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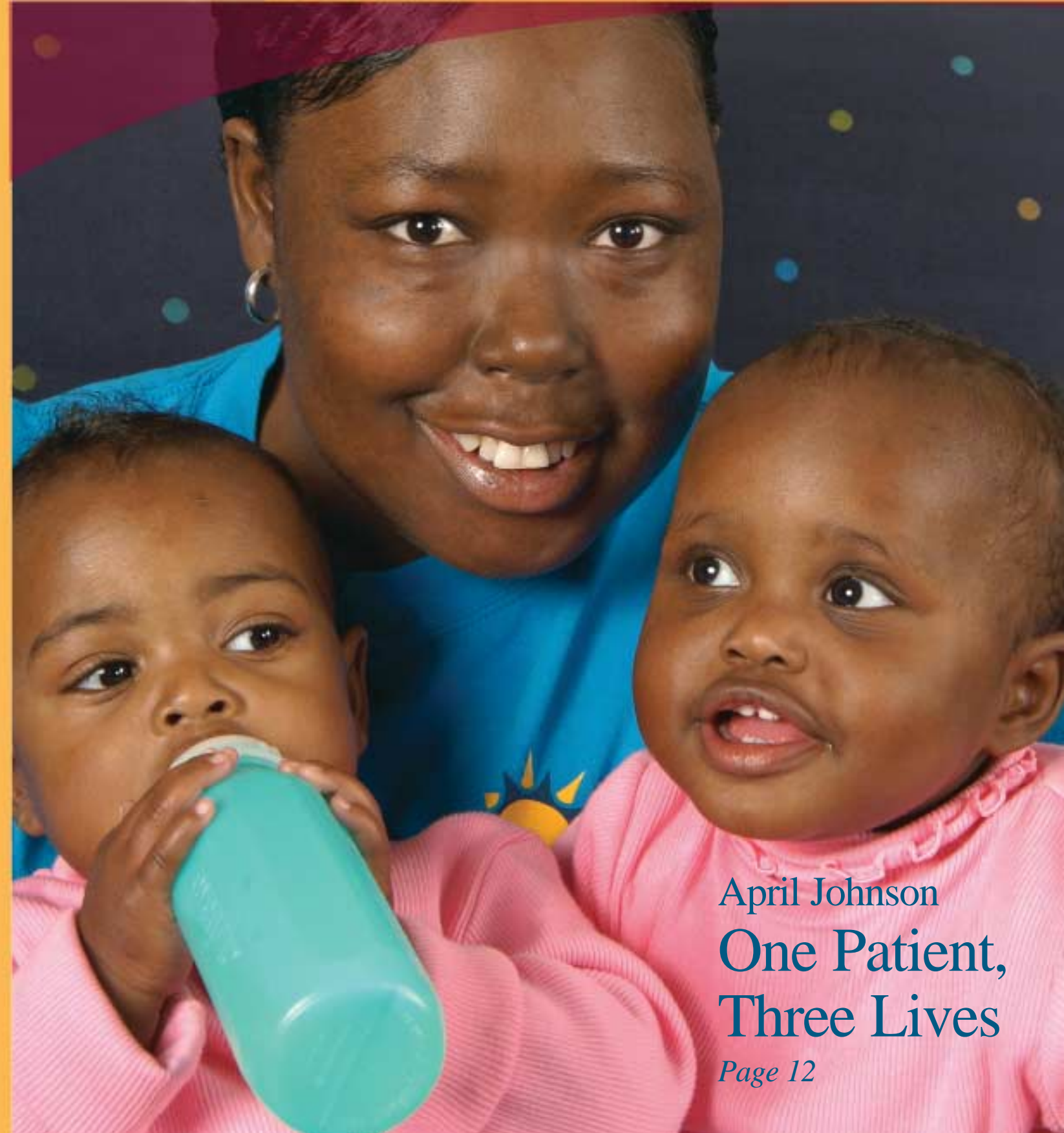


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Finding cures. Saving children.



April Johnson
**One Patient,
Three Lives**

Page 12

St. Jude Children's Research Hospital was founded by the late entertainer Danny Thomas. It opened February 4, 1962. The institution was created because of a promise Danny made during the depression era to St. Jude Thaddeus, the patron saint of the hopeless.

"Show me my way in life," Danny prayed. In return, Danny promised to build St. Jude Thaddeus a shrine. That shrine became a world-class research institution that treats children regardless of race, color, creed or their ability to pay. This remarkable event also inspired the name of this magazine,

Promise.



St. Jude Children's Research Hospital, Memphis, Tennessee

Promise

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332 N. Lauderdale St.
Memphis, Tennessee 38105

St. Jude Children's Research Hospital's mission is to find cures for children with catastrophic diseases through research and treatment.

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A publication of St. Jude Children's Research Hospital Summer 2004

Features

4 Command Performance

The show must go on

7 Service over Self

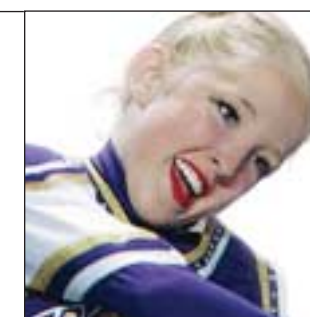
A continuing commitment

8 Spa Kids

Massage and humor

12 One Patient, Three Lives

April Johnson's Faith and Miracle



16 A Peek Under the Hood

Scientists study molecular motors

18 On the Road to Peoria

Running for a reason

21 Parkinson's Progress

Research for both kids and adults



Highlights

2 Achievements and Events

Perspective

24 Amber Valletta

A Call to Action



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On the cover: April Johnson with daughters Faith (on left) and Miracle (see article, page 12). Photo by Laura Hajar.

Highlights

A missing link

Researchers at St. Jude and Mayo Clinic have discovered that inactivation of the *CBP* gene in certain immature white blood cells causes lymphoma in laboratory models. The cancer is accompanied by changes in the expression of specific genes associated with development of the disease.

“One finding that was particularly surprising was the specific effect the loss of *CBP* had,” said article co-author Paul Brindle, PhD, of St. Jude Biochemistry. “It is commonly believed that *CBP* is involved in the control of many genes. Yet the absence of *CBP* appears to promote lymphoma by cooperating with a narrow set of dysregulated genes.”

Another unexpected finding was the lack of association between the loss of *CBP* function and a gene called *p53*. *CBP* is known to help activate *p53*, but the loss of *CBP* in white blood cells triggered cancer even though *p53* activity appeared normal. The findings were published in *Cancer Cell*, February 2004.

The wizardry of Ozz

Research conducted by St. Jude scientists may help uncover the genetic cause of certain muscle diseases that occur for unknown reasons in children.

A team led by Alessandra d’Azzo, PhD, of St. Jude Genetics and Tumor Cell Biology found that a novel protein, Ozz, directs the destruction of a structural protein in muscle that helps organize and stabilize muscle growth. The researchers also discovered the *Ozz* gene overlaps another gene, which codes for an enzyme called protective protein/cathepsin A or PPCA. This enzyme is deficient in the metabolic disease galactosialidosis.

The *Ozz* and *PPCA* genes share a genetic “on-switch” that controls their expression; thus mutations in *PPCA*



St. Jude patient David Moore and Debbie Crom, RN, PhD, of the After Completion of Therapy (ACT) Clinic, discuss the importance of promoting strong bones after cancer therapy. Their discussion occurred at the Eighth Annual St. Jude Cancer Survivor’s Day conference, which also marked the 20th anniversary of the ACT Clinic. Although Crom dressed as a skeleton to make learning about bones fun, she experienced many poignant moments during the conference. “It is very moving to have survivors say, ‘Do you remember me?’ and to be able to respond, ‘We not only remember you; we hold you in our hearts and we are dedicated to you having as healthy a future as possible,’” Crom says.

could alter the normal expression of *Ozz* and could cause the muscle problems of children with galactosialidosis.

d’Azzo, who holds the Jewelers Charity Fund Endowed Chair in Genetics and Gene Therapy, was senior author of a report on the findings, which appeared in the February 2004 *Developmental Cell*.

