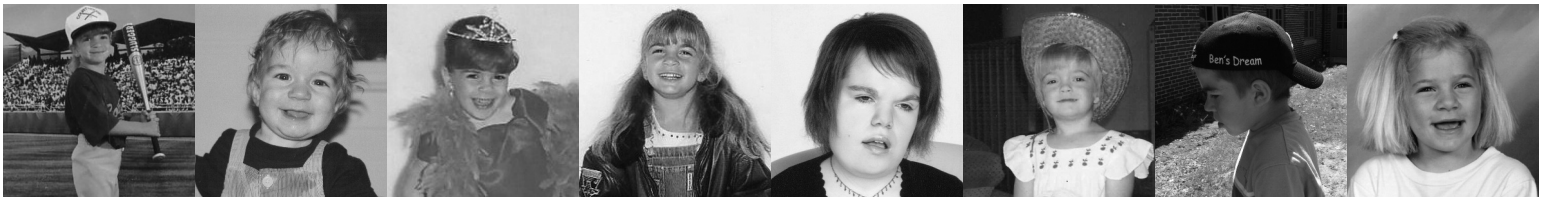
The Children's
Medical Research
Foundation, Inc.®

KirbyGram

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

December 2010

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



Dear Friends,

Brad and I formed this Foundation because of our four-year-old daughter, Kirby, the disease she was afflicted with, and the hope that Sanfilippo and its devastating progression could not possibly manifest itself within her -- our beautiful bundle of joy. The solution seemed simple. Raise funds to enable researchers to advance and expand their work to find a cure. We chose to fight this disease.

Now 16 years later, although Sanfilippo has taken its toll on Kirby, she continues to defy her affliction with seemingly endless resolve, all the time with a smile. A smile that brings us reassurance of her comfort and delight in her moments of happiness -- a reminder of her amazing grace. She is our hero.

As her battle continues, our dream of a cure could come true, for Brad and I have received news of a breakthrough this year. Dr. Haiyan Fu of the Center for Gene Therapy at The Research Institute at Nationwide Children's Hospital in Columbus, Ohio, is ready to bring her 10-year-old gene therapy program to human clinical trial. Joining forces with other families and foundations, we hope to raise $1 million to fund the studies required by the FDA to bring her work to fruition.

The price to fund this and continue to support other valuable research might seem insurmountable. But all Brad and I have to do is remember what doctors first told us 16 years ago: Nothing can be done. Enjoy her while you have her. Then our thoughts turn to Kirby. Her fortitude must not be in vain. No matter what the future holds for her, our mission is still for her. Because it is her story that is repeated in hundreds of families around the world, hundreds of stories shaped by one cure. And it has been your faithful belief in our mission that has allowed Kirby's story to be written and your unwavering support of The Foundation that has helped research to reach this level. It can be done.

This holiday season, Brad and I wish for your families and you the same joy Kirby brings to our lives each day. We ask that you think of Kirby, and in her honor, continue to support The Children's Medical Research Foundation and its mission of a cure.

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

Sue and Brad Wilson

Fundraising News

"Fore" Kirby

June 4th was the date of the Fifteenth Annual "Fore" Kirby Golf Fun Raiser at Ruffled Feathers Golf Club in Lemont. This year's event had just 15 participants yet raised more than $25,000 "fore" Kirby!

The Foundation is actively seeking new participants for this unique golf outing. The event is held each year on one of the first Fridays of summer. Participants are given pledge cards and are asked to secure pledges from friends and associates for each of the 18 holes of golf to be played.

Fred Sammons

Sue comments, "This is always a fun event for Brad and me as it enables us to relax with friends yet raise an incredible amount of money each year. We are very fortunate to have these people in our lives, always willing to help us as a family or do whatever it takes for The Foundation to succeed."

Talking about fun a longtime supporter but first time participant, Fred Sammons, made his debut with a hole-in-one on the third hole. Even more fun, it was his third one! We're thinking three is a pretty lucky number for him!

Upon completion of the round, score cards are collected from each player, and The Foundation then contacts all of those who have pledged with the results of their player's round and the total amount due. Participants also are asked to pay for their round of golf, which means that 100% of the donations go directly to The Foundation! Cocktails and dinner are served immediately following at the Wilsons' home.

