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 2010

What is Sanfilippo Syndrome?

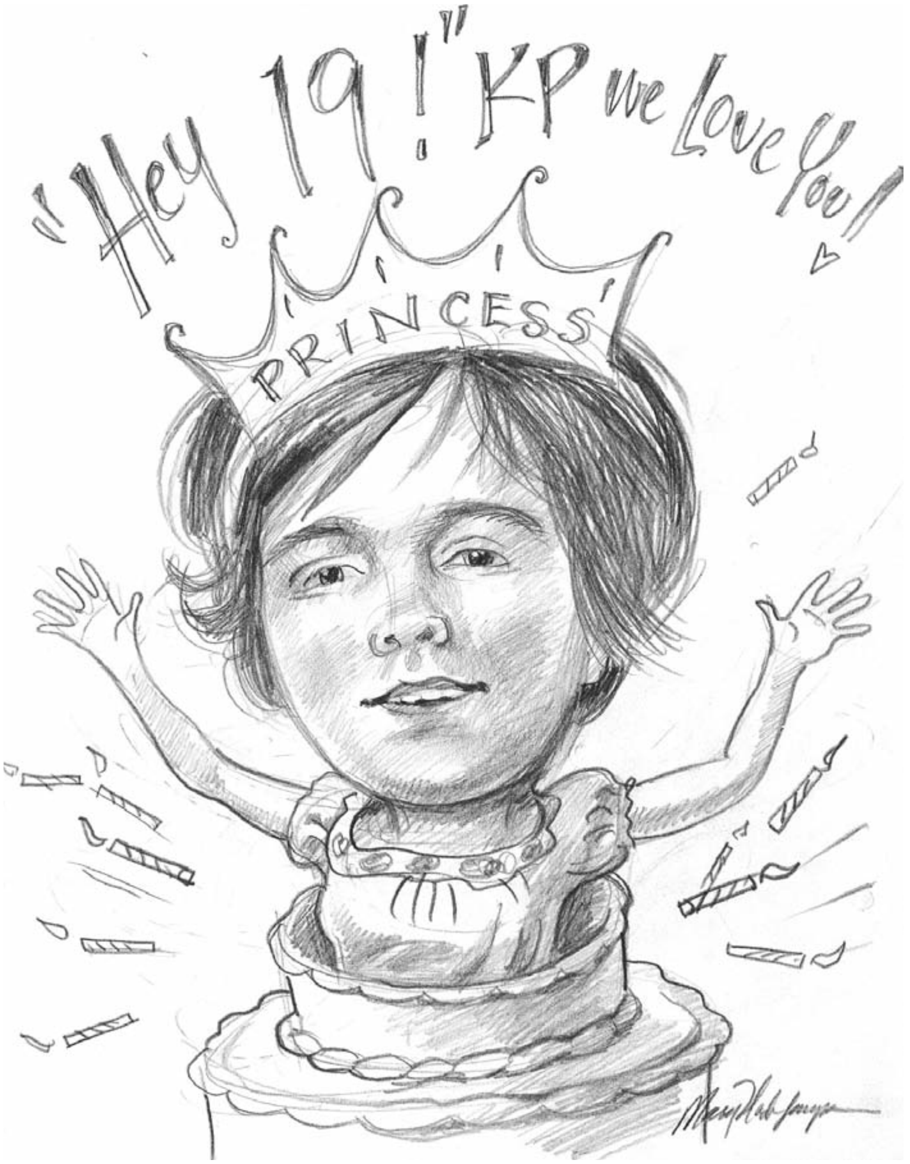
Sanfilippo Syndrome is one of seven Mucopolysaccharide (MPS) disorders. There are four different enzyme deficiencies that cause Sanfilippo. The Sanfilippo disorders are described as type A, B, C, or D. There is very little difference between the four types, though there have been a few very mild cases 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 Wilsons are busy celebrating!! Kirby turned 19 years old on April 15th , and big sister Maggie will be graduating from college on May 23rd. Brad and Sue are excited and grateful for this special time with their children and wish all the Foundation's supporters a very happy and fun-filled summer with family and friends.



Kirby's classroom aide, Mary Lempa, captures a smile from the birthday princess on her special day.

FUNDRAISING NEWS

Oh What A Night!

Thanks to Karin Matusiak, Mary Swiontek and their group of volunteers, the Foundation held its first Trivia Night last November, and oh what a night it was!! It was a casual, bring-your-own- everything kind of night where teams of eight gathered with their own food, beverages and table décor, ready to compete for the tacky yet oh so coveted first place crowns. Our thanks to Donna Yelnick for volunteering to share her expertise in MCing the event, handling the questions and crowd in a way that kept the evening running smoothly with seemingly non-stop laughter. The best news is that this small but very tenacious group of volunteers raised $14,946 for research, and some of whom the Wilsons met for the first time just prior to the event.

