The Children's
Medical Research
Foundation, Inc.®

KirbyGram

The latest news on Kirby Wilson and friends and the search for a cure for Sanfilippo Syndrome

December 2013

Our goal is to create awareness of Sanfilippo Syndrome and other neuro-genetic disorders, fund medical research and find a cure.

Dear Friends,

As our dream of a cure grows ever closer to coming true, Brad and I can't help but reflect back on our journey. It began with Kirby as a four-year-old bundle of energy and joy who delighted in song, dance and smiles. "Happy?" is a question she asked daily – a voice we will never forget and a question that we remain mindful of each day. Brad and I are grateful for her continued comfort, and we delight in her moments of happiness.

We also think of you and the blessings you have brought to our lives. Our own angels - guardians of our dream and mission, who have stood strongly by our sides for 19 years, like Kirby was your very own. We reflect on the success story you are helping to create. The story of happiness for thousands of children. The story of honor for Kirby. Brad and I are blessed by your devotion to our family, and your certainty of our mission continues to be our good fortune.

This holiday season, our wish for your families is happiness, the same happiness Kirby brings to our lives. We ask that you think of Kirby, and in her honor, continue to support The Children's Medical Research Foundation as it strives to provide funds needed to support a human trial in 2014 and make our dream of a cure a reality.

May the blessings of the season be yours, now and always,

~ Sue and Brad Wilson

A year of happy for Kirby and the Wilsons

Fundraising News

Junior Board Cruises

The Foundation's Junior Board hosted its second fundraiser, "Cruising for a Cure," on August 23rd in Chicago. Maggie Wilson and fellow Board members Joe Avram, Kelly Brummet, Ryan Brummet and Bob Karpiak organized this two-hour evening cruise on Lake Michigan, complete with music, cocktails, food and raffle.

The event raised more than $2,800 with 85 guests. A special thanks goes to Broadway in Chicago and the Brummet, Karpiak and Sorensen families for their contributions toward the success of the evening. Brad and Sue were delighted to attend the event and to see, firsthand, this Board's enthusiasm toward being a part of the Foundation's mission of the cure.

BonVoyage!

Oh What A Night!

Thanks to Karin Matusiak and Mary Swiontek and their group of Trivia volunteers, the Foundation held its third Trivia Night November15th, and oh what a night it was!! This casual, bring-your-own- everything kind of night saw teams of ten gathered with their own food, beverages and table décor, ready to compete for the tacky, yet oh so coveted, first place crowns. Karin and Mary also took on the task of MCing the event, handling the questions and crowd in a way that kept the evening running smoothly with seemingly non-stop laughter. The lucky, or should we say smart, team of Lyons Township High School seniors won its rights to the crowns by correctly answering 62 of 80 questions. The best news was that Trivia Night's small but very tenacious group of volunteers raised more than $9,350 for research completely on its own, asking nothing of the Wilsons. Sue comments, "I know how much work goes into fundraising, and this night could not have been done without the considerable time and enthusiasm of some pretty special friends, for which we give thanks. It was a rare and special treat to sit back and enjoy an evening benefiting the Foundation."

Top Team Crowned!

The Foundation Gives Thanks…

To **Donna Logan-Gabel, Margaret Dawe, Nicholas Megofna, Ralph Siegel, Raymond Brazell, and Gregory Miller,** who designated the Foundation as their charity of choice in their employers' United Way campaigns. Thanks for uniting for Kirby!

To **Achim Seifert and Eric Wolfe** for their donations and to their employers **Cornerstone Real Estate Advisors** and **LEGO Children's Fund** for their matching gifts, which doubled the donations!

To the many friends and family who donated to the Foundation in fond memory of **Tom Thomas,** a longtime family friend of the Wilsons.

To Kirby's grandmother, **Joanne Wilson,** for her donations in memory of **Rev. Barbara Teeter** and **Gloria Balaban.**

To board member **Barbara Cummings** for her donations in fond memory of her sister-in-law **Lorie Cummings, Norm Vogt, Bob Heidrick** and **Casey Vallee.**

To **Kirschbaum's Bakery** and **Casey's Market,** both from Kirby's hometown of Western Springs, for their continuous fundraising efforts using cash jars. And to the people of the community who fill them and have helped to raise more than $720 to date this year, your "hometown girl" thanks you from the bottom of her little heart.