Interested in joining the fun? Please contact Sue at (708) 784-0631 to learn more.

The Foundation Gives Thanks….

To **Margaret Dawe, Nicholas Megofna, Donna Logan-Gabel and Carrisa Osle-Sherman,** who designated The Foundation as their charity of choice in their employers' United Way campaigns. Thanks for uniting for Kirby!

To The Marmon Group for its matching contribution, doubling employee **James Angus's** donation to The Foundation. It's a great match for Kirby!

To **Barbara Cummings** for her donation in memory of **John Schroeder**.

To the many contributors who used the donation envelopes as an opportunity to give to The Foundation. Donations from our June newsletter totaled $730.

To **Kirschbaum's Bakery** and **Casey's Market**, all 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 $470 to date this year, your "hometown girl" thanks you from the bottom of her little heart.

And To The Families Working Together For The Cure….

To Jim and Mary Jane Baier and Drs. Glenn Bloiso and Margaret Crabtree for their contributions in honor of Hunter and Sydney Moff of Williamsport, PA.

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Fundraising News

The **Kidwell Family** was busy celebrating this past May and June. Not only did both **Brooke and Ashleigh** have birthdays but Ashleigh graduated from high school on June 1st. We thank **Mr. and Mrs. Antonio Ruiz, Robert Allen, Mr. and Mrs. Arthur Kidwell, Mr. and Mrs. Mark Leavitt, Mr. and Mrs. Terri Fox and Mr. and Mrs. Darryl Lawson** for their donations in celebration of the girls' happy days.

Brooke the birthday girl.

Ashleigh with her proud parents, Anna and Dave.

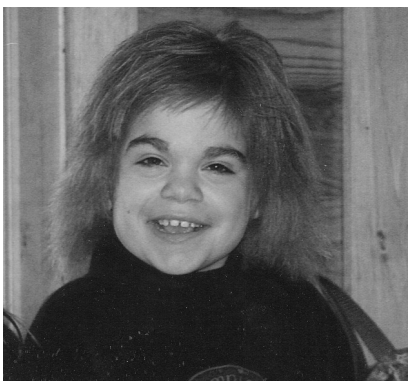
News From Connecticut

A Note From Rhianna's Mom –

"Never doubt that a small group of thoughtful, committed citizens can change the world. Indeed, it is the only thing that ever has."

– Margaret Mead

I first heard this quote at a United Way event, and I thought it spoke clearly to our fundraising efforts. We are truly grateful for the *"thoughtful and committed"* who remain strong in our lives. I thank each of you who continue to donate on behalf of Rhianna. Many of you have been supporting our efforts since the beginning over 14 years ago. As I speak of longevity, words cannot express our appreciation for the dedication of Sue and Brad Wilson. Their hard work has now brought us a promising breakthrough to a cure. As they continue to care for Kirby each day, they have remarkably found the energy to kick it up, set a goal and make this breakthrough a reality. May they be blessed with ongoing strength and courage.



Rhianna Logan

I must not forget that within our *"small group"* are the researchers, many of whom have dedicated their lifelong careers to finding a cure. Without them, *"change"* would not be possible. To each of them, my heartfelt gratitude and all of Rhianna's very special smiles.

My hope soars. Thank you so very much.

– Cynthia Logan

Our thanks goes to **Tabitha and Justin Manafort** for once again giving the proceeds of the **Manafort Family Foundation's** annual golf outing to The Foundation.

Len and Gail Roberts of the **Clinton S. Roberts Foundation** continue to support our mission of a cure with a donation in honor of Rhianna.

Dennis and Laurel Colgan of **Picture Fame** continued their support of "Rhianna's Hope" with a donation to The Foundation.

Peter and Joanne Brandien honored longtime supporters and friends of the Logans, **Alan and Donna Theriault**, with a donation.

Research Update

Update from the Laboratory of Dr. Elizabeth F. Neufeld, Department of Biological Chemistry at UCLA, November, 2010

For many years, we have focused on two questions: why is the brain so severely affected in patients with Sanfilippo syndrome, and how can we develop treatment for this disease, using our mouse model of Sanfilippo syndrome type B (MPS IIIB)? We believe that we are now close to an answer to both questions.

