts of laundry, mealtimes and being prepared with medications and supplies for travel or emergencies.

We had two extraordinary fundraisers this year – our Ski Race in April and our Bike Race in September – which combined raised approximately $200,000.

24 HOURS OF SCHWEITZER

"Faster than a speeding bullet," summed up performances at the *24 Hours of Schweitzer* fundraiser at the end of March, held in our hometown of Sandpoint, Idaho. Nearly 130 skiers and snowboarders – ages 5 to 74 – displayed heroic efforts in spite of stormy weather that caused the first delay in the ski relay's four-year history.

Despite the challenges the event raised a record $165,000.

Participants from Sandpoint, Spokane, Ellensburg, Issaquah and around the region, and as far away as California, Colorado, Oregon and New York took to the slopes with a mission to complete the most runs possible in 24 hours straight. Mother Nature, however, had plans of her own. Gusty winds and pounding rain closed most of Schweitzer Mountain Resort for the day and caused a 7½ hour delay before participants' runs were officially counted.

Once counting was underway, skiers and boarders made up for lost time, logging an impressive 7,774 runs or 7,064,310 vertical feet in just 16 ½ hours. The all-day, all-night ski event concluded with an auction dinner/ awards party attended by 375 people, with many dressed in costume to celebrate the event's *Hank's Heroes: Mission Possible* superhero theme.

This year's race was down to the wire, with three-time defending champion Matt Gillis sealing his fourth victory after narrowly edging Eric Jensen to finish with 143 runs. Gillis also individually raised a record $33,000, earning repeat honors as the event's top fundraiser and doubling his personal fundraising total from last year's event.

In the four-person team category, Team "Hank E Panky" took first place with 501 runs, while Team "Fill the Bank for Hank" placed second with 480 runs. Team "Blue Eyed Bombers" logged 381 runs to earn first-place honors for the second year in the three-person team category.

Finan Lund, age 12 of Sandpoint, was the top finisher of "Kids 12 and Under" with 126 runs; and Sam Timmons, age 8 of Denver, Colorado, was the top youth fundraiser with $5,223 in pledges. Other standouts included Slate Fragoso, age 7 of Sandpoint, who logged 71 runs and raised $4,000, and Crosby Schmidt, age 5 of Sandpoint, who raised $2,425 and completed 43 official runs.


Henry and Matt Gillis

Reporters Mark Peterson, Kris Crocker and Robyn Nance from KXLY-TV in Spokane gave new meaning to the term "media mogul" after carving 40 runs down the mountain and raising more than $2,000 toward the cause.

Other participants included 17-year-old Paul Flerchinger of Spokane Valley, who skied in honor of his 8-year-old cousin Tina Flerchinger of Clarkston, Washington, who also has cystinosis. Paul's three-man team from Gonzaga Prep completed 268 runs.

"We were continually amazed at the incredible endurance, dedication and spirit demonstrated day and night throughout the event, in spite of the very challenging weather conditions. Every participant is a super hero in our book," said Brian Sturgis, Hank's dad and one of the event organizers. Schweitzer Mountain Resort stayed open all night, with lift operators encouraging participants throughout the evening, ski patrol on stand-by to provide assistance, event crews coordinating rope lines and signage, and employees helping with lodging and meals.

More than 40 volunteers helped around the clock with planning, coordination and on-site assistance at the ski event and auction to make this year's event the most successful ever.

MARK YOUR CALENDAR
March 22–23, 2013
Planning is already underway for the 5th Annual *24 Hours of Schweitzer* ski race at Schweitzer Mountain Resort.

CYCLING FOR CYSTINOSIS

HENRY

At the *24 Hour Bike Race* a fun-time was had by all. Special thanks to our wonderful hosts Mike and Jeanne Rosenberger of Sandpoint, Idaho who graciously allowed us to use their property to run the event.

We also couldn't do it without all the volunteers who worked at multiple locations along the 19-mile loop, counting riders as they completed laps throughout the night.

There were amazing performances all around as 68 bike participants and one outstanding runner, ranging in age from 3 to 74 years old, combined to raise more than $40,000 to help find a cure for Henry and all those with cystinosis. Sandpoint cyclist Jacob Styer won the solo division, turning the pedals to the tune of 418 miles, which equaled 22 laps.

Local runner Chuy Fragoso stole the show, running 106 miles in 23.5 hours, raising more than $23,000 on his own, which was more than half of the total amount raised. He had hoped to run 200 miles in 40 hours and raise $25,000 for a cause that has become very close to his heart. A nagging hip injury proved too painful, and forced him to stop. Chuy wrote to his supporters on Facebook: "I am proud to say that more than $22,000 was raised and money is still coming in! Going into this I had three goals: to raise money for cystinosis research, to raise awareness of cystinosis, and to push my body to its physical limit. Lucky for me this endeavor was not a race or a competition, it was an effort to raise funds for a cause that I am extremely passionate about. Although I did not complete the 200 miles, I did push my body to its limit. A nagging left hip (for the last 6–7 weeks) brought on other issues and pain that ultimately made progress extremely slow and painful and the decision was made to call it a day at 106.25 miles in 23.5 hours! I cannot thank you enough for your contributions in helping me achieve my most important goal, changing the lives of children and families with cystinosis. This entire experience has been extremely humbling, when I say this I am not referring to my physical performance but to the performance of all who heard my voice, in this my cry for help, for this cause. Never underestimate the good that is in all of us."

Matt Gillis and Chuy Fragoso

We want to thank our family, friends, volunteers, community, Henry's doctors and health care providers, researchers studying cystinosis and last but not least, Nancy and Jeff Stack of the Cystinosis Research Foundation. You all give us so much hope!

By Paul Flerchinger, Tina Flerchinger's cousin

GETTING WILD AND CRAZY

While visiting my Aunt Denice (Flerchinger) one day, she mentioned the idea of skiing for 24 hours to help her daughter and my cousin, Tina, fundraise for a cure for cystinosis. I thought to myself, *skiing for 24 hours … that would be wild and crazy; why not!*

FOR HANK, TINA AND A CURE

Paul Flerchinger, Cameron Dolsby and Matt Baker

I started asking friends about their skiing abilities and whether they would want to ski for 24 hours to help Tina. My good friends Cameron Dolsby and Matt Baker said, "Skiing for 24 hours straight? That would be awesome!"

After we actually committed, I started fundraising like mad. I began at home going through my parents' contacts. When I sent out the emails, I didn't expect anyone to respond, let alone give money. Honestly, I was amazed at the generosity of so many people.

Then, I went to school and had an all-school announcement made to donate to *24 Hours for Hank.* My physics teacher allowed me to show a short clip to the class about Tina because, "a picture is worth a thousand words." In that class alone, I received more than $50 and had people asking what else they could do to help. This nearly brought tears to my eyes. It really shows that people care about others and want to help in any way they can.

Tina, Julie and Paul

When people saw Tina's picture, they immediately said, "She is the perfect candidate for this disease. She is so cute and has an awesome smile – who wouldn't want to help her."

The race itself was exhilarating. We started at 8 a.m. and it was already raining. We all thought the whole trip would be miserable with the weather, but we just kept skiing. A couple of hours passed, and we got to move off of the bunny hill where the weather gradually started to change to snow. Our spirits lifted, we began powering through runs. On the lifts up, we would plan our next route and talk with the others on the lift. Between 2 a.m. and 5 a.m. there was a bit of a mental fog and my team and I seemed to laugh at everything anyone said.

As the end of the race was closing in, it began to get harder and harder to continue even though we knew we were close to finishing. Our legs really started to fatigue, yet with an hour left, we knew we couldn't stop. At 7:50 a.m. we all gathered to ski down as a crowd to the finish. Everyone clapped and was happy to be done with the 24 hours of skiing.

When we went inside to find out how many laps Matt, Cameron and I had skied, the board said "298." We were disappointed to miss our goal of 300 laps but it was great knowing that we had tried our best and had a ton of fun doing it. And it means that Matt, Cameron and I will have to come back next year to get those last two runs in.

This truly is one of my favorite memories and a great way to help the Cystinosis Research Foundation, Tina Flerchinger, Henry Sturgis and all others with this terrible disease.

Tina is one of my favorite cousins and together with the Cystinosis Research Foundation, we will find the cure.

Paul Flerchinger, Tina Flerchinger's 18-year-old cousin, lives in Spokane, Washington and during the ski event he was a senior at Gonzaga Preparatory High School, along with buddies Cameron Dolsby and Matt Baker. Paul is now attending Washington State University, pursing a Mechanical Engineering degree. When not busy helping to raise money for Tina, Paul is a private pilot flying as much as he can, he builds and flies RC planes, and plays tennis along with many other outdoor activities. He enjoys family time, especially with his older sister Julie and younger sister Dana.

Matt and Cameron are also off to college this year, where socializing, being outdoors and helping others are always on their list of things to do.

Many Hands Make Lite Work

TOGETHER WE ARE MAKING A DIFFERENCE

KICK'N UP KOUNTRY MUSIC FESTIVAL

On Thursday, June 14, 2012, Caleb Gowan was one of the opening acts for the three-day long *Kick'n Up Kountry* music festival in his hometown of Karlstad, Minnesota. Caleb won the "Little Kickers" karaoke contest for the eight-and-younger age group with his version of the Zac Brown Band song, *Knee Deep*. Caleb's friend, Roxie made baked goods and raised $540 for cystinosis research. Unfortunately, it rained the last two days of the festival but it was a lot of fun educating others about cystinosis. Caleb had a blast and hopes to enter the contest again next year!

Caleb lives with cystinosis but he is still an active and bright young man who always sees the glass half full. Way to go Caleb!

LOTS OF LOVE FOR Landon

Benefiting the Cystinosis Research Foundation

LOTS OF LOVE FOR LANDON GOLF OUTING

The *Lots of Love for Landon* Golf Event took place on July 6, 2012 at the Ponderosa Golf Course in Hookstown, Pennsylvania. Golfers included Landon's family and friends, as well as local business people.

The event included a 50/50 raffle, Chinese auction, and skill prizes in addition to 18 holes of golf.

Landon is a loving, funny and energetic 2 ½ year old, who was diagnosed with cystinosis in June of 2011. He is thriving now after his diagnosis last year. Landon and his parents are excited to welcome a baby brother in January.

Landon's uncle, Jason Whitfield along with his friend and colleague Chris Krasny organized the event with support from Landon's parents, Jimmy and Lauren, his grandparents, and his aunts and uncles.

Approximately $7,500 was raised at the golf event.

HALLOWEEN EVENT FOR LANDON

Jimmy, Lauren and Landon Hartz are excited to announce the 2nd Annual *Lots of Love for Landon* Halloween Event. The event was held on Saturday, November 3, 2012 in Pittsburgh, Pennsylvania.

Watch for an update in our next issue of *Cystinosis Magazine.*

For information about future *Lots of Love for Landon* events or to be included on our guest list, contact Jimmy and Lauren at 412-841-3594 or LaurenLHartz@gmail.com

Music for Mary

A BENEFIT CONCERT BY THE OLY MOUNTAIN BOYS

Music for Mary, was held on October 5 at the Tacoma Sportsman's Club in Puyallup, Washington. It was the first event organized by Melissa and J.R. Head in honor of their four-year-old daughter Mary, who has cystinosis.

More than 200 guests attended the event that featured entertainment by popular local band Oly Mountain Boys, a real crowd favorite. There was also a silent auction with 65 items and a live auction.

Guests enjoyed an Italian soda bar during the silent auction and dined on a delicious buffet dinner. But the evening's real dining surprise was the dessert raffle. Guests at each table drew numbers to determine when they would get to visit the table at the back of the room showcasing 25 luscious desserts.

In addition to music by the Oly Mountain Boys, MC "Uncle Gary," entertained guests between sets with a great game of Heads and Tails that had everyone in the room rollicking.

After watching an emotional video about cystinosis, there was an energetic live auction with 10 items. Initially, Mary was proud of herself because she didn't cry when she went on stage! That quickly changed as she ended up being a terrific auction assistant, madly waving bid numbers and driving up prices.

Mary was clearly the belle of the ball throughout the evening, visiting with old friends and making new ones in between helping herself to the buffet and desserts.

The evening was a tremendous success, raising more than $17,000 for the Cystinosis Research Foundation.

Melissa and J.R. say plans are already underway for next year's event!

THE AKINS CONCERT TO BENEFIT CAMDEN AND CYSTINOSIS RESEARCH

With The Akins – three brothers and a dad – their faith and family values shape everything they do. Their musical talent, tight family harmonies, and live instruments create a unique sound that is enjoyed by all ages.

On Saturday, November 10, The Akins performed their second concert to benefit Camden and the Cystinosis Research Foundation. The event took place in the Gray United Methodist Church in Gray, Georgia.

Look for an update of this successful event in our next issue of *Cystinosis Magazine.*

Bailey Believes
Ride for a Cure

By Jessica Dedio, Bailey's mom

It started with five people who wanted to find a cure for Bailey – Bailey, Jay and me, of course – and my mom, Sherry, and step dad, Tim Boucher. It was all about love, hard work, determination, dedication and never giving up on your dreams. The event was all the more special because it is Bailey's love of riding dirt bikes that started our journey to the first annual *Bailey Believes Ride for a Cure* on Saturday, October 20.

On Friday, the day before the event, we drove to Barstow, in the middle of the desert, to get the camp ready. Every time a truck, toy hauler or motor home pulled up, I looked up and thanked God that people were actually coming out to help us raise money to find a cure for cystinosis.

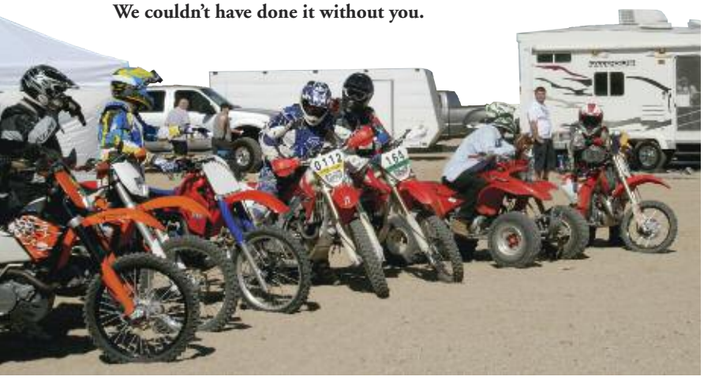
I was so nervous about how the event would turn out, I didn't sleep a wink that night. At 9:30 am on Saturday, when people started to walk through the registration line, I was overwhelmed with love. I wanted to hug every one of them and let them know how much this meant to us.

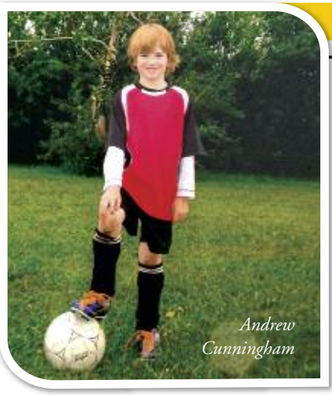
There were three groups: Pro, Intermediate and Beginner, and when they started up their motorcycles I got chills all over my body. Fortunately, everyone came back from the ride safe and with a big smile on their face.

For lunch, we grilled sausages and hot dogs, had potato salad and chips, and drank sodas, water and beer. Everyone mingled and had a great time. Of course, Bailey was quickly back on his bike riding with his friends Dustin, Amanda and Brandon – he was in heaven.

At 3:30 pm, our raffle/silent auction began, and like the rest of the day, it was a wonderful success, helping us raise $12,215 for the event. All of the money will go to the Cystinosis Research Foundation to help find a cure.

We want to thank everyone who helped make our first *Bailey Believes Ride for a Cure* a success, from the bottom of our hearts. We couldn't have done it without you.





Andrew Cunningham

FORE FATHERS – JCFG MEMORIAL
GOLF TOURNAMENT

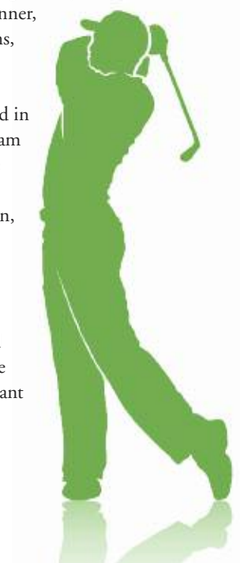
Karen McCullagh-Cunningham and her family organized the *First Annual Fore Fathers – JCFG Memorial Golf Tournament* at the Boulder Creek Golf Course in Alberta, Canada. The event, held on September 29, hosted 144 enthusiastic golfers and was supported by 20 volunteers. The goal was to raise awareness and money for both heart disease and cystinosis.

The event raised $25,000 – with $10,000 going to support cystinosis research. Charitable donations were directed to CARE (Cystinosis Awareness & Research Effort) of Canada and non-charitable donations were sent directly to the Cystinosis Research Foundation.

The tournament sold out in six days and turned into a day filled with fun, laughter and friendly competition. Following the day of golf, 200 guests enjoyed dinner, awards, live and silent auctions, and entertainment by Karen's brother Alan.

The tournament was held in honour of Andrew Cunningham and in memory of four of the organizer's fathers – John McCullagh, Conway Cameron, Frank Halluk and Gordon Cunningham – who all died of heart attacks in their 60s.

Karen and Don's son Andrew, age 9, was diagnosed with cystinosis in 2005, so the whole family felt it was important to do something to support research in hopes of a cure.



WET TEE-SHOT

Tina's Hope for a Cure

TINA

The *Wet Tee-Shot* has been a staple of Pacific Empire Radio's summer events for six years. The venue has changed since the first event but it has grown stronger each year. The *Wet Tee-Shot* this year was held at The Lewiston Golf & Country Club and sponsored by Kendall Motors. Listeners responded in a huge way when Kendall Motors set up the largest Grand Prize to date: $30,000 in cash or a car!

Each Thursday for six weeks, participants had the opportunity to hit one free golf shot into floating rings on the driving range. They could then purchase three additional shots for $5. Those who made it into one of the rings during the qualifying nights were invited back for a chance at the Grand Prize on the final night. The *Wet Tee-Shot* is a fun-filled competition that will be going on for many years.

Pacific Empire Radio has been a wonderful friend to Tina, donating 100 percent of the proceeds for the additional balls purchased by contestants to *Tina's Hope for a Cure* and the Cystinosis Research Foundation. More than $1,200 was raised during this year's event!