News From Connecticut

Holiday fundraising efforts by **Artisan's Marketplace** raised $1,100 for the Foundation. This annual event reminds the Logans each year that the fundraiser's name, "Stars for Hope," is not just about ornaments, but also the generosity of the many "stars" within their community who keep Rhianna's Hope shining bright.

Gene and Cynthia are also grateful to those who brightened their holiday with donations to the Foundation in honor of Rhianna in lieu of gifts.

(Continued on Page 3)

Fundraising News

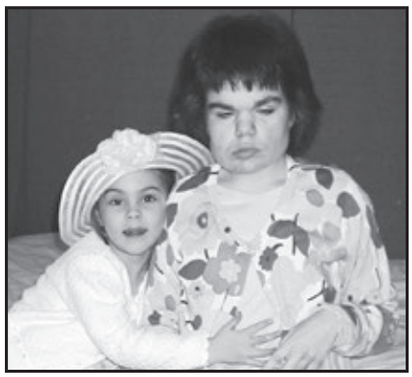
The **Bristol Auto Club** revved up its support of the Foundation by making a donation in honor of Rhianna. We appreciate the group's never-ending drive to find a cure.

Rhianna's grandparents, **James and Martha Couture,** and longtime supporters and friends **Alan and Donna Theriault** celebrated Rhianna's 21th birthday with donations to the Foundation.

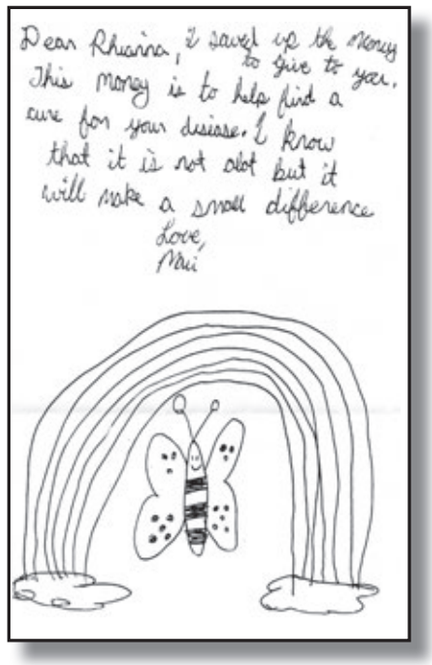
The Theriault's friends **Peter and Joanne Brandien** also honored Rhianna with a donation, as did **Dennis and Laurel Colgan** of **Picture Fame,** who contributed for "Rhianna and the kids."

Donations were received in memory of Gene and Cynthia Logan's longtime friend, **Alta M. Saunders,** from the **Logans, Frank and Lola Guglietta,** and members of the **Delta Kappa Gamma Society, MU Chapter.**

Our thanks to the Logans' friends **Tabitha** and **Justin Manafort** for honoring Rhianna with a donation from their annual **Manafort Family Foundation** golf outing. The Logans are truly grateful for the Manafort Foundation's continued support of Rhianna. It contributes generously to so many of the local charities that it is a blessing that a cure for Rhianna remains a priority in the family's heart.



Rhianna and friend Marianna



And last, but certainly not least, we ask that you read the note above from the Logans' 11-year-old neighbor, Marianna Belanger, that accompanied a $117.00 donation. We beg to differ with this wonderful girl – her words and donation mean a lot and make all the difference in the world to families like the Logans and Wilsons.

A note from Cynthia Logan

What word can best describe the emotions as Rhianna turns 21? Amazed, grateful, unbelievable – all seem inadequate.