The primary defect in Sanfilippo syndrome type B is mutation in *NAGLU*, a gene encoding a lysosomal enzyme needed to degrade heparan sulfate and the resulting storage of heparan sulfate in lysosomes. The original hypothesis was that the storage itself caused disease, perhaps because the enlarged lysosomes occupy a lot of space within the cell. But it has seemed paradoxical that the storage of a large amount of heparan sulfate in lysosomes of the liver and kidney don't cause liver and kidney disease, while the storage of much smaller amounts of heparan sulfate in the brain cause profound mental retardation and dementia in patients with Sanfilippo syndrome. We reported last year that the pathology in the MPS IIIB mouse brain was much more complicated than just lysosomal storage of heparan sulfate.

Briefly, the MPS IIIB (and also MPS IIIA) mouse brain accumulates a number of substances besides heparan sulfate. Of particular interest are proteins that are known to aggregate: lysozyme, amyloid beta and hyperphosphorylated tau (P-tau). The last two are known to accumulate in Alzheimer disease. But the Sanfilippo syndrome is not full blown Alzheimer disease: First of all, in Sanfilippo syndrome these substances accumulate mostly in a very small area of the brain, called the medial entorhinal cortex, whereas Alzheimer disease starts in the human equivalent of this area but then spreads to other parts of the brain. The P-tau in our MPS IIIB mice is detected by some but not all antibodies generated against Alzheimer P-tau. And finally P-tau and beta amyloid aggregates found in the MPS III B mouse are smaller than those found in Alzheimer disease, as determined by their staining properties. Nevertheless, the presence of amyloid beta and P-tau aggregates in the MEC (and of one form of P-tau in the dentate gyrus) is significant because MEC and the dentate gyrus are very important areas for learning and memory. The aggregates of amyloid and especially of P-tau may interfere with some of the pathways needed for forming memories.

The view that the accumulation of heparan sulfate starts a pathogenic cascade that ends in the accumulation of aggregates of amyloid beta and P-tau suggests possible treatments. We are specifically looking for small molecules that can cross the blood brain barrier. Any compound that would reduce the accumulation of heparan sulfate should be beneficial. Genistein might be such a compound, as would be compounds specifically synthesized to interfere with the biosynthesis of heparan sulfate. But it would also be necessary to have compounds that act toward the end of the pathogenic cascade. Last year we reported trying lithium chloride because it was a good inhibitor of the enzyme GSK3beta, which is responsible for the formation of P-tau; but at the time the experiment had not been successful. We then tried another dose of lithium chloride, which did produce a significant lowering of P-tau in the dentate gyrus, though not to normal levels. Since lithium chloride has significant problems of toxicity, and its effect was only partial, it is not recommended for testing in Sanfilippo patients.

However, there are drugs being developed for Alzheimer disease that work by preventing the aggregation of P-tau and/or breaking up the aggregates once formed. We are testing one such drug at this time and are planning to test others. But inhibiting one step at a time is not likely to produce the optimal treatment. We believe that it will be necessary to use a combination of drugs, working at the beginning and the end of the pathogenic cascade, and perhaps at some intermediate steps as well, in order to

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Research Update

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significantly affect the course of the Sanfilippo syndrome and make a difference in the quality of life for the children. Any promising strategy developed with the mice will be brought to the attention of our clinical colleagues to work toward a clinical trial.

This work was made possible by grants from The Children's Medical Research Foundation and from the National Institutes of Health.

Update from Haiyan Fu, PhD, Center for Gene Therapy, The Research Institute at Nationwide Children's Hospital

Mucopolysaccharidosis (MPS) IIIB (Sanfilippo B) is a devastating lysosomal storage disease (LSD) with severe neurological disorders. The disease is caused by inherited defect in α -N-acetylglucosaminidase (NAGLU), a lysosomal enzyme required for breaking done glycosaminoglycan (GAG) in cells. The lack of NAGLU enzyme activity causes the accumulation of GAG in cells. Infants with MPS IIIB appear normal at birth, but then develop severe progressive neurological manifestations. The neurological damages lead to high mortality and premature death. The somatic manifestations in MPS IIIB are mild, relative to other forms of MPS.

