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

June 2012

What is Sanfilippo Syndrome?

Sanfilippo Syndrome is one of seven Mucopolysaccharide (MPS) disorders. There are four different enzyme deficiencies that cause Sanfilippo. The Sanfilippo disorders are described as type A, B, C, or D. There is very little difference between the four types, though there have been a few very mild cases of the B form reported where the children have remained relatively healthy into early adult life.

Children with Sanfilippo are missing an essential enzyme that breaks down a complex body sugar called heparan sulfate. This sugar slowly builds in the brain, stopping normal development and causing hyperactivity, sleep disorders, loss of speech, dementia and typically, death before adulthood. There is no cure yet.

While Sanfilippo occurs once in 24,000 births, successful research into the disease could apply directly to many of 5,000 other genetic disorders.

KIRBY UPDATE

The Birthday Princess

April 15th was a very special day for the Wilson family. Kirby turned 21 years old on that beautiful, sunny Sunday. The family's day started at Highlands Presbyterian Church's morning service, attended by devoted members who have supported Kirby from the first days of her diagnosis with their prayers and The Foundation with their years of donations. A champagne brunch followed with family and friends. The day's celebration concluded with Kirby and her family enjoying her favorite dinner of pizza and Coke and a birthday cake befitting a princess, made by special friend and neighbor Claudia Saranecki.

Sue comments, "The day was magnificent from start to finish because we had so very much to celebrate and be thankful for. First, of course, is Kirby's continued comfort as she reached a great milestone for any young adult. It is a day such as this that we are reminded of the blessing of having her with us and the joy she has brought to our lives. We are able to celebrate this milestone because of her perseverance, determination and joyfulness. It is she who has shown us the way."

As Brad and Sue begin to think about Kirby's journey into adulthood, they appreciate more and more the exemplary experience Lyons Township High School has provided for her over the years. Such services and staff cannot be duplicated in the adult world for people with disabilities such as Kirby's. Sue comments, "As I have mentioned before, Brad and I are grateful for Kirby's teacher, Jackie Gay, the therapists and aides who have worked tirelessly to assist Kirby in being the best she can be. They have created a model situation for Kirby and children like her that quite simply can't be beat. Our daughter Maggie posted on The Foundation's website blog about this attitude that we feel is LT at its best." We have printed it on the following page.

DEFYING LIMITATIONS

January 8, 2012

Every day, I take the train into downtown Chicago and walk nearly a mile to get into my Michigan Avenue office. Although some days I have to dodge the unruly cab driver or elbow my way through Union Station, the city's beauty never ceases to amaze me.

However, what amazed me more was the passion Kirby's special ed teacher showed toward her students. I don't know if I could name another person who'd be willing to take a class full of wheelchair-bound students downtown on public transportation. Yes, that means loading all the students on a train, navigating through the bustling Union Station, and making that mile-long trek to Michigan Avenue. All so that each of these students could enjoy the beauty of Millennium Park. So, naturally I took the opportunity to step out of the office and enjoy the afternoon with her.

It felt incredible to know that Kirby spends her days with a teacher who is devoted to allowing her students to experience life like any other high school student. As I walk to work each day, I'm so grateful that Kirby is in the hands of a woman who helps her explore this beautiful city.

Maggie

Maggie, Kirby and The Bean

Kirby's Going Green!

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 NEWS

17 Years for the Sweetheart

The Four Seasons Hotel Chicago was where 164 sweethearts gathered February 10th for the 17th Annual Sweetheart Dinner Dance. After enjoying a champagne cocktail reception, guests were treated to an elegant dinner and entertainment by Michael Lerich's talented group of musicians. Many guests reported that it was the best dinner dance yet! The evening's generous sponsors, along with some enthusiastic bidding in both the live and silent auctions, enabled The Foundation to raise over $61,000.

Sue comments, "The Sweetheart Dinner Dance is a special evening for us, as its loyal guests are a reminder to us of the compassion and commitment shown to our family and mission. The economic times continue to challenge not-for-profits and supporters alike. Yet, The Foundation has been able to continue its critical mission of funding researchers, enabling science to advance ever closer toward a cure. Brad and I are honored by the depth of these donors' devotion and are blessed by their presence in our lives."