Brain cancer progress

Completion of a pilot study brings researchers closer to an international clinical trial aimed at improving guidelines for treatment of medulloblastoma, a common type of childhood brain cancer.

The study is the first to demonstrate that medulloblastoma samples can be rapidly delivered to a central research institu-

tion and analyzed. The findings confirmed that samples shipped from institutions in the United States and Australia can be analyzed at St. Jude for genetic abnormalities rapidly enough to provide physicians with information to guide their treatment decisions.

The study also demonstrated that by detecting the presence of a protein called ERBB2 in tumor samples, doctors might be able to predict which children with medulloblastoma will require more intensive treatment.

A report on this study, led by Richard Gilbertson, MD, PhD, of Developmental Neurobiology and Amar Gajjar, MD, of Hematology-Oncology, appeared in the March 2004 *Journal of Clinical Oncology*.

Order from disorder

St. Jude investigators have demonstrated for the first time that—contrary to the assumption that proteins must maintain a rigid structure in order to perform an assigned task—many proteins exploit disorderliness in their structure to perform various jobs. The research findings appeared in the April 2004 *Nature Structural and Molecular Biology*.

The St. Jude finding explains how many proteins can adapt their structures to the needs of the moment, binding to different molecules depending on the job at hand.

“The potential importance of disorder in the function of some proteins has been discussed by researchers for several years,” said Richard Kriwacki, PhD, of St. Jude Structural Biology, the report’s senior author. “But until now no one had actually demonstrated how such flexibility allows a protein to interact with different molecules. We’ve taken a big step in understanding the subtle details of a critical biochemical process in the life of the cell.”

To view an online movie illustrating the movement of a protein, visit www.stjuderesearch.org/data/kriwackilab/p27.html.

A fresh look

St. Jude scientists have discovered that a tumor-suppressor protein called Rb is required for proper retinal development in laboratory models. This is a major step toward understanding why some children develop the devastating eye cancer called retinoblastoma. The discovery should eventually help scientists design a better treatment for this disease.

The St. Jude team showed that Rb limits growth of immature retinal cells so the retina develops to a normal size. The Rb protein also prompts specific cells to develop into light-sensitive cells called rods.

“What we’re learning could eventually help us to block the molecular signals that trigger retinoblastoma in children,” said Michael Dyer, PhD, of St. Jude Neurobiology, senior author of a February 2004 *Nature Genetics* article about this research.

Tricks of the trade

A genetic trick that viruses use to replicate themselves has been adapted for the laboratory to build complex protein structures required by immune system cells, according to St. Jude investigators.

The approach could also be used to

develop new gene therapy vectors in cases when cells must be modified to make high levels of different proteins. A vector is a DNA molecule used to ferry specific genes into cells in order to give those cells the ability to make particular proteins.

St. Jude researchers are also conducting Phase I clinical trials with investigational drugs to treat cases of ALL that have resisted previous therapies.

The achievement gives researchers a way to study the roles of complex proteins in living cells and to produce therapeutically useful amounts of multiple proteins. The new technique would

permit scientists either to restore complex protein structures that are missing in certain cells or make multiple proteins that act together as potent drugs against cancer and other diseases.

Dario Vignali, PhD, of St. Jude Immunology is senior author of a report on this work, which appears in the May 2004 issue of *Nature Biotechnology*.

Rising rates

The cure rate for pediatric acute lymphoblastic leukemia (ALL) might continue to rise with improved use of conventional therapies. But even more effective and less toxic therapies based on genetic and pharmacogenetic studies may one day push the success rate close to 100 percent, according to an article published by Ching-Hon Pui, MD, Leukemia/ Lymphoma division director; Mary Relling, PharmD, Pharmaceutical Sciences chair; and James Downing, MD, Pathology chair.

The article appeared in the April 2004 edition of the *New England Journal of Medicine*.

The researchers based their prediction on a review of leukemic cell genetic abnormalities and host normal cell genetic characteristics. The genetic approach to ALL treatment increases physicians’ ability to identify which gene mutations are linked to responsiveness to anti-leukemic drugs. Clinical trials are underway to test the safety and efficacy of drugs targeting a variety of gene mutations.

St. Jude researchers are also conducting Phase I clinical trials with investigational drugs to treat cases of ALL that have resisted previous therapies.

These news items reflect only a handful of the lifesaving projects occurring at St. Jude Children’s Research Hospital. For information about other recent discoveries, visit our Web site at www.stjude.org/media.



Marlo Thomas, St. Jude National Outreach director, and Joe Mirro Jr., MD, the hospital’s chief medical officer, appeared before Congress in April to discuss the need for more funding for pediatric brain tumor research and treatment. Mirro also talked about the hospital’s efforts toward individualized treatment. Thomas and Mirro were joined by Thomas’ husband, Phil Donahue (pictured in background), ALSAC National Executive Director Richard Shadyac and two St. Jude brain tumor patients and their families.

Command Performance

For Lindsay Harwell, the show must go on. Dance and theater activities help her concentrate on a life beyond cancer.

By Victoria Tilney McDonough

When Lindsay Harwell steps on a stage to perform, she loses herself—in the dance, the song, the words. Although she is a private person, something about performing sets her free. Having started dance at age 2, Lindsay loves to move her limbs to music and to the sound of her own spirit. “I like to get up and show everyone what I can do, to do my best,” the 16-year-old says. “I like hip-hop the most. It’s flowy; you just have to go with it.”

These days, Lindsay’s biggest challenges are no longer strained muscles or tough dance routines. These days, Lindsay knows how lucky she is to dance, to have friends and to have her family close. In December 2003, she found that her sore leg was not the result of a pulled ligament but of a tumor the size of a grapefruit lodged near her right hip. She had osteosarcoma, the most common type of bone cancer in children and adolescents.

“Lindsay has always had a high tolerance for pain,” explains her mother, Carla. “So when she continued to complain about her leg and then could barely walk at all, I knew it was serious. A mother just knows these things.”

Because the pain in her leg intensified around Christmas 2003, it took several weeks to get answers. “We had bone scans and consultations, but we never heard back for sure. It was probably an infection, the doctors told us,” says Carla. “Everyone was out for the holidays. The waiting, for us, was excruciating. When we finally got a call, they told me to come with Lindsay and Tony, my husband. That’s when I knew. Why else would they have insisted that Tony come, too? I froze. It all felt like a dream.”

The night they found out, Lindsay wanted to sleep in her mother’s bed.

“In the dark, she said, ‘Mama, can I talk to you?’ She said she was worried that she wouldn’t be able to swim or water ski or be her normal self with the Hickman line,” says Carla. A Hickman line is a tube that is inserted into a major blood vessel through the chest. St. Jude patients receive chemotherapy and other drugs through this line, which eliminates the need for repeated needle sticks.

“With no hair,” Lindsay whispered to her mother, “I’m worried boys won’t like me.” Carla told Lindsay that she was beautiful—inside and out.

“That night was the only time I’ve seen her cry since we found out,” Carla says.

Keep moving

Lindsay started 48 weeks of chemotherapy in January. She has felt tired but hasn’t been sick from the drugs. But even sickness wouldn’t have stopped the determined sophomore from competing in the Universal Dance Association National Championships. “We were practicing hard after the holidays in preparation for Nationals at the end of January,” says Robin Crane, dance sponsor for Lindsay’s high school team. “These kids have known each other for several years and are very close. They’ve been supportive of Lindsay. She’s been teaching them a life lesson. Even when she’s tired or feels faint, she

takes a minute then keeps going. She doesn’t let anything get her down.”

