



KirbyGram

June 2001

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

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, mental retardation, dementia and finally death by age 10-15 years. 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

Spring was a special time for the Wilsons. In March, they traveled to Key Largo, Florida, where Kirby and her big sister Maggie attended a five-day program at the Island Dolphin Care facility. Brad and Sue had the pleasure of watching their children interact and swim with some very special dolphins. Out of all the opportunities to touch, play and swim with the dolphins, Kirby's favorite time was when her dolphin friend, Tiffany, would spit water at her! It was a wish come true for the entire family, thanks to the generosity of The Make-A-Wish Foundation, whose "wish makers," Debbie Fey and Kirby Purjet, orchestrated every detail of the trip. Sue comments, "Make-A-Wish made us feel like royalty, and the people at Island Dolphin Care went above and beyond to ensure that Kirby's dolphin experience was a happy one."

April brought Kirby's 10th birthday and joy to the Wilsons. Her special day was spent taking an "adventure" walk through the woods, singing all her favorite songs. A pizza dinner and cake with family topped the day. Laughter filled the room when Kirby decided that the use of a fork just wasn't fast enough for the cake so she



The birthday girl

decided to use a two-handed approach. The left hand still used the fork as the right simply dug in to fill the obviously unacceptable lapse of time!

"We are blessed that the past six months have brought no obvious regression in our dear daughter. Her laughter fills our hearts with joy," Sue comments. "She remains our teacher, reminding us to never forget the power of the simple things. Her smiles, kisses and hugs allow our spirits to soar. Brad and I have a truly privileged life as her very proud parents."

FUNDRAISING NEWS

A "Sweetheart" of a Night for the Foundation

The Sixth Annual Sweetheart Dinner Dance, held this past February, raised more than \$84,000 for the Foundation! This is the largest jump in profits the Foundation has ever realized, thanks to the generosity of the 281 guests in attendance. "It is the continued support of these people that makes these huge achievements possible for the Foundation," Sue states. "They are our "enablers," for whom we will always be grateful."

FUNDRAISING NEWS

Fun for All at UIC's Winter Ball

The University of Illinois at Chicago College of Medicine's Class of 2003 selected the Foundation as the benefactor of its annual Winter Ball. This annual student-run fundraiser was held at the Harold Washington Library Winter Garden in January. The gala featured a Tango demonstration, dancing and silent auction. Final

numbers are not in yet, but the students expect to exceed \$6,500 for the Foundation. The Wilsons were amazed at the hard work put forth by the students in the planning of the event, which was certainly apparent throughout the evening.

"Brad and I give thanks to all the medical students not only for their efforts on behalf of the Foundation but also for the concern and compassion shown toward Kirby and the disease that afflicts her. It was a wonderful experience for Brad and me as parents and an obvious benefit to the Foundation," Sue comments.

"Score for Kirby"

Score Tennis in Countryside hosted a lock-in tennis "fun" raiser, "Score for Kirby," on April 21st. Thirty of Score's players volunteered to

participate in this 12-hour tennis marathon, for which they collected pledges from family and friends for each hour of tennis they played. The event raised \$3,200 for the Foundation. The Wilsons never cease to be amazed at the people who gather around them to do whatever possible to help. "The players and coaches of Score put forth an amazing effort to raise awareness and funds for the Foundation. Their



Score's players are winners for Kirby

enthusiasm was incredible," Sue explains.

And Then There's The Women.....

The LaGrange Highlands Woman's Club has chosen the Foundation as one of the Club's benefactors for the sixth year with contributions totaling \$7,800. "These women all live within our community, and I am honored to have them as friends and neighbors. They have never lost faith in our mission, and it means the world to me," Sue says.

The **Indian Head Park Woman's Club** once again chose the Foundation as a benefactor of their generosity with a \$300 donation in the name of Kirby and her "Grandma," Shirley Malek.

The **St. Cletus Council of Catholic Women** honored the Foundation with a donation from its fundraising efforts for the second year. The Council stated that it recognizes the

importance of our charity and sent the members' blessings as well. The Foundation gives thanks for the Council members' commitment and faith in its mission.

And of course, the Wilson's dear friend, **Ellie Rounce**, never stops when it comes to fundraising for her "little Kirby." This

time she gathered friends for a "House of Lloyds" party, which not only raised funds for the Foundation but also allowed Sue Wilson to pick items for the "Sweetheart" silent auction from the wonderful selection of gifts and houseware items. Ellie is truly Kirby's sweetheart.