Kirby's cousin Molly with Anna Kidwell

(continued on page 3)

FUNDRAISING NEWS

Marquette University Continues for Kirby

Marquette University's Student-Athlete Advisory Council (SAAC) hosted its sixth annual Cure for Kirby fundraiser. It was held at the January 24th Golden Eagles men's basketball game against USF at the Bradley Center. A video clip on The Foundation was presented during the game, and at its conclusion, student-athletes were available for more information. Online donations were accepted January 24th through February 7th. This event was started in 2007 as a way of honoring fellow athlete Maggie's little sister, Kirby. Members have chosen to continue their fundraising on behalf of Kirby, even after Maggie's graduation. A special thanks to Qdoba Mexican Grill in Milwaukee for its donation on behalf of this great group of student-athletes.

The Foundation Gives Thanks . . .

To **Bulley & Andrews** in Chicago for its holiday donation "in honor of our clients, colleagues and friends."

To the many friends who donated in celebration of **Kirby's** 21st birthday. A perfect way to celebrate her life.

To **Penny Kahan** for her donation in celebration of **Noel Hertz's** and **Sharon Eisman's** anniversary.

To **Margaret Dawe, Nicholas Megofna, Mark Leavitt and Donna Logan-Gabel, Raymond Donato, Ronald Odrobinak, William Leonard and Renata Fetzer and the anonymous donor** from **Adams and Knight**, who designated The Foundation as their charity of choice in their employers' United Way campaigns. Thanks for uniting for Kirby!

To **Mr. & Mrs. Robert Nardozzi** for their donation in the name of **Madeline Capodanno** in celebration of Christmas.

To **The Marmon Group LLC** for its matching contribution, doubling employee **James Angus's** donation. And, to **LEGO Children's Fund** for doubling employee **Erick Wolfe's** contribution. They are a perfect match for The Foundation.

To **Barbara Cummings** for her donations in memory of **Bud Vockel and Viola White**.

To **Mike and Katie Lynch** for their donation in memory of **Virginia Myers.**

To the many contributors who used the donation envelopes as an opportunity to give to The Foundation. Donations from our December newsletter totaled $3,060.

The Wilson family wishes to thank the many people who donated to The Foundation in memory of Sue's mom, **Shirley Malek**. Known to many as Grandma, she was a woman of incredible strength who lived to love and support her family. The Wilsons are grateful for the kind words and memories people shared with them about Shirley.

As Sue reflects, "Sometimes we talk of an encounter with a person who has said or done something that made us feel special. We feel blessed to have been the recipient of his or her good will, generosity or compassion. Touched by an angel is a phrase that describes a feeling we have for a moment in time, yet it's so profound we remember that moment for a lifetime.

For me, that moment in time lasted 54 years. That angel was my mother. Fifty-four years of special moments and memories where there were just no negatives. Hers was a lifetime of doing good for her family. She was a quietly powerful woman. An angel by definition who possessed unparalled love, patience, understanding and forgiveness.

Grandma

(continued on page 4)

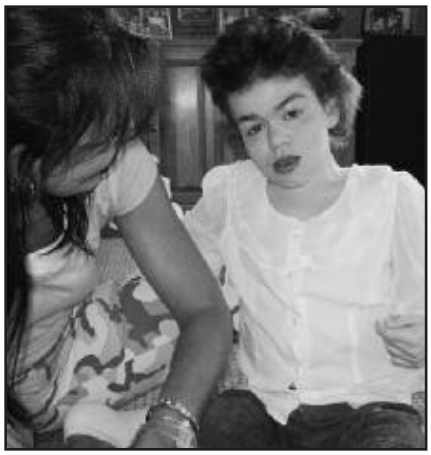
FUNDRAISING NEWS

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

To **Mr. & Mrs. Arthur Kidwell** for celebrating Christmas with a donation in honor of their granddaughters, **Brooke and Ashleigh Kidwell**.

To **Michelle Dick** for her Christmas donation in honor of her cousins, **Brooke and Ashleigh**.

To **the Fowler family - Betsy, Steve and Jeff** - for their Christmas gift and blessing to The Foundation in honor of their **daughter and sister Kimberly**, their "bit of sunshine from Heaven to our hearts."