The team traveled to Orlando, Florida, and won fourth place in the competition.

While on that trip, both Lindsay and her friends realized that a cancer diagnosis shouldn’t set her apart. “I think Lindsay really accepted her cancer and everything that comes with it that first night in Orlando,” says her mother. “Her friends saw her Hickman line, saw me flushing it, and that was that. It was no big deal. Lindsay’s teammates—and Lindsay, herself—realized that even with the line, even without her own hair, she is still Lindsay.”

One step at a time

For some patients and families at St. Jude, traversing between two worlds—their “old” world and that of St. Jude—can feel a bit like stepping back and forth through Alice’s looking glass. But for Lindsay, life still has a keen sense of normalcy. She’s been lucky, she admits, that she’s been able to continue with most of her activities and that St. Jude has accommodated her schedule. As she told a television reporter, “Everything happens for a reason. You can’t change the past; you can only make the future better. I’m just taking one day at a time.”

Lindsay’s friends, family and community have helped her maintain as normal a life as possible. They have also made her



SETH DIXON



Whether she’s waving pom poms or playing a nun in *The Sound of Music*, Lindsay Harwell (far right) is determined to continue doing the things she loves while undergoing treatment for osteosarcoma, a type of bone cancer. “Everything happens for a reason,” she says. “You can’t change the past; you can only make the future better. I’m just taking one day at a time.”

realize how loved and supported she is. Her dance squad raised \$1,600 for a wig to match her cornsilk-blond hair. The football team presented her with a huge card and a big stuffed Jaguar, their mascot. “Who would’ve thought those muscle boys could be so sensitive?” Carla laughs.

Students and faculty at the school where Lindsay’s grandmother teaches donated money from their annual fund-raiser to Lindsay. “They gave us part of the hope chain created from the fund-raiser,” Carla says. Each paper link in the chain cost five cents. The more paper links, the more money raised. This year’s chain snaked from classroom to classroom, down corridors, into the lunchroom and down stairwells.

“The section they gave Lindsay was so long we had to hang it in the garage!”

Stepping in character

Last summer, before Lindsay knew her life would change, she auditioned at her town’s local community theater for *The Sound of Music*. In early April, she donned a habit and stepped on stage for several weeks to play one of the nuns. Like dance, singing and acting is a release for her.

“I started taking voice lessons a few years ago and really love it. My older sister took them first; I always want to do what she does,” she says. “My sister has more of an opera voice. I have more of a country singer voice.” Lindsay met several country stars during Country Cares for St. Jude Kids®, which inspired her to practice more seriously.

Keeping busy, especially in group activities, seems to help her stay strong. “Lindsay looks out for everyone; that’s just her nature,” says her mother. “The first night of chemo, when Lindsay was an inpatient, I was so tired, I passed out on the couch in her room. When the nurses came in, Lindsay said, ‘Shhh, my mama’s asleep. She’s very tired.’”

Top: Lindsay may spend her days at St. Jude Children’s Research Hospital, but evenings are a different matter altogether. That’s when she participates in theater and dance—concentrating on greasepaint and costume changes instead of chemotherapy and cancer therapy.

Bottom: Mother and daughter have gained strength from each other during the rigors of cancer treatment. “I have been so impressed with how strong Lindsay’s been through all of this,” Carla says. “She holds me up sometimes, saying, ‘Mama, don’t worry. You worry too much. It’s going to be okay.’”

Carla thinks Lindsay is a great deal like her own mother. “My mother has always been my rock,” she says. “I can cry with her. She helps me see more clearly when I need to. Lindsay is a lot like her. They’re always looking out for others. They’re as close to angels as can be. I have been so impressed with how strong Lindsay’s been through all of this. She holds me up sometimes, saying, ‘Mama, don’t worry. You worry too much. It’s going to be okay.’”

Looking forward

Today is the day after Lindsay’s sweet sixteenth birthday party. She is starting 31 days of radiation on top of what’s remaining of her chemotherapy regimen. The tumor has shrunk to less than half its original size, and the Harwells hope that these treatments will do it—that surgery won’t be necessary since the tumor is so close to her hip bones and ovaries. Waiting for their appointment, mother and daughter feel tired from last night’s festivities.

“We were still up celebrating at 3 a.m.,” says Lindsay, who shows a picture of a three-layer cake that a family friend made for the occasion. When asked if she has a birthday wish, she answers quietly, “I wish I could be cured.”●

PHOTOS BY SETH DIXON



SERVICE *over* Self

Mom continues her daughter’s battle against cancer by raising funds for St. Jude.



All Shirley Castell has to do is think of her daughter, and she is reminded of why she made the commitment to help the children of St. Jude Children’s Research Hospital. In December 1969, Shirley found out that her 16-year-old daughter, Janet Castell, had leukemia. Not long after receiving this life-changing news, Shirley learned about St. Jude, and thus began her mission to support the hospital.

Janet’s particular form of leukemia was not being treated at St. Jude, so she was unable to go to Memphis for treatment. Nevertheless, Shirley decided to help other children at the hospital who were suffering from cancer. In 1970, she and her daughter held a fund-raiser for St. Jude that raised \$1,500. Janet didn’t survive her fight with cancer, but Shirley dedicated her life to helping other children win their battles with the disease.

Through the years, Shirley has held many other events to benefit St. Jude, including grocery raffles and bingo games, which she coordinated weekly through the local Jaycees—a national organization established to provide opportunities for young adults to develop personal and leadership skills through service to others. She fondly remembers a special donation she presented to St. Jude.

“I remember one particular time when Danny Thomas came to California to accept a check for \$30,000 raised through bingo games,” says Shirley. “I wish everyone had had a chance to meet Danny. He was so dedicated and really cared about the kids at the hospital.”

Dedicated is also a word that could be used to describe Shirley, who has spent the past 34 years raising money to support St. Jude. To honor her commitment to the institution, the Jaycees made a donation to the hospital in memory of Janet.

“That is one of the nicest things anyone has ever done for me,” says Shirley. “Some people ask why I support St. Jude way back in Memphis, but it’s more than that. The protocols and research at St. Jude are shared everywhere.”

As a testament to her dedication, Shirley spent many years volunteering for the hospital’s radiothons and golf tournaments in addition to the events she organized herself. She has cut back on the amount of time spent working bingo games, but the organization donates annually in her honor to thank her for her monthly participation in bingo.

“Sometimes I get tired and think I’ve volunteered long enough, but then I think about the kids at St. Jude, and I know I have to go on,” says Shirley. “I just want every child to have a childhood. Children should be healthy and happy; they shouldn’t be sick. St. Jude gives children a chance to live.”

To learn more about ways to give, call ALSAC Gift Planning at (901) 578-2081 or toll free at (800) 830-8119 ext. 2081. ●

By Alicia H. Matthews

Spa

BY CARRIE L. STREHLAU

Kids

A new study brings massage into the patient's room. But this treatment involves more than just back rubs. Think whoopee cushions. Think *Three Stooges*. Think relief from pain and anxiety.

ughter may be the best medicine, but a good massage is a close second. Markie Lambert—a 12-year-old patient

at St. Jude Children's Research Hospital—got the best of both worlds.

Markie and his mother, Margaret, volunteered to be part of an ongoing study using humor and massage conducted by staff in the hospital's Behavioral Medicine division.

Researchers created the study to explore whether massage and humor therapy can reduce the distress experienced by patients undergoing stem cell transplants.

