Cover story

12  Defying the Odds
    Natural killer cells help Jordan James thrive.

Features

6  Strength Through Sharing
    Shared resources help scientists make discoveries quickly and economically.

9  Trikeathon: 25 Years of Kids Helping Kids
    Successful program teaches tots valuable lessons.

10  Sweet Relief
    New pain management method turns tears into smiles.

11  Serious about Support
    One trip to St. Jude was all it took.

16  St. Jude for LIFE
    Adults return to St. Jude for a unique follow-up study.

19  Run for your Life
    Thanks to St. Jude, Broox Middleton hits his stride.

23  Teen Spirit
    Volunteers share their energy and enthusiasm.

Research Highlights

2  News and Achievements

Perspective

24  Charkelcy Keyone Docher
    Hope is a Remedy

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Research reveals lipid’s unexpected role

The lipid that accumulates in brain cells of individuals with an inherited enzyme disorder also drives the cell death that is a hallmark of the disease, according to research led by St. Jude investigators.

Children with a disease called GM1-gangliosidosis are born without the instructions for making an enzyme that breaks down a lipid, or fat molecule, called GM1-ganglioside. The disorder causes developmental and movement problems, seizures and early death.

St. Jude researchers provided the first evidence that a lipid can initiate a suicidal response in cells. Investigators discovered how GM1 accumulation inside certain structures in brain cells disrupts their internal calcium balance. This imbalance ultimately leads to programmed cell death.

“The finding is essential for understanding the causes of progressive loss of brain cells characteristic of this disease,” said Alessandra d’Azzo, PhD, of St. Jude Genetics and Tumor Cell Biology. d’Azzo is senior author of a report on this work, which appeared in the journal *Molecular Cell*. This work was subsequently featured in *Nature Chemical Biology*. The research also provides hints for a strategy to intervene in the disease process.

Statins may protect against infections

Medication already widely used to combat high cholesterol and heart disease might also help protect individuals with sickle cell disease and certain other forms of chronic inflammation from life-threatening bacterial infections.

Laboratory findings from St. Jude provide a foundation for future research to determine whether the drugs, known as statins, protect children with sickle cell disease from pneumococcal infections.

Researchers found that statins worked in several ways. Along with disrupting the ability of toxins to enter healthy cells, statins reduced the protein on the cell surface that the bacteria use to infect cells and spread throughout the body.

Elaine Tuomanen, MD, Infectious Diseases chair, said the findings suggest statins might also protect against an entire class of bacteria, including diphtheria, tetanus, listeria and group A streptococcus, the so-called flesh-eating bacteria. Tuomanen is senior co-author of a report on this study that appeared in *The Journal of Clinical Investigation*. 
Research offers clues to brain complication

New evidence from St. Jude investigators strengthens the link between a devastating complication of brain tumor surgery and disruption of a pathway that functions like a fiber optic cable connecting important structures in the brain.

The complication is posterior fossa syndrome (PFS), which strikes about 25 percent of children who undergo surgery to remove malignant brain tumors, primarily medulloblastoma. Despite more than two decades of research, PFS remains a puzzling problem.

“Posterior fossa syndrome is an extreme example of how brain function is altered in this population,” said Robert Ogg, PhD, Radiological Sciences, senior author of a report on this study that appeared in the journal Brain.

The St. Jude study marks the first time an advanced neuro-imaging technique known as diffusion tensor imaging has been combined with magnetic resonance imaging to compare changes in the brains of patients who did and did not develop PFS.

The research adds to growing evidence that PFS may be caused by the disruption of tracts located on both sides of the brainstem. These tracts are the primary communication link between two areas that house regions of the brain charged with advanced functions such as language, thought and emotional regulation.

Survivors urged to get HPV vaccine

In a recent edition of the journal Cancer, St. Jude investigators reported that childhood cancer survivors—especially young women whose treatment included hematopoietic stem cell transplants—are at high risk for cervical cancer later in life. Researchers encourage these individuals to receive the human papillomavirus (HPV) vaccine as protection against cervical cancer.

Melissa Hudson, MD, St. Jude Cancer Survivorship Division director, said hematopoietic stem cell transplants are linked to a 13-fold increased risk of cervical cancer. The therapy involves extreme, sometimes prