

Family Conference Agenda

Wednesday, July 15 12:00 pm – 4:00 pm	CRN Board of Directors Meeting <i>Closed Session</i>	Room Wintergreen
Thursday, July 16 8:00 am – 5:00 pm	Neurological Testing with Dr. Trauner's team <i>Angela Ballantyne, Chelsea Hurt, Monica Lopez, and Sharon Nichols</i>	Room Heather, Hibiscus, & Honeysuckle
12:00 pm – 8:00 pm	Registration / Information Desk	Conference Registration Desk
1:00 pm – 4:00 pm	CRN Scientific Review Board Meeting <i>Closed Session</i>	Wintergreen
5:00 pm – 8:00 pm	CRN Welcome Reception <i>Complimentary</i> <i>Hosts: The Smith Family and the Friend Family</i> Family Introductions 6:30 pm	Rotunda, Resort Deck, & Pool Deck
Friday, July 17 7:00 am – 8:30 am	Continental Breakfast <i>Complimentary</i>	Room Continuous Break Area outside Salons DEFG
8:00 am – 5:00 pm	Neurological Testing with Dr. Trauner's team <i>Angela Ballantyne, Chelsea Hurt, Monica Lopez, and Sharon Nichols</i>	Heather, Hibiscus, & Honeysuckle
8:00 am – 5:30 pm	Registration / Information Desk	Conference Registration Desk
8:00 am – 5:30 pm	Child Care Open	Willow
8:30 am – 8:45 am	Welcome & Opening Remarks <i>Host: Christy Greeley, President and Executive Director</i>	Salons D, E, F, G
8:45 am - 9:15 am	Cystinosis Research Network – Your Advocacy Group <i>Christy Greeley, President and Executive Director</i> Meet the CRN Board of Directors and learn more about how CRN works to achieve its stated vision of the discovery of improved treatments and ultimately a cure for cystinosis and mission of supporting and advocating research, providing family assistance, and educating the public and medical communities about cystinosis.	Salons D, E, F, G
9:15 am – 10:00 am	Keynote Address <i>Jess Thoene, M.D</i> Cystinosis has a century-long history of clinical and laboratory investigations by a wide variety of scientists from Europe and America. This presentation will review the history of cystinosis- where we've been and where we are, and look forward to where we hope to be. Emphasis will be place on key events in the story, with the inclusion of some original findings to impart the flavor of scientific discovery, and the serendipitous nature of the research process. .	Salons D, E, F, G
10:00 am – 10:15 am	Break	

<p>10:15 am - 10:30 am</p>	<p>Plenary Session</p> <p>CRN Sponsored Research Updates Introduction <i>Host: Elva Smith, VP Research</i> An introduction to CRN's research program will be given. Currently funded CRN investigators and others will then provide brief updates on their current research projects.</p>	<p>Salons D, E, F, G</p>
<p>10:30 am – 10:40 am</p>	<p>Newborn Screening Study at NIH <i>Thierry Vilboux, Ph.D.</i> The diagnosis of cystinosis is confirmed by determining the cystine content of polymorphonuclear leukocytes, or by CTNS mutation analysis. Prenatal diagnosis can be obtained by genetic analysis in families with a previous affected child, or by measuring the cystine content of amniocytes or chorionic villi. An effective treatment for cystinosis is oral cysteamine, which lowers lysosomal cystine concentrations, thereby slowing the progression to renal failure. For efficient treatment, cysteamine should be given as early in life as possible, so early diagnosis is invaluable. We explored possibilities to include a cystinosis testing in newborn screening programs. However, not enough leukocytes are present in a bloodspot to determine the cystine content of leukocytes on biochemical grounds. Therefore, we evaluated possibilities for screening on molecular grounds. Specifically, from a newborn blood spot, the technique should be able to discriminate all the known mutations (single base mutations, insertions and deletions) involved in infantile cystinosis and be able to differentiate carriers from patients; in addition, the technique should be rapid and able to be performed in high throughput. Different approaches are considered, including the flow cytometry-like technique from Luminex (XMAP) and the MALDI-TOF mass spectrometry from Sequenom (Iplex). Based on one of these techniques, it would be possible to analyze a variety of known mutations within the same experiment/sample well. Pilot experiments are designed to show effectiveness of each of these techniques, using our large group of cystinosis patients' DNA samples as templates. So far, newborn screening tests based on molecular grounds are not available or implemented. Cystinosis is a prototypic disease for proof of principle for newborn screening on molecular grounds, after which it is likely that screening for other genetic diseases will follow.</p>	<p>Salons D, E, F, G</p>