"We're asking the question about whether brief, positive experiences might serve as a sort of medicine," says Sean Phipps, PhD, clinical psychologist and lead researcher for the study. "There is some evidence to suggest that a brief, positive experience impacts your ability to tolerate negative experiences. And it may serve as a stress buffer, as well as an antidote against the physical effects of stress."

Relaxation station

Funded by a National Cancer Institute grant, the project is the result of two earlier pilot studies. "We looked at techniques that kids could use during the day and that were transportable to their hospital rooms," Phipps says. "Of the techniques we tried, the most well-liked and widely used were massage and humor therapy."

Margaret can understand why. "I'd be sitting up all day and night praying for Markie," she recalls. "I would go into the relaxation room, put on my headphones and listen to my CD. I was feeling so tense, and as soon as I would start to relax, I would feel more comfortable. The massage

therapist had to wake me up once because I'd truly been asleep."

Margaret and her son participated in one part of the three-tiered study. In the first group, children receive a massage three times a week along with humor therapy intervention. The second group receives the same interventions, along with massage and relaxation therapy sessions for a participating parent.

"We bring the parents to a room with a big, soft, comfy recliner with dim lighting," says Beth Gray, a lead clinical research associate who also serves as the study's main massage therapist. "We encourage the parents to focus on their breathing and help them to relax each muscle group. Then we

PHOTOS BY SETH DIXON



Twelve-year-old Markie Lambert tries out a wacky toy from the Comedy Cart. Desirée Louwerse of Behavioral Medicine brings laughter and fun to patients' rooms as part of a project evaluating the effect of massage and humor therapy. The study is funded by a grant from the National Cancer Institute.



encourage them to imagine a safe and peaceful place before beginning the relaxation imagery.”

“The relaxation imagery is related to competence in parenting so they can feel more confident in parenting an ill child,” Phipps adds.

The third group receives standard care. To participate in the study, a patient must be 6 to 18 years of age and undergoing a stem cell transplant from a matched sibling, mismatched family member or an unrelated donor.

“What we’re doing here is complementary in nature,” Gray says. “It is not meant to replace any of the medical treatments. We want to show some things that could help improve a patient and parent’s quality of life.”

Ahh, there’s the rub

Gray is also responsible for coordinating study results from the other participating institutions in Toronto, Canada; Columbus, Ohio; and Philadelphia, Pennsylvania.

“When I go in the child’s hospital room, I let them know it’s massage time,” she says. “I

Beth Gray, the study’s main massage therapist, works her magic on Markie Lambert. “What we’re doing here is complementary in nature,” Gray says. “It is not meant to replace any of the medical treatments. We want to show some things that could help improve a patient and parent’s quality of life.” Gray also coordinates study results from participating institutions in Toronto, Canada; Columbus, Ohio; and Philadelphia, Pennsylvania.



In addition to receiving massages, parents participating in the study learn to use relaxation techniques while lounging in comfy recliners. “There is some evidence to suggest that a brief, positive experience impacts your ability to tolerate negative experiences, says Sean Phipps, PhD, clinical psychologist and lead researcher for the study. “And it may serve as a stress buffer as well as an antidote against the physical effects of stress.”

usually have my CD player with relaxing music. I always ask the patient if it’s okay to have a massage that day. If they say yes, I start with their hands, then arms, legs and feet, shoulder, neck, scalp and back. But it is all based on what the child allows.”

According to Gray, some children fall asleep and some want to keep an eye on everything. “Sometimes the child may feel nauseated, be in pain or not be in the mood to have a massage,” she says. “We are flexible. We let the children know that they are in charge.”

For the parents, Beth brings a special table into another room and performs a full-body massage for about 30 minutes. “I take the portable massage table with fresh linens into the parent room, and I also have my CD player with relaxing music and some very light lotion,” Gray says.

“Parents seem to be so appreciative of the chance to relax because of what they’re going through,” Gray continues. “Parents carry so much stress to stay on top of what they are required to do. This offers them a time to take care of themselves, which is a new concept for many of the parents.”

Humor me

Study participants complete forms to determine how they feel before and after the humor and massage

intervention, as well as to track their mood, physical well-being and activity levels across the acute phase of transplant.

“It seemed like Markie rested better and didn’t complain about aches as much after he had a massage,” Margaret recalls. Other study outcomes include monitoring the use of medications for pain and nausea and the number of days spent in the hospital.

“If some patients require fewer pain medications or get out of the hospital a day sooner, that would more than cover the cost of the interventions,” Phipps says.

Markie says he really enjoyed having his hands massaged. But his absolute favorite part of the study? The whoopee cushion. “I want to buy one of my own,” he says.

The whoopee cushion is part of the Comedy Cart—a large, brightly painted box on wheels that travels to each patient’s room. Coordinated by Desirée Louwse in Behavioral Medicine, the Comedy Cart includes funny glasses, sports bloopers and classic movies like *The Three Stooges*. A patient can choose an item from the cart or Louwse will order an item that a patient may think is humorous but is not already included in the cart.

“We encourage the kids to take a laugh break every day,” Phipps says.

“In fact, we recognize that there may be some days when they don’t feel like it, and we stress that those are the days that are best for them to do it. Our research assistants encourage the kids to take items off the cart. Along with this, we try to plant the seed that there are aspects of their own environment that they may find humorous.”

That may be a funny voice a nurse makes or a humorous mannerism of a doctor. “The goal is to educate the patients and parents about adding laughter to each day,” he adds.

For Markie, it’s his younger cousin. “She always makes me laugh just by the things she does and the way she dances,” he says.

“Markie is the one who makes me laugh,” adds his mother.

From the results of this study, researchers will later be able to study the physiological effects of humor and massage on patients and examine the mechanisms by which these interventions produce positive outcomes.

“This is really still a preliminary study just to see if it works,” Phipps says. “We’re in the very early stages, but anecdotally, it is being well received.”

Markie and Margaret were glad to be part of the study, and Gray could see the results. “When they laugh, you know they feel better,” she says. •



Laura Hallar

Deloris Johnson awoke with a gasp. Bolting out of bed, she peered into the darkness, heart pounding, body trembling. This was the third time that her deceased mother had appeared to her in a dream. The first time, the message had been cryptic: “You need to check on somebody,” Deloris’ mother admonished. But this time the message was frantic. “You’re gonna wait too late! You’re gonna wait too late!” warned the apparition.

“I jumped up, and when I blinked she was gone,” recalls Deloris. “That’s how I found out April was sick.”

In January of 1996, Deloris’ niece, April Johnson, complained of swollen lymph nodes. Sure enough, when Deloris took the 14-year-old to the doctor, she learned that April had cancer. “Take her to St. Jude,” advised Deloris’ boss. “That’s the best place to go.”

The next day, April traveled to St. Jude Children’s Research Hospital on the first leg of a journey that would demand courage and determination, faith and more than one miracle.

At left: April and Efreem have hearts full of gratitude and hands full of babies, aptly named Miracle and Faith.

Below: Son Marlon visits April just after her stem cell transplant.

One Patient Three Lives

By Elizabeth Jane Walker

When this St. Jude patient experienced a relapse of her cancer, three lives were at stake.

Karen Pulfer Focht



Family matters

April and Deloris were nervous about leaving their home. For more than a decade, April and her two sisters had lived with Deloris and her two daughters in a small apartment. Now the family would be separated for months.

“That was my first time being away from home and my other children,” Deloris says. “But when we went to St. Jude, it was like they rolled out the red carpet. They treated us like we were the queen of England. It was like I was the President’s wife or something! I never dreamed it would be like that.”

At St. Jude, April discovered that she had acute lymphoblastic leukemia (ALL). The disease was in complete remission after 120 weeks of treatment. For the next few years, April regularly returned to Memphis for checkups. In the meantime, she had a son, whom she named Marlon.