No treatment is currently available for MPS IIIB. The disease is not amenable to either recombinant enzyme replacement therapy or hematopoietic stem cell transplantation that are currently available for treating the somatic diseases of MPS I, II and VI. To date, the biggest challenge in developing therapies for MPS III, and many other neurological diseases, is how to efficiently deliver the therapeutic materials into the CNS. This is because MPS IIIB affects the entire nervous system, and the blood brain barrier (BBB) prevents efficient therapeutic delivery to the central nervous system (CNS).

Gene therapy has been considered an ideal approach for treating LSDs because it has potential to mediate long-term restoration of the missing enzyme activity. In addition, the NAGLU enzyme is secreted and can be taken up and used by neighboring cells. Therefore, it is not necessary to reach 100% of cells by gene therapy vector to treat MPS IIIB.

We have been working on developing gene therapy for MPS IIIB with the support from the NIH, Ben's Dream – The Sanfilippo Research Foundation, and Cure Kirby – The Children's Medical Research Foundation. Our research over the last 10 years has been focused on developing efficient approaches to deliver the therapeutic AAV vectors into the CNS for global or broad effects. Using these clinically relevant approaches to deliver the human NAGLU gene, we have achieved significant neurological benefits in adult MPS IIIB mice, with correction of cognitive and motor function and extended survival. Recently, we have demonstrated the best long-term therapeutic impacts to date in treating MPS IIIB in mice using a single intravenous (IV) injection, an AAV serotype 9 (AAV9) vector. The AAV9 vector has the unique ability to cross the BBB from the vasculature without additional treatment. Because of this BBB-crossing ability, the IV-injected AAV9 vector can reach more brain cells, and relatively low vector dose is needed to achieve clinical benefits, compared with other serotypes we have used. This will overcome one of the major challenges in the translation of gene therapy procedures from mouse to human, the scalability (and the cost) of vector production. Importantly, this IV rAAV9 gene delivery procedure is minimally invasive and poses minimal burden to patients if translated to clinical application. Therefore, we strongly believe that we are well-positioned to move our rAAV9 MPS IIIB gene therapy program toward clinical trial. We are currently working toward submitting an IND application to the FDA for approval of AAV9 gene therapy clinical trial in patients with MPS IIIB. Furthermore, this AAV9 gene delivery procedure is also applicable for treating other forms of MPS/LSDs with neurological manifestations.

Fundraising Opportunities

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.

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!

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.

Go Kasual For Kirby

Tired of wearing those heels, hose or ties five days a week? Why not suggest a **"Go Kasual For Kirby Day"** to your employer? It's a great way to give a "relaxing feel" to a workday and raise funds for The Foundation. Simply send a memo to co-workers explaining the day and set the "fee" to participate.

Still in school but want to help? How about a **"Hat Day"** done the same way! It's fun for the kids and a great way for them to participate in a good cause. No "fee," just leave an amount up to them.

The Sweetheart Dinner Dance

February 11, 2011 • The Ritz-Carlton Chicago

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

The 16th annual Sweetheart Dinner Dance will be held Friday, February 11, 2011, in the Ballroom of The Ritz-Carlton Chicago.

This elegant venue is the setting for The Foundation's celebration of its 16th year, brightened by hope that a breakthrough to a cure is here for Kirby and the other children.

Executive Chef Mark Payne will serve a signature four-course dinner from his award-winning kitchen, following a champagne reception in the adjoining Loge.

We will be treated to the magical sounds of the Michael Lerich Orchestra, which has entertained us for the past 15 years! And silent auction packages promise to tempt sports, travel, dining, spa and shopping enthusiasts.

Reservations are $225 per person or $2,250 for a table of ten and must be made in advance. Invitations will be mailed in December. 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. Please contact Sue Wilson at (708)784-0631 with any questions.

The 16th 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) _____

Address (required for cc processing) _____

City _____ State _____ Zip Code _____

Phone Number _____

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, or fax to (708) 784-1978 or call (708) 784-0631.

The Children's
Medical Research
Foundation, Inc.®

P.O. Box 70
Western Springs, IL 60558

KirbyGram

Save The Date

Friday, February 11, 2011

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 call **(708)784-0631** now for reservations.

Then on February 11th enjoy sipping champagne, dining in the Ballroom of the Ritz-Carlton Chicago and dancing to the music of the Michael Lerich Orchestra.