<p>10:45 am – 10:55 am</p>	<p>Tissue Repository for Cystinosis <i>Jess G. Thoene, M.D.</i> The description of atubular glomeruli (ATG) in diabetic nephropathy, and the occurrence of the "swan neck" deformity in the proximal renal tubule in cystinosis prompted a pilot study in one cystinotic kidney to determine the occurrence of ATG in cystinotic kidney specimens. The results were encouraging, and CRN then funded a cystinosis tissue repository at the University of Michigan that has enabled us to obtain renal tissue post transplantation. Three separate patient samples have now been evaluated by thick section microscopy and 3D glomerular re-construction (performed by Patrick Walker and associates at Nephropath in Little Rock, Arkansas), with a fourth under study. The results are highly statistically significant in the difference in incidence between ATG in cystinotic renal tissue (81%) compared to normal control tissue (4%) $p < 0.0001$. This finding may help to explain the long time course and evolution of glomerular failure in cystinosis.</p>	<p>Salons D, E, F, G</p>
<p>11:00 am – 11:10 am</p>	<p>Study of ATP metabolism in human cystinotic proximal tubular cells and in humans with cystinosis in vivo <i>Elena Levchenko, M.D., Ph.D.</i> We have extensively studied ATP metabolism in skin fibroblasts and proximal tubular cells of patients with cystinosis. Despite a slight decrease in intracellular ATP levels, mitochondrial ATP generation and the activity of Na⁺, K⁺-ATP-ase were normal in both cell types. These results contrast previous data obtained in proximal tubular cells loaded with cystine dimethylester. Cysteamine treatment normalized intracellular cystine, but did not influence intracellular ATP content.</p>	<p>Salons D, E, F, G</p>
<p>11:15 am – 11:25 am</p>	<p>Development of a cysteamine in situ gelling system for the topical treatment of corneal crystals in cystinosis <i>Olufemi Rabi; BPharm, PhD</i> Corneal cystine crystal deposition is an early diagnostic feature of nephropathic cystinosis and leads to photophobia, blurred vision and corneal erosions. Current treatment is with topical cysteamine 0.55% eye drops, with hourly administration which limits compliance and efficacy. Our aim is to formulate a gelling system which increases ocular contact time of the cysteamine and reduces the lachrymal drainage. As a result bioavailability can be increased with less frequent administration which would greatly improve the quality of life of cystinotic patients. Temperature induced gelation systems consisting of a mixture of poloxamers and a cellulose derivative were investigated. These polymers are suitable for the eye and were selected due to their compatibility with cysteamine, their rheological behaviour under different conditions (shear rates, temperature, dilution with simulated tear fluid) and the <i>in vitro</i> cysteamine drug release characteristics. In parallel, commercial preparations containing other drugs were used for bench marking. Studies <i>in vitro</i> showed slower rate of release of cysteamine as the concentration of the polymers increased while maintaining dropability and good rheological profiles. We predict good tolerability of cysteamine eye gel in line with other commercial gels or <i>in situ</i> gelling systems.</p>	<p>Salons D, E, F, G</p>

11:30 am – 11:40 am	<p>Functional Characterization of Cystinosin – LKG <i>Francesco Emma, M.D.</i> We recently identified an isoform of the cystinosin protein, termed "cystinosin-LKG" based on its last amino acid sequence. The expression of this isoform is not restricted to the lysosomal compartment and the protein is also expressed in other intracellular vesicular structures and to the plasma membrane. Further studies have shown that cystinosin-LKG represents approximately 15-20% of CTNS gene transcripts in most tissues, except in the testis where it accounts for approximately 50% of the transcripts. Up-regulation of the CTNS gene in different experimental conditions does not modify the relative expression of the two major cystinosin isoforms. These data and data on the characterization of cystinosin-LKG sub-cellular compartments will be presented.</p>	Salons D, E, F, G