April found out she was pregnant again in 2001. But an early sonogram indicated that her pregnancy was anything but routine.

“The doctor started dancing around the room and singing a song,” April recalls. “I said, ‘What are you singing for?’ He said, ‘Because I see two babies!’” April and her fiancé, Efram Coleman, were elated. “He’d been telling me I was going to have twins because he had them in his family,” April says.

But the couple’s joy soon turned to concern, as April began suffering from unexplained gastric problems, chest pains and dehydration. After many trips to the local doctor, they learned the cause: April’s leukemia had returned with a vengeance.

Miracle and Faith

Local medical professionals advised April to abort the babies so that she could obtain appropriate treatment. But Efram and April would not consider that option. “I told the doctor, ‘If God blessed me with these twins, he must want me to have them,’ April says. Again the family turned to St. Jude for help.



LARINA HAJAR

To survive relapsed T-cell leukemia, April endured aggressive chemotherapy followed by a stem cell transplant. Afterward, she suffered a range of potentially deadly side effects. Today, April is rebuilding her life with the help of Efram and the inspiration of her children.

April’s case posed a challenge to her longtime St. Jude physician, Ching-Hon Pui, MD. Not only was April pregnant, but she had T-cell ALL, a type of leukemia with a dismal prognosis.

“In general, patients with relapsed

T-cell leukemia only have a 10 percent cure rate,” Pui observes. “The goal, obviously, was to save the twins and the mother.”

In order to survive relapsed T-cell leukemia, April would need to undergo

**This hasn’t been an easy time for me,
And as one who cares about me,
There have been so many moments when I’ve wished
I could have
somehow been spared some of the pain or at least
cushioned the blows.**

**But it seems that I have my own roads to travel in life.
For a while I’m on a smooth, well-worn path,
Then suddenly the road swarms.**

**But you know what?
I’ve watched myself with admiration
As I’ve faced difficulty with strength and courage.**

**And even in those times when I wanted to give up,
Somehow I found it in myself to carry on,
And I just know I’ll continue to do so.**

**I’m a remarkable person,
And even though this is a road to travel,
I’ll be sure to look along the side from time to time.
The person I see there will be cheering me on.**

—Poem by April Johnson

aggressive chemotherapy so that she could obtain a second remission followed by a stem cell transplant. Pui knew that the situation was precarious. “I could not give her the routine induction therapy for relapse of leukemia, because it would carry a high risk of losing the twins,” Pui says, “and I had to use drugs that would not affect fetal development.”

As the babies grew within her, April could not help but worry. Would her twins survive? If she waited to begin aggressive treatment, would she be able to defeat the disease? Every day that she waited, the leukemic cells were multiplying—reducing her survival odds even further.

Wren Kennedy, MSN, a pediatric nurse practitioner in St. Jude Hematology-Oncology, says April’s priority was clear. “She never lost sight of the fact that she wanted to try to give those babies life even at the expense of her own,” Kennedy says. “Even though we were staying away from all the drugs that are known to cause birth defects, the treatment was making her fairly ill. She was having low white blood counts and getting infections and ending up in the hospital on broad-spectrum antibiotics.”

In her 29th week of pregnancy, April returned home so that her obstetrician could deliver the twins. Although they weighed just a little more than 2 pounds each, the babies were healthy and beautiful. April and Efram named their tiny daughters Miracle and Faith.

Overcoming challenges

After the babies’ birth, April returned to St. Jude, where she underwent an intensive chemotherapy regimen that finally induced a solid remission. Then she needed a stem cell transplant.

St. Jude doctors found that April’s older sister, Myesha, was a perfect match. The transplant occurred in September of 2002. “I’m not used to needles, and it was really an experience to go through,” admits Myesha, “but I was glad to do it because that was my baby sister.”

About a month afterward, April’s condition started to deteriorate. Already damaged from the chemotherapy, her

As the babies grew within her, April could not help but worry. Would her twins survive? If she waited to begin aggressive treatment, would she be able to defeat the disease? Every day that she waited, the leukemic cells were multiplying—reducing her survival odds even further.

lungs quit functioning properly. She ended up in the Intensive Care Unit on a ventilator. “They thought I was going to die,” says April.

“All of us made a trip to St. Jude because they told us that she could go at any time,” Deloris remembers. “But God told me, ‘Not yet.’ The next day she got better, and they took her off the respirator.”

Then April developed graft-versus-host disease (GVHD). This potentially fatal complication of stem cell transplantation occurred when the new immune system (Myesha’s cells) recognized April’s cells as foreign and began destroying them. As her body attacked itself, April experienced excruciating pain, diarrhea and weight loss, which necessitated a feeding tube. She also underwent operations for related complications.

To control the disease, April received a new treatment that shows promise for patients with chronic GVHD. Extracorporeal photopheresis is much like a blood transfusion. A machine removes blood from the patient’s body. T-cells from the blood are combined with a drug, and the mixture is exposed to ultraviolet light, which activates the drug. The treated blood is then reinfused into the patient.

“Photopheresis worked well for April, and it allowed us to reduce other drugs, like steroids, which cause a lot of side effects,” says Rupert Handgretinger, MD, PhD, director of Stem Cell Transplantation at St. Jude.

Handgretinger says that April is slowly recovering from GVHD, and he antici-

pates a bright future for April and her family. Her leukemia is in remission, and Handgretinger says a relapse is unlikely. “Normally, these leukemias relapse early if they’re going to do so,” he says. “So her chance to be cured now is extremely high.”

Doubly blessed

Looking back on her ordeal, April credits Efram with helping her survive the stresses of relapse, transplant and treatment-induced separations from her children. Efram quit his job so that he could be in Memphis during the transplant and its aftermath.

“He won’t let me do laundry or sweeping or mopping or washing dishes,” said April, during their yearlong stint at Target House. Other family members pulled together at home, taking care of Marlon, Miracle and Faith when the children could not be with their parents.

Today, April and Efram have returned to their hometown, where Efram has been rehired by his former employer. As April’s health slowly improves, Efram continues to demonstrate his expertise at changing diapers and chasing children.

“He’s a very good dad,” observes Deloris, who says that God has helped the family endure their trials. “You just can’t give up,” she says. “You don’t give up. You just keep going. And you keep praying.”

“I’ve been through a whole lot,” says April, quietly. “And I thank God every night for being here and for letting me have my three kids.”●

A Peek under the Hood at MOLECULAR MOTORS

BY MARC KUSINITZ AND
ELIZABETH JANE WALKER

Motors propel cars along highways and tractors on farms; they run air conditioners in office buildings, refrigerators at home and conveyor belts in factories. Motors are everywhere, even inside the cells of your body.

Structural biologists at St. Jude Children's Research Hospital are studying two types of biological motors critical to a cell's ability to divide and produce healthy daughter cells. Those motors are called helicases and kinesins. Helicases help a cell make copies of all its chromosomes so that each daughter cell gets a full set. Kinesins transport each of those chromosomes into the daughter cells.

Understanding the structure of these tiny protein motors may help scientists eventually bring the growth of cancer cells to a screeching halt.

Helicases to the rescue

The DNA molecule that makes up a chromosome is like a rubber ladder that is twisted into a coil, called a double helix. The cell contains two copies of each chromosome, one from the mother and one from the father.

In cells preparing for division, every chromosome from both the mother and father must be copied, or replicated, so

that each of the two daughter cells has a complete set of chromosomes. This requires the cell to uncoil each chromosome, split the "ladder" apart and rebuild the halves. The result is two copies of each chromosome.

One type of helicase enzyme unwinds the double-stranded DNA molecule. If this process jams and stalls, the cell activates "rescue" helicases to cut through the gridlock and allow the DNA to continue the replication process.

