

A Life Line for Liam

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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 Thomas made during the depression era to St. Jude Thaddeus, the patron saint of the hopeless.

"Show me my way in life," Thomas prayed. In return, Thomas promised to build St. Jude Thaddeus a shrine. That shrine became a world-class research institution that treats children regardless of race, religion or the family's 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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St. Jude Children's Research Hospital's mission is to advance cures, and means of prevention, for pediatric catastrophic diseases through research and treatment. Consistent with the vision of our founder, Danny Thomas, no child is denied treatment based on race, religion or a family's ability to pay.

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Promise

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On the cover: St. Jude patient Liam Reinier. Story on page 18; photo by Ann-Margaret Hedges.

GIANTS

GENTLE

America's
best-loved
retailers pull out
all the stops to
connect
customers and
employees
with the
incredible
work of
St. Jude.



PHOTOS BY BIOMEDICAL COMMUNICATIONS

Amid the happy hubbub of holiday shopping, pay special attention to the opportunities to support St. Jude as the third annual *Thanks and Giving* campaign rolls out across America in stores like CVS/pharmacy, Domino's Pizza, Kay Jewelers, Target and Williams-Sonoma Inc.

Created by Marlo Thomas, St. Jude national outreach director and daughter of founder Danny Thomas, along with her sister

and brother, board members Terre and Tony Thomas, the *Thanks and Giving* campaign is an unprecedented coming together of celebrities, media, retail and corporate partners. This unique national program asks consumers to give thanks for the healthy kids in their lives and give to those who are not.

Timed as it is with the holiday season, the program resonates with retailers and shoppers alike. One of the most popular

ways to participate in the *Thanks and Giving* campaign is to add a donation to St. Jude at checkout.

“Our corporate partners came up with the great idea of the add-on at retail, which is a very uncomplicated way for a consumer to contribute. And it gives a peek into the hearts of the American people, whose generosity is very inspiring to me,” Thomas says. “At CVS, for example, where the average purchase is \$10, 1.8 million customers added a dollar for *Thanks and Giving*. Even though they’re making a small purchase, they’re willing to add a dollar to their bill to give to the children of St. Jude. It shows how the American public has embraced this campaign and the work of St. Jude. It’s very moving.”

Domino’s Pizza is one partner that participates in the add-on program for *Thanks and Giving*. The company has been with the program since its inaugural year.

“St. Jude has done an outstanding job of building excitement around the campaign and building awareness for all the corporate partners,” says David A. Brandon, chairman and CEO of Domino’s Pizza, who is excited to be back for the company’s third year. Last year, Domino’s raised \$1.2 million during *Thanks and Giving* and helped raise awareness for St. Jude by printing the campaign logo on millions of pizza boxes.

Merchandise offerings abound this year as well, ranging from the classic wrap dress by Diane von Furstenberg—who will donate \$1 to St. Jude for each dress manufactured—to the huggable plush puppy “Graham” from Kay Jewelers. Graham is eighth in a series of limited-edition collectibles offered to Kay Jewelers’ customers. The puppy’s ear tag and gift bag feature artwork created by St. Jude patients.

“Our participation in the *Thanks and Giving* campaign gives us an opportunity to help generate awareness and funds to help the kids at St. Jude,” says Terry Burman, executive chairman of Sterling Jewelers Inc., another partner in the program since its inception. “Year after year we see the remarkable life-saving work performed at St. Jude, and we are very proud of our partnership.”

Target Stores will offer stuffed elephant gift card holders, which will be featured prominently at the register. Cute and cuddly with huge, floppy ears decorated with snowflakes drawn by a St. Jude patient, these precious pachyderms will make great stocking stuffers. For every plush elephant sold at \$2.99, a minimum of \$1.50 will go to St. Jude (representing 100 percent of net profits).



“The American public has embraced the *Thanks and Giving* campaign and the work of St. Jude. It’s very moving,” says Marlo Thomas, the hospital’s national outreach director.

Opposite page: This cuddly elephant gift card holder from Target is an example of how retailers and corporate partners across the nation are finding creative and fun ways to raise money for St. Jude.

Twenty companies joined St. Jude in 2004 for the inaugural year of *Thanks and Giving*, but with this year’s campaign, the number of corporate partners has ballooned to 42. New partners for 2006 include Saks Fifth Avenue, GNC, Coffee Beanery, Dollar General, Club Libby Lu, AutoZone, Sag Harbor and Gymboree.

“Our partners’ *Thanks and Giving* revenue increased significantly last year—several more than doubled their first year revenue—and our online donations increased by 150 percent from year one to year two,” Thomas says. “Results like these create great excitement and momentum as we head into year three.”

Thomas attributes the program’s expanding success to the unique bond that is forged

with each corporate partner. “We listen closely to our partners and actively seek their ideas. They’re experts about what works with retail, and we are blessed to be partnered with some of the most successful and innovative companies in the world.”

Williams-Sonoma Inc. joined *Thanks and Giving* in 2005 and saw immediate results. “The response far exceeded our expectations,” said Pat Connolly, its executive vice president and chief marketing officer. The company raised nearly \$1 million in its first year through add-on donations and employee giving.

Indeed, retail employees are crucial in bringing *Thanks and Giving* to the customers’ attention. Brandon says the inspiring public service announcements really helped keep his Domino’s team members motivated to raise money throughout the entire campaign.

Several partners relate stories of customers who want to share with associates how their own lives have been touched by St. Jude. It’s a story that Thomas has heard again and again—and one that never fails to motivate her.

“I am invited to many of our partners’ national meetings and employee events, and I go to let them know how much their role in *Thanks and Giving* means to me and my family,” Thomas says. “And it’s amazing; I am always approached by people who tell me how they, or a family they know well, have been helped by St. Jude. They speak of a cousin or a neighbor or a friend at work—people who have been directly affected by St. Jude and the work St. Jude does.”

“That’s very inspiring to me—to know how far our reach truly extends, and to hear, again and again, how St. Jude is the place families have been able to turn to when there seem to be no help or answers anywhere else.”●

Highlights

PETER BARTA



In 1968, Rudolph Jackson, MD (at left), was hired to work at St. Jude. In addition to studying and treating childhood leukemia, he worked alongside Lemuel Diggs, MD, and Alfred Kraus, MD, to establish the hospital's sickle cell program. Jackson's distinguished career also included stints at the National Institutes of Health and Morehouse School of Medicine. After more than 30 years, Jackson, now retired, recently visited St. Jude, where he discussed the hospital's current sickle cell disease program with Russell Ware, MD, PhD, Hematology chair.

Third Pew Scholar

Joseph Opferman, PhD, of Biochemistry has been named a Pew Scholar in the Biomedical Sciences. Identified by the Pew Scholars Program as one of 15 of the country's most gifted biomedical scientists, Opferman will receive \$240,000 during the next four years to support his research, which focuses on processes that control lymphocyte development.

Pew Scholars are junior faculty members at medical schools and research institutions who show outstanding promise in the basic and clinical sciences. Previous scholars have gone on to win the Nobel Prize, the MacArthur Award and the Albert Lasker Medical Research Award.

Brenda Schulman, PhD, of Structural Biology and Genetics and Tumor Cell Biology, and Michael Dyer, PhD, of

Developmental Neurobiology were named as Pew Scholars in 2002 and 2004, respectively.

A dose a week

Children with cancer who develop anemia during chemotherapy can benefit from a weekly dose of erythropoietin (EPO), according to St. Jude researchers. The drug reduces the need for red blood cell transfusions and improves the quality of life in children whose anemia is corrected by this treatment.

Anemia is a condition caused by an abnormally low level of hemoglobin (Hb), the oxygen-carrying protein in red blood cells; EPO is a natural hormone that stimulates production of Hb-containing red blood cells.

This is the first large-scale study of anemic children with cancer that ran-

domly assigned patients to receive either EPO or a placebo (inactive "drug") intravenously; it was also the first to measure EPO's effect on quality of life in children. Bassem Razzouk, MD, of Oncology was lead author of a report on this study that appears in *Journal of Clinical Oncology*, August 2006.

H5N1 vaccine update

St. Jude scientists have announced that a vaccine they developed a few years ago against one antigenic variant of the avian influenza virus H5N1 may protect humans against future variants of the virus. Vaccines based on this model might therefore be suitable for stockpiling for use during a pandemic (worldwide epidemic) until a new vaccine could be developed against the variant causing the outbreak. An antigen is an inactivated whole-virus vaccine produced by reverse genetics that stimulates production of antibodies by the immune system.

Elena Govorkova, PhD, of Infectious Diseases was lead author of a report on the study, which appears in the July 2006 issue of *Journal of Infectious Diseases*. Robert Webster, PhD, of Infectious Diseases and holder of the Rose Marie Thomas Chair at St. Jude, was the report's senior author.