Thank you to everyone who made the 2012 *Wet Tee-Shot* a success. We hope to see you again next year!

Freek Wonnink of Kampen, Holland organized his first fundraising event in May to help the Cystinosis Research Foundation. Surrounded by a very supportive and generous community, Freek raised $3,200 at the event, which featured two live bands, an amazing DJ and an incredible laser light show. The venue, called The Trunk, that accommodated the more than 150 guests was a unique theater and was offered free of charge by the owners. Most of the evening's beverages were donated by Horecagroothandel Brouwer, a local beverage wholesaler. The event, which went into the early morning hours, was designed to raise awareness and money for research. Plans are underway for the next fundraiser in May 2013.

Freek, who is CEO of his own software development company, was diagnosed with cystinosis 30 years ago. He loves to travel and makes about four trips to the United States each year. In August he stopped by the CRF offices to present his check to CRF Board Treasurer Don Solsby.

BIDDING HIGH FOR A CURE

Friends of *Joshua's Journey of Hope* worked diligently for months organizing its Second Online Fundraising Auction held from September 6 through September 16. Those efforts paid off handsomely, raising more than $10,000 to support Joshua Clarke and cystinosis research.

More than 250 items were donated from generous merchants and points-of-interest across the nation. Most of the items offered discounts of up to 50 percent. The auction provided bargains from theme park tickets, restaurants and golf course gift certificates to wine tasting tours, vintage items and collectibles plus special hotel packages and exotic vacation getaways. There were more than 1,000 bids and nearly every item was sold!

Since many of the items were from national companies, more than half of the bidders were from outside of California. Even Hawaii was represented. This broad exposure helped to increase awareness about cystinosis to a wide variety of people in a non-traditional way.

Joshua's Journey of Hope

The JJOH board is already planning its third online auction in September 2013. To learn more about Joshua and the JJOH activities visit www.joshuasjourney.org

PARTIAL LIST OF AUCTION ITEM DONORS

American Girl
Angels Baseball
Aquarium of the Bay
Bay Area Discovery Museum
Build-A-Bear
Charles Schultz Museum
Disneyland
Golden State Warriors
Hearst Castle
Knott's Berry Farm
Legoland & Sea Life Aquarium
Los Angeles Dodgers
Palm Springs Aerial Tramway
Ripley's Believe It or Not
San Diego Zoo
Sea World San Diego
Six Flags Magic Mountain
Toyota Speedway
USS Hornet Museum
V. Sattui Winery
VANS (Off the wall)
Walt Disney Family Museum
Winchester Mystery House

I'm gonna change the world somehow . . .

Much has been written about the power of the pen to change the world and make it a better place. Couple that power with the wonderful voice of a young girl mature beyond her years and you have indeed experienced a remarkable accomplishment.

Such is the case with a recording by Samantha Catalano, which is creating a broader awareness of Natalie Stack's wish ***to have my disease go away forever.***

Samantha is the 17-year-old daughter of Lisa and Tony Catalano, a Sares-Regis colleague of Jeff Stack. The Catalano's are longtime supporters of the Cystinosis Research Foundation. Samantha recently decided she could do even more, using some very special gifts of her own. She recorded a song she wrote – words and music – (as well as designing the CD jacket) to help Natalie and all those with cystinosis.

In words that belie her young age, Samantha writes of Natalie, "I'm gonna change the world somehow." Given the exceptional talents she demonstrates on her recording of *Natalie's Wish,* Samantha clearly has that same ability.

Thank you, Samantha for your powerful music and sentiments. Thanks also for reminding us, that we all have the ability – regardless of age, position or financial status – to make a difference in the journey to finding a cure for cystinosis.

People who hear about the Cystinosis Research Foundation often ask, "How can we help?"

Erin and Chad Little have joined the growing ranks of cystinosis families who have come up with their own unique way to answer that question.

STEP UP FOR A CURE

Erin and Chad Little of Ontario, Canada are the parents of two-year-old Olivia, who was diagnosed with cystinosis when she was 18 months old. Today, Olivia weighs 25 pounds, her cystine levels are good and she is doing well. Eating is a never-ending battle for Olivia, so Erin is constantly counting her calories and chasing her with food.

Erin runs a full-time child care business from her home so Olivia is always on the go, keeping up with the others. Olivia loves to cook, play stickers, read stories and swing on the "big boy" swings. She is full of life and never misses a beat. From the outside you'd never know she was dying on the inside.

Caring for Olivia doesn't leave much time for outside activities, but like so many parents of children with cystinosis, Erin and Chad wanted to find a way to support the Cystinosis Research Foundation. In 2010, Erin started building and selling small stools that are as handy as they are cute. Today, the small family-run business – ***Step Up For A Cure*** – seems to have caught on.

Erin, who is genuinely surprised says, "The stools were a hit almost from the beginning. And now, the orders just keep rolling in for the stools."

A local firm, the Southampton Market in Ontario, builds the stools and sells them to Chad's mom and dad at a discount. "Bruce and Dianne then give them to Chad and me, and we sand, paint and decorate them," Erin says. "Chad and I pay for the sandpaper, paint, brushes and other supplies. Bruce and Dianne sell the stools in a store they own at the beach and we also sell them on Facebook, so 100 percent of the profits go to CRF"

"People can order standard designs: *Time Out, Penalty Box* and *This Stool is Mine,* or I can create custom designs for a slightly higher price. One woman has a son who loves pirates, so I used skulls instead of polka dots. Then I added his name," Erin said.

Erin and Chad set a goal of raising $2,000 this summer. They exceeded that goal, and are now hoping to raise an additional $2,000 by selling 50 more stools by Christmas.

"We're thrilled that people like our product. This has been a hobby of mine since 2010. I would dibble dabble with it and sell a few. Then when Olivia got sick in 2011, we made the decision that in 2012 we would donate the money for research," Erin adds.

PRICES:

Time Out, Penalty Box and This Stool is Mine are $40.

Adding a name costs $5.

Zebra or other animal prints are $50

Shipping costs vary but typically range from $25 – $40.

For information or to order a stool, email Erin at ce.little@bmts.com

I have always found inspiration from the wisdom of others and tried to leverage it in a meaningful way. I think that in and of itself it is one of the greatest gifts you can give yourself. The ability to be an enthusiastic learner and to leverage what you learn for the good of others is paramount to creating not only a positive sense of community but also a key driver in your quest to accomplish your dreams.

LIFE LESSONS

As we head into the heart of the fall football season, I am continually reminded that this is the time of year when I learned many of the most important lessons my father passed down to my brothers and me.

My dad was a salesperson by trade but his passion was coaching youth sports. I'm not sure why he wanted to be a coach. Maybe it was his natural competitive spirit, a need to connect in a meaningful way with others or maybe he simply realized that he had a gift for it and he wanted to see where this gift would take him. Coaching was what he was born to do – it was in his DNA and he was really good at it.

Looking back, I realize that his passion was only partially about the actual coaching of the sport. Beyond wanting to win, coaching was his platform for making a contribution to the world. He used that platform to teach life lessons to area youth. He certainly wanted to win but he also wanted to produce good citizens who were productive and contributing members of the community.

Dad passed away in 1999 from cancer and I often reflect on many of the lessons he taught me and my teammates growing up.

As a member of the cystinosis community I think it would be benefical to share a few of dad's memorable quotes and lessons with you. His lessons are not only a foundation for sports but they can also help each of us in the cystinosis community. As my good friend Kris Elftmann reminded me, "These concepts are critical to CRF's mission of finding a cure. They bind cystinosis patients, family members, friends, doctors, donors and supporters together. Every member of these groups brings different gifts and strengths – some large, some small, but all essential to victory. By doing and giving what and where we can, we are all able to contribute to finding the cure."

I hope you find inspiration from my dad and leverage his wisdom in a way that helps move your own goals and dreams forward, as well as those of the Cystinosis Research Foundation.

"Dad" Grier and two of his sons at a game, of course!

"If it's to be, it's up to me." *(The importance of hard work)* – If this doesn't describe Nancy Stack perfectly in a single sentence, I don't know what does. She is tireless in promoting the mission of the CRF – better treatments and ultimately a cure. I've never met anyone more determined, more laser-focused and more driven. Yet, she is equally compassionate, caring and generous.

"Winners never quit, quitters never win." *(Dedication)* – Think about cystinosis patients and their parents who work 24/7/365 to maintain onerous dosing schedules. A six-hour schedule is hard to do every day for one week. Now imagine how difficult it is for a cystinosis patient to maintain that schedule day in and day out *without ever getting a break.* They are simply amazing. They are heroes and it is because of their courage that we all stand beside them and take on this challenge.

"If it was easy, everyone would do it." *(Commitment)* – All the families across the country who have poured their hearts into fundraising. Whether it's $5 or $50,000, every dollar sent to CRF goes directly to research – research that is making a difference. Each of us has our own struggles – struggles that come in all shapes and sizes. Fundraising isn't easy and it's not much fun. If it was, everyone would do it. We are so close to reaching our goals but it does take a village. It isn't easy for sure, but don't quit.