Stephen White, DPhil, Structural Biology chair, is studying how these rescue helicases work by using an enzyme called T4 helicase, which is found in the *Escherichia coli* (or *E. coli*) bacterium.

"As structural biologists, we like to look at simple things," White explains. "If you're trying to look at a giant, human complex to understand how it works, it's very difficult. But if you can find an equivalent complex in a bacterium or a virus that does essentially the same thing, it's much easier to look at. So we're looking at this in T4, a virus that invades *E. coli*. T4 has a helicase that acts like human helicases but in a much, much simpler system."

Using a technique called X-ray crystallography, White has created a model of the enzyme, which gives an intimate look at the graceful loops and

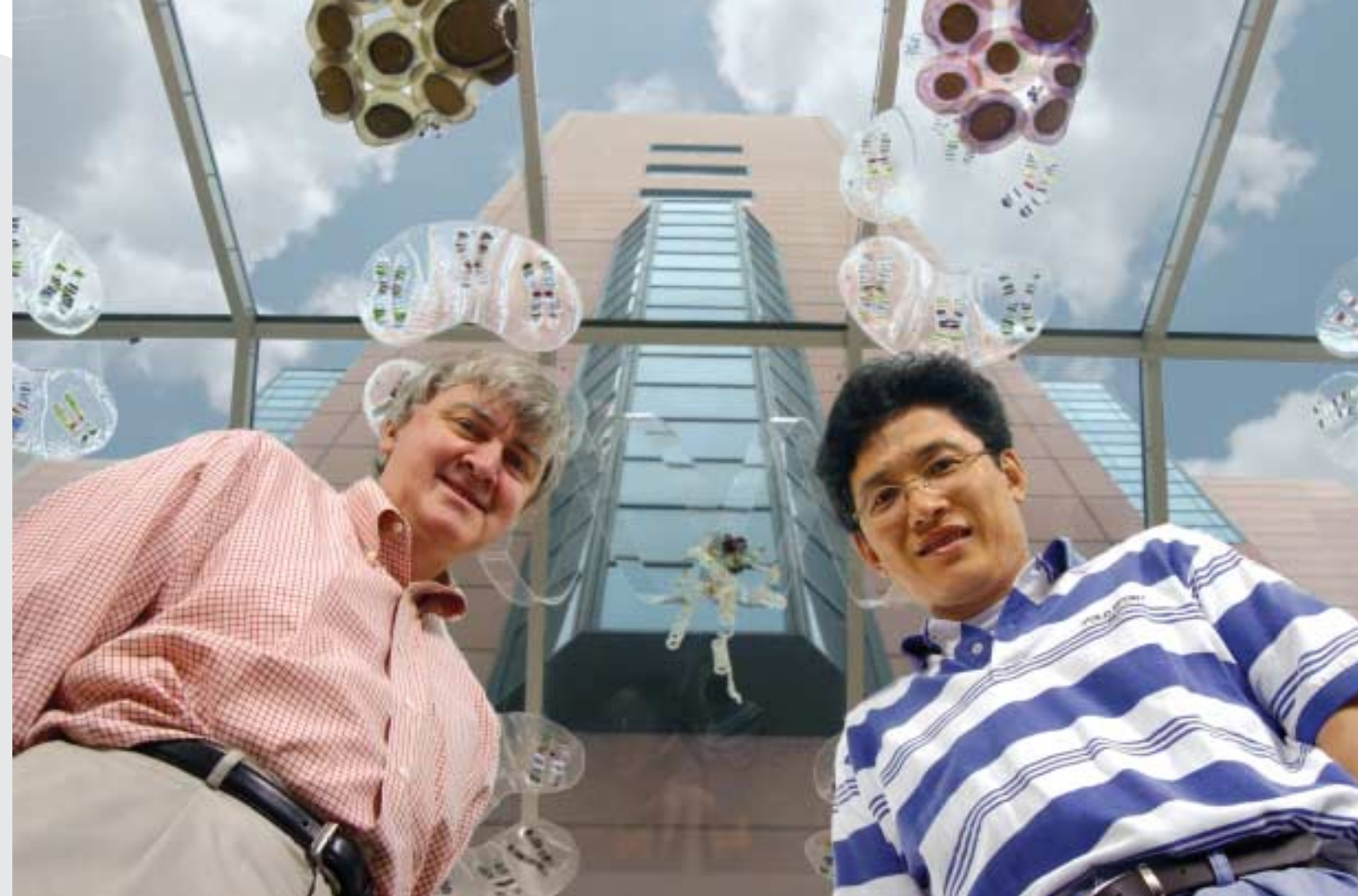
turns that make up T4's structure. Such images are helping White understand how these rescue helicases work. These enzymes are important because if they are defective, the cell might die or become a cancer cell.

Movin' down the highway

Just before the parent cell divides, other motors, called kinesins, move chromosomes into place so that each daughter cell has a complete set of the same chromosomes the parent cell had. The kinesins transport the chromosomes along microscopic highways called microtubules.

Two sets of microtubules lead, like east and west routes of a highway, to opposite sides of the cell. Kinesin II motors carry chromosomes from each set along one of those microtubule highways. When the cell divides down the center, each daughter cell then has a complete set of chromosomes.

Hee-Won Park, PhD, of Structural Biology created an image of a kinesin motor called Ncd from the fruit fly *Drosophila*. "We picked the kinesin protein from *Drosophila* because we believe that it's similar to the human version," Park says. "This is important because cancer cells divide like crazy, and in cancer cells these kinesin proteins are used for DNA division."



ANN-MARGARET HEDGES

St. Jude structural biologists such as department Chair Stephen White, DPhil, and Hee-Won Park, PhD, are studying molecular "motors" called helicases and kinesins. "If mutations in DNA are not fixed properly, they produce mutated proteins," White says. "If the protein doesn't do its job right, you end up with cancer." Usually, cells can repair mutations. But if something is wrong with the "motor" that does the overhaul, then the DNA doesn't get repaired properly. Scientists hope to treat certain diseases by shutting down such defective motors.

Using the fruit fly model, Park developed a working theory of how this protein "walks" along the microtubule, carrying the chromosome with it. One end of each microtubule strand is called the positive or "plus" end to distinguish it from the other, negative or "minus" end. Scientists have long assumed that kinesin proteins travel toward the "plus" end of a microtubule. But Park discovered that Ncd steadily moves toward the more stable "minus" end by grasping the microtubule and letting go, grasping and letting go in what he calls a "lever-arm model."

"Somehow the different types of kinesins know which end they're supposed to move to," Park says. "We are

interested in learning how they know which end they're supposed to travel to when they bind to the microtubule."

Learning about the Ncd motor is only one part of a mind-boggling picture. "There are about 124 different kinds of kinesins in the cell," Park says. "This is only one of those." Although the discovery process is arduous, it is also exciting. "It takes a couple of years to crystallize each protein," he says, "but it's a glorious thing to work on."

Malfunctions, misfolds and mutations

When proteins malfunction, misfold or mutate, the outcome can be catastrophic. "DNA repair is the root cause

of most cancers," observes White. "If mutations in the DNA are not fixed properly, they produce mutated proteins. If the protein doesn't do its job right, you end up with cancer."