A recent webinar describes the reality of human trials for Sanfilippo and the wonderful supporters who have been with us for the past 17 years. To listen as doctors describe their success with gene therapy in their mouse models and their goal of human trials as soon as next year sends our hope soaring. That followed by a direct thank you to The Children's Medical Research Foundation for funding the research from the start 15 years ago sends our gratitude soaring. Each fundraiser and all the special people who made it successful, every note of encouragement, all the newspaper articles, TV coverage, the other MPS families we have met and, of course the unending dedication of Sue and Brad Wilson all run through my mind.

To realize these efforts have had an impact is an incredible feeling. I do believe we will see a cure. What we thought could only be a miracle will be a miraculous accomplishment. My sincere gratitude to all who have and continue to support Rhianna's Hope, to the dedicated researchers who continue to work so diligently, and of course, to the Wilsons who while caring for Kirby continue to fundraise and work so hard to keep it all moving forward.

And To The Families Working Together For The Cure . . .

We thank **Michelle Dick**, **Carol Lawson, Judy Bible, Robert Allen** and **Grandma and Grandpa Kidwell** for their donations to the Foundation in celebration of **Brooke Kidwell's** high school graduation, as well as her and her sister **Ashleigh's** birthdays. What a great year of celebrations for the **Kidwell family**.

Brooke and Brad having a moment, with Ashleigh in the background

Research Update

Haiyan Fu, Ph.D and Douglas McCarty, Ph.D, Center for Gene Therapy, The Research Institute at Nationwide Children's Hospital

October, 2013

We have developed effective gene therapy approaches for the treatment of the most common two forms of Sanfilippo Syndrome, MPS IIIB and IIIA. We have tested these approaches and shown functional benefits in mouse models. Currently, we are in the process of moving these two approaches toward gene therapy clinical trials in patients with MPS IIIB and A. Dr. Kevin Flanigan will lead our team at Nationwide Children's Hospital (NCH) for this move. The following are the ongoing and planned projects in preparation for the proposed clinical trials.

1. Natural History in Mucopolysaccharidosis Type III

The Institutional Review Board (IRB) at NCH has recently approved this study.

This study – generously supported by Ben's Dream, The Sanfilippo Children's Research Foundation, and The Children's Medical Research Foundation – has the following goals:

- To assess our ability to measure changes in mental function and mobility
- To study the natural history and progress of the disease
- To establish normal ranges of function in patients who will be potential subjects for a future treatment study using gene therapy
- To find indicators of disease progression over one year. This will include changes in brain activity and in cerebrospinal fluid which will require MRI and lumbar puncture procedures.

The enrollment of study subjects will begin soon.

2. MPS IIIB Gene Therapy

1) **Pre-IND meeting with the FDA for MPS IIIB gene therapy clinical trial**
Pre-IND meeting with the FDA was held on Aug. 23, 2013, to discuss issues regarding our planned GLP-toxicology testing of our gene therapy vector product and the clinical trials. We are waiting for the feedback from the FDA while preparing the toxicology testing.
2) **GLP-toxicology testing of AAV9-hNAGLU vector (Sponsor: NIH/NINDS):** The tox testing will begin as soon as we receive the nod from the FDA.
3) **Submit an IND application to the FDA for a phase I/II MPS IIIB gene therapy clinical trial (Sponsor: NIH/NINDS)**
Upon the completion of the GLP-toxicology testing, we will submit an IND application to the FDA for a phase I/II gene therapy clinical trial in patients with MPS IIIB.
4) ***Produce clinical-grade AAV9-hNAGLU vector for the proposed trial:**
To prepare for the proposed MPS IIIB clinical trial, we will initiate the production of clinical-grade AAV9-hNAGLU vector as soon as receiving financial support for it. The vector production and validation will take 6-8 months. The vector will be stable when stored at -80ºC.
5) **Phase I/II MPS IIIB gene therapy clinical trial***