"Be willing to do what others aren't." *(Sacrifice)* – Dr. Stéphanie Cherqui and her ability to step outside the box – to "go for it." I can't help but wonder where we would be if she didn't do what she does. I don't know, but I'm glad that she and other researchers are willing to do what so many others will not do! Thank you Dr. Cherqui!

"Don't sit on your helmet; you'll warp it." *(I'm convinced that dad made this one up)* – While I still don't think you can warp a football helmet by sitting on it, dad was trying to convey respect for what you have. Whether it was untying your shoes before you put them on or putting things back in their place, he taught me the importance of having respect for, and taking care of, your equipment. As I think about the CRF, the equipment is our base of friends and family and even strangers. Communication is our equipment and it is key to ensuring that you are apprised of the progress that is being made.

Now for Holt! He is thriving!

Simply put – the 12-hour dose has changed his life and is giving him the opportunity to compete. He is active and energetic, and enthusiastic about spending time with others. And he is performing at a high level in school. Chrissy recently came home from his first parent-teacher conference. I came in after being out of town and she had tears in her eyes. I was prepared for the worst. What I didn't realize was that they were tears of joy. She said, "He is doing well in his class – towards the top! He is reading beyond expectations and his attention to detail is off the charts. He is creative and participates in class … the teacher didn't have enough positive things to say." I couldn't believe it. I immediately broke down with her in the middle of the kitchen.

Thank you to all of our supporters who have given Holt the opportunity to compete … much like his grandfather it's in his DNA. He just needed the chance and you gave it to him.

Love,
Jason and Chrissy Grier
Charlotte, North Carolina

Neveen A. Soliman, MD, PhD, Joins CCIR Advisory Board

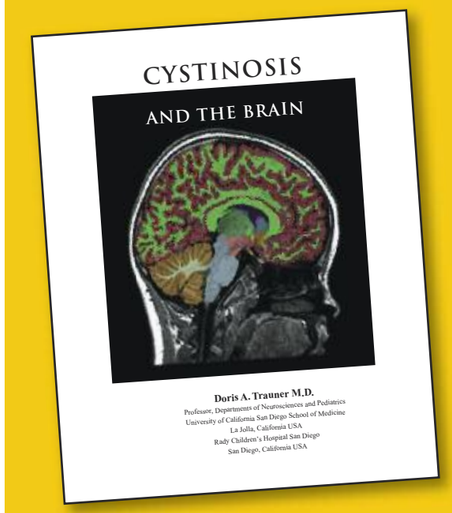
Neveen A. Soliman is a professor of pediatrics and pediatric nephrology, Kasr Al Ainy School of Medicine, Cairo University. She holds a medical doctorate degree in pediatrics from Cairo University, 1993. She performed her postdoctoral training at Guy's Hospital, London working as a clinical and research fellow. In 2001, she helped create the Center of Pediatric Nephrology & Transplantation, Children's Hospital, Cairo University.

Her research is focused on genetic and metabolic renal diseases including cystinosis. Another of her research interests is the clinical and molecular characterization of cystic kidney diseases and other ciliopathies like Bardet-Biedl, Joubert, and Meckel-Gruber syndrome, as well as genetic and steroid resistant nephrotic syndrome.

In 2003, she founded the Egyptian Group for Orphan Renal Diseases (EGORD), the first group of its kind in Egypt and the region to care for rare kidney diseases. Through EGORD Dr. Soliman and her team managed to diagnose cystinosis for the first time in Egyptian children, provide patients with both Cystagon® and cysteamine eye drops, and publish their experience with the largest reported patients' series in the region. She heads a team of 10 coworkers, which established a national database for many inherited renal diseases including cystinosis, genetic nephrotic syndrome, nephronophthisis and primary hyperoxaluria.

Dr. Soliman is a member of several pediatric nephrology and genetics scientific societies, authored and co-authored many publications in peer-reviewed international journals. She is the 2011 recipient of the Global Kidney Academy/International Nephrology Education Foundation "Leadership & Education in Nephrology Award."

FOR PATIENTS & FAMILIES, FAMILY PRACTITIONERS & MEDICAL SPECIALISTS, TEACHERS & ADMINISTRATORS



A New Publication to Better Understand Cystinosis and Its Impact on the Brain

The Cystinosis Research Foundation is pleased to announce that it has published *Cystinosis and the Brain*. The book is an invaluable resource for cystinosis families, patients, caregivers and clinicians. The book, written by Dr. Doris Trauner, is a compilation of every CRF-funded study by Dr. Trauner and her colleagues at the University of California, San Diego. To date, the CRF has issued over $1,000,000 in research grants to Dr. Trauner and her team. Although many journal publications have resulted from their work, until now the research results have not been integrated and summarized into a practical book for parents and patients.

The book covers important topics including, Neurological Problems in Cystinosis, Cognitive Function in Cystinosis, Behavioral Issues in Cystinosis and Myopathy. The book also has a chapter on various interventions.

***Cystinosis and the Brain* is an invaluable resource for the cystinosis community. If you would like a free copy, please contact Nancy Stack at nstack@cystinosisresearch.org.**

Heartfelt Thanks and a Sad Goodbye

It is with sadness that we announce that Dr. William Rizzo has resigned from the CRF Scientific Review Board (SRB). Dr. Rizzo, a nephrologist at the University of Nebraska Medical Center, has served as a SRB member for over six years.

Dr. Rizzo joined the CRF SRB at a time of tremendous growth. The CRF was raising over a million dollars each year, which meant we were committed to funding that same amount in research. Unlike most non-profit foundations, the CRF announces two calls for research applications each year in an effort to get money into the hands of researchers as quickly as possible. Our goal was to create a dynamic cycle of research in an effort to accelerate research progress and further our mission to find better treatments and a cure for cystinosis.

Dr. Rizzo met his first cystinosis patient over 30 years ago and that personal knowledge of cystinosis and his close relationship with cystinosis patients brought a unique approach and insight to the grant evaluation process. It was with warmth and heart, as well as intellect and expertise that Dr. Rizzo evaluated every grant submitted to CRF since 2006. His ability to balance the science with the needs of the patients, ensured that the patients' welfare was always front and center.

Dr. Rizzo has been part of a seven-member Scientific Review Board that has, since 2006, reviewed over 130 grant applications for their scientific merit and has recommended over $16 million in new grants. Dr. Rizzo, along with the other CRF SRB members have guided this foundation, and by doing so we have achieved major milestones: a delayed-release form of cysteamine and the first allogeneic stem cell treatment for cystinosis.

We are deeply indebted to Dr. Rizzo for his invaluable commitment, dedication and embrace of CRF and the cystinosis community. We are grateful for his service and only wish we could find the words to thank him for his part in changing the course of cystinosis research.

Dr. Rizzo will always be a part of the CRF family. He had this to say about his tenure as a SRB member, "I have been privileged to serve on the Scientific Review Board for more than six years during which time we've seen some remarkable advances in cystinosis research and therapy. The past several years, however, have been particularly spectacular … and the next few years promise even more. You have kept your eye on the prize by supporting the most promising research that will translate into new therapies for our cystinotic children. As a direct result of the CRF, we now stand at the most exciting time for cystinosis and can finally see innovative new therapies, such as hematopoietic stem cell transplantation, come to fruition. And gene therapy is on the horizon."

Dr. Julie Ingelfinger, SRB Member, Receives Prestigious Award

Julie Ingelfinger, MD, Harvard Medical School, Boston, Massachusetts, who serves on the CRF Scientific Review Board, is the recipient of the 2012 American Society of Pediatric Nephrology's Founder's Award.

This prestigious award is given annually to individuals who have made a "unique and lasting contribution to the field of pediatric nephrology."

In addition to her role at MassGeneral Hospital for Children, Dr. Ingelfinger does basic and clinical research, is professor of pediatrics at Harvard Medical School, and has served as a deputy editor for the *New England Journal of Medicine* since 2001.

Earlier this year Dr. Ingelfinger co-chaired the Third CRF International Cystinosis Research Symposium with Corinne Antignac, MD, PhD, Paris, France; Stéphanie Cherqui, PhD, University of California, San Diego; and Elena Levtchenko, MD, PhD, Leuven, Belgium.

Published Studies (since spring 2012 issue)

Hematopoietic Stem Cell Gene Therapy for Multisystemic Lysosomal Storage Disorder Cystinosis – Published in *Molecular Therapy* by Stéphanie Cherqui, PhD, Department of Molecular and Experimental Medicine, The Scripps Research Institute, La Jolla, California.

Treatment of Cystinosis with Delayed-Release Cysteamine: 6-Year Follow-up – Published in the September 2012 issue of *Pediatric Nephrology* by Ranjan Dohil, MD, Department of Pediatrics, Rady Children's Hospital, University of California, San Diego.

Cystinosin is a Melanosomal Protein that Regulates Melanin Synthesis – A research paper by Robert Ballotti, PhD, INSERM, Nice, France, has been accepted for future publication in *The FASEB Journal.*

A Potential New Method to Estimate Tissue Cystine Content in Nephropathic Cystinosis – Published March 2012 in *The Journal of Pediatrics* by Ranjan Dohil, MD, Department of Pediatrics, Rady Children's Hospital, University of California, San Diego.

Pharmacokinetics of Cysteamine Bitartrate Following Intraduodenal Delivery – Published in *Fundamental & Clinical Pharmacology* by Ranjan Dohil, MD, Department of Pediatrics, Rady Children's Hospital, University of California, San Diego.