Our DNA is bombarded constantly, so the cell's DNA-repair mechanisms must work overtime to compensate. Usually, the cell can repair mutations. But if something is wrong with the actual apparatus—the motor—that does the overhaul, then the DNA doesn't get repaired properly. Scientists hope to shut down such defective motors to treat certain diseases. And like the microscopic motors themselves, St. Jude researchers are working constantly, moving inexorably toward their destination. •

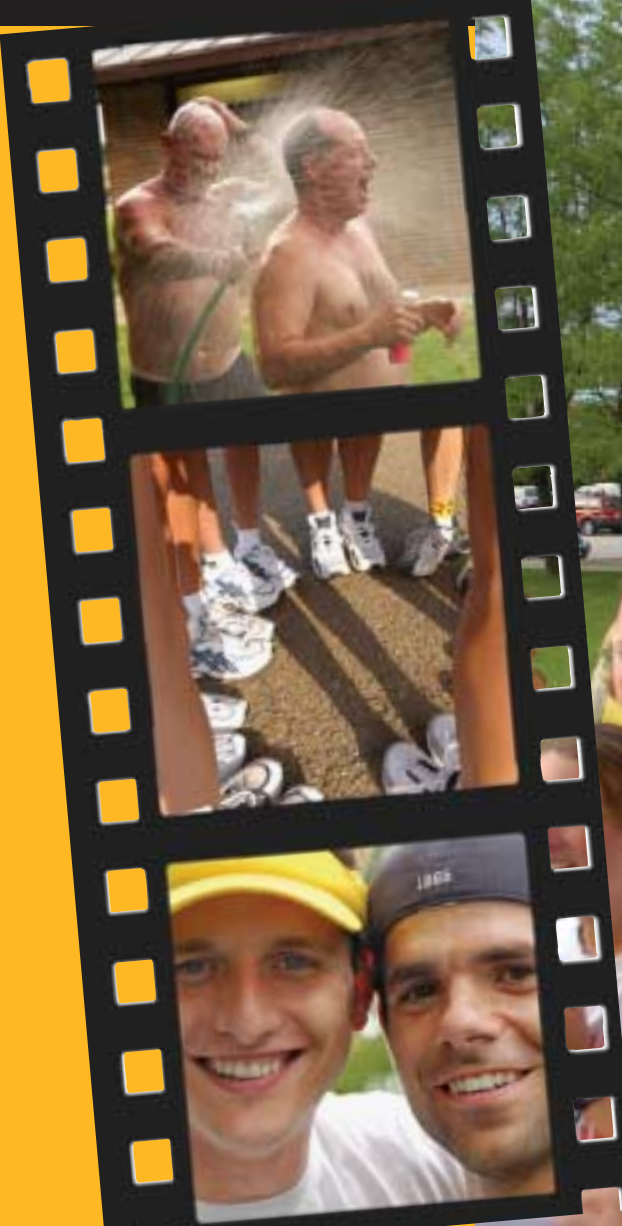
On the Road to **PEORIA**



Text and photos by Laura Hajar

What inspires 150 people to run, relay-style, 465 miles from Memphis, Tennessee, to Peoria, Illinois? What prompts them to spend three sleepless nights in cramped—and often smelly—RVs? What possesses them to set out in the blazing summer heat, with nothing in sight but corn fields and the occasional downhill slope? These are only a few of the questions one might

have asked runners participating in the 22nd St. Jude Memphis to Peoria Run last summer.



The horde of runners in last year's Memphis to Peoria Run included 14 St. Jude employees who joined the trek. Runners were organized into two teams, which "leap frogged" through Tennessee, Kentucky and Southern Illinois.

It does not take long for first-time participants to discover why so many people take part in this event. Answers come in conversations at dinner and while running in the cool dawn air. An answer comes from an elderly woman, waiting at the end of her driveway in the middle of the night, who hands a check to a group of people running through her neighborhood.

But perhaps the most compelling answer is emblazoned on a T-shirt worn by a runner and former St. Jude patient: a picture of herself after treatment with the words "St. Jude Survivor" stamped below.



Upon arriving in Peoria, the Memphis runners join individuals who have done auxiliary runs from such cities as Chicago, Springfield, Champaign/Urbana, and St. Louis. Together, they run into the Peoria Civic Center where a telethon for St. Jude is underway. The 2003 St. Jude Memphis to Peoria Run raised \$1,221,571 for research and treatment. The 23rd annual St. Jude Memphis to Peoria Run will begin August 4, 2004, at the front door of the hospital and conclude August 7. To make a pledge or donation, call toll-free (800) 713-8223 or visit www.stjuderuns.org and click on the "Donate" button.



Parkinson's *Progress*

By Tanuja Coletta

Everyone knows that Parkinson's disease affects adults.

*But by studying this disease,
St. Jude scientists may help children, as well.*



ANN-MARGARET HEDGES

Richard Smeyne, PhD, gets the same reaction every time he gives a tour of his laboratory. Visitors cock their heads, furl their brows and ask the obvious question: “Why would the world’s premier center for the research and treatment of childhood illnesses be studying Parkinson’s disease?”

Smeyne draws his answer from the U.S. space program — the “Tang effect” (yes, the orange powder drink mix).

“We spent millions of dollars to go to the moon, and the things that came out of it for the general public include Tang, ear thermometers and smoke detectors,” he explains. “In that same vein, while our mission is to treat children, our research goals are to study basic developmental mechanisms that aren’t necessarily limited to childhood cancer. So while we hope to find the underlying basis of Parkinson’s disease, this research may also have applications for the children we treat.”

Smeyne and his colleagues in St. Jude Developmental Neurobiology are searching for the exact location of genes that could be used to screen people at risk for Parkinson’s disease. St. Jude is home to one of a handful of programs in the world taking a serious look at the benefits exer-

cise could have on curbing the disease’s symptoms and progression. The findings could offer clues to a variety of neurodegenerative diseases, as well as pediatric and adult brain tumors.

Escaping the trap

Parkinson’s disease can turn even the simple act of waving a hand into a battle between the brain and the nerves. The progressive disease afflicts 1 million Americans and 2 percent of all people older than 55, making it the third most common neurological disease after Alzheimer’s and a form of dementia. Many people recognize Parkinson’s characteristic symptoms — tremors and the loss of balance and coordination — from seeing celebrities like Michael J. Fox, Pope John Paul II, Janet Reno and Muhammad Ali cope with the disease.

Although it exacts a hefty physical toll on its victims, Parkinson’s disease rarely affects the intellect.

“This is a disease where in most cases, your mental faculties don’t deteriorate, but you physically become immobile,” Smeyne says. “In the end stages, it’s like being trapped in your own body.”

The trap is set when nerve cells, or neurons, in a portion of the brain called the *substantia nigra* are damaged or destroyed. As a result, the cells can no longer release dopamine, a chemical that helps keep muscle movement smooth and controlled. The symptoms of Parkinson’s disease appear when most neurons in the *substantia nigra* die.

“Until 70 percent of these cells are dead, you don’t get one symptom,” Smeyne says. “But the bad part is that once you get the disease, those neurons cannot be rescued. You can’t turn them back on or get them to work better. They’re gone for good.”

Smeyne is trying to figure out why this happens and, specifically, how to predict who will succumb to the disease. While the cause of Parkinson’s disease is largely unknown, Smeyne thinks it is most likely due to a genetic susceptibility to environmental agents such as certain pesticides and other toxins. The current gold standard in treatment is the drug levodopa, or L-dopa, which neurons can convert into dopamine to replenish the brain’s dwindling supply. Although the drug is remarkable at stopping Parkinson’s symptoms, it isn’t a permanent cure.

“It wears off,” Smeyne says. “Eventually it doesn’t work anymore, and the cells even regulate against it. Also, some people think — and we’re among them — that giving L-dopa actually causes the disease to progress faster.”

Gaining a better understanding of how the brain cells work could lead to earlier detection and more effective treatment.

A new approach

Because Parkinson’s symptoms appear late — sometimes several years after onset — and are often coupled with other illnesses of aging, understanding the disease’s basic cell biology was limited until an accidental discovery 22 years ago. That’s when a group of California drug users botched an attempt to make synthetic heroin and instead produced a neurotoxin known as MPTP. The next day, the addicts were catatonic with severe parkinsonian symptoms. All of the patients improved immediately with L-dopa.