The Foundation Gives Thanks....

To **Lyons Township High School's choir** for, once again, singing for Kirby. This year, the evening included the **Armstrong High School's choir**, who traveled from

FUNDRAISING NEWS

Minnesota to join in the event. The Foundation gives its heartfelt thanks to the directors, Mike Wolniakowski and Stephanie Trump, as well as their most talented students for an outstanding performance for Kirby and others like her.

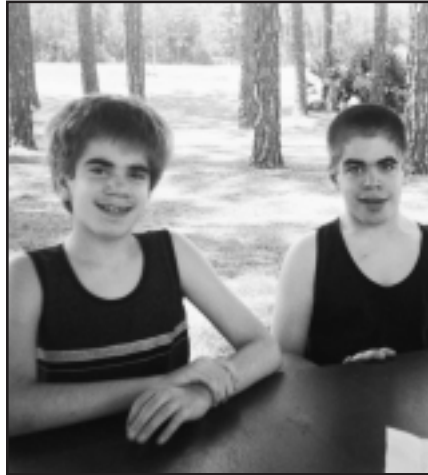
To **Lyons Township High School's Peaceable Schools Initiative** group for raising \$300 from a car wash fundraiser. Kirby thanks these students for shining cars to brighten her future!

To **Kim Sheehan** for going "over the hill" for Kirby! To celebrate her 40th, she asked guests to donate to the Foundation in lieu of gifts. Her celebration raised \$795 for the Foundation. Now that's a party!

To **Tom Ostdiek**, owner of **Carpet Tech Services**, for his February fundraising efforts and donating \$306....that's a clean sweep for Kirby and friends!

To **White Hen Pantry, Kirschbaum's Bakery** and **Casey's Market**, all from Kirby's hometown of Western Springs, for their continuous fundraising efforts with cash jars. And to the people of the community who filled them and helped to raise almost \$2900 last year, your "hometown girl" thanks you from the bottom of her little heart.

To **Rich and Debbie Vanderpool**, parents of **Jason**, who also asked that donations be made to the Foundation to celebrate



Jason, with brother Jon, enjoying the day

Jason's 10th birthday. Jason's special day raised \$340 for the Foundation!

To **Steve and Betsy Fowler** for donating to the Foundation in honor of their daughter **Kimberly's** 13th birthday.

To the **Sprosty Bag Employees** for collecting \$100 in donations in honor of **T.J. Catanzarite**.

To **Catherine and Judy Bracken** for hosting a fundraiser at **The Cottage** and raising \$359 for the Foundation through the sale of "Shelby Stars," in honor of **Shelby George**. Shelby is a star!



Kimberly's eyes speak a thousand words



Shelby - the shining star

The IPA Wives Club is Flying High!

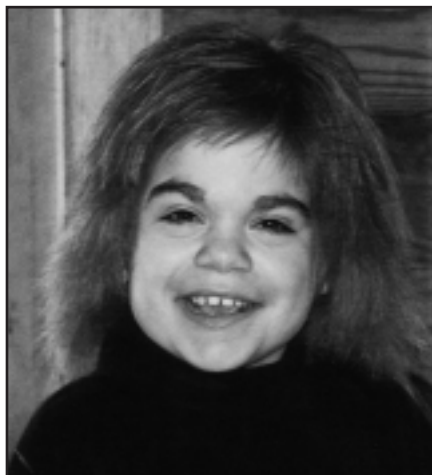
The **IPA (Independent Pilots Association - a UPS pilots union) Wives Club** honored **Ashleigh and Brooke Kidwell**, daughters of fellow member Anna Kidwell and UPS pilot David, with a silent auction fundraiser in which all proceeds were donated to the Foundation. This March

10th event raised \$13,040! This is a magnificent gift, and the Foundation thanks the Wives Club for its most generous contribution to help give all children like Ashleigh and Brooke a "flying start" for a bright future.