CRF Science Report and Research Grant Updates

CRF research grant progress reports are published in the *Research* section on our website: **www.cystinosisresearch.org**. As updates are received they appear in our monthly *Star Facts* e-newsletter.

SCIENTIFIC REVIEW BOARD

The Scientific Review Board 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 submitted and advising the CRF on the scientific merit of each proposal.

2012 Call for Funding Proposals

The ultimate goal of the Cystinosis Research Foundation is to find a cure for cystinosis. Global calls for grant and fellowship applications are announced bi-annually in March and September. Research and fellowship awards will be given for up to 3 years. The number and value of the awards will depend on the number of outstanding proposals received and the value of the funds available at the time.

The CRF announced its Fall 2012 call for proposals on September 10, 2012. Currently CRF has $400,000 available for new grants The deadline for applications was Wednesday, October 24, 2012.

New research grants and fellowships will be announced by the end of January 2013. Visit **www.cystinosisresearch.org/For-Researchers** for details.

2012 Spring Grants Funded

Total: $1,663,781

Corinne Antignac, MD, PhD, Principal Investigator
Necker Hospital, Paris, France
"Characterization of Proteins Interacting with Cystinosin"
$212,000 – 2-year grant

Corinne Antignac, MD, PhD, Research Mentor
Zuzanna Andrzejewska, Research Fellow
Necker Hospital, Paris, France
"Role of Cystinosin in Vesicular Trafficking and Membrane Fusion"
$63,000 – 1-year grant

Bruce Barshop, MD, PhD, Research Mentor
Ilya Gertsman, PhD, Research Fellow
University of California, San Diego
"Identification of Protein Thiol Modifications and Metabolic Markers of Disease in Cystinosis"
$63,625 – 1-year grant

Sergio Catz, PhD, Principal Investigator
The Scripps Research Institute, La Jolla, California
"Molecular Mechanisms to Repair the Vesicular Transport System in Cystinosis"
$72,375 – 1-year grant

Robert Chevalier, MD, Principal Investigator
University of Virginia, Charlottesville
"Oxidant Injury to Proximal Tubular Loss in Cystinosis"
$219,099 – 2-year grant

Pierre Courtoy, MD, PhD, Principal Investigator
Héloïse Gaide Chevronnay, PhD, Co-Principal Investigator
De Duve Institute, Brussels, Belgium
"Integrated Cellular and Tissular Physiopathology of Cystinosis in Cystinosin KO Mice and Correction Mechanisms upon Haematopoietic Stem Cell Grafting"
$210,000 – 2-year grant

Alan Davidson, PhD, Principal Investigator
University of Auckland, New Zealand
"Differentiation of Cystinotic Pluripotent Stem Cells into Kidney Tissue"
$46,449 – 1-year grant

Olivier Devuyst, MD, PhD, Principal Investigator
Sara Terryn, PhD, Co-Principal Investigator
University of Zurich, Switzerland
"Defective Transport and Epithelial Dedifferentiation: Genesis of Key Events in Nephropathic Cystinosis"
$212,500 – 2-year grant

Bruno Gasnier, PhD, Principal Investigator and Mentor
Bruno André, PhD, Co-Principal Investigator
Quinton Verdon, PhD, Research Fellow
Université Paris Descartes, France
"Molecular Study of a Cystinosin Homologue and its Impact on Cystinosis and Cysteamine Therapy"
$214,984 – 2-year grant

Robert Mak, MD, PhD, Principal Investigator
University of California, San Diego
"Vitamin D and Muscle Wasting in Nephropathic Cystinosis"
$150,000 – 2-year grant

Jennifer Simpson, MD, Principal Investigator
University of California, Irvine
Ghanashyam Acharya, PhD, Co-Principal Investigator
Baylor College of Medicine, Houston, Texas
"Nanowafer Drug Delivery for Corneal Cystinosis: Sustained-Release Cysteamine"
$199,749 – 2-year grant

See Lay Abstracts on following pages

CYSTINOSIS RESEARCH FOUNDATION

Lay Abstracts – Spring 2012 Grants

Corinne Antignac, MD, PhD, Principal Investigator, Necker Hospital, Paris, France

Project Title: Role of Cystinosin in Vesicular Trafficking and Membrane Fusion

Objective/Rationale: The cystinosis gene encodes a lysosomal cystin transporter, cystinosin. Cells overexpressing cystinosin fused to a green-fluorescent protein (cystinosin-GFP) to allow its easy identification under fluorescent microscopy, displayed aggregation of lysosomes, which suggests the role of cystinosin in membrane fusion events. Moreover, little is known about the way cystinosin is targeted to the lysosomes and the role of its two sorting signals in this process. Our proposal is a one-year follow up of the initial project, to complete the data on lysosomal targeting of cystinosin. Moreover, we will analyze the possible function of cystinosin in mechanisms of vesicle fusion.

Project Description: The studies on targeting of lysosomal membrane proteins indicate the existence of direct (intracellular) and indirect (via plasma membrane) pathways by which proteins can be sorted to these organelles, mediated by distinct adaptor protein complexes. To verify the way cystinosin is targeted to lysosomes, we will analyze the impact of depletion of different adaptor proteins on the possible mislocalization of cystinosin-GFP to cellular compartments other than lysosomes by confocal microscopy. Our previous study indicates that cystinosin is mainly targeted via the direct pathway omitting plasma membrane. This will be further analyzed using TIRF (total internal reflection fluorescence) microscopy and cell surface biotinylation, both methods permitting to determine the level of cystinosin at the cell surface.

Moreover, when overexpressing cystinosin-GFP, we could observe the expansion of the Vti1b positive compartment. Vti1b had recently been described as the protein involved in the fusion of autophagosomes with lysosomes, suggesting that enlarged structures observed could be of autolysosomal origin. We will further analyze if these vesicles are functional autolysosomes and the role of cystinosin in their formation.

Relevance to the Understanding and/or Treatment of Cystinosis: The study of cystinosin trafficking will help us to better understand process targeting cystinosin to the lysosome and especially the role of the unconventional lysosomal targeting motif cystinosin bears. Moreover, the finding of additional functions for cystinosin could explain why some symptoms of cystinosis (i.e. the Fanconi syndrome) are not improved by lysosomal cystine depletion using cysteamine, and provide insight into the complex processes governing vesicular fusion.

Anticipated Outcome: We expect to unravel the way cystinosin is targeted to the lysosomes and the role of its both sorting motifs in this process. Moreover, by analyzing the impact of cystinosin in vesicular fusion, we hope to better understand its function additional to the cystin transport and thus the pathophysiological mechanisms underlying cystinosis.

Alan Davidson, PhD, Principal Investigator, University of Auckland, New Zealand

Project Title: Differentiation of Cystinotic Pluripotent Stem Cells into Kidney Tissue

Objective/Rationale: In the majority of patients, nephropathic cystinosis leads to renal Fanconi syndrome progressing to kidney failure. However, raised levels of cystine are found in all organs and it is not clear why the kidney is particularly affected. To address this, we plan to generate cystinotic kidney tissue from induced pluripotent stem (iPS) cells that we have generated from a patient with nephropathic cystinosis. iPS cells, like cells from an embryo, have the potential to form any cell type in the body.

Project Description: In this project we will examine the potential of cystinotic-iPS cells to mature into kidney cells. We will first induce the iPS cells to undergo an embryonic-like program of growth in a petri dish. This results in so-called 'embryoid bodies,' which are balls of embryonic tissues such as muscle, blood, and kidney. Then using a method we have developed, we will isolate the kidney 'precursor' cells in order to get a pure population of cells that can be further matured into kidney tissue. If successful, we will be able to study the cystinotic-kidney tissue and learn more about why it is so sensitive to cystine accumulation.

Relevance to the Understanding and/or Treatment of Cystinosis: By generating cystinotic kidney tissue in a dish, we will be able to study in detail the effect of increased cystine levels on kidney cell function – something that is currently difficult to do in patients. Hopefully, this work will identify the cause of the renal Fanconi syndrome in nephropathic cystinosis and lead to the development of new therapies.

Anticipated Outcome: We expect to optimize our methods to induce and purify kidney precursors from cystinotic iPS cells and demonstrate the formation of mature kidney tissue in a dish.

Bruce Barshop, MD, PhD, Research Mentor
Ilya Gertsman, PhD, Research Fellow
University of California, San Diego

Project Title: Identification of Thiol Modifications and Metabolic Biomarkers in Cystinosis

Objective/Rationale: It was previously shown that excess cystine in cystinotic cells causes modification of an important cell regulating protein. We have been investigating in a comprehensive way, the proteins that are getting modified by cysteine, as well as protein modifications caused by oxidative stress in fibroblast cells. We found a number of potentially modified proteins which we plan to verify in other cell lines like renal tubular epithelial cells. We will also study changes in metabolites related to these proteins.