11:45 am – 11:55 am	<p>Determination of Intraleucocitary Cystine by High Performance Liquid Chromatography (HPLC) in Patients with Cystinosis <i>Leticia Belmont, M.D.</i> In México we do not utilize any methodology for the determination of cystine in order to follow the therapy of our patients, which have to travel to other countries for monitoring their cysteamine treatment. This HPLC methodology is adequate for quantification of cysteine in leukocytes for diagnosis and monitoring treatment of cystinosis patients. The objective of the present work is to implement in México a methodology for the quantification of cystine in leukocytes by HPLC. The support of this has been made possible by CRN.</p>	Salons D, E, F, G
12:00 pm – 12:10 pm	<p>Successful treatment of the murine model of cystinosis using bone marrow cell transplantation <i>Stephanie Cherqui, Ph.D.</i> The long-term objective of this project is to use the patient's own bone marrow stem cells for transplantation and to genetically modify them <i>ex vivo</i> to introduce a functional version of the defective gene (<i>CTNS</i>). This will create a reservoir of healthy stem cells in the bone marrow that can migrate to and integrate in the different organs as a function of the progressive tissue damage for the life of the patient. As pre-clinical studies, we are using the mouse model for cystinosis, <i>Ctns</i>^{-/-} mice, that accumulates cystine in all the tissues and develops similar defects to those of the human children. We transplanted three types of bone marrow stem cells: the whole bone marrow cell (BMC), hematopoietic stem cells (HSC) and mesenchymal stem cell (MSC). The cells were from the GFP-transgenic mice, which have the advantages to express a functional <i>Ctns</i> gene and a reporter gene, the Green Fluorescent Protein (GFP), that allow the identification of the transplanted cells in each organ of the transplanted mice. Four months post-transplant, organ-specific cystine content was reduced by 57% to 94% in all organs tested in the BMC or HSC-treated mice. A large quantity of transplanted BMC and HSC was revealed in all organs tested. Most of these cells were part of the intrinsic structure of the organ. The natural progression of renal dysfunction was prevented and deposition of corneal cystine crystals was significantly improved in the BMC and HSC-treated mice. In contrast, MSC did not integrate efficiently in any organ. We are currently analyzing the long-term transplantation impact of BMC and HSC-transplanted <i>Ctns</i>^{-/-} mice when they reach 15 months old (a mouse with cystinosis lives ~2 years). Our preliminary data showed that BMC transplantation lead to a preservation of the intraocular pressure, the neuromotor activity, the bone density and can improve the renal function. The cystine content in each tissue was kept significantly low compared to the non-treated <i>Ctns</i>^{-/-} mice. Transplantation of BMC or HSC but not MSC results in the successful treatment of cystinosis in our mouse model demonstrated by high levels of tissue integration, significant reductions in tissue cystine content and preservation of organs function.</p>	Salons D, E, F, G
12:15 pm – 12:25 pm	<p>Gene Transfer Studies for Cystinosis <i>Vasiliki Kalatzis, Ph.D.</i> We performed the first viral-mediated <i>CTNS</i> gene transfer studies and evaluated the feasibility of this strategy as an alternative or complementary treatment for cystinosis. Initially, we treated human <i>CTNS</i>^{-/-} fibroblast cell lines and primary murine <i>Ctns</i>^{-/-} hepatocyte cultures with <i>CTNS</i>-expressing adenovirus vectors <i>in vitro</i> and demonstrated that gene transfer can reduce cystine storage. However, <i>in vitro</i> treatment of hepatocytes from young and older mice suggested that the efficiency of correction was age-dependent. We validated these observations <i>in vivo</i> by performing a) short- and b) long-term <i>CTNS</i>-transfer studies in the liver of <i>Ctns</i>^{-/-} mice. a) Short-term <i>CTNS</i> gene transfer in young <i>Ctns</i>^{-/-} mice resulted in a significant decrease in cystine levels as compared to levels in non-treated mice. In contrast, <i>CTNS</i> gene transfer in older mice did not significantly reduce cystine levels. A possible explanation for