Chili's cares

On June 22, St. Jude announced that Chili's Grill and Bar will donate \$50 million to the hospital during a 10-year period—making it the largest donation in the hospital's history. St. Jude has earmarked part of this donation for a state-of-the-art building that will house the Department of Radiological Sciences, The Pediatric Brain Tumor Consortium, inpatient activities areas and new research laboratories. The new Chili's Care Center is scheduled to open in the fall of 2007. ●

Leap of Faith

In uncertain times, one family gave to St. Jude anyway—and was richly rewarded.

BY BETSY TAYLOR

Tim and Betsy Katen's lives are a testament to faith—in each other, in hard work and in God.

Indeed, their story hearkens back to that of Danny Thomas, a struggling entertainer with a devout belief who prayed to a patron saint for career advice with spectacular results. In gratitude, Thomas founded St. Jude Children's Research Hospital, a worldwide beacon of hope for children suffering from catastrophic diseases.

Tim could have settled easily into a successful career with an established business, but he chose instead, with the help of his wife, to blaze his own path.

"Tim has always had an entrepreneurial spirit," Betsy explains.

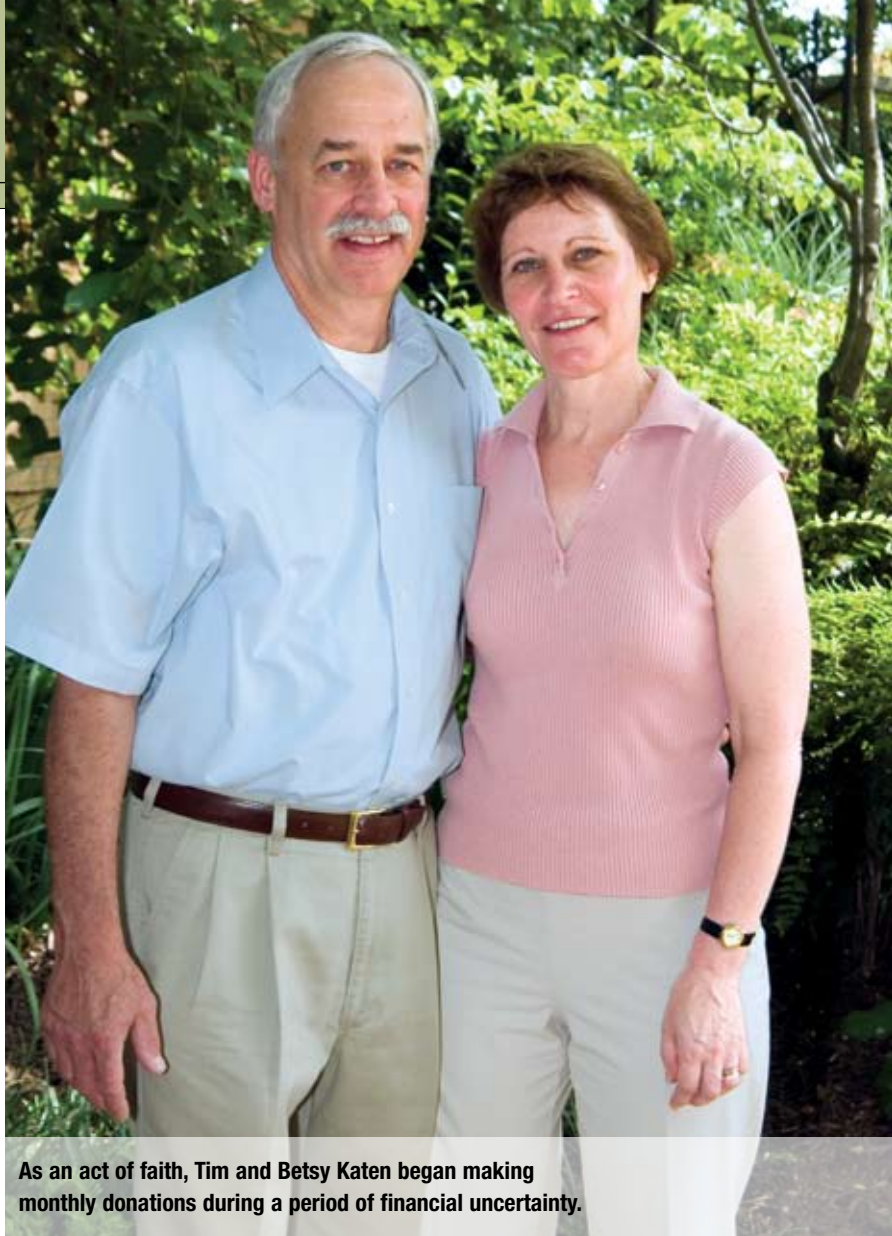
In 1978, Tim borrowed money to start a company from a rented Pennsylvania garage, designing and making molds for small plastic parts to go in computers and other products. Tim jokes that, to get his loan, the bank had to take "everything but my wife." (It's a good thing they didn't—she's an incredible ally.)

Then in 1982, the recession hit. The Katen family, shortly after the birth of their third child, worried about whether their business would survive.

Inspired by Thomas, Tim and Betsy prayed to St. Jude Thaddeus for guidance and help. As an act of faith, they began donating \$15 a month to the hospital.

"We first heard about St. Jude while watching a telethon," Betsy says. "We were touched by the stories of the children and the medical conditions that they were facing."

Circumstances may have made their livelihoods temporarily uncertain, but the



As an act of faith, Tim and Betsy Katen began making monthly donations during a period of financial uncertainty.

Katens were thankful for what they had. Their children were happy and healthy, and their hearts ached for the families at St. Jude.

So they gave...and never stopped giving.

During the next 10 to 15 years, their business prospered. Tim even opened a second company. The two flourishing firms now employ more than 130 people.

As the Katens' financial means have grown, they've substantially increased their cash contributions to the hospital.

Like Thomas, the Katen family believes that St. Jude Thaddeus answered their prayers.

"Many prayers were said to St. Jude, and our prayers were heard," Betsy says.

Tim and Betsy are proud to have instilled a philanthropic spirit in their

three children. Their oldest child, Philip, already donates to St. Jude.

Betsy explains that they're eager to help others "because we can." She adds, "What if it were me? I would want others to help."

A recent visit to the hospital further reinforced the Katens' dedication to giving.

Betsy remembers the smile of one boy on a tricycle, who proudly declared that he'd be going home soon.

"It made us feel good to be part of the family who helped this little boy," she says.

To learn more about making a gift to St. Jude or other planned giving opportunities, call ALSAC Gift Planning at (800) 395-1087 or e-mail giftplanning@stjude.org. ●

EYE STORM of the

Just when KJ Milligan thought he had weathered the storm of a lifetime, cancer swept back in with gale-force strength. Then Hurricane Katrina destroyed his home. But this teen courageously fought on, supported by a swirling group of family, friends, firefighters and his dedicated team at St. Jude.

BY ELIZABETH JANE WALKER

Sometimes cancer creeps in like a fog, slowly and stealthily; other times, it swoops in like a hurricane.

Kenny Milligan was unaware of gathering clouds on the day he took his son, KJ, to the doctor for an ear infection. But within hours, Kenny and his wife, Lori, knew that a Category 5 cancerous storm was buffeting KJ's body—a tempest that would put the family's faith and fortitude to the test.

Looking back, the diagnosis seems almost accidental. After all, how often does a doctor order a chest X-ray for a teen with an ear ache? And what are the odds of finding a softball-sized mass planted ominously in the middle of that image?

A physician in KJ's hometown wanted him to undergo an operation almost immediately. "No sir," Kenny responded. "We're going to check around before you cut him open." For advice, the family turned to Lori's uncle, who had lost a child to a rare tumor.

"What would you do if you were in my position?" Kenny asked.

"I'd do anything I could do to get to St. Jude Children's Research Hospital," he responded.

Without warning

When the Milligans arrived at St. Jude, they learned that KJ had an extremely rare kind of tumor called a mediastinal germ cell tumor. Less than 3 percent of all pediatric cancers fall into that classification. The disease develops when germ cells take a wrong turn during the embryonic and fetal stages of development. Instead of migrating to the gonads, where they normally settle, they move to other places, where they become malignant.

"Germ cell tumors can develop in sites like the brain or abdomen or chest," explains Carlos Rodriguez-Galindo, MD, of St. Jude Oncology. "This kind of cancer is usually fairly aggressive, but in KJ's


case, the cancer was even more aggressive than usual."

At St. Jude, KJ received four courses of chemotherapy and then underwent an operation to remove the tumor. But soon after the operation, tests showed a tiny bit of residual tumor. Before KJ could undergo a second operation, the cancer began to grow at an astounding pace. Within a week, it had spread to his lungs.