Project Description: We will culture renal tubular epithelial cells as well as additional fibroblast cells, both cystinotic and control, and use a protein labeling method to quantitate modified proteins in cystinosis. The cellular proteins will be quantified using mass spectrometry. We will use the non-protein portion of each cell preparation and evaluate the metabolite profile from both cystinotic and control cells. Using a Q-tof mass spectrometry instrument, we are able to evaluate and compare metabolite concentrations of thousands of different compounds. We hope to uncover metabolites that are either altered in composition or quantity in order to understand the metabolic consequence of the disease and if these metabolites are related to the modified proteins that we have found. Protein modifications and metabolite concentrations will also be studied with and without cysteamine treatment.

Relevance to the Understanding and/on Treatment of Cystinosis: Though we currently know the severe impact of accumulated cystine in cystinosis patients, it is still very unclear as to what the impact of this compound has on all of the important cellular mechanisms. We plan to study the biochemical consequences of excess cystine and hopefully uncover uncharacterized pathways which can potentially be treated to limit the severity of the disease.

Anticipated Outcome: We expect to verify that the proteins we have seen to be modified in fibroblasts are also altered in other cell lines, though we expect to find a number of new affected proteins in the most symptomatic cell line, the renal proximal tubular cell. We then expect that substrate metabolites of proteins that are modified by oxidation for example, will have altered composition or concentrations. By studying the cells post cysteamine treatment, we will also be able to evaluate which compounds are bound to the drug, and at which rates these are broken down or excreted from the cell.

Sergio Catz, PhD, Principal Investigator, The Scripps Research Institute, La Jolla, California

Project Title: Molecular Mechanisms to Repair the Vesicular Transport System in Cystinosis

Objective/Rationale: Organic substances are broken down in intracellular compartments called lysosomes. For example, proteins are digested inside these compartments to release amino acids which are recycled so they become available to synthesize new proteins. In cystinosis the transporter that is essential for the release of the amino acid "cystine" from these degradative compartments is defective. This leads to cellular dysfunction. We propose to use molecular approaches to facilitate the release of the accumulated amino acid cystine from the degradative compartment of cystinotic cells directly into the extracellular space. The cells will then restore normal cellular function.

Project Description: To achieve our goals, we will increase the expression of molecules that specifically induce the release of the content of the degradative compartments of the cells into the extracellular space. These molecules are specific proteins that facilitate the directional movement of degradative compartments. This will force the release of the content of these compartments and restore normal cellular function. We will test several proteins and approaches including molecules that facilitate vesicular transport and vesicular fusion. We will measure the decrease of accumulated cystine in cystinotic cells utilizing various approaches including fluorescence microscopy and mass spectrometry.

Relevance to the Understanding and/or Treatment of Cystinosis: The significance of this research is that therapies that decrease accumulation of amino acids in degradative compartments may lead to effective strategies for treating cystinosis. This could have implications for prevention of injurious consequences of cystine accumulation in infantile cystinosis and retardation of late complications in post-transplanted patients. This project may also lead to a better understanding of the physiopathology of cystinosis.

Anticipated Outcome: Novel mechanism of cellular regulation in cystinosis will be identified. Important molecules that improve the function of cystinotic cells and organisms will be discovered. Small molecules (pharmacological compounds) with potential beneficial effect on cells and organisms with cystinosis will be tested and characterized.

Lay Abstracts — Spring 2012 Grants

Robert Chevalier, MD, Principal Investigator, University of Virginia, Charlottesville

Project Title: Oxidant Injury in Proximal Tubular Loss in Cystinosis

Objective/Rationale: Most children with cystinosis develop kidney failure by the second decade of life. In cystinotic children undergoing kidney transplantation, almost all nephrons (the functional units of the kidney) have undergone destruction of the connection between the filtering unit and the tubule. There is increasing evidence that this damage results from cellular oxidant injury due to cystine accumulation. Inhibition of this process, particularly early in the course of cystinosis, may slow or prevent progressive kidney damage.

Project Description: Using a newly developed mouse model of cystinosis, this project will test the hypothesis that oxidant cell damage is a key stimulus to progressive kidney injury in this disease. Animals will be treated from birth with a novel antioxidant, MitoQ, which is targeted to mitochondria (the source of cellular energy and the structures susceptible to injury from cystine accumulation in kidney tubules). Blood and urine markers of kidney function and injury will be measured. Kidney tissue will be analyzed for specific cell damage (including various forms of cell death) due to oxidant injury. In addition, a newly developed digital imaging technique will be used to measure changes in the mass of kidney tubules in response to normal maturation and to the superimposed injury to mitochondria due to cystine accumulation. Similar techniques will be applied to kidney tissue from cystinotic patients, to validate the animal model.

Relevance to the Understanding and/or Treatment of Cystinosis: Kidney failure is a major consequence of cystinosis, and kidney damage first appears in children between 6 and 12 months of age. Although cysteamine can slow this process, most patients develop kidney failure by adulthood. This project will investigate a novel early intervention that will demonstrate the role of mitochondrial oxidative injury in this process, as well as providing preliminary evidence for a new preventive treatment to preserve the functioning units of the kidney, the nephrons.

Anticipated Outcome: For over 30 years, our laboratory has explored the cellular mechanisms of kidney injury resulting from the most common cause of kidney failure in children: birth defects of the urinary tract resulting in obstruction to urine flow. We have discovered that the same cells are injured by cystinosis, one of the rarest causes of kidney failure. We expect that the use of these techniques will reveal the mechanisms and timing of kidney cell injury in cystinosis, and will point to new therapies to slow or prevent KIDNEY DAMAGE.

Pierre Courtoy, MD, PhD, Principal Investigator
Héloïse Gaide Chevronnay, PhD, Co-Principal Investigator
De Duve Institute, Brussels, Belgium

Project Title: Integrated Cellular and Tissular Physiopathology of Cystinosis in Cystinosin KO Mice and Correction Mechanisms Upon Hematopoietic Stem Cells (HSCs) Grafting

Objective/Rationale: Our investigations aim at better understanding the natural course of cystinosis and of its correction by stem cell therapy in a mouse model. The two major objectives are (i) to evaluate the role of apical receptor-mediated endocytosis (ARME) of ultrafiltrated low molecular weight proteins (LMWP), as the key source of cystine, in the longitudinal progression of nephropathic cystinosis; and (ii) to better define the (sub)cellular mechanisms of HSC correction in kidneys, thyroid and liver.

Project Description: The model we propose for longitudinal progression of proximal tubular cells atrophy, based on distal transfer of endocytic load, will be experimentally tested by interrupting ARME supply of LMWP. Megalin being the key actor driving ARME, cystinotic mice will be crossed with kidney-specific megalin knock-out congeners. Kidney protection in double KO mice will be evaluated by comprehensive morphological analysis. Mechanisms underlying cystinosis correction by HSCs grafting will be estimated using combination of high resolution fluorescence imaging and development of a new tool allowing in *vivo* HSCs tracking by electron microscopy. Emphasis will be placed on local factors favoring HSCs grafting in different host tissues and on HSCs/host cells physical interface, in order to identify how corrective signals are transferred between these cells.

Relevance to the Understanding and/or Treatment of Cystinosis: Further understanding the physiopathology of cystinosis progression and mechanisms of its correction by HSCs grafting are crucial to identify and correctly evaluate end-points and potential toxicity issues for the planned clinical trial of stem cell therapy.

Anticipated Outcome: These investigations should lead to better understand the atrophy program expanding in cystinotic kidneys and demonstrate the role of LMWP endocytosis in disease progression. We also hope to narrow down likely processes involved in correction of epithelial atrophy by HSCs so as help maximize HSCs grafting procedure and resulting correction of cystinotic cells.

Olivier Devuyst, MD, PhD, Principal Investigator
Sara Terryn, PhD, Co-Principal Investigator
University of Zurich, Switzerland

Project Title: Defective Transport and Epithelial Dedifferentiation: Genesis of Key Events in Nephropathic Cystinosis

Objective/Rationale: Nephropathic cystinosis is characterized by a progressive dysfunction of proximal tubule cells that appears by 6 to 12 months of age. In absence of treatment with cysteamine, end-stage renal disease is reached around 10 years of age. The pathogenesis of defective transport processes in cystinosis remains unclear, reflecting limitations of cellular and animal model systems. A new line of *Ctns* KO mice shows accumulation of cystin in the kidney, with signs of tubulopathy and severe histological lesions leading to chronic renal failure. The availability of this strain provides an excellent opportunity to address the cellular mechanisms underlying specific transport defects in cystinosis.

Project Description: The overall goal of this project is to take advantage of a detailed characterization of the new *Ctns* mouse model and the availability of cutting-edge methods to analyze cellular mechanisms of transport defects in the early stage of cystinosis (i.e. before the onset of renal failure). These transport defects play an essential role in the burden of disease (renal Fanconi syndrome) and are probably instrumental for renal disease progression. The specific aims include: (1) To characterize specific transport defects *in vivo* and *ex vivo,* using the *Ctns* mouse model; (2) To investigate the mechanisms of altered transport using primary cultures derived from micro-dissected tubular segments; (3) To evaluate the influence of residual activity of cystinosin (and the extent of cystine accumulation) on transport processes.

Relevance to the Understanding and/or Treatment of Cystinosis: Obtaining insights into the early chain of events leading to proximal tubule transport defects, before structural damage, may provide new targets for interventions which, in turn, could alleviate the burden caused by the urinary loss of vital metabolites in patients with nephropathic cystinosis.