Since then, MPTP has opened the doors for researchers to create lab models to study Parkinson’s disease. While the chemical is devastating to humans, it does not kill enough neurons in laboratory mice for them to develop the debilitating symptoms of the disease. Observing that some strains of mice were naturally resistant to MPTP’s effects, Smeyne and his colleagues compared genetic differences and identified the exact chromosomal location of the genes involved in Parkinson’s disease.

“We took a neurogenetic approach to the disease that no one was really doing at the time on an experimental level,” Smeyne says.

Now his lab is homing in on the genes that can lead individuals to develop Parkinson’s disease.

“We’ve actually shown in our lab that the nerve cells die only after they interact with another type of cell in the brain called a glial cell,” Smeyne says. Glial cells make up the brain’s support tissue and do not conduct electrical impulses as do neurons. While popular belief holds that glial cells are the glue that holds neurons together, Smeyne takes another view.

“We believe that glia do not only support neurons, but play a much more critical role in brain function,” he says. “I believe that Parkinson’s disease will ultimately be found to be a disease of glial cells that affect neurons through their interactions.”

Smeyne’s lab is now testing ways to interfere with the process and keep cell death under 70 percent. “If we do that, we will stop the symptoms from ever arising, which is an effective cure in itself,” Smeyne says.

He was surprised to learn that exercise might be the key.

Deluxe mouse pad

Besides L-dopa and other drugs, current Parkinson treatments range from stem cell transplantation to deep brain stimulation, where a pacemaker conducts impulses to electrodes surgically inserted in the brain.

“Right now, there’s a huge emphasis in biotech and pharmaceutical companies

on using compounds called neurotrophins, or growth factors, as therapies because it’s been shown that those chemicals protect the neurons that die in Parkinson’s disease,” Smeyne says. “The problem is with the delivery of these compounds into the brain; there is very little control. So my lab is looking for ways to stop the process without using these drugs.”

A lab member suggested they test mice exposed to MPTP by using the centuries-old “enriched environment” concept — which relies on social, mental and physical stimulation to increase brain function. Research had shown that ani-

protected in both experiments, Smeyne’s lab deduced that something external was protecting the neurons.

They found that mice raised in the deluxe cages had increased neurotrophin levels. “So when neurons get injured by the toxin, the extra neurotrophins are there to support them through the toxic insult and recover,” Smeyne says.

Next the researchers broke the enriched environments down to cages that either contained mazes, open space or exercise wheels. “It was the aerobic exercise that was working. Just running on those wheels was enough to offer protec-

While we hope to find the underlying basis of Parkinson’s disease, this research may also have applications for the children we treat.

mals raised in this environment had stronger neurons with more dendrites and synapses, which help neurons send signals to other cells. But Smeyne was skeptical about how the process would affect toxins.

The researchers moved groups of 14 MPTP-exposed mice from normal cages, which usually house about five mice with food, water and little else, into spacious cages filled with toys, mazes and exercise wheels — what Smeyne calls the Trump Plaza of mouse housing.

The results were amazing.

“Three months later, there was zero cell loss,” he says. “They were 100 percent protected in this enriched environment. We couldn’t believe it.”

Wanting to see if the reaction was specific to Parkinson’s disease, the researchers ran the experiment in lab models of pediatric seizures. Again, the neurons were completely protected.

Because the way cells die in Parkinson’s disease and pediatric seizures is different and because neurons were

tion.” The outcome was equally good for adult mice, proving that “it’s never too late” to start exercising to be protected. Now, Smeyne is studying how much exercise is needed and how long the neuron protection lasts.

St. Jude researchers think the findings may be useful for children who undergo cancer therapy. Studies have shown that about four years after receiving full cranial radiation, some children experience a decrease in their IQ levels. The cause is unknown, but neuron loss could be one reason, says Smeyne.

Putting the “Tang effect” into practice, St. Jude scientists are discussing a research project to see if exercise can help reduce nerve cell death in these children. “This research that came out of Parkinson’s disease may work well with handling some of the secondary effects that we see from chemotherapy and radiation,” Smeyne says. “This is the kind of thing that can only happen at St. Jude, where our research can be translated to the clinic almost seamlessly.”●



Richard Smeyne, PhD, of St. Jude Developmental Neurobiology is searching for the exact location of genes that could be used to screen people at risk for Parkinson’s disease. St. Jude is one of a handful of programs in the world studying the benefits exercise could have on curbing the disease’s symptoms and progression. The findings could offer clues to a variety of neurodegenerative diseases, as well as pediatric and adult brain tumors.

Perspective

A Call to Action

By Amber Valletta

When I was a kid attending Catholic schools in Tulsa, Oklahoma, I participated in Math-A-Thons® for St. Jude Children's Research Hospital. With my classmates, I watched videos of Danny Thomas and his family talking about the hospital and its patients. I remember thinking, "Those kids are my age," and I felt so bad for them.

But it wasn't until I was an adult working in New York that a little girl made St. Jude real to me—by issuing a request that I couldn't ignore. Haley Hubbard didn't know me, but we were from the same hometown. She had seen newspaper articles about my involvement with charity events in Tulsa. Convinced

that I cared about children, she told the people at St. Jude, "This woman will help us. Call her!"

So a St. Jude doctor called and talked to me. I was touched to hear about the hospital again and to learn about the children and their families.

I was crying by the end of the conversation, saying, "I'll do anything! What do you want me to do?"

Thank God for Haley and for the faith that she had! Haley

and I met for the first time at the hospital, where I held her hand while she underwent a medical procedure. Since then, I have watched her grow, seen her prom pictures and served as a sort of long-distance big sister.

Now she's graduating from high school and going to college.

I help St. Jude because it gives kids like Haley a chance to grow up. Children have the right to live and to experience life to its fullest. That's why people do the hard and diligent work they do for St. Jude—so that they can see these children smile and someday have normal lives.

The research and development at

St. Jude is by far the best in the world. And they share their information with everyone. I think it is extraordinary in our day and age that St. Jude is willing to share information and not hoard it for its own financial advantage. The hospital goes into countries that can't afford the medicine or the technology and helps them cure cancers and catastrophic diseases.

I have a little boy. That's definitely a reason for me to help. God forbid that it should happen, but if I ever had a sick child, I'd know exactly where to go.

The doctors and nurses, the researchers, the Thomas family, the fund-raisers at ALSAC—they're all healers who are saving lives and making changes in the world.

It's up to you and me to help them.●

Actress and supermodel Amber Valletta is a member of the hospital's Professional Advisory Board. She has been heavily involved in such St. Jude fund-raising events as Runway for Life, the L.A. Gala and the Monaco Gala. Valletta is the celebrity spokesperson for The Night for the Children Gala, which will be held July 23 at the Monte Carlo Sporting Club, Monaco. (See www.nightforthechildren.com for more information.)

"It wasn't until I was an adult working in New York that a little girl made St. Jude real to me—by issuing a request that I couldn't ignore."



St. Jude patient Haley Hubbard didn't know supermodel Amber Valletta, but she had heard about Valletta, since they were from the same hometown. The girl just knew that Valletta would embrace the St. Jude mission, once she heard about it. Sure enough, when Valletta learned about St. Jude, she threw her influence and energy into helping the kids of St. Jude.



Got smiles?

Crystal Smith, RN, assists patient Krista Kellon with her milk mustache for the "Got Milk?/Shake Stuff Up" photo contest. The contest was part of the hospital's celebration of National Nutrition Month. The theme was milk and dairy. Patient Courtney Hayworth was selected as the photo contest winner for Memphis. One local "Shake Stuff Up" winner is selected in each city and one grand-prize winner will win an ad in Rolling Stone magazine for the milk campaign.