"That was a scary time for KJ and his family," observes St. Jude Hematology-Oncology Fellow Sarah Sherr, MD. "When we saw how quickly the tumor had grown in one week, we didn't know if we were going to be able to stop it."

Gently, Rodriguez-Galindo and Sherr explained the situation to the family. "They said he had nine new tumors," Kenny recalls. "I wasn't prepared for that news, and it was just about more than I could take."

When KJ saw his father's pain, he climbed off the examining table and tenderly placed his hand on Kenny's knee.



“It’s okay, Dad. We’ll get through it,” he said. Tears in his eyes, Kenny looked at his son and knew he spoke the truth. “I was supposed to be taking care of him,” Kenny says, “and he was looking after me.”

SETH DIXON

Lessons from Job

Doctors told KJ that they would need to attack the cancer from several directions. He would undergo brutal rounds of chemotherapy, followed by another operation and a stem cell transplant.

In August 2005, KJ and his family took a short break from chemotherapy treatments to return home to the Alabama Gulf Coast. During that visit, Kenny spent some time with the pastor of his church. The two discussed KJ’s illness and the fact that Kenny was unable to work as a firefighter during his son’s treatment. Kenny had recently studied the biblical character Job, who was tested by God by losing his health, his wealth and his home.

"Do you feel kind of Job-like?" the minister asked. "No, Job lost his house," Kenny replied. "I'll never lose my house."

A few days later, Hurricane Katrina gained strength and began moving in their direction. Even though KJ was not yet due back at St. Jude, Kenny packed up the family and their dogs and headed north. The Milligans were staying in a hotel near Memphis when the hurricane filled their home with six feet of water. The only items that escaped damage were a few pictures on the wall.

"Everything was gone," Kenny says. When he learned about the devastation, Kenny remembered the conversation with his pastor. "All I could do was sit there and laugh," Kenny recalls. "I gained strength through the story of Job. He went through so much, but he got back more than he had when he started."

Smiling through the storm

Back at St. Jude, KJ continued his chemotherapy treatments in preparation for surgery and a stem cell transplant. The next few months were brutal. When he wasn't sick, KJ spent his time playing a video game called Zelda, watching college football and joking with his dad, with whom he shares a close relationship

marked by frequent hugs, laughter and nearly constant jokes.

Throughout his treatment, KJ never lost his positive attitude. For instance, when he learned that one of his doctors hailed from Spain, KJ made an effort to learn a few words of Spanish.

"Even when he was very sick, he would always greet me with a smile when I opened the door," Rodriguez-Galindo recalls. "Sometimes he would be throwing up when I would come in. He would try to stop throwing up and say, 'Hola, Dr. Rodriguez!'" and then continue throwing up. And I could never leave without getting a hug from him."

Sherr was amazed at KJ's ability to be cheerful and optimistic even in the toughest situations. "I remember one time when he was waking up from surgery," she says. "There he was, with an incision in his chest. As he blinked his eyes open, I said, 'Hey, KJ, how are you?' and he said, 'Oh, I'm great!' What he went through was really tough, but he kept his spirits up all the time."

Mark Brown, a St. Jude chaplain, became particularly close to KJ and his family. Brown attributes KJ's optimism in part to his faith. "KJ is the kind of kid who really feels deeply for other people and can focus on that even when he's not feeling well," Brown explains. "He and

his dad have an amazing sense of trust that no matter what happens, KJ is safe and secure in an ultimate sense. When KJ was worried or afraid during treatment, he would say to me, 'I'm not in charge here. God is in charge, and that's going to be good enough for me.'"

Firefighters to the rescue

While Kenny stayed with KJ, Lori returned to their hometown and found a house to buy. The Milligans knew that they would eventually need to purchase furniture and update the home, but they decided to worry about that later. Now was the time to focus on KJ's battle for survival.

At St. Jude, KJ underwent an autologous stem cell transplant. Before he had begun treatment, technicians had removed healthy stem cells from KJ's own marrow. These cells had been stored while he received extremely high doses of chemotherapy. Although it kills tumors, chemotherapy also damages the bone marrow. To make KJ's bone marrow recover, clinicians then transplanted the previously harvested stem cells. The treatment was difficult, and KJ's recovery was slow, with side effects ranging from a gruesome skin rash to severe hearing loss.





While Kenny and Lori cared for KJ, Kenny's fellow firefighters attended to their coworker's needs. Every month, they donated sick leave for Kenny. "For 14 or 15 months, I didn't work a day," Kenny says. "I ran out of vacation and holidays quickly, but I never missed a paycheck." The firefighters also collected donations to help the Milligans with household expenses.

What Kenny did not know was that his colleagues were also spearheading a secret renovation project. Firefighters Dale Shaw and Chris Turner led a community effort to raise money and renovate the house the Milligans had purchased. People in KJ's hometown donated \$30,000 toward the effort. Workmen installed gleaming ceramic tile, lustrous hardwood floors and a luxury bath. Every room was furnished and beautifully decorated. Aware that KJ is a fan of Auburn University, the firefighters even decorated his room in orange and blue.

Facing page, from left: An aspiring video game designer, 16-year-old KJ teaches Carlos Rodriguez-Galindo, MD, a thing or two about technology; and while he draws strength from his dad's dedication, the affectionate teen also constantly teaches Kenny lessons about faith and persistence.

Above, from left: Whether clowning around with Hematology-Oncology Fellow Sarah Sherr, MD, or riding horses at camp, KJ does everything with enthusiasm and panache.

"I didn't know the scope of what they were doing," Kenny says. "I knew they were going to help us a little, but I thought they were just going to paint the house, clean the carpets and maybe put in new miniblinds."

In April 2006, KJ finally got to return home. He was surprised to discover that he was sad to leave the hospital. "You get so attached to this place," he says. "You make all these new friends, and it's really hard to say goodbye."

When the Milligans finally drove onto their street, they were astounded to see fire trucks and TV vans parked in front of their house, with dozens of people crowded in the yard.

"There were cheers, laughter, pride, relief, joy and tears as we walked through two lines of people that started at our front door and stretched almost to the street," Kenny wrote in an e-mail. "Every room was beautiful, just like something in a magazine. We are so blessed to have people in our lives like that. God has been so faithful to us. He promised me a fully restored child and a house for my family. As always, he does it in abundance."

Safe harbor

Although their home may look like a decorator showcase, KJ claims that he lives in a house divided. The high school freshman is a rabid fan of Auburn and LSU. The rest of his family—even his brother, Tyler—roots for the University of Alabama. "This boy just bumped his

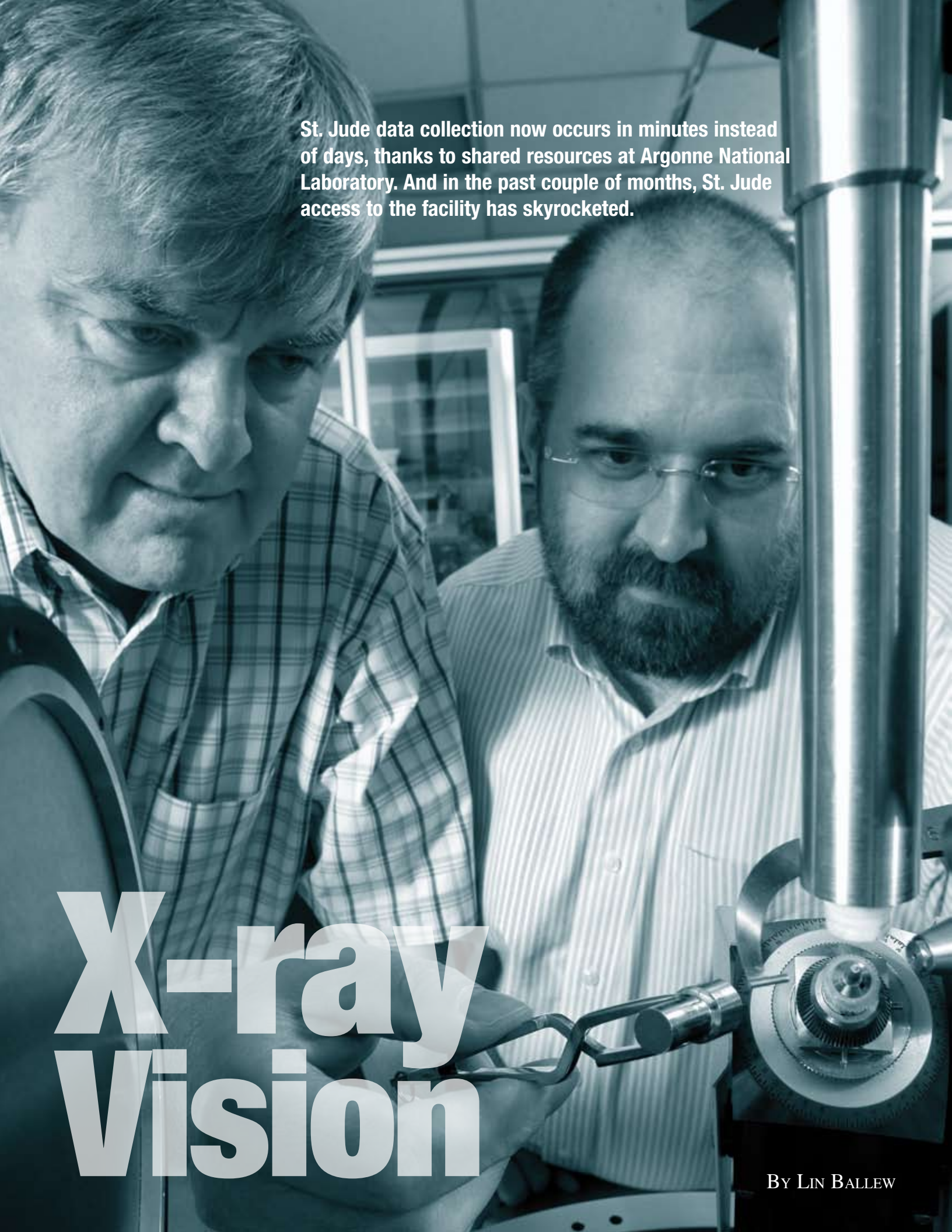
head somewhere along the line," Kenny explains with a grin. Quick as lightening, KJ retaliates. "I have to live with these jokers!" he says, with mock exasperation.