Anticipated Outcome: These translational investigations will address the early stage of cystinosis, which may point to cellular pathways that could be targeted (or monitored) before any irreversible damage of the kidney. Being able to correct some of the early transport defects in cystinosis could alleviate major clinical consequences of increased urinary losses of vitamins and solutes. The mechanisms identified in early 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.

Bruno Gasnier, PhD, Principal Investigator and Mentor
Bruno André, PhD, Co-Principal Investigator
Quinton Verdon, PhD, Research Fellow
Université Paris Descartes, France

Project Title: Molecular Study of a Cystinosin Homologue and Its Impact on Cystinosis and Cysteamine Therapy

Objective/Rationale: Cysteamine therapy remains the main treatment for cystinosis. The compound permeates cellular and lysosomal membranes and condenses with cystine in the lysosome, thus generating a molecular species that resembles the amino acid lysine. This new compound then leaves the lysosome through a hitherto unknown lysine transporter, thus depleting lysosomal cystine. We recently identified this transporter as a novel lysosomal membrane protein termed PQLC2. This breakthrough suggests novel rationales for improving cysteamine efficiency.

Project Description: We used diverse experimental approaches including baker yeast genetics, mammalian cell biology, biochemistry, and electrical recording of frog eggs to elucidate the biological function of PQLC2. This powerful association between mammalian cell biology and yeast genetics will be pursued to characterize further PQLC2 and explore its therapeutical interest. We will analyze the transport properties of PQLC2 and its expression mechanism, before exploring whether its stimulation or upregulation might potentiate cystine depletion. Using yeast, we will study the interactions of PQLC2, or its yeast equivalent, with other proteins, characterize its function in a cellular context, and investigate a paradoxical toxicity of the cystine/cysteamine reaction product in this species.

Relevance to the Understanding and/or Treatment of Cystinosis: The project will improve our understanding of the molecular actions of cysteamine. The interaction of cysteamine and lysosomal cystine induces a biochemical cycle of sulfur compounds across the lysosomal membrane that reverses cystine storage. This cycle requires at least two small-molecule transporters non-affected by the disease to permeate the lysosomal membrane. Our study focuses on the first identified of these key transporters, PQLC2, the second remaining unknown.

Anticipated Outcome: Knowledge of the properties of PQLC2 and of its consequences at cellular level should suggest rationales for improving cysteamine therapy or discover alternative, more efficient cystine-depleting drugs.

Lay Abstracts — Spring 2012 Grants

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

Project Title: Vitamin D and Muscle Wasting in Nephropathic Cystinosis

Objective/Rationale: Cystinosis is a rare genetic disorder. Muscle wasting is a common complication in patients with cystinosis and negatively impacts the quality of life. The underlying mechanism of muscle wasting in cystinosis is unknown. The cystinosis transgenic mouse model provides an excellent opportunity to study pathophysiology of muscle wasting in cystinosis. We observed low serum concentrations of vitamin D metabolites in this mouse model. Thus, we aim to investigate whether supplementation of vitamin D metabolites will be able to improve muscle wasting in cystinosis.

Project Description: We hypothesize that vitamin D deficiency signals through the inflammatory cytokine interleukin-6 and results in muscle wasting in patients with cystinosis. Chronic kidney disease was observed in aging cystinosis transgenic mice. We will test whether early supplementation of vitamin D metabolites will be able to prevent muscle wasting in young cystinosis transgenic mouse, prior to the onset of chronic kidney disease. We will also test whether supplementation of vitamin D metabolites will be able to reverse muscle wasting in old cystinosis transgenic mouse. Lastly, we will test whether genetic manipulation of interleukin-6 will be able to arrest muscle wasting in cystinosis transgenic mouse by using a double genetic knockout strategy.

Relevance to the Understanding and/or Treatment of Cystinosis: Muscle wasting is a common complication in cystinosis. Myopathy and swallowing difficulties were noted in patients with cystinosis. The underlying mechanism of this muscle wasting is not well understood. Our preliminary results highlight the significance of vitamin D deficiency in the pathogenesis of muscle wasting in cystinosis. If confirmed, these findings will raise awareness of vitamin D deficiency in cystinosis and potentially improve muscle wasting and quality of life in patients with cystinosis.

Anticipated Outcome: We anticipate that vitamin D deficiency is an important cause of muscle wasting in cystinosis and supplementation of vitamin D metabolites will prevent and reverse muscle wasting in cystinosis.

Jennifer Simpson, MD, Principal Investigator
University of California, Irvine
Ghanashyam Acharya, PhD, Co-Principal Investigator
Baylor College of Medicine, Houston, Texas

Project Title: Nanowafer Drug Delivery for Corneal Cystinosis: Sustained Release Cysteamine

Objective/Rationale: The treatment of corneal cystinosis requires the hourly application of cysteamine eye drops in order to reduce corneal cystine crystals. This frequent dosing regimen is due in part to the rapid clearance of the drug from the ocular surface. Hourly dosing negatively impacts medication compliance and patient quality of life. Hence, there is an unmet need for a programmable drug delivery system that can release the drug in therapeutically effective concentrations for longer duration of time with the goal of improving drug efficacy, patient compliance and quality of life.

Project Description: By integrating current nanofabrication technologies with controlled drug delivery strategies, this research project aims to develop a nanowafer that can deliver cysteamine for a longer duration of time i.e., a day to a week. The nanowafer will be fabricated by hydrogel template strategy using biocompatible hydrogel material. The wafer contains an array of nano-reservoirs into which cysteamine can be loaded. Upon installation of nanowafer on the ocular conjunctiva, the cysteamine molecules slowly diffuse out from the nano-reservoirs into the surrounding tissue, thus enabling the drug availability for a longer duration of time. In addition, the desired drug release profiles can be obtained by fabricating nanowafers containing drug reservoirs of different dimensions. The polymer matrix of the nanowafer protects cysteamine from oxidation to its disulfide form: cystamine. The efficacy of the nanowafers will be evaluated in the Cystinosin knockout mouse model and compared to topical cysteamine therapy.

Relevance to the Understanding and/or Treatment of Cystinosis: The goal of this research is to fill an unmet medical need in the treatment of corneal cystinosis by reducing drug dosing requirements and improving patient compliance and quality of life.

Anticipated Outcome: The cysteamine nanowafer, upon successful development can release cysteamine in a controlled fashion, thus enhancing drug efficacy and improving patient compliance.

New CRF SRB Members

Lisa M. Guay-Woodford, MD

Dr. Lisa M. Guay-Woodford is the Hudson Professor of Pediatrics at the Children's National Medical Center (CNMC), a pediatric nephrologist, and an internationally recognized investigator whose research focuses on identifying clinical and genetic factors involved in the pathogenesis of inherited renal disorders, most notably autosomal recessive polycystic kidney disease (ARPKD). Her laboratory has identified the disease-causing genes in several mouse models of recessive polycystic kidney disease and her group participated in the identification of the human ARPKD gene as part of the ARPKD Consortium. In addition, her laboratory was the first to identify a candidate modifier gene for recessive polycystic kidney disease. Dr. Guay-Woodford has over 100 peer-reviewed publications based on research performed in her own laboratory or as a member of several national and international consortia. She has directed the NIDDK P30-funded Hepato-Renal Fibrocystic Disease Research and Translational Core Center, initially established at the University of Alabama at Birmingham in 2005, and continues to serve as co-Director since moving to CNMC in 2012. Her research program has been funded by the NIH, the Burroughs Wellcome Fund Clinical Scientist Award in Translational Research, and the Polycystic Kidney Disease Foundation. In 2009, Dr. Guay-Woodford was awarded the Lillian Jean Kaplan International Prize for Advancement in the Understanding of Polycystic Kidney Disease, given by the PKD Foundation and the International Society of Nephrology.

In addition to her investigative work, Dr. Guay-Woodford has established and serves as Director of the CNMC Inherited Renal Disorders Program. She is the Director of the Center for Translational Science, as well as Director of the Clinical and Translational Science Institute at Children's National Medical Center (CTSI-CN), which is funded by the NIH CTSA program. She has served on several editorial boards for journals in her field. She has been a permanent member and Chair of the NIH Cellular and Molecular Biology of the Kidney Study Section. She is the Past President of the Society for Pediatric Research and Councilor for the International Pediatric Nephrology Association.

Martin Konrad, MD

Martin Konrad is working as a Pediatrician at the University Children's Hospital in Münster, Germany.

He is the head of the Department for Pediatric Nephrology since 2007. He studied Medicine at the University of Heidelberg, Germany and received his MD degree in 1992. After a two-year period as a research fellow in renal genetics in Corinne Antignac's laboratory at the Necker hospital in Paris, France he got his training in Pediatrics and the subspeciality in Pediatric Nephrology at the University Children's Hospital in Marburg, Germany.

Martin Konrad has a long-standing interest in the molecular genetics of inherited renal disorders, especially renal tubular disorders. Current research activities focus on renal salt and electrolyte losing disorders and inherited disturbances of calcium/magnesium metabolism.

Pierre Courtoy, MD, PhD

Pierre Courtoy was trained as MD, PhD, and is a board-certified internist. He is the Head of the Cell Biology Laboratory at de Duve Institute, Brussels, and of the Platform for Imaging of Cells and Tissues at the Brussels campus of the Université catholique de Louvain, where he teaches Cell biology and General pathology. Trained by Georges Palade and Marilyn Farquhar at Yale and by Christian de Duve at Louvain (thus two Nobel prizes), he spent three decades scrutinizing the endocytic apparatus in a variety of experimental systems and methods, with strong emphasis on advanced morphology.