The Graduate

Our congratulations to 18-year-old Carley Trocheck, daughter of Dave and Barb Trocheck of Diamond, OH, who will be graduating on May 25th from Happy Day School. Another great milestone for another very special child.

News From Connecticut

Holiday fundraising efforts by **Artisan's Marketplace** raised $450 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.

Our thanks to longtime supporters **Martha and Jim Couture, Donna and Alan Theriault** and **Lynn and Joseph Fuda** for their donations in celebration of Rhianna's birthday;

To **Joanne and Peter Brandien and Wendall Theriault of Quality Components** for their donation honoring Rhianna, in **Donna and Alan Theriault's** name;

To **The Bristol Auto Club** for donating $1,500, which were the proceeds of its annual **"Cruisin' for Rhianna" Auto Show**. The Logans and The Foundation appreciate the club members' years of commitment to their "drive" to find a cure for Sanfilippo; and to **Dennis and Laurel Colgan** of **Picture Fame** who continued their support of "Rhianna's Hope" with a donation to The Foundation.

Gene Logan's father passed away on December 30th. He spent many hours caring for Rhianna. Gene and Cynthia have wonderful memories of the many trips he took to the horse barn with Rhianna, giving up his own hobby to support her. The Foundation received many memorial donations in his honor. Our deepest sympathy goes out to the Logan family for their loss.

Rhianna's friend Shane and his prom date Amber share some time with Rhianna.

RESEARCH UPDATE

Robert K. Yu, Ph.D., Med.Sc.D
Professor, Institute of Molecular Medicine and Genetics, Georgia Health Sciences University, Augusta, GA

July 1, 2011 – June 30, 2012

Dr. Yu's laboratory has engaged in research, with the continued encouragement and generous support of The Children's Medical Research Foundation, Inc., Chicago, for an effective and safe therapy for Sanfilippo disease. This commitment has never diminished. Sanfilippo disease is known as Mucopolysaccharidosis III (MPS III), genetic disorder occurring in one out of 24,000 births. It belongs to a broader group of genetic disorders known as Lysosomal Storage Diseases (LSD). These diseases share a common feature in that a certain enzymatic defect can cause the accumulation of biological materials in body cells. In MPS, these materials are collectively known as mucopolysacchrides or heparin sulfates, sugar-containing substances that are essential for the body to develop and function normally. Children afflicted with Sanfilippo Syndrome, however, are missing certain essential enzymes that break down these substances. As a result, these substances accumulate in the body, especially in the brain, causing progressive damage to tissues. A Sanfilippo child may appear normal at birth and seems to develop normally for the first year or two, but as more and more cells become damaged, clinical symptoms begin to appear. These symptoms include hyperactivity, sleep disorders, loss of speech, mental retardation, dementia, and finally death. Life expectancy for a child with Sanfilippo Syndrome is shortened. To date, four different enzyme deficiencies have been found to cause Sanfilippo disease. For this reason, development of effective therapeutic strategies for the treatment of these disorders is urgently needed.

Current treatment strategies do not effectively treat those diseases due to the complicated nature of the brain anatomy and disease pathology. Thus, devising a novel therapeutic strategy urgently needs a well-characterized disease model with a quantifiable measurement for evaluating therapeutic efficacy. For this reason, a major effort undertaken by Dr. Yu's team has been the use of neural stem cell (NSC)-based therapy in the pathological brain of Sanfilippo Syndrome A (MPS IIIA) using the naturally existing Mucopolysaccharidosis type III (MPS IIIA) mutant mouse as a disease model. MPS IIIA is characterized by severe central nervous system degeneration due to a deficiency of a lysosomal enzyme, sulfamidase, for degradation of body sugar, heparin sulfate. To tackle this problem, a novel *micro-piggyBac* system has been developed by Dr. Yu and his team, and it promises to be safer than the traditional *mini-piggyBac*. By integrating the *micro-piggyBac* system with NSC technology, an innovated *micro-piggyBac*-NSC MPS IIIA genetic disease model will be established. This disease model will be adopted to address the possibility of correcting neural defects of Sanfilippo Syndrome using *micropiggyBac*-NSC-mediated gene and stem cell therapy. The long-term objective of this therapeutic strategy using *micropiggyBac*-engineered-NSCs should be able to readily apply to other forms of MPSs. In addition, Dr. Yu hopes to apply the disease specific NSCs (such as the MPS IIIA NSCs in this work) as a drug screening system to identify small molecules for treating the specific diseases.