Pretty as a picture - Ashleigh and Brooke Kidwel

FUNDRAISING NEWS



Rhianna, all smiles after riding horseback

News From Connecticut

Gene and Cynthia Logan's friends, **Alan and Donna Theriault**, once again organized their annual event, "**Rockin' for Rhianna**," which was held November 21st in honor of the Logan's daughter, Rhianna. This event just keeps getting bigger and bigger for the Foundation. With the help and generosity of many volunteers and contributors, it raised \$19,000. The Foundation thanks Alan and Donna, their volunteers and donors for their steadfast commitment to Rhianna and others like her.

Rhianna's Hope (the committee formed by the Logan family to raise research funds) is busy with last-minute plans for its Fifth Annual "**Cut-Against-Time**" fundraiser to be held June 10th. This was the first event ever held for Rhianna, and the committee's members show no signs of slowing down with their continued efforts to bring new ideas in each year. We wish them the best!

Mr. **Harvey Wilson** and **The Bristol Auto Club** are still cruisin' too with their "**Cruisin' for Rhianna**" fundraiser, which raised \$5,000 for the Foundation. Now that's a smooth ride!

Martha Couture of **An Artisan's Marketplace** (and Rhianna's grandmother) was able to raise \$1,000 with a "**Santa for Hope**" raffle. Thanks, Grandma!

Cory and Donna Gabel, Rhianna's aunt and uncle, raised \$600 for the Foundation with the sale of Cory's own solo piano instrumental CD, "**One Road.**" The cover's artwork was created by Donna. A great family effort!

Our thanks to Mr. **Joseph Beaulieu** and the **CT Area Classic Thunderbird Club** for their donation of \$150 in honor of Rhianna.

And of course, thanks to **Mary Lou Cassille** of **Cassille's Restaurant** and her loyal customers for their continuous support of Rhianna and the Foundation through their contributions to the cash jar.

As always, the Logans give thanks to the many supporters within their community who realize how precious their time is and continue to put forth such an incredible effort on behalf of their dear daughter.

Ben's Dream

Poorman-Douglas Company of Portland, OR, and **Xerox** teamed up to put on **The Haunted House and Harvest Festival** last October and attracted more than 600 people. Thanks to Ben Siedman's uncle, **Howard Carpenter III**, a P-D employee, for spreading awareness about Ben and the Foundation. All proceeds from the three-day event, which totaled \$4932, were donated to the Foundation. Fun, food and fundraising, a great combination for Ben and his friends!

The **Lisa James Salon** of Wellesley, MA, hosted a **Cut Against Time** fundraiser last November in honor of



Ben's day on the farm

one of its very special customers, Ben. Through advertising, flyers and word of mouth, haircuts and raffle ticket sales turned into a \$6941 donation to the Foundation. Our thanks to salon owner **James Mortenson**, **Nancy Pizzotti** and salon employees for sharing their talents and helping to "cut" the time for a cure!

A big thank you goes to **The Florence & Edgar Leslie Charitable Trust** for their most generous contribution of \$5,000 toward Ben's Dream, and thereby to the Foundation.

MPS UPDATE

Our congratulations and thanks to MPS Board Member and Chairman of the Committee on Federal Regulations, **Les Sheaffer**. His hard work and commitment to making our legislators aware of all MPS disorders and the need for federal funding for research have paid off. He recently got language specific to MPS written into the Senate LHHS committee appropriations bill report, a bill established by Congress which determines the funding level for the NIH and emphasizes the priorities of the Senate committee. This language

MPS UPDATE

has resulted in a projected \$9.2 million worth of funding for MPS research for the fiscal year 2001.

Also, because of the relationships Les has built over the years with people in Congress, he, Linda Shine and Barbara Wedehase of the National MPS Society had meetings with top officials at NIH. These meetings resulted in NIH's desire to

host a scientific workshop and symposium at its headquarters in Bethesda MD. The main focus will be areas of study relating to MPS disorders, including the blood brain barrier and other critical MPS research issues. This meeting is proposed for the summer of 2002.

Quite simply, Les, we think you're the best!

And to all of you, we give thanks for your letters to your legislators in support of MPS research that have helped Les achieve these goals, as well as the most generous donations you make to the Foundation that enable researchers to bring their work to the level of consideration by the NIH. It's this type of combination that will bring the cure!