His main achievements are the demonstration that osteoclasts resorb bones by developing an acidified extracellular lysosome while the cycling human endometrium programs itself-renewal by matrix metalloproteinases; the first assessment of clathrin-independent endocytosis and purification of endosome-specific subcompartments; and the first evidence of an endocytic recycling defect in a genetic kidney disease, leading to the serendipitous discovery of a novel mechanism of lysosome biogenesis in this organ.

Since last decade, he focused on apical endocytosis for which kidney proximal tubular cells are a model of efficiency, in collaboration with E.I. Christensen, O. Devuyst, C. Antignac and S. Cherqui. Current interests in the kidney field are the regulatory machineries of apical recycling, the physiopathology of cystinosis, and the mechanisms underlying its correction by stem cell grafting. Pierre Courtoy was the founder of the european endocytosis network two decades ago and an active member of several international consortia. He has published more than 150 peer-reviewed papers and his work has received close to 6400 citations (h index, 40).

William E. Smoyer, MD

William E. Smoyer, MD is the Vice President for Clinical and Translational Research and Director of the Center for Clinical and Translational Research at The Research Institute at Nationwide Children's Hospital. Dr. Smoyer was also awarded the C. Robert Kidder Endowed Chair of Clinical and Translational Research in July, 2008.

He is a co-founder and steering committee member of the Midwest Pediatric Nephrology Consortium, a national clinical and translational research consortium comprised of 40 member centers dedicated to advancing the care of children with renal disease. As a basic and clinical scientist, Dr. Smoyer also has a long-standing track record of NIH and other extramural funding supporting his research on the molecular mechanisms of podocyte injury and recovery during nephrotic syndrome, one of the most common kidney diseases seen in children.

Dr. Smoyer received his undergraduate (Biomedical Engineering) and medical degrees from the University of Florida. He then completed his pediatric residency at the University of Texas Medical Branch, followed by clinical fellowships in pediatric nephrology at the Children's Hospital of Philadelphia as well as Children's Hospital, Boston. He also completed a research fellowship at the University of Pennsylvania.

He is the author or co-author of more than 80 peer-reviewed publications and book chapters. He is a member of the Society for Pediatric Research and the American Society of Pediatric Nephrology as well as a fellow of the American Academy of Pediatrics, among other numerous associations. He also has been consistently listed among the Best Doctors in America since 2005.

We are indebted to everyone who serves on a Cystinosis Research Foundation Board for their leadership, guidance and commitment to helping our children.

CYSTINOSIS RESEARCH FOUNDATION

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. CRF has dedicated almost $17 million in ten years to cystinosis research in an effort to find a cure.

EDUCATION

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

CURE CYSTINOSIS INTERNATIONAL REGISTRY

The Cure Cystinosis International Registry (CCIR) is a collaborative effort by the leaders in the cystinosis community to establish a comprehensive, global patient registry for cystinosis. The purpose is to connect those with cystinosis to the research community in an effort to find a cure for cystinosis.

CCIR BOARD OF ADVISORS

The CCIR Advisory Board is dedicated to promoting and facilitating current research and medical information to the global cystinosis community in an effort to inform the community of current treatments, clinical trials and studies and patient care.

Bruce A. Barshop, MD, PhD
University of California, San Diego

Kyle Brown, CEO, Innolyst, Inc.

Betty L. Cabrera, MPH, University of California, San Diego

Paul Goodyer, MD, Montreal Children's Hospital, Canada

Whitney Glaize, Cystinosis Research Foundation

Jean Hobbs-Hotz, Cystinosis Foundation

Valerie Hotz, Cystinosis Foundation

Tom Melang, Cystinosis Patient Advocate

Patrick Niaudet, MD
Hôpital Necker-Enfants Malades,
Université Paris Descartes, Paris, France

Teresa Partington, Jenna and Patrick's Foundation of Hope

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

Neveen A. Soliman, MBBCh, MSc, PhD
Cairo University and Director of the Egyptian Group for Orphan Renal Diseases (EGORD)

Nancy Stack, Cystinosis Research Foundation

Jody Strauss, Cystinosis Awareness & Research Effort

Tricia Sturgis, 24 Hours for Hank

Doris A. Trauner, MD
University of California, San Diego

CCIR MEDICAL AND SCIENTIFIC COUNCIL

The CCIR Medical and Scientific Council was instrumental in the development, design and content of the medical questionnaire for the registry. The Council provides ongoing guidance relating to the scientific and clinical aspects of the registry.

In addition, Dr. Barshop, Dr. Goodyer, Dr. Schneider and Dr. Trauner are members of the *Ask An Expert* subcommittee that addresses questions from cystinosis patients.

Bruce A. Barshop, MD, PhD
University of California, San Diego

Stéphanie Cherqui, PhD
University of California, San Diego

Ranjan Dohil, MD
University of California, San Diego

Paul Goodyer, MD
Montreal Children's Hospital, Canada

Daniel R. Salomon, MD
The Scripps Research Institute, La Jolla

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

Doris A. Trauner, MD
University of California, San Diego

www.cystinosisregistry.org

Ordinary People *Changing the World*

One morning, thousands of starfish lay on the beach after a terrible storm had washed them ashore.

An old fisherman named Safran Smith hobbled along the beach slowly tossing one star fish after another back into the ocean. A group of young surfers stopped to watch him. After a while, one of them said, "Hey buddy, there are thousands of starfish on this beach. Even if you spend all day here you won't make a difference."

Safran looked up with a puzzled expression on his face. Finally, he reached down and picked up another starfish. He tossed it back into the water and then turned to the young men and pointed to where the starfish landed.

"I can't do everything," Safran said, "but I certainly did make a difference in the life of *that* starfish."

Startled, the young men looked at Safran and thought about what he had said and done. One by one they joined him, helping to save many more starfish than they could ever have dreamed.

As we enter the holiday season we hope that each of you will keep the 2,000 children and young adults worldwide with cystinosis in your thoughts and prayers.

We also ask you to consider making a gift to the Cystinosis Research Foundation. Like Safran Smith, each of us holds the power to change – and even save – a life.

Perseverance against insurmountable odds and a refusal to accept failure are the hallmarks of bravery and hope.

They are also the cornerstones on which the Cystinosis Research Foundation was built. When Nancy and Jeff Stack founded CRF in 2003, they understood the monumental challenges they faced in finding a cure for cystinosis. They recognized how long and winding the road might be, but they took the first critical steps.

Along the way, others joined the quest. Today, thousands of people across the United States have helped to raise more than $20 million for cystinosis research.

With each passing day we draw closer to reaching CRF's bold vision of finding the cure for cystinosis. While much has already been done, there is still much more to do.

CYSTINOSIS RESEARCH FOUNDATION

To make a gift to the Cystinosis Research Foundation, call 949-223-7610 or visit www.cystinosisresearch.org.

Cystinosis Research Foundation is a non-profit, tax-exempt entity pursuant to Section 501(c)3. Federal Tax ID #32-0067668. 100 percent of the funds raised will support cystinosis research. All gifts are tax deductible.

Photo by Rick Lundh
Story adapted from *The Star Thrower* by Loren Eisley

TOGETHER WE ARE MAKING A DIFFERENCE.

SAVE THE DATES

THERE'S MORE THAN ONE WAY TO ...

We're always impressed and excited to see the creative ways CRF supporters find to raise money for cystinosis research. With help from so many wonderful friends we are getting closer to a cure.

Sunday, December 9, 2012
Dallas Marathon
Running for Nicole – Nicole Hall
Dallas, Texas

Saturday, February 13, 2013
Hope for Holt – Holt Grier
Hearts for Holt Gala
Charlotte, North Carolina

HOPE FOR HOLT
REACHING FOR A CURE

Friday, March 22 – Saturday, March 23, 2013
24 Hours for Hank – Henry Sturgis
24 Hours of Schweitzer Ski Event
Schweitzer Mountain Resort, Sandpoint, Idaho

24 HoursforHank

Thursday, April 18 – 20, 2013
Cystinosis Research Foundation
Day of Hope Family Conference
Balboa Bay Club, Newport Beach, CA

CYSTINOSIS RESEARCH FOUNDATION

Saturday, May 18, 2013
Tina's Hope for a Cure – Tina Flerchinger
Fifth Annual Wine, Stein and Dine Event
Lewiston, Idaho

Tina's Hope for a Cure

May 20–21, 2013
Jenna and Patrick's Foundation of Hope – Jenna and Patrick Partington
CBS Radio Hosts: Golf and Guitars
Haggins Oak Golf Course, Sacramento, CA

Jenna & Patrick's Foundation of HOPE

September 2013
Joshua's Journey of Hope – Joshua Clarke
Third Online Fundraising Auction

Joshua's Journey of Hope

For information about other upcoming CRF events, visit www.cystinosisresearch.org .

2013 NATALIE'S WISH GALA

Miracles, Milestones AND THE POWER OF ONE

SATURDAY, APRIL 20, 2013 ★ BALBOA BAY CLUB, NEWPORT BEACH, CALIFORNIA