"KJ's got all these plans about being a video game designer or a game tester or a pit crew member when he grows up," Kenny replies. "But he's gonna wind up being a comedian."

Today, the storm seems to be over, and the future looks sunny for the Milligan family. In retrospect, Kenny says he wouldn't change a thing about the experience. "People think that it was a tragedy," he says. "You find out your son's got cancer, you go through everything we did at St. Jude—and then in the middle of it, you lose your house and you're homeless. But last year was the greatest year in my life. I grew more, I learned more, I became closer with my family and I got to see God's work every day."

As the Milligans' St. Jude chaplain, Brown was able to see how the family coped, and he watched them as they grew through their experiences.

"Right in the middle of the toughest experiences in the world, the Milligans had this great blessing in which they have really come to know the care of people at St. Jude and the care of their community," Brown observes. "It's kind of an ironic thing that you sometimes learn that in the moment of your deepest need." ●

A black and white photograph of two men in a laboratory setting. The man on the left, with grey hair and a plaid shirt, is looking down at a piece of equipment. The man on the right, with a beard and glasses, is also looking down at the same equipment. They are both holding a small, cylindrical object. In the background, there is a large, complex piece of machinery, likely an X-ray diffractometer, with a vertical column and a circular base. The overall tone is professional and scientific.

St. Jude data collection now occurs in minutes instead of days, thanks to shared resources at Argonne National Laboratory. And in the past couple of months, St. Jude access to the facility has skyrocketed.

X-ray Vision

BY LIN BALLEW

Topping what is already the best and brightest is hard, but that's just what researchers at St. Jude Children's Research Hospital have done. For several years, St. Jude investigators have been tapping into X-ray crystallography—the process of using high-powered X-ray beams to probe protein crystals and reveal their secrets—but the process was hampered by limited technology. Until recently, St. Jude scientists only had two moderately powerful X-ray crystallography machines they could use. Collecting the data was laborious and time consuming, and the resulting image quality was limited.

More than 100,000 kinds of proteins exist in the human body, from those in the hair and skin and muscles to ones that aid in digestion. Some proteins fight infection, while others speed up important chemical reactions. “Most diseases occur when things go wrong with proteins,” says Stephen White, DPhil, Structural Biology chair. Consequently, understanding what these proteins do is crucial to advancing medical research.

That is where high-powered X-ray technology comes into play. The Advanced Photon Source (APS), located at the Argonne National Laboratory in Chicago, Illinois, is a place where St. Jude structural biologists can collect data on proteins in minutes instead of days. APS is the only such center in the United States, and only the third center of its caliber in the world. The facility is so large that a professional sports arena could fit inside it. And size does matter. While the complex is huge, the crystals the scientists are concerned with are unbelievably small and fragile.

“It's difficult to appreciate just how many atoms there are in a crystal,” White says. “A crystal is less than a millimeter in size. One way to think about it is that if the typical distance between atoms were a centimeter, then one crystal would fit on top of Memphis.”

However, while the crystal itself is miniscule, the macromolecular structure that holds the key information is extremely large at the atomic level. Only a super-powerful radiation beam can determine that structure with clarity. And it is the atomic structure of the macromolecules of protein or DNA complexes that scientists really want to see.

Scientists have solved part of that problem by forcing the macromolecules to crystallize—a time-consuming process—so that the structures can more easily be handled. However, unlike the strong crystals school children create with sugar or salt, protein crystals are delicate, “like cubes of jelly—very small and just as fragile,” White explains.

The sheer size of the task is why advances at APS are such a big deal. Freed from limitations of time, space and quality, scientists can get nearly instant results that are much richer in

data quality and magnitude. But it gets even better. For the past few years, St. Jude researchers have had to take the crystals to Chicago, load them and personally run the equipment to yield the desired results. Now, permanent staff in place at APS can process crystals that have been shipped overnight from St. Jude. In the past few weeks, St. Jude scientists have even acquired the ability to sit at their computers in Memphis and manipulate the crystal remotely by computer.

The Argonne laboratory, which was created and is maintained by the Department of Energy through the efforts of the University of Chicago, is a fantastic resource for St. Jude. The hospital is a founding member of the Southeast Regional Collaborative Access Team, otherwise known as SER-CAT, and White is the board's Tennessee representative.

SER-CAT includes 24 other members from such prestigious organizations as the National Institutes of Health, the National Aeronautics and Space Administration, Wyeth Pharmaceuticals, Georgia Tech Research Corp. and a host of top-notch universities and medical centers. The new facility offers one of the world's most sophisticated X-ray capabilities to macromolecular crystallographers and structural biologists. Instead of having access to one beamline, or super-X-ray tract, St. Jude now has access to two such beamlines. This is significant because the second beamline only recently became operational, and the amount of X-ray time available to St. Jude scientists has doubled. With the hospital's participation in the SER-CAT consortium, beamline access is guaranteed, which allows time-sensitive St. Jude research to proceed without delay.

The hospital's new department of Chemical Biology and Therapeutics will have an increasing need for structural information, so the enhanced access will be beneficial to them as well. “Rapid access to crystal structures of inhibitors bound to their target proteins is crucial for drug discovery,” says Kip Guy, PhD, the department's chair. “Without access to a facility like the APS through SER-CAT, we would be severely hampered in optimizing inhibitors.”

APS has become one of the most productive facilities in the world, with government, industry and medicine sharing its resources. St. Jude continues to stand on the threshold of tomorrow, looking for ways to understand the diseases of children and prevent the suffering of other kids. SER-CAT and the Advanced Photon Source at the Argonne National Laboratory are making that hope a reality. ●

Enhanced access to the Advanced Photon Source at Argonne National Laboratory will help Stephen White, DPhil (at left), Structural Biology chair, and Kip Guy, PhD, Chemical Biology and Therapeutics chair, collect data even more quickly.



ARGONNE NATIONAL LABORATORY PHOTO

Thinking Out

BY CARRIE L. STREHLAU

GENE THERAPY has come a long way since it was successfully used to treat a disorder that was billed in the popular press as "Bubble Boy disease." At St. Jude, researchers are blazing a trail toward making gene therapy a safer and even more effective treatment for a wide range of diseases.



side The Bubble

Replacing a bad gene with a good gene to help cure disease... It sounds like a script from a science fiction movie. In fact, one sci-fi TV show, *Stargate Atlantis*, is centered around this concept. But, sci-fi sounding or not, gene therapy is real and is making great strides at St. Jude Children's Research Hospital.

A fairly young area of research, gene therapy studies began in the 1980s. Then in 1990, the National Institutes of Health performed the first approved gene therapy procedure on a young child with a rare genetic disease called severe combined immune deficiency. Although not a cure, it was a crucial step for the field.

"The basic concept of gene therapy is to insert a properly designed gene, made in the laboratory, into the appropriate cells in order to confer a therapeutic effect either by fixing a broken gene or by endowing the cell with a new property," says Brian Sorrentino, MD, director of Experimental Hematology and co-director of Transplantation and Gene Therapy.

A carrier molecule known as a vector is used to deliver the "normal" gene into the target cells.

"A vector is a virus that has been disabled," Sorrentino explains. "It has a 'payload' that we insert. It efficiently infects the cell—as a virus should; but after it inserts the normal gene into the chromosome, it's done its job and the virus is then permanently disabled."