RESEARCH UPDATE

Dr. Elizabeth F. Neufeld, UCLA "The Mouse Model of Sanfilippo Syndrome Type B" May, 2001

We continue to study the mouse model of Sanfilippo Syndrome Type B, particularly with respect to the brain pathology. Changes occur not only in neurons, but also in other cells of the brain, and are especially prominent in microglia. These are cells of the macrophage system, which are part of the body's defense against invaders but which can also react to disease of the body's own cells. Electron microscopy shows that the microglia of the Sanfilippo B mouse have very swollen vacuoles with the characteristic appearance of lysosomes in MPS storage disease. They also appear to store GM 2 and GM 3 gangliosides. Activated microglia can be seen very early in the disease process (when the mice are one month old) and become more numerous with time. We believe that the microglia become activated as they attempt to dispose of heparan sulfate and possibly of damaged neurons. The activated microglia may produce compounds that are toxic to neurons, thereby

compounding the injury. While this is all hypothesis at the present time, it can be tested, and if found correct, would have implications to treatment of the disease.

We have distributed the Sanfilippo Type B mice to a number of laboratories. But to make them more widely available, we have sent them to the Jackson Laboratory, Bar Harbor, ME, a central repository for mutant mice. The Jackson Laboratory will maintain the Sanfilippo Type B mice and breed them into a colony. This will take some time, but meanwhile anyone interested in obtaining these mice is urged to contact the Laboratory so that they can anticipate the demand. The URL for the Jackson lab is <http://jaxmice.jax.org/index.shtml>. See <New Jax mice strains> and <New strains under development that are not yet available>. Finally, scroll down to Naglu (#003827).

Dr. Robert K. Yu, MCG Research Institute "Neurochemical Studies of Sanfilippo Disease" May, 2001

During the past year, we have completed a detailed analysis of the

ganglioside composition of the brains of goats affected with Sanfilippo D disease (MPS IIID). In addition, we have characterized the ganglioside composition of a mouse embryonal stem cell line with the goal of setting the stage for using stem cells for developing a cell transplantation therapy for MPS III. In addition to testing drug therapy regimens, which are ongoing, we plan to further develop the cell transplantation therapy strategy. The latter plan promises a more permanent correction of the metabolic defects in MPS III. We have also established a Sanfilippo mouse colony in our laboratory from founder mice provided to us by Dr. Elizabeth Neufeld, UCLA. These animals will be used for testing our proposed treatment plans using drugs and cell transplantation; both are in progress.

Dr. Joseph Muenzer, University of No. Carolina at Chapel Hill "Neurological Correction of Mucopolysaccharidosis by AAV Gene Therapy" May, 2001

The focus of MPS research at the University of North Carolina, Chapel Hill, North Carolina, in the laboratory

RESEARCH UPDATE

of Dr. Joseph Muenzer has been to develop adeno-associated viral (AAV) gene therapy as a treatment for the central nervous system in MPS IIIB. An AAV vector is a delivery system to allow the human MPS IIIB gene to be taken into cells and then incorporated into the cell's genetic material. Once the MPS IIIB gene is in the nucleus of the cell, the missing enzyme in MPS IIIB can be made and the storage of mucopolysaccharides reversed.

In previous research, we have made AAV vectors containing the human MPS IIIB gene, produced the missing enzyme in MPS IIIB in cultured skin cells and mouse MPS IIIB brain and corrected the storage of mucopolysaccharides in cultured cells using AAV vectors. Although these advances are significant, we had not been previously able to demonstrate correction of the storage in the brain on MPS IIIB animals. In the past year, we have demonstrated long-term localized correction of lysosomal storage in the brain of MPS III mice after a single direction injection of an AAV vector. With the correction of lysosomal storage in the brain of MPS IIIB mice, we have demonstrated that AAV gene therapy is a potential treatment for neurological disease in MPS IIIB. One last step however is needed before human gene therapy clinical trial can be considered for MPS IIIB. A significant improvement in vector spread or delivery of the AAV vector to much larger area of the brain needs to be achieved.

Recently, significant advances have occurred in AAV gene therapy. Exciting studies with reporter genes have shown that by changing the covering or coat of the AAV vector, the vector is more widely distributed after direct injection into the brain of

animals. In addition, the modified or new vectors appear to be more capable of entering cells thus allowing higher expression of the missing enzyme and greater possibilities of correcting the stored material. Studies are in process to utilize these advances to develop more efficient AAV vectors and gene therapy methods for MPS IIIB. These promising studies are not possible without the support of basic research at the University of North Carolina by the Children's Medical Research Foundation, Inc.