Sue comments, "We have never received feedback from any event like we did with the Trivia Night. Attendees immediately were asking about the date of the next one and how it might be expanded to include awards for the best table theme and décor. Over six months later, people are still talking about what a great time they had. 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."

Our first place team is crowned!

Marquette University's Student-Athletes Chose Kirby

Marquette University's Student-Athlete Advisory Council (SAAC) chose to fundraise for the Foundation for the fourth year in a row to honor fellow member Maggie Wilson's little sister, Kirby. This year's "Beating the Buzzer for Sanfilippo" was held at the March 2nd Golden Eagles men's basketball game at the Bradley Center. A video clip on the Foundation was presented during the game, and at its conclusion, more than 50 student-athletes canvassed the crowd collecting over $1,300. Sue Wilson comments, "SAAC is a special group of students who realize the importance of giving back and somehow find the time, even with their academic and team schedule, to help others in need. We are thrilled Maggie was able to be a part of SAAC for four years and will always be grateful that this very special group of student-athletes chose to honor the Foundation with its fundraising endeavors."

A Sweetheart of a Night

The Four Seasons Hotel Chicago was where 149 sweethearts gathered this past February for the 15th Annual Sweetheart Dinner Dance.

Auction winners - Kevin and Zoe McMillen.

After enjoying a champagne cocktail reception, guests were treated to an elegant dinner with entertainment by Michael Lerich and his 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 $65,000.

Sue comments, "The Sweetheart Dinner Dance is a special evening

FUNDRAISING NEWS

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 blessed by their presence in our lives."

The Foundation Gives Thanks . . . .

To **Margaret Dawe, Nicholas Megofna, Ray Donato, Ron Odrobinak, Roland Pisoni, William Hellenbach, Carissa R. Osle-Sherman and Donna Logan Gabel,** who designated the Foundation as their charity of choice in their employer's United Way campaigns. Thanks for uniting for Kirby!

To the **Lego Children's Fund** for doubling employee **Eric Wolfe's** donation to the Foundation. It's a great match for Kirby!

To Kirby's aunt **Linda MacDonald** for her contribution in memory of **Bob Pollack**.

To **Bob and Paulette Harnach** for their donation in memory of **Beatrice Lenertz**.

To **Barbara Cummings** for her donation in fond memory of her mother **Mary Jane Seamans** and **Dennis Maurer**.

And to the many contributors who used the donation envelopes to give to the Foundation. Donations from our December newsletter totaled $1,505.

To the Families Working Together for the Cure . . . .

John and Joan Bellontine, proud parents of nine-year-old **Grace**, have again donated a portion of the proceeds from their Grace for a Cure fundraising efforts to the Foundation "to help in your efforts to find a cure for Sanfilippo Syndrome." The letter was signed with "Peace, Love & Grace" and a $10,000 donation was enclosed. Brad and Sue appreciate the Bellontine's faith in the Foundation and willingness to join them in a most important mission.

Angela's House held its second annual fundraiser called "A Night for a Cure," which this year supported 15 rare diseases. A check for $375 was received in Grace's honor.

Anna Kidwell, mother to **Brooke and Ashleigh**, made her annual drive from their home in Kentucky to Chicago to help with the Sweetheart Dinner Dance, this year bringing her eldest daughter, **Danielle**. Sue is always happy to see extra talent lend an artistic hand in the day's set-up. Anna, along with her husband, **Dave**, were also sponsors of the event in honor of their children.

Kent and Judy Bible celebrated the Kidwell girls' birthdays and Ashleigh's high school graduation with a donation in their honor to the Foundation.

Grandpa and Grandma (Arthur and Roberta) Kidwell also celebrated Ashleigh's high school graduation as well as her 21st birthday with a donation to the Foundation.

The Joseph Bianco Family celebrated Ashleigh's graduation with a donation, stating "The Kidwell family continually inspires

Danielle and Anna Kidwell at the Sweetheart.

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Cynthia's mom, Martha, (Mimi to Rhianna) with Rhianna and Gloria Brown with her granddaughter Brooke.

us with their love and commitment to Ashleigh and Brooke."

Larry and Susan Kirch of LaCrosse, WI, donated in honor of their daughter **Allison Rose Kirch**.

Steve and Betsy Fowler of Shelby Twp., MI, donated in honor of their daughter **Kimberly Fowler**.

News From Connecticut

A note from Cynthia Logan --

It seems it was just yesterday when Rhianna celebrated her 17th birthday, and here we are almost halfway through 2010. Fourteen years ago when we had our first cut-a-thon to raise funds for research, our slogan was "cut against time." Today it feels as though time has a real advantage over us, and that is why each and every donation touches our hearts in a very big way.