3. MPS IIIA Gene Therapy

1) **Produce AAV9-hSGSH vector for GLP toxicology testing***
We will initiate the production of AAV9-hSGSH vector for GLP toxicology testing, which is required by the FDA.
2) **Submit pre-IND application to the FDA**
We will submit a pre-IND application to the FDA in a few months to request for pre-IND meeting with the FDA to discuss our GLP toxicology testing of AAV9-hSGSH vector, for a phase I/II MPS IIIA gene therapy clinical trial.
3) **GLP-toxicology testing of AAV9-hSGSH vector***
The GLP-toxicolocy testing will be performed following the FDA advices at the pre-IND meeting.
4) **Submit an IND application to the FDA for a phase I/II MPS IIIA gene therapy clinical trial***
Upon the completion of the GLP-toxicology testing, we will submit an IND application to the FDA for a phase I/II gene therapy clinical trial in patients with MPS IIIA.
5) **Produce clinical-grade AAV9-hSGSH vector for the proposed MPS IIIA gene therapy clinical** trial*
6) **Phase I/II MPS IIIA gene therapy clinical trial***

4. Identification of brain-specific biomarkers for MPS IIIA and IIIB ($200,000)*

No effective outcome measures for MPS III are currently available for the evaluation of therapeutic benefits. This will be a critical challenge for our planned gene therapy clinical trials. In our recent preliminary studies, we have developed a minimally invasive approach that can detect neuropathology changes in the brain in MPS IIIA and IIIB mice. The majority (>94%) of these changes (>300) can be corrected by our AAV9 gene therapy treatment in both MPS IIIA and IIIB mice. Further studies are needed to identify potential brain-specific markers and test this approach in MPS patients. They can then be further tested in our planned gene therapy clinical trials.

*Unfunded projects

(Continued on Page 5)

Research Update

Svitlana Garbuzova-Davis, Ph.D., D.Sc.
Paul R. Sanberg, Ph. D., D.Sc.
Center for Aging & Brain Repair
Department of Neurosurgery
University of South Florida
College of Medicine

September, 2013

For more than a decade, researchers at the University of South Florida have studied the potential of human umbilical cord blood (hUCB) stem cells to treat various neurodegenerative disorders, as well as brain and spinal cord injuries. The mononuclear cell portion from hUCB (MNC hUCB) is a diverse group, which includes stem cells, lymphocytes, and monocytes. A single cell dose has been shown to provide benefits in animal models of Alzheimer's disease, amyotrophic lateral sclerosis, stroke, and Parkinson's disease, suggesting that MNC hUCB cells are able to repair a damaged or defective nervous system.

The research team lead by Dr. Sanberg has been investigating a new cell therapy approach for Sanfilippo Syndrome Type B (MPS III B) by administration of MNC hUCB cells. A deficiency of the *Naglu* enzyme, causing accumulation of heparan sulfate, is a major feature of this disease, and MNC hUCB cells might be preferable to other cell sources for delivering the missing enzyme. The initial study (Garbuzova-Davis S, Willing AE, Desjarlais T, Davis CD, Sanberg PR. *Transplantation of human umbilical cord blood cells benefits an animal model of Sanfilippo syndrome type B.* Stem Cells Dev, 14(4): 384-394, 2005) demonstrated that administration of MNC hUCB cells into the lateral brain ventricle of early symptomatic mice modeling MPS III B has positive effects. Administered cells survived for a long time (7 months), migrated into different brain structures, improved neuronal architecture in the hippocampus and cerebellum, and reduced GAG accumulation in the liver of treated mice. Although all of these results indicate the benefits of MNC hUCB cells, we approached a less invasive method of cell delivery. In another study (Garbuzova-Davis S, Klasko SK, Sanberg PR. *Intravenous administration of human umbilical cord blood cells in an animal model of MPS III B.* Comp Neurol, 515(1): 93-101, 2009), a single dose of MNC hUCB cells was administered into the veins of Sanfilippo mice at early or late stage disease. Results showed behavioral improvements in enzyme-deficient mice, survival and wide distribution of administered cells within and outside the central nervous system. Also, heparan sulfate accumulation was reduced in the liver and spleen of mutant mice, 6 months after receiving hUCB cells.

Additionally, an anti-inflammatory effect by MNC hUCB cell transplantation was determined.