A new frontier

Gene therapy became a focus for St. Jude in the 1990s and was made a formal program by then-director Arthur Nienhuis, MD, now a member in the Department of Hematology.

St. Jude has studies devoted to the development of gene therapy in several areas including acute lymphoblastic leukemia (ALL), hemophilia, sickle cell disease, solid tumors and inherited immunodeficiencies. In collaboration with other St. Jude programs, the Transplantation and Gene Therapy Program is exploring research to advance the treatment of these catastrophic childhood diseases.

"The gene therapy activities at St. Jude are now taking place in both the Comprehensive Cancer Center and the Sickle Cell Disease Center," Sorrentino says.

In one of the most recent studies, St. Jude researchers developed a model for studying new gene therapy vectors. This model has also been used to explain why gene therapy used to treat children with X-linked severe combined immunodeficiency (XSCID) at an institution in Europe caused some of the patients to develop leukemia.

Back to the future

XSCID is caused by a mutation in a gene called *gamma C* that prevents the immune system from forming B and T lymphocytes. B lymphocytes produce

antibodies, and T lymphocytes perform a variety of tasks such as helping B cells and killing cells that are infected with viruses.

XSCID was the first disease to be successfully treated with gene therapy and was made famous by the story of the so-called "Bubble Boy" who lived inside a plastic bubble to shield him from infections.

In 2002, French researchers inserted normal *gamma C* genes into bone marrow stem cells removed from young children with the disease. Clinicians then infused the genetically modified stem cells back into the patients, restoring the ability of 11 children to develop normal immune systems. However, three of the patients eventually developed leukemia, an event that caused gene therapy researchers to pause and reconsider the safety of this approach.

"The pursuit of clinical trials was stalled by this unanticipated event, causing us and other investigators in the field to go back and restudy the problem of insertional mutagenesis, which is the random activation of cancer-causing genes by the gene therapy vector," Sorrentino recalls.

Researchers later determined that the *gamma C* gene added to the stem cells had inserted itself into oncogenes (cancer-causing genes). The genetic on-switch that was part of the *gamma C* gene had turned on the oncogenes in the blood cells and

“We have an outstanding gene therapy group that is second to none. Having a high level of expertise in vector science along with the GMP facility on our campus is key and gives us a unique edge.”

caused them to multiply uncontrollably, causing leukemia.

Based on recent St. Jude studies, researchers concluded that XSCID itself may make children with this disease particularly susceptible to cancer caused by gene therapy.

“One important implication of this finding is that gene therapy for other forms of genetic blood diseases will likely pose less risk for causing cancer than was previously thought,” Sorrentino says.

Genetic pioneers

Another St. Jude gene therapy study—a collaboration with the University of Cincinnati—focuses on making chemotherapy for brain tumors safer and more effective.

By inserting a gene into bone marrow cells, researchers can protect those cells against chemotherapy’s effects, which otherwise cause low blood counts. This approach is designed to allow researchers to give higher doses of the chemotherapy drug along with a second drug that improves the effectiveness of that chemotherapy in killing tumor cells.

“St. Jude was responsible for creating the vector for this study,” Sorrentino says.

Investigators at the hospital are also working on promising gene therapy studies for ALL. In this approach, Dario Campana, MD, of Oncology and his colleagues put a new gene into a certain type of immune system cell that can then attack and kill leukemia cells. Researchers anticipate that this approach will have fewer severe side effects than other forms of leukemia therapy.

Current therapy for hemophilia (a rare bleeding disorder that prevents blood from clotting properly) involves a specialized type of blood transfusion that is costly, must be given repeatedly and does not cure the disease. St. Jude researchers have developed a gene-therapy approach for curing hemophilia. Investigators are currently at the point of making clinical material in the Children’s GMP, LLC, a facility on the hospital campus that produces biological products and drugs.

Scientists at St. Jude are also developing a gene therapy approach to treat sickle cell disease, with the ultimate goal of a cure. The strategy is to insert the normal hemoglobin gene into the patient’s own bone marrow cells.

In addition, St. Jude is pioneering the use of genetically modified bone marrow

cells to treat children who have a neurodegenerative disorder called lysosomal storage disease. This genetic disease kills brain cells and is lethal in infants and children.

Hope on the horizon

Three diseases have been “unequivocally cured” through gene therapy studies, Sorrentino says. They are XSCID, adenosine deaminase deficiency (a rare genetic disorder caused by receiving a deficient *ADA* gene from both parents) and chronic granulomatous disease (a group of rare, inherited disorders of the immune system caused by defects in certain immune system cells). “The tools for gene therapy have steadily improved over the past several years allowing gene therapy researchers to achieve proof of principle in the clinical realm,” Sorrentino says.

He adds that St. Jude is in a strong position to lead the field in clinical gene therapy. “We have an outstanding gene therapy group that is second to none,” he says. “Having a high level of expertise in vector science along with the GMP facility on our campus is key and gives us a unique edge. Our focus for the immediate future is to expand our studies into clinical trials and to make an impact on the diseases that we have targeted with this approach.” ●



A few of the scientists who are on the front lines of gene therapy research at St. Jude include (from left) Jim Allay, Children’s GMP, LLC; Andrew Davidoff, MD, Surgery; John Cunningham, MD, Hematology; Arthur Nienhuis, MD, Hematology; Brian Sorrentino, MD, Hematology; John Coleman, Therapeutics Production & Quality; John Gray, PhD, Hematology; Dario Campana, MD, Oncology; and Derek Persons, MD, PhD, Hematology.

PETER BARTIA

Bouncing BACK

St. Jude patient and gymnast Morgan Rathke earns a perfect score against medulloblastoma.

BY LOIS M. YOUNG

With 10 national titles to her name, twice as many state championships and a fierce determination to succeed, Morgan Rathke was well on her way to becoming a top-level gymnast. Then, last fall, her priorities took a dramatic flip when doctors found a tumor on her brain. Suddenly, Morgan was faced with her greatest challenge ever—a competition she must win to save her own life.

Already a winner

Before her illness, Morgan moved through her days with what seemed like endless energy. Along with working out at the gymnastics academy four to five days a week and competing in meets on weekends, Morgan earned straight As at her middle school in Illinois. She was also a cheerleader and member of the track team.

The youngest of four siblings, Morgan grew up in the gym. She started training at only 4 years old. Her older sisters, Kristin and Lauren, were also gymnasts. “At one time, I had all three girls competing at the same meets at the same time,” says their mother, Pam Rathke.





Pediatric Nurse Practitioner Valerie Groben, RN, tests Morgan Rathke's strength during an examination.

Morgan's sisters still use their gymnastics skills—Lauren as a high school cheerleader and Kristin as a college cheerleader and gymnastics instructor.

Looking back, Pam believes that all the physical training and can-do mindset Morgan acquired as a gymnast helped her daughter compete against her most formidable opponent.

Preparing for the meet

In early November 2005, Morgan started feeling dizzy during gymnastics practice. Pam took her to a specialist who thought Morgan had an inner ear problem. Despite treatment, she started having severe headaches and began vomiting.

Pam called the doctor's office to explain Morgan's new symptoms. They said, "Our treatment doesn't cause that; she must have the flu."

"After a week I told our regular doctor, 'This is not the flu,'" Pam says. That doctor saw Morgan right away and scheduled an MRI for the following morning.

At 2 p.m. the doctor called Morgan's father, David Rathke, and said, "You need to get Morgan to the hospital; we have a surgeon waiting. We found something on the MRI."

Morgan was barely checked into her hospital room and her parents were in the

hall, when the surgeon told Morgan, "You have a brain tumor."

Morgan knew what that was but says, "I didn't know what to think."

"I know we were in shock," Pam says. "I can't imagine how she felt."

Morgan had medulloblastoma, the most common malignant brain tumor in children, and she needed immediate surgery to remove the growth. The Rathkes feel lucky that an experienced neurosurgeon happened to be in their small-town hospital that week. He performed the surgery but told the Rathke family that Morgan needed to go elsewhere for follow-up treatment.

Joining a new team

That night in the hospital, Pam could not sleep. At about 4 a.m., she turned on the television and started flipping channels. She came upon a St. Jude commercial. It showed actor and comedian Robin Williams asking a 13-year-old St. Jude patient what his next plans were. The boy said, "To be in the seventh grade." At the time, Morgan was in the sixth grade and a few months from her 13th birthday. That St. Jude patient had survived the same kind of brain tumor.

Pam recalls, "A couple of hours later when the doctor came in, I said, 'God

wants us to be at St. Jude.' I had never seen that commercial before, but I just knew that was where we were supposed to be." The doctor agreed and made the phone call, referring Morgan to St. Jude.