We are truly grateful to the Brown family for honoring Rhianna with donations in memory of their dear mother, Gloria Brown. Mrs. Brown was a lifelong family friend, a real friend, the kind that doesn't come along often. When I came home with new baby Rhianna there she was to offer a helping hand. Her sincere concern and prayers have given us strength over the years. We will miss her.

Our gratitude goes out to the customers of Cassille's Restaurant who continue their support of Rhianna's Hope. A little closer to home are the customers of Artisan's Marketplace, who along with their donations, continually send their messages of compassion and prayer to Rhianna. It is the ongoing love and generosity that keep our hope and spirits alive; we are more than thankful.

My reflection on time makes me realize how much my appreciation of the Wilsons has grown, Brad and Sue's steadfast commitment to funding research while caring for Kirby is truly remarkable. Their diligence over the past 15 years has built the foundation for the future success of Sanfilippo research and the ultimate gift of a cure for the many children affected. May our heartfelt thanks bless them with peace at the end of each day.

— Gene and Cynthia Logan

Annual holiday fundraising efforts by **Artisan's Marketplace** paid off in a big way this year, netting $968 for the Foundation. This really does show the Logans that the fundraising name "Stars for Hope" is not just about ornaments but also the generosity of the many "stars" within their community that keep Rhianna's Hope shining bright.

Dennis Colgan of **Picture Fame** sent a donation in celebration of "Rhianna, Kirby and the Kids."

Wendall Theriault sent in a Christmas donation honoring Rhianna in the name of his son and longtime Foundation supporters **Alan and Donna Theriault.**

Mr. and Mrs. Robert Nardozzi sent a Christmas donation in the name of **Miss Madeline Capodanno**.

Donations were also received from **Alta M. Saunders and Louis Bohomi** in honor of Rhianna.

RESEARCH UPDATE

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

Development of Stem Cell Transplantation Therapy for Sanfilippo Disease: Recent Advances in Cell-based Gene Therapy – April, 2010

For many years, Dr. Yu has studied the biology of stem cells for the purpose of developing a cell transplantation therapy to correct the genetic defects of neurodegenerative disorders, including such lysosomal disorders as Sanfilippo disease (mucopolysaccharidosis III). The stem cells are derived from the inner cell mass in blastocytes at early embryonic stages. In recent years, it has been recognized that stem cells can also be harvested from other sources, such as umbilical cord blood. These cells are self-renewable and pluripotent, meaning that they can develop into different cells types, such as nerve, muscle, and bone cells, etc. Thus, they are amenable for use for tissue regeneration and repair. Dr. Yu has induced them to differentiate into neural stem cells (NSCs) or neural progenitor cells (NPCs) that are committed to developing into brain cells for use in neurodegenerative disorders. They are then harvested and transplanted into damaged brain to re-regenerate and repair the damaged areas. This transplantation therapy therefore represents an effective therapeutic approach for repairing injured brain tissues. This strategy has already been recognized by many leading laboratories as a viable and most promising approach, as evidenced by a number of publications in the scientific literature. In Dr. Yu's laboratory, a major focus is to develop and modify a relatively new technology, the so-called "transposon or piggyBac" technology, for making the cell transplantation strategy even more effective. This relatively novel technology can be used to replace missing or defective genes, such as those in mucopolysaccharidosis III, in the host chromosomes. This technology enables the transplanted gene to integrate permanently inside the cells, thus achieving long-term therapy. This technique is gaining momentum in the gene therapy field. Ongoing research in Dr. Yu's laboratory has shown that it is feasible to fortify neural stem cells with specific enzymes that are missing in mucopolysaccharidosis III. He plans to transplant those engineered cells into animal brains in order to restore biological functions in patients suffering from this disease. He is keenly aware that the safety and efficacy of these strategies must be fully evaluated before their use in humans with mucopolysaccharidosis III.

In addition to the above, Dr. Yu and his team have learned much about the biological properties of NSCs/NPCs and how one can control them from becoming malignant cells, which can occur in certain conditions and jeopardize the safety of patients receiving stem cell treatment. In particular, he is focusing on the role of cell surface molecules that help define the properties of these cells and govern how they behave in the brain. These molecules are critical in determining the properties of cells and the way they become different types of nerve cells. More importantly, they play crucial roles in determining how they interact with each other, so once the neural stem cells are transplanted into the damaged brain, they can be correctly integrated with existing brain architecture. This basic knowledge is essential because Dr. Yu wants to make sure the donor cells survive, migrate, and grow normally within the recipient's brain, and to avoid abnormal or excessive growth, for example to become tumors. To achieve this goal, he has employed a relatively new technique, called "neurospheres formation method," to isolate and purify these cells. The work assures that there will be well-defined cell populations for therapeutic use. In the past year, Dr. Yu and his team have successfully transplanted these cells into the brain of animal models with mucopolysaccharidosis III to see if they can correct the storage of heparan sulfate. Preliminary studies have shown that these cells grow and integrate inside the brain after transplantation. More importantly the recipient animals survive the transplantation surgery for a prolonged time. Animals with mucopolysaccharidosis appear to have improved biological function, as assessed by behavioral tests. The results are very encouraging.