However, most observed behavioral benefits in Sanfilippo mice were limited to a short period after transplantation, possibly due to declining production of the missing enzyme. This scarcity and the progressive nature of MPS III B disease suggested that repeated injections of lower cell doses might prove more effective than a single dose. To address this possibility, we investigated the effect of repeated MNC hUCB cell infusions. In this study (Willing A E, Garbuzova-Davis S N, Zayko O, Derasari HM, Rawls AE, James CR, Kuzmin-Nichols N, Sanberg CD, Sanberg PR. *Repeated administrations of human umbilical cord blood cells improve disease outcomes in a mouse model of Sanfilippo syndrome type III B.* Cell Transplantation, under review), we tested whether repeated low doses of MNC hUCB cells would be more beneficial than a single dose of cells. The MNC hUCB cells were intravenously administered into *Naglu* mice monthly for 6 months. Behavioral (spontaneous locomotor activity and cognition) and various neuropathological tests were performed in these mice, and results were compared to *Naglu* mice receiving a single: low cell dose, high cell dose, or media injection. Briefly, our study results showed that repeated cell doses reduced stereotyped behaviors and restored normal anxiety-like behavior in these mice. The repeated cell administrations also restored hippocampal cytoarchitecture, decreased GM3 ganglioside accumulation and decreased microglial activation, particularly in the hippocampus and cortex. It is our conclusion that the neuroprotective effect of MNC hUCB can be enhanced by repeated cell administrations and is likely associated with continuous delivery of the missing enzyme.

Thus, repeated MNC hUCB cell injections are likely to provide long-term benefit by affording sustained *Naglu* enzyme replacement in MPS III B, as well as long-term trophic support against the progressive neuronal degeneration. In addition, the multiple smaller doses better translate to clinical settings. These studies therefore provide the groundwork for more comprehensive investigations to optimize the frequency and size of multiple injections in relation to safety and clinical applicability.

We are grateful for the support of our studies by The Children's Medical Research Foundation, Inc. We especially want to thank Susan M. and R. Bradford Wilson for their marvelous support.

Robert K. Yu, Ph.D., Med.Sc.D
Institute of Molecular Medicine and Genetics, Medical College of Georgia

September, 2013

Dr. Yu's major research efforts concern the chemistry, metabolism and biological function of complex glycoconjugates, particularly glycosphingolipids. These compounds play crucial roles in determining cellular properties such as intercellular interactions, recognition, and adhesion. In particular, he and his team are

(Continued on Page 6)

Research Update

developing an understanding of the role of glycoconjugates in cell proliferation and differentiation, as well as the metabolic basis and regulatory mechanisms for changes of their expression in the developing nervous system. A major thrust of his more recent effort, supported by grants from CMRF and NIH, is on the glycobiology of neural stem cells. He is developing an understanding of the role of stage-specific glycoconjugates in governing events in cell differentiation and cell-fate determination via several signaling pathways. During the past year, he has discovered many so-called stage-specific glycolipids and glycoproteins that are important for cell fate determination. Most interestingly, he has found an association of a cell surface ganglioside, called GD3, in rapidly proliferating cells, such as neural stem cells. This association results in regulation of the activity of a mitogen (epithelial growth factor) receptor that controls cellular proliferation. An understanding of how cell growth is controlled is critically important in utilizing them for cell transplantation studies. The ultimate goal is to utilize those cells for the treatment of a variety of neurodegenerative diseases, such as Sanfilippo disease, Alzheimer's disease, Parkinson's disease, and brain injury.

Kirby's Going Green!

We no longer issue the June edition of the *KirbyGram*.
But, you can receive late-breaking news and event updates
while helping the Foundation to go green and
save much-needed funds at the same time.
Please e-mail your name and phone number to curekirby@sbcglobal.net
to help us start a new, greener database of our supporters.

Fundraising Opportunities

Have Fun With This Office "Fun" Raiser – Kirby Dares You!

Here's a fundraising idea that can be challenging and fun for everyone in your office. Are you willing to take a dare for Kirby? Here's how it works. Your company pledges a total amount it would be willing to donate to the Foundation. Then each employee willing to take on a dare chooses the dare and the amount to be donated if he or she follows through. There can be a list of suggested dares with donation amounts, or you can leave it up to the employees to get creative and have some fun. Do a dance or perform a song on the street, or for the office, wear heels for a day (that would be a guy thing), get a Mohawk, do cartwheels down a hall, eat or drink a mystery concoction….all for fun and a great cause.