A week later, the Rathke family arrived at the hospital. "You don't know what to expect," Pam says. "You are still in shock. We got here, and both my husband and I felt better. We felt relief, like a weight was lifted off our shoulders."

Competing at a new level

Morgan doesn't remember much about arriving at St. Jude. She had many complications from surgery. She could not walk, write, use her left arm or talk much.

But Pam remembers, "From the time we walked in the door, we heard, 'Dr. Gajjar is the best; you're going to love him.' And we did from the minute we met him."

Amar Gajjar, MD, is co-chair of the St. Jude Oncology department, director of the Neuro-Oncology Division and co-leader of the St. Jude Brain Tumor Program.

"Morgan comes from a very loving family," Gajjar says. "She was upbeat and positive about her therapy, which really helped the staff and her recovery."

Morgan's treatment involved six weeks of radiation therapy to her head and spine with heavier radiation at the tumor site. Then she had four cycles of high-dose chemotherapy. After each dose of chemo, she received some of her own bone marrow stem cells to help her body recover faster from the treatments.

All-around good sport

The radiation was not too bad, Morgan says. She was able to go home for a few weeks in February before starting chemotherapy. Along with physical therapy and occupational therapy during that break, she met with her gymnastics coach about four times a week. He had her running; climbing the rope; and doing

push-ups, pull-ups, and a few minor tricks on the bar and the floor.

"Chemo kind of knocked her back down," Pam says, "but she hasn't stopped working on getting her strength back."

What does Morgan think about all that has happened to her? "I just try not to think about it that much," she says.

Pam praises her efforts. "Morgan has been amazing. She has not complained through the whole thing. She just works harder and harder. I think she just tries to go beyond what has happened."

Morgan has what her coach calls, "stick-to-it-ness."

"She was always that way with all her hard gymnastics tricks—never giving up, just trying again and again and again until she got it," Pam says. "I really think gymnastics made a difference in her attitude toward this illness and her recovery."

Loving supporters

Another critical factor in Morgan's recovery was the support she received from many people. Her family and coaches called almost every day. At one point, she was feeling down because she had to miss her brother Brian's high school graduation. Her coach drove eight hours to Memphis for a daylong cheer-up visit.

At least twice a week, she received uplifting cards, letters and packages from her Chemo Angels, which are similar to pen pals.

Despite having only about 800 residents, her hometown held a successful walk-a-thon in Morgan's name to benefit St. Jude.

"My friends made special T-shirts for the event," she says. "They sent me one that had 'Our Hero' on it."

The gymnastics community offered support through St. Jude fund-raisers and words of encouragement. At one meet that Morgan had to miss, all the kids wrote messages to her on paper stars. They posted them at the meet and afterward sent all the greetings to Morgan. She even received a hand-written letter from U.S. Olympic medalist Courtney Kupets.

For many years, Peoria, Illinois, has held a gymnastics meet to benefit the St. Jude affiliate there. The Rathke sisters

competed in that meet for years before Morgan became a patient. This year, Morgan was one of the poster kids for the event.

As for St. Jude supporters, Morgan reeled off a long list of staff members who have helped her. The ones who seem to stand out most are Gajjar, Kim Kasow, DO, and St. Jude schoolteacher Erin Brick. "Erin and Morgan hit it off right away because Erin was a gymnast, too," Pam says. "Erin understood what Morgan was going through and what she was missing."

Brick was a member of the Penn State University gymnastics team in the early 1990s. Morgan was quiet until they found that mutual interest, but Brick says with a smile, "She's definitely not quiet now." Brick was impressed with how hard Morgan worked on schoolwork and physical therapy throughout her treatments. "There's no stopping her," Brick contends. "She worked right through everything."

New challenges lie ahead

In July, Morgan showed no signs of her disease, so that wonderful day had finally come for her to travel home.

Soft-spoken yet mature for her age, Morgan already has lofty goals. Even before the tumor, she was talking about going to college to become a doctor or nurse. This experience cemented that idea. "Maybe someday I'll come back and work at St. Jude," she says.

For now, Morgan just wants to get back in shape for gymnastics and start competing again. Like most 13-year-olds, she wants to hang out with

her friends and chat with them on the Internet.

"I think something like this changes your perspective," Pam says. "Before, Morgan was very serious about competing and winning. Now, she just wants to get back to gymnastics and being with her friends. Just doing it because she loves it—that's what really matters now."

At first, Morgan will return to St. Jude every three months, so the staff can monitor her recovery and make sure her tumor does not return.

"Dr. Gajjar wants to see her cart-wheel down the hallway," Pam laughs. "That will be no problem when you come back—right, girl?" Morgan just nods and smiles in her quiet, confident way. ●

Morgan performs at the 8th Annual World Class Gateway Challenge.



**One phone
call can
make all the
difference
in the world,
especially
when your
child's life is
on the line.**



Life Line

BY BONNIE KOURVELAS

“Oh, thank God.”

The young mother has been trying to be calm, but finally her voice on the telephone wavers and breaks. She has just learned that the one thing she wants most in life—her little boy’s rare disease to stay in remission—has happened, and against all the odds.

On the other end of the line, a physician at St. Jude Children’s Research Hospital intently studies test results that have turned out even better than he could have hoped. He has just called Gina Reinier to tell her that instead of settling in for many more months of treatment, she and 4-year-old Liam will be able to get on a plane and go home to Iowa.

All Liam knows is that he gets to see Daddy again...and his brothers and his best friend, Sean, and his room and his beloved Harry Potter video game. Liam can’t pronounce the name of the cancer that has threatened his life, but he knows that at least for now, there won’t be any more needles and hospital beds. He does not realize how slim the chances were that this moment would arrive, but his mom does.

A higher calling

One day last fall, Gina, a high school biology teacher, noticed a reddish, circular mark on Liam’s leg. The next day, his legs were covered with spots like chickenpox; then his appetite disappeared and he began sleeping all the time. As Gina remembers that October day, she glances over at her son, who plays nearby.

“Liam never, ever stops,” Gina says, “so I knew right away that something was

wrong.” The pediatrician examined the bruises on Liam’s legs and asked to do some blood work.

“My science background was telling me, ‘Oh, she’s looking for hemophilia because of the bruising,’” Gina recalls. “I knew he wasn’t hemophiliac, or we would have figured that out by now, and so I was fine with it—no problem. The doctor came in about 20 minutes later with tears in her eyes...” Gina’s voice trails off.

“Look how good I did,” immediately chirps Liam, who has been busily coloring, yet has not missed a word of his mother’s recount of that day.

“Oh my goodness, you’re putting a lot of details on there,” Gina says, proudly admiring her son’s work. “I like it.”

She collects herself and returns to that day in the doctor’s office. “She came in

with tears in her eyes and said, ‘I’m going to pray for you.’ And I thought, ‘When the doctor leaves medicine behind and goes to religion I know I’m in trouble,’” Gina recalls.

Wrong number

Assuming that Liam had leukemia, the physician referred Liam to an oncologist and then handed Gina a business card. “She said I could call any time, day or night,” Gina says. “So that told me we were really bad off.”

The oncologist ran tests and immediately ruled out leukemia, so he told the family it must have been a virus after all. But after further testing, joy turned to utter shock when the phone rang at the Reiniers’ house two weeks later. The oncologist said Liam had something that was worse than leukemia.

What Liam had is myelodysplastic syndrome (MDS). The name comes from myelo (dealing with bone marrow) and dysplasia (the proliferation of abnormal cells). It is a blood cancer so rare that most people have never heard of it. The cause is unknown, although a genetic component exists. MDS can give the appearance of leukemia.

“When he called, the oncologist said that genetic studies revealed Liam was missing a chromosome that is a big indicator of MDS. I was trying to write all this down while I was on the phone,” Gina says. “And he said, ‘This is very serious; I have very bad news for you.’ But I was still thinking, ‘It’s OK, we can do this.’ I asked, ‘This is survivable, isn’t it?’

“And he said, ‘No. Not really.’



JOY TURNED TO UTTER SHOCK WHEN THE PHONE RANG AT THE REINIERS' HOUSE. THE ONCOLOGIST SAID LIAM HAD SOMETHING THAT WAS WORSE THAN LEUKEMIA.



"I said, 'What? Not really survivable?' And he said, 'No.' That was the end of the phone call, because I had no ability left to talk."

Well-meaning doctors in Iowa gently urged Gina and Jeremy Reinier to accept that Liam was not going to grow up.

"At home we were told that we should wait until it progressed into leukemia, because it often does, and that we might as well get all the good days out of him that we could and say goodbye," she says.

Just a phone call away

Determined not to give up, Gina sat down at her computer and found St. Jude.

"St. Jude was the only place I could find that talked about MDS being survivable," she says. "I told my doctor I wanted to take Liam there. He shrugged and said we could do that if we wanted to, but he really didn't see what good it would do."