To ensure an adequate supply of stem cells, Dr. Yu has established an Umbilical Cord Blood Stem Cell Core Facility in the Medical College of Georgia. This Core is currently directed by Dr. Yu and is in full operation. This Core has provided researchers at MCG and other institutions with fresh and defined hematopoietic stem cells from cord blood. He is hoping to expand the operation of this Core to provide researchers and clinicians with an alternative source of stem cells for clinical investigations, including Sanfilippo disease. Two major instruments, a

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fluorescence-assisted cell sorter and a confocal microscope have been purchased using a substantial amount of funding from the State of Georgia. These instruments are in full operation for sorting of the myriad of cells in cord blood and for their characterization. These are essential steps to bring these cells for use in the clinic.

Dr. Yu is fully committed to continuing his research into mucopolysaccharidosis based on encouraging accumulated data. The financial support of the Children's Medical Research Foundation and more importantly, its encouragement, have provided the necessary incentive for continuing this work, which Dr. Yu hopes to be able to quickly bring to fruition.

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

During the last few years, our research group at the University of South Florida has studied the potential of human umbilical cord blood (hUCB) stem cells to treat various neurodegenerative disorders (stroke, ALS, Parkinson's disease) as well as brain and spinal cord injuries. Data suggest that these cells are able to repair a damaged or defective nervous system. We have also shown that hUCB cells reduced disease related changes after intravenous (iv) injection into an animal model of Sanfilippo Syndrome type B. In Sanfilippo syndrome type B, a deficiency of the Naglu enzyme leads to accumulation of heparan sulfate, a major feature of this disease, which may be ameliorated by hUCB cell therapy. Although administered hUCB cells were found widely distributed among different brain structures, the mechanism of cell migration to the brain is still unclear. One possibility is that cell migration to damaged areas of the brain occurs due to "signaling" substances in damaged tissues, substances that attract the transplanted cells. Another possible mechanism of transplant cell migration may be crossing of a damaged blood-brain barrier (BBB). Previously we showed BBB dysfunction, indicated by leakage of IV injected Evans Blue (EB) dye and serum protein (albumin) in microvessels of various brain structures, in Naglu mice at early and late stages of disease. These novel findings point to functional alterations of the BBB in a mouse model of MPS III B. However, soundness of the BBB structure in this disease model is uncertain. The aim of this study was to determine whether structural integrity of the BBB is impaired in a mouse model of Sanfilippo type B at different stages of disease. Microvessel ultrastructure in various brain structures (cerebral cortex, hippocampus, cerebellum, and striatum) from Naglu mutant mice at early or late stage disease and from wild type mice (controls) was examined with an electron microscope (EM). Also, immunohistochemical staining for GM3 ganglioside was performed in serial brain sections to detect glycosaminoglycan accumulation within the vascular endothelium. Results showed that BBB structural integrity was affected in microvessels of various brain structures in early and late symptomatic male and female mice modeling MPS III B. Capillary ultrastructure revealed endothelial cell degeneration, which, along with pericyte degeneration, compromised the BBB, resulting in vascular leakage. Endothelial cells and pericytes, cells composing vascular wall, were highly vacuolated and contained GM3 gangliosides leading to cell damage. Significant structural abnormalities were observed in capillary endothelia of late symptomatic mice. Also, a microaneurysm was identified adjacent to ruptured endothelia, which led to vascular leakage.

Importantly, BBB structural damage, confirming our previous functional BBB impairment, was determined in brain structures known to experience pathological changes, such as neuron vacuolization leading to neuron degeneration. This new discovery of microvascular functional and structural damage in a mouse model of MPS III B even at early disease stage may have implications for disease pathogenesis in human Sanfilippo disease. The important role that blood-brain barrier dysfunction could play in Sanfilippo pathology make it necessary to investigate this possible damage in MPS III patients. To our knowledge, no direct examinations have been undertaken to verify BBB disruption or dysfunction in patients with MPS III. Determining competence of BBB in patients with MPS III is important for understanding additional mechanisms of disease pathogenesis and to developing pharmacological treatment.

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.

Save The Date...

16th Annual Sweetheart Dinner Dance

Plans will soon be underway for the
16th Annual Sweetheart Dinner Dance to be held
February 11, 2011,
at The Ritz-Carlton Chicago.

Reservations will be $225 per person
and must be made in advance.

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.

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