The above studies have been supported in part by a CMRF grant and in part by a USPHS/NIH grant awarded to Dr. Yu. Acknowledgment of the generous support from those agencies has been indicated in the following publications.

1. Meir, Y.-J. J., Weirauch, M. T., Yang, H.-S., Chung, P-C., Yu, R. K., and Wu, S. C.-Y., Genome-wide target profiling of piggyBac and Tol2 in HEK 293: pros and cons for gene discovery and gene therapy. BMC Biotechnology 11:28, 2011, (http:/www.biomedcentral.com/1472-6750/11-28).
2. Yanagisawa, M., Yoshimura, S., and Yu, R. K. Expression of GD2 and GD3 gangliosides in human embryonic neural stem cells, ASN Neuro (2011) doi:10.1042/AN20110006. PMC 3072763.
3. Yu, R. K., Tsai, Y.Z., Ariga, T., and Yanagisawa, M. Structure, biosynthesis, and function of gangliosides: An overview. J. Oleo Sci. 60: 534-44, 2011. PMID:21937855.
4. Yu, R. K., Tsai, Y.-T., and Ariga, T. Functional roles of gangliosides in neurodevelopment: An overview of recent advances. Neurochem. Res. 37: 1230-1244, 2012. doi: 10.1007/s11064-012-0744-y.
5. Yagi, H., Saito, T., Yanagisawa, M., Yu, R. K., and Kato, K. Lewis X containing N-glycans predominately expressed on mouse embryonic stem cells regulate proliferation of the cells via the Notch signaling pathway. J. Biol. Chem. (in revision).

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

In April of 2012 at the 19th annual meeting of the American Society for Neural Therapy and Repair in Clearwater, Florida, Dr. Paul Sanberg, Director of the University of South Florida's Center of Excellence for Aging and Brain Repair, and Dr. Svitlana Garbuzova-Davis, an Assistant Professor at the Center, delivered two presentations related to Sanfilippo Syndrome.

Dr. Sanberg emphasized that cell therapy has great potential for the treatment of various

(continued on page 6)

neurodegenerative diseases. The mononuclear cell portion from human umbilical cord blood (HUCBCs) is a diverse group, which includes stem cells, lymphocytes, and monocytes. A single high dose of HUCBCs has been shown to provide benefits in animal models of Alzheimer's disease (AD), amyotrophic lateral sclerosis (ALS), and Sanfilippo Syndrome type B (Mucopolysaccharidosis III B; MPS III B). However, very few of these administered cells remain a few months after a single injection. This scarcity and the progressive nature of these diseases suggested that repeated injections of lower cell doses might prove more effective than a single dose. Studies showed that multiple low doses of HUCBCs administered intravenously are more beneficial than a single high cell dose. Repeated cell injections are likely to provide long-term benefit against these progressive diseases by affording sustained *Naglu* enzyme replacement in MPS III B, as well as long-term trophic support against the progressive degeneration in AD and ALS. In addition, smaller doses translate better 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.

Dr. Garbuzova-Davis and her team have been investigating blood-brain barrier (BBB) condition in Sanfilippo Syndrome. Based on her recently published study (PLoS ONE, 2011) showing severe BBB breakdown in a MPS III B mouse model, the current investigation focused on structural and functional integrity of the BBB in MPS III patients. Since brain damage is a common factor in all MPS III types, and the BBB normally protects the brain from harmful blood born substances, determining BBB competence may be important to discovering potential additional disease mechanisms. Analyzing post-mortem tissues from patients with MPS III A and MPS III D obtained from the NICHD Brain and Tissue Bank for Development Disorders, University of Maryland (Baltimore, MD) with a variety of techniques, significant BBB impairment was determined in microvessels from various brain structures. Degeneration of major BBB cellular components, severe fluid buildup around capillaries, vascular leakage, and extensive lysosomal accumulation in brain microvessel endothelium were noted. These new findings of BBB structural and functional impairments, although from only two cases, MPS III A and MPS III D, should be considered in developing treatments for MPS III. Special attention should be given to endothelial cell function in view of possible deterioration of BBB transport systems needed to maintain proper balance of the central nervous system.