Gina takes a deep breath. "And then we came down here, and the doctors were very positive. There definitely is a mortality rate with this—it's a very serious disorder and requires a bone marrow

transplant. But we went from being told 'that was it' to 'here's how we can help you.' I know the word 'hope' is used so much that it's almost overused, but they gave us hope, and we really didn't have any when we came down here.

"We looked into a couple of other places, just to make sure. Some of them promised higher success rates but they couldn't give me any reasons why; they couldn't give me any statistics to back it up. And it really felt like a sales campaign. They seemed to like that he had a rare disorder because it was a new number for their books. But at St. Jude, that didn't seem to be the case. They knew me by name, they responded to my e-mails, they would call me on the phone, and it really was how they could help Liam, not how Liam could help them," she says.

Life on the line

At St. Jude, Liam's doctor, Greg Hale, MD, is interim chief of Bone Marrow Transplantation. "MDS is a malignant disorder in which bone marrow cells grow abnormally, so that they don't become the normal cells that carry oxygen, clot the blood or fight infections,"

he explains. "Most people who get MDS are elderly—it's quite rare in pediatrics. In Liam's case, studies identified monosomy 7, which means part of the DNA on chromosome number 7 was missing."

Liam's only hope was a bone marrow transplant, and he came to the right place for it. One of the largest pediatric transplant centers in the world, St. Jude has been named a Center of Excellence by the MDS Foundation. In Liam's case, family members were not close matches for him, so an unrelated donor was selected. The only thing the family knows about the donor is that she is a 21-year-old female, somewhere out there in the world. A year from now, if they wish, Liam and his donor can exchange personal information. Gina hopes to do that—so she can say thank you.

Whoever the donor is, she gave a piece of herself to Liam, and now her healthy blood cells are taking over and fighting Liam's diseased blood cells. That's the good news that Hale called to tell Gina.

"When he called me, I was lying on the couch, holding the phone to my chest," Gina recalls. "I really thought we were going to stay here for another transplant. But when he said, 'You can go home,' my heart just about leaped out."

For the next year, she and Liam will journey from Iowa back to St. Jude every month for bone marrow studies and testing.

"At the end of his first year of transplant, he will undergo a complete re-evaluation, including bone marrow studies," Hale explains. "MDS can be hard to follow, so we have to look carefully."

In the meantime, the Reinier family strives to resume a normal existence. For Liam, that means a return to his room, his friends, his video games and the ability to eat restaurant pizza again for the first time in months. For Gina and Jeremy, it means they can enjoy every day with their energetic little boy, while at the same time, finally daring to hope for his future. ●

A microscopic image of cells, likely from a tissue sample, showing a cluster of cells with prominent nuclei and cytoplasm. The cells are stained, with some appearing in shades of orange and yellow, and others in darker brown tones. The background is dark, making the cellular structures stand out.

RUTH ANN
HENSLEY

A “Howdunit” MYSTERY

It's a plot that turns on a cell's precarious dance of life and death. St. Jude scientists are determined to write the book on cell suicide.

A “Howdunit” MYSTERY

RUTH ANN
HENSLEY

If Doug Green, PhD, were to give you the shirt off his back, chances are it would sport big, bright tropical flowers. It is hard to imagine that this joyful, Hawaiian-shirt-wearing scientist who describes certain proteins as “outrageously cool” is the same man who penned scientific reviews titled “Ten Minutes to Dead,” “A Matter of Life and Death” and “At the Gates of Death.” This Don Ho-meets-Stephen King dichotomy mirrors the good-versus-evil, protagonist-versus-antagonist dynamic that Green studies—apoptosis, or cell death.

In a multi-cellular organism like the human body, the death of a cell is just as important as the proliferation of tissue in sustaining life. Just as in a good thriller, it’s when those factors become out of balance that trouble begins. By studying apoptosis, researchers hope to understand the delicate equilibrium between cellular life-and-death forces. With that knowledge, scientists may one day have the ability to make life-saving plot changes when the story line takes a turn for the worst.

STRANGER THAN FICTION

Clearly, the main character of the cell death saga is the cell itself. But unlike most murder mysteries, this is no “whodunit.” There is no smoking gun in the library—rather, the cell kills itself. Thus, researchers at St. Jude Children’s Research Hospital are intrigued with the “howdunit” of the process.

“The remarkable thing we have learned is that cells in our body, which are dying all the time, don’t *always* die the way we usually think of death, as being worn out, torn up or broken apart. A cell receives a signal from the body when it’s infected or if it’s a cancer, and then it commits suicide. That remarkable process of a cell killing itself is the study of apoptosis,” says Green, who holds the Peter Doherty Chair

in Immunology at St. Jude. “We can also refer to the process as active cell death. Because the cell wasn’t killed *by* something—it actively killed itself.”

Green, one of the top 20 most-cited scientists in the country, explains that a cell can die from many causes, but the two most common ways are through apoptosis and necrosis. A cell has a choice of whether or not to undergo apoptosis, but it has no choice in necrosis. In the latter process, the cell may burst, become torn or be destroyed by external forces. This distinction is important because when cells die by necrosis, a powerful signal activates an immune response. This response typically results in inflammation and can pose serious health issues. Apoptotic cell death, however, proceeds silently.

“It’s like the cell was never there,” Green says. “It’s more than silent, it’s aggressively silent, and there is no inflammatory response.”

Why is the focus on apoptosis important in the treatment of diseases such as cancer?

“Everything we do in the attempt to kill a cancer is involved in inducing apoptosis in the cancerous cells,” Green explains. “And every problem we have in performing that induction is related either to the cancer not undergoing apoptosis or to healthy cells dying.”

INVESTIGATING THE MYSTERY

The human body is composed of millions of cells. Every day tremendous numbers of cells in our body die and are replaced by other cells. If just one of them becomes cancerous, it can kill us.

Safeguards built into our biology prevent that. Most of those protective mechanisms rely on the cell realizing something is wrong. When this altered cell gets the message to start reproducing with no constraints, it responds to the signal by committing suicide—apoptosis.

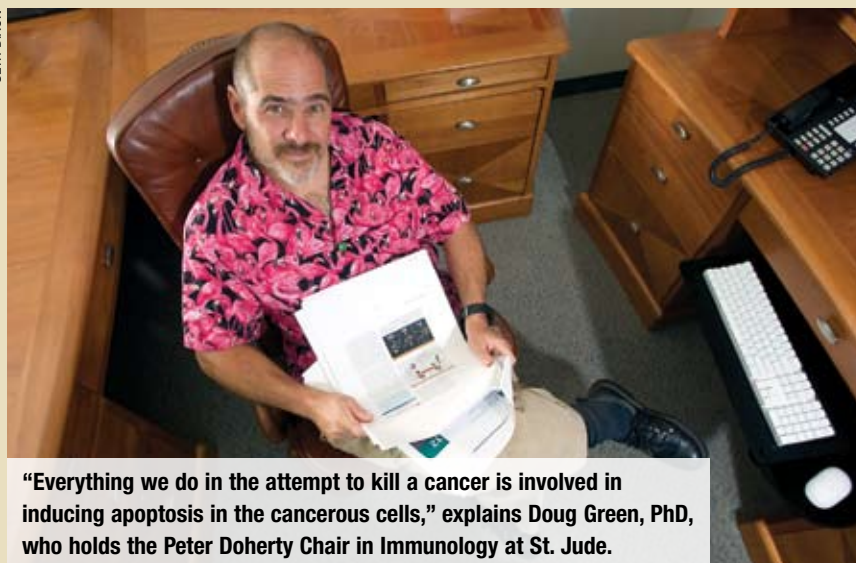
“Otherwise, every one of us would have cancer by the time we were 7 months old,” Green says. “As a good friend of mine once said, the question isn’t why there is so much cancer; the question is why there is so little.”

Apoptosis is one answer. It’s a central component in halting the reproduction of cancerous cells, according to Green, who is a pioneer in the field.