A Match For Kirby

Does your company have a matching gift program? It could double your support of the Foundation.

United Way Can Be For Kirby, Too

Does your company have United Way pledges at your workplace? Although we are not a United Way member, you can designate The Children's Medical Research Foundation as your recipient, and the funds will be forwarded to us through the United Way Campaign! Simply give your local United Way agency the Foundation name, address and our Federal ID #36-4033667.

Give Kirby Security

Tired of taxes? The Foundation now has a brokerage account available that allows you to donate appreciated securities. Why pay tax on the gains when you can realize a charitable deduction of the full market value of your stocks . . . and it's for Kirby, too! Contact Sue Wilson at (708) 784-0631 to learn more.

A Gift Like No Other

This holiday season give clients a donation to The Children's Medical Research Foundation in their name. It's a gift that won't gather dust and goes far beyond any other.

Celebrate, And Make It For Kirby

Is there a special birthday coming up for a family member or friend? Are you looking for an alternative to the typical "over the hill" gift? Be different. In lieu of gifts, donate to The Children's Medical Research Foundation. Kirby always loves a party!

The Sweetheart Dinner Dance
Friday, February 14, 2014
at the
Four Seasons Hotel Chicago

An elegant setting at one of the world's finest hotels

The 19th annual Sweetheart Dinner Dance will be held Friday, February 14, 2014, in the Ballroom of the Four Seasons Hotel Chicago.

Executive Chef Kevin Hickey will serve a four-course dinner in contemporary American style enhanced by the great bounty of the Midwest.

We will be treated to the magical sounds of the Michael Lerich Orchestra, which has entertained us for the past 18 years! And silent auction packages promise to tempt sports, travel, dining, spa and shopping enthusiasts.

Reservations are $250 per person or $2,500 for a table of ten and must be made in advance. Invitations will be mailed in December, or you can reserve your place now online at www.curekirby.org.
Please plan to join us by marking your calendars now.

We need your help to make it a success

This dinner dance is the primary fundraising event of the year, and we're asking you to help ensure its success.

We have designated five sponsorship levels for the Sweetheart Dinner Dance, as listed below. In appreciation of your sponsorship, you will receive prominent event recognition. We ask that you indicate your wishes on the following Reply Form and return it to The Foundation or visit us online at www.curekirby.org. Please contact Sue Wilson at (708) 784-0631 or curekirby@sbcglobal.net with any questions.

The 19th Annual Sweetheart Dinner Dance

SPONSORSHIP REPLY FORM

Sponsorship				
❑ Diamond	$10,000	❑ Silver	$ 1,000
❑ Platinum	$ 5,000	❑ Sweetheart	$ 500
❑ Gold	$ 3,000		

Name as you want it to appear (please print) _____

❑ Check Enclosed

Please charge my (check one) ❑ Visa/MC ❑ American Express

Cardholder Name (print) _____

Account Number _____

Expiration Date _____

Signature _____

Please return this form to: **The Children's Medical Research Foundation, Inc., P. O. Box 70, Western Springs, IL 60558, fax to (708) 784-1978 or call (708) 784-0631.**

Please include your phone number _____

The Children's Medical Research Foundation, Inc.®

P.O. Box 70
Western Springs, IL 60558

KirbyGram

Save the Date

Friday, February 14, 2014

The Sweetheart Dinner Dance Makes a Romantic Holiday Gift

This holiday season, give your sweetheart a gift of good cheer –
a romantic evening at the Sweetheart Dinner Dance.

You'll avoid last minute shopping in crowded stores when you go
online (www.curekirby.org) or call (708) 784-0631 now for reservations.

Then enjoy February 14th in taffeta and tux, sipping champagne,
dining at the Four Seasons Hotel Chicago and
dancing to the music of the Michael Lerich Orchestra. Cheers!