the age-dependent efficiency of cystine clearance is that a longer post-injection period is required to reduce the higher cystine levels in older mice. b) Interestingly, and consistent with our short-term data, long-term gene transfer significantly reduced cystine levels in young <i>Ctns</i>^{-/-} mice but not in older mice. Our observations suggest that the age-dependent phenomenon may be due to a factor other than duration of cystinosis expression. Taken together, our data provide the proof-of-concept that gene transfer is feasible for correcting defective lysosomal transport and suggest that, in the case of cystinosis, it may be preventive but not curative in some tissues.</p>	Salons D, E, F, G
12:30 pm – 1:45 pm	<p>Luncheon <i>Complimentary</i></p>	Waterside Restaurant

1:45 pm – 3:00 pm	<p>Poster Sessions This session will showcase a mix of science, medicine, industry and advocacy group, and patient experiences to provide an interactive experience for both family and professional attendees. Researchers, clinicians, industry, advocacy representatives, students, patients, and caregivers will be invited to exhibit their latest research findings, treatment breakthroughs, advocacy group updates, and real patient and family experiences. This will be an interactive session where exhibitors will be available to discuss their work or experiences with those attending. We invite you to browse the posters and take this opportunity to ask the authors and presenters questions.</p>	Rhododendron
3:00 pm – 3:15 pm	Break	
3:15 pm – 3:45 pm	<p>Cystoran™ (Cysteamine Hydrochloride Ophthalmic Solution): Project Update <i>Gianfranco Fornasini, Ph.D., Senior VP, Scientific Affairs, Sigma Tau Pharmaceuticals, Inc.</i></p>	Salons, D, E, F, G
3:45 pm – 5:00 pm	<p>Medical Panel <i>Moderator: Bill Gahl, M.D., Ph.D.</i> Please join the entire group for the unique and informative opportunity to have your questions and concerns addressed by the leading physicians and researchers in cystinosis. All of the doctors who have presented at the Family Conference, all attending Medical Advisory Board and Scientific Review Board members, as well as other health care professionals involved in treating and researching cystinosis are scheduled to participate. Questions for the panel will be collected during the proceedings today.</p>	Salons D, E, F, G
5:00 pm – 5:30 pm	<p>Session Wrap-Up <i>Christy Greeley, CRN President and Executive Director</i></p>	Salons D, E, F, G
6:30 pm	<p>Speaker/Guest Dinner <i>Closed Session</i></p>	Balsam
Saturday, July 18 7:00 am – 8:45 am	<p>Continental Breakfast <i>Complimentary</i></p>	Room Continuous Break Area outside Salons DEFG
8:00 am – 5:00 pm	<p>Neurological Testing with Dr. Trauner's team <i>Angela Ballantyne, Chelsea Hurt, Monica Lopez, and Sharon Nichols</i></p>	Heather, Hibiscus, & Honeysuckle
8:00 am – 5:30 pm	Registration / Information Desk	Conference Registration Desk
8:00 am – 5:30 pm	Child Care Open	Willow
8:45 am – 9:00 am	<p>Opening Comments <i>Host: Marybeth Kruppenacker, Director, Education and Awareness Committee Member</i> CRN Education and Awareness program overview will be given.</p>	Salons D, E, F, G
9:00 am – 10:00 am	<p>Patient Panel Presentation <i>Moderators: Marybeth Kruppenacker and Pam Woodward</i> <i>Panelists: Mack Maxwell, Tom Melang, Sarah Melang, Eddie Langley, Karen Gledhill, Morgan Friend, Tahnje Woodward, Laura McGinnis, and Christian Morales</i> Patient panel presentation during which panel members will answer prepared questions and address topics related to the use of coping mechanisms through the ups and downs that cystinosis brings related to not only developmental and transitional issues of daily life but also medical issues. Teens and adults living with cystinosis will be featured and will share how they have recognized and lived to their full potential given the challenges they have faced. Audience participation will be encouraged.</p>	Salons D, E, F, G
10:00 am – 10:15 am	Break	
10:15 am – 10:45 am	<p>Cystinosis Research Foundation Update <i>Nancy Stack, President and Jason Grier, Board Member, CRF</i> The Cystinosis Research Foundation is the largest fund provider of cystinosis research in the world. We have funded over fifty-four research studies in our quest to find better treatments and a cure for cystinosis. We will provide an overview of the CRF, discuss the current research funded by the CRF and present the 2009 CRF video.</p>	Salons D, E, F, G