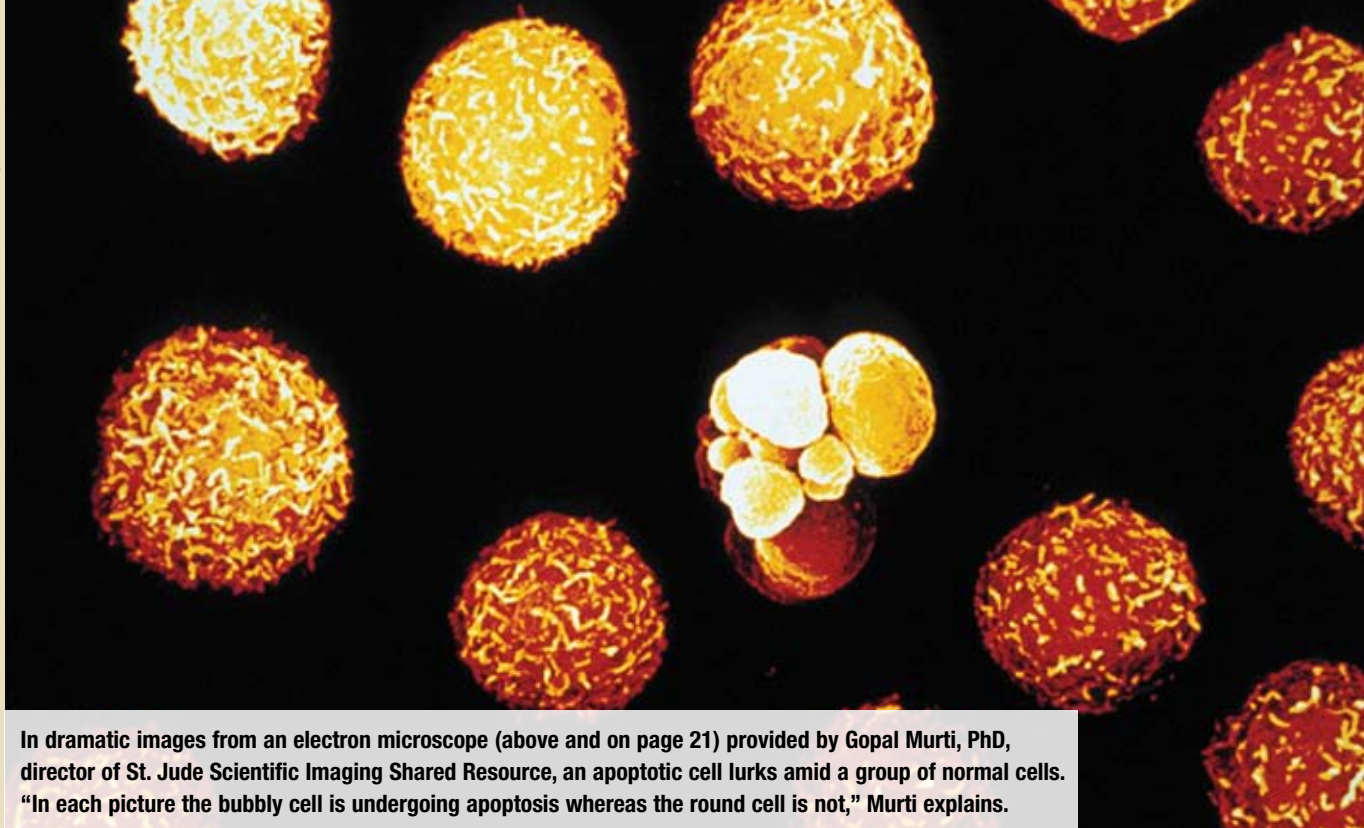
THE PLOT THICKENS

If apoptosis is the good guy in this story, what is stopping its heroic measures? That is where the plot thickens.

SETH DIXON



“Everything we do in the attempt to kill a cancer is involved in inducing apoptosis in the cancerous cells,” explains Doug Green, PhD, who holds the Peter Doherty Chair in Immunology at St. Jude.



In dramatic images from an electron microscope (above and on page 21) provided by Gopal Murti, PhD, director of St. Jude Scientific Imaging Shared Resource, an apoptotic cell lurks amid a group of normal cells. "In each picture the bubbly cell is undergoing apoptosis whereas the round cell is not," Murti explains.

"We have a paradox," Green says. "Cells are poised to die, but in cells that have a mutation or some other defect, the same signal that tells the cell to die will activate oncogenes [cancer genes] and cause the cell to start reproducing. If we can get a grasp on that signaling process, we can get cancer."

Unfortunately that isn't as simple as sending in apoptosis on a white horse.

"Killing the cancer isn't the problem; it's keeping the patient alive," Green explains. "You can kill Godzilla, but if you take out Tokyo in the process, it didn't do any good."

The key in treatment is to find that delicate balance between a cell's life-and-death mechanisms—to induce apoptosis in cancerous cells while minimizing cell death in normal cells.

"I think that's achievable," Green says. "Our real success in cancer treatment comes from combined treatments and therapies that work together to prevent collateral damage to the patient, while being effective against the cancer."

Green says when he began studying apoptosis it wasn't a household word in the scientific community. Today the subject is studied by scientists in disciplines such as genetics, molecular pharmacology and infectious diseases, to name a few.

A crucial discovery occurred when researchers identified a family of proteins called Bcl-2, which play a key role in apoptosis.

"We are learning that there are some members of this protein family that block cell death, but there are other members of the family called Bax and Bak that are absolutely required for apoptosis to occur," Green explains. "So now the question is, 'How are Bax and Bak activated?' It's a very controversial, active area of investigation."

A TANTALIZING CLIFFHANGER

What sounds like a bad family reunion may lead to the next chapter in this page-turning cell death thriller.

"A lot of attention and excitement is being paid to a new class of drugs that inhibit Bcl-2," Green says. "In the simplest form, diseases are caused by too much or too little cell death. So the hope is that the more we can understand about that balance at the fundamental level, the better our chances are to manipulate it."

It was that kind of hope that inspired Green to come to St. Jude last year.

"I came here because of the incredible promise of St. Jude—of what we are able to do here, of the fantastic advances we are already making. At St. Jude, an overlying mission surrounds us, which is driven by kids with catastrophic diseases. No one can say that is not a worthwhile and personally important mission," he says.

Green admits that finding cures for catastrophic diseases is not an open-and-shut case.

"Every day for the last 15 years the newspapers have announced possible cures for cancer. So where is this victory cure we were promised years ago?" Green asks. "These things take time. There's nothing that we're doing in the lab today that I can make any prediction about except to say, 'I hope we're going to learn something from it.'"

Inspired by that hope, Green vigilantly studies the fragile balance of life and death at the cellular level. When he seeks balance in his own life, he finds it by spending time with his family, playing the guitar and inventorying his collection of 150 Hawaiian shirts. But when it comes to his research, it's much like a good book—he can't put it down until he figures out "howdunit."●

Perspective

Let Me Count the Differences

BY TOM DUNBAR

“St. Jude is unique because its vision, created by the incomparable Danny Thomas, is more focused than that of any other hospital treating children.”



Tom Dunbar and his son, Evan, who lost his battle with neuroblastoma in 2001. Today, Tom and his wife, Lynn, help St. Jude raise money to help other kids.

What makes St. Jude Children’s Research Hospital different from any other hospital? My family knows the answer to that question all too well.

When our son, Evan, was 4 years old we found out that he had neuroblastoma, a solid tumor of the nervous system. For the next two years we stood by our little guy as he fought his battle with courage and good humor.

Kids at St. Jude really are heroes—whether they are survivors, like so many are these days, or angels, like my Evan, forever 6 years old. All of these children are essential to advancing cures, targeting therapies, minimizing side effects and

allowing survivors to fully participate in life.

St. Jude is unique because its vision, created by the incomparable Danny Thomas, is more focused than that of any other hospital treating children. The vision is to cure every single child afflicted by a life-threatening disease—period. They do that without regard to ethnic background, country of origin, cause of the disease or ability to pay for treatment.

At another hospital we visited, no treatment could begin until we had deposited \$70,000 via wire transfer to the hospital, despite the fact that we had excellent medical insurance. But at St. Jude, they

welcomed us. They did eventually ask us about whether we had insurance, but it never came close to influencing treatment in any way. That difference alone meant the world to us.

St. Jude is the closest thing to a pure research institution for childhood disease that you will ever find. I was awed, on a recent trip to Memphis, with the huge amount of research St. Jude undertakes. This was a side we never really saw while there with Evan. Their capabilities are truly amazing, but fund raising is crucial to supporting this massive effort.

Essentially, for St. Jude, the buck stops with you and me. Without our ongoing gifts, research simply will not continue, the suffering of children will not stop and more children like our Evan will die. Because of Danny’s vision, because of the unbelievable efforts of the physicians and researchers there, because of the continuing successes, and because of your generosity, St. Jude is a place full of hope.

Danny Thomas himself said it best: “No child should die in the dawn of life.” Because of his vision and because of his ability to share that vision with the world, people just like you have given and continue to give their hard-earned dollars so that all aspects of research and treatment are able to continue without interruption. I hope and pray that you continue to support Danny’s dream. Together, we can save the lives of even more innocent children. Please do it in Evan’s memory. ●

Tom Dunbar and his wife, Lynn, lost their son, Evan Thomas Joseph Dunbar, in July 2001. They help keep his memory alive through the Evan Dunbar Foundation and through their generous support of St. Jude.

**Most kids
feel better with
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and a kiss.**

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need a cure.**

Peter, 2 - Prostatectomy

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