Dr. Chester Whitley, University of Minnesota "Gene Therapy for Sanfilippo "B" Syndrome" May, 2001

In this laboratory, CMRF has supported several new discoveries necessary to develop a systemic therapy for Sanfilippo Syndrome. An initial step was to devise a method of automated gene sequencing of the entire human alpha-N-acetylglucosaminidase (NAGLU) coding region (Aronovich et al. 1996; Zhao et al. 1998). This facilitated identification of mutations in affected children and differentiation of a more "attenuated" condition. Most recently, these same methods have been extended to determine the sequence of an analogous gene in emu and to identify a specific mutation causing Sanfilippo Syndrome type B in commercial breeding stocks of these birds (Aronovich et al. 2001). Significantly, this work brings another laboratory (University of Pennsylvania) into this area of research, stimulating studies in this new model. More importantly, comparison of the human, mouse and emu gene to analogous genes in more distant organisms (e.g., tobacco, the

laboratory worm *C. elegans*) provides the background for genetically-engineering synthetic NAGLU genes. Similar work in this laboratory has identified the normal sequence of another gene in dogs and identified its mutation causing Sanfilippo Syndrome type A in Dachshunds (Aronovich et al. 2000).

To deliver such genes to patients, the major thrust of work in this laboratory has been to investigate potential gene therapy delivery vehicles, known as "vectors," for the ability to deliver a normal NAGLU gene to relevant tissues.

A vector that holds particular promise is derived from the HIV virus. However, social concern about the use of HIV is a major impediment to development of clinical therapy. Alternatively, non-viral synthetic integrating system has recently become available. Discovery of Sleeping Beauty transposon at the University of Minnesota provides a means of accomplishing some of the integrating function of HIV, but in a non-viral gene delivery system. Current work is exploring delivery of lysosomal enzyme genes; initial work has developed an MPS marker gene transposon and is currently under investigation in MPS cells grown in tissue culture. In the coming year, it is hoped that this work can be extended to studies of a Sleeping Beauty transposon with NAGLU in the colony of Sanfilippo Syndrome mice (Li et al. 1999) recently introduced into this laboratory.

FUNDRAISING IDEAS

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! Our United Way Chicago "Agency Number" is 3025558. For those of you out of state, wishing to participate, please supply your local United Way agency with the Foundation name, address and our Federal ID #36-4033667.

Our thanks to the employees of University of Chicago Hospitals, Sears, CSC Consulting, Wellpoint Health Network, UPS and Pitney Bowes for designating their United Way pledges to the Foundation.

Give Kirby Security

Tired of taxes? The Foundation now has a brokerage account available which 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 Brad or 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

Soon the time will come when your company will wonder what it should give clients for Christmas. How about 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.

TIME TO SHOP? DO IT ONLINE

If you plan to surf the Web for online purchases and gifts, make your starting point our GreaterGood.com shopping portal. As a registered partner with GreaterGood.com, The Children's Medical Research Foundation will receive a cash donation of up to 15% of every purchase.

GreaterGood builds and manages "online shopping villages" for not-for-profit partner sites like ours, where every purchase benefits our cause. Our village includes a broad assortment of brand-name merchandise offered by leading retailers such as:

1-800-Flowers, Amazon.com, the BabyCenter, the DisneyStore, FogDog Sports, the Gap,

igoGolf.com, J.Jill, j.crew, K-Bkids, Nordstrom, REI, Starbucks and others.

When you shop through our online village, you support our mission - at no additional cost to you!

It's simple to help. Just click on The Children's Medical Research Foundation's "Shopping" button on our website - www.curekirby.org - to automatically benefit the Foundation. You can enjoy your purchase knowing that you've made a valuable contribution to our cause.



FUNDRAISING EVENTS

7th Annual Sweetheart Dinner Dance

Plans are now underway for the Foundation's Seventh Annual Sweetheart Dinner Dance, which again will be held at The Drake Hotel in Chicago on February 8, 2002. Do you know an individual or business that might be interested in sponsorship or in making a donation of an item or service for the auction? We have a full range of sponsorship opportunities, and our auction consists of children's toys, sports tickets and memorabilia, vacations, art, and gift certificates for hotels, dining and a variety of services. Please contact us for further details.

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