10:50 am – 11:20 am	<p>National Organization for Rare Disorders (NORD): It's All About Collaboration <i>Jean Campbell, NORD Vice President for Membership Development</i> <i>"Never doubt that a small group of thoughtful, committed people can change the world: indeed it's the only thing that ever has!"</i> Since 1983, NORD has been the voice for the rare disease community, venturing into the un-chartered territory seeking to improve the lives of individuals diagnosed with a rare disease. Learning about NORD's programs and services will reveal our common threads that woven together produce a unique and compelling tapestry.</p>	Salons D, E, F, G
11:25 am – 12:15 pm	<p>Envisioning Transition <i>Maya Doyle, LCSW and Leslie Clogston, CCLS, MS</i> Will review the concept of transitioning for children with special health care needs and transition as a process common to all people and life stages. Will assist families to visualize their children's transition to adulthood. Will provide age-appropriate suggestions to build independence and medical self-management and provide resources on transitioning for families and health care providers.</p>	Salons D, E, F, G
12:15 pm – 1:30 pm	<p>Luncheon <i>Complimentary</i></p>	Waterside Restaurant
1:30 pm – 3:00 pm	<p>Workshop Session A These topic specific workshops will allow families to tailor their conference experience to meet their specific needs. Families will have the opportunity to discuss and share their own experiences regarding the latest research, management techniques, and therapies with leading experts as well as with other families with similar issues and concerns. Sessions will be repeated so that participants may attend more than one workshop.</p> <p>A1 – Gastrointestinal Issues and ER Cysteamine Formulation/Eye Drops and Ocular Issues <i>Host: Jen Wyman</i> <i>Panelists: Bill Gahl, Ranjan Dohil, Robert Kleta, Olufemi Rabi, Bruce Barshop</i></p> <p>A2 – Transplantation/Pediatric to Adult Care Transition Issues <i>Host: Pam Woodward</i> <i>Panelists: Allan Kirk, Rick Kaskel, Mark Benfield</i> Teens with cystinosis are encouraged to attend this session.</p> <p>A3 – Neurology and Educational Issues <i>Host: Brittney LeBeau</i> <i>Panelists: Doris Trauner and staff</i></p> <p>A4 – Nephrology/Fanconi's Syndrome/Growth Issues <i>Host: Frankie McGinnis</i> <i>Panelists: Craig Langman, Ewa Elenberg, Jess Thoene, Elena Levchenko, Leticia Belmont, Francesco Emma</i></p> <p>A5 – Siblings Only <i>Moderators: Maya Doyle, LCSW and Leslie Clogston, CCLS, MS</i> For siblings of children with cystinosis age 6-16. Will explore the experience of being a sibling of a child with Cystinosis using discussion, storytelling, and art activities. Siblings should have some awareness of the illness if they are attending this session.</p>	<p>Salon A</p> <p>Salon B</p> <p>Salon C</p> <p>Dogwood A</p> <p>Dogwood B</p>
3:00 pm – 3:15 pm	<p>Break</p>	

<p>3:15 pm – 4:45 pm</p>	<p>Workshop Session B</p> <p>B1 – Gastrointestinal Issues and ER Cysteamine Formulation/Eye Drops and Ocular Issues <i>Host: Mack Maxwell</i> <i>Panelists: Bill Gahl, Ranjan Dohil, Robert Kleta, Olufemi Rabi, Bruce Barshop</i></p> <p>B2 – Transplantation/Pediatric to Adult Care Transition Issues <i>Host: José Morales</i> <i>Panelists: Allan Kirk, Rick Kaskel, Mark Benfield</i> Parents are encouraged to attend this session.</p> <p>B3 – Neurology and Educational Issues <i>Host: Frankie McGinnis</i> <i>Panelists: Doris Trauner and staff</i></p> <p>B4 – Nephrology/Fanconi’s Syndrome/Growth Issues <i>Host: Brittney LeBeau</i> <i>Panelists: Craig Langman, Ewa Elenberg, Jess Thoene, Elena Levchenko, Leticia Belmont, Francesco Emma</i></p> <p>B5– Siblings and Children with Cystinosis <i>Moderators: Maya Doyle, LCSW and Leslie Clogston, CCLS, MS</i> For siblings and Cystinosis kids, aged 6-16. Will bring both groups together using discussion and medical play to explore the experience of being a sibling or a child with Cystinosis.</p>	<p>Salon A</p> <p>Salon B</p> <p>Salon C</p> <p>Dogwood A</p> <p>Dogwood B</p>
<p>5:00 pm – 5:30 pm</p>	<p>Conference Wrap Up <i>Christy Greeley, President and Executive Director</i> Summary of conference proceedings and announcement of “Above and Beyond” Achievement Award.</p>	<p>Salons D, E, F, G</p>