Currently, Dr. Garbuzova-Davis and her team are focusing on strategies for BBB repair. Since HUCBC administration shows benefit in MPS III B by delivering the missing enzyme, these cells might also restore BBB integrity by replacing endothelial cells.

Supported by: The Children's Medical Research Foundation

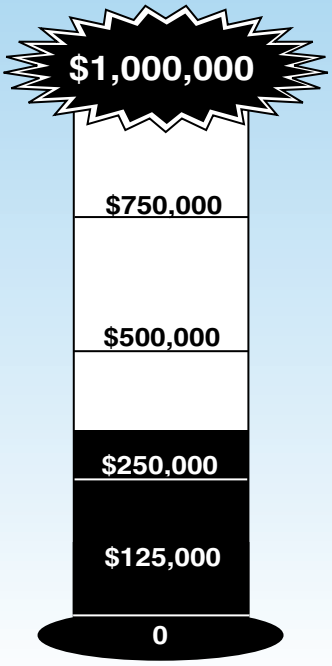
A Summation of the Update Received From Haiyan Fu, PhD, Center for Gene Therapy, The Research Institute at Nationwide Children's Hospital, Columbus, OH

Dr. Fu has recently completed a longevity study in mice afflicted with Sanfilippo Type B (MPS IIIB) that were treated with their AAV9-NaGlu gene therapy vector by a single intravenous injection. The data showed that the majority of these mice survived to a life within normal range of their lifespan. This finding further demonstrates the therapeutic potential of this gene therapy delivery system as a treatment for MPS IIIB.

Dr. Fu and her team are currently focusing on moving this gene therapy approach toward a clinical trial in patients with Sanfilippo B. They have started the interaction with the FDA and are currently working on finding the best dose regimen for the trial. They are also planning for the toxicology studies that are required by the FDA.

In addition, Dr. Fu's team is testing its methodology in older, more affected mice to compare the results with previous testing on younger models. Dr. Fu feels it is important to investigate whether advanced manifestations can be treated with the current approach, as many patients are not diagnosed until after significant damage has occurred. To date, her preliminary data suggest the gene delivery system may be beneficial for treating advanced MPS IIIB but stress the importance of more experiments to obtain more significant functional data.

Her current funding needs focus on the clinical vector development of the AAV9-NaGlu gene therapy product that will be tested to ensure its identity, strength, purity and quality. This testing is required in order to receive the necessary Certificate of Analysis from the government's regulatory agency as she moves toward her goal of FDA approval of a human trial.



Update On Funding Studies

Over the past year, we have spoken to you about our campaign to raise $1,000,000 to support Dr. Haiyan Fu of The Research Institute at Nationwide Children's Hospital in Columbus, OH, and the studies required for FDA approval of human trial.

We are happy to report that through your support and the efforts of other families and foundations, funds have been raised and grants issued to Dr. Fu and The Research Institute at Nationwide that now total $275,000. And, with each passing month, more and more families are joining forces to make the $1 million a reality.

It is The Children's Medical Research Foundation's goal to continue to support these studies, as well as other research offering hope of a livesaving treatment.

We are asking you to visit our website at www.curekirby.org and go to its Blog. Click on "A Cure is Within Our Reach." It will allow you to watch our You Tube video. Donate what you can, whether it be $1, $5 or $100. Then tell friends and ask them to do the same. Help us to make a cure for Sanfilippo the next You Tube sensation!

Want to get involved? Please read on and take a look at the ways you can help us achieve our mission of a cure with these fundraising ideas.

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.

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 names. It's a gift that won't gather dust and goes far beyond any other.

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SAVE THE DATE

The 18th Annual Sweetheart Dinner Dance

Plans soon will be underway for the
18th Annual Sweetheart Dinner Dance to be held February 8, 2013,
at The Ritz-Carlton Chicago.

Please contact the Foundation at (708) 784-0631 for further details and to learn how you can help to make it a "sweetheart" of a night for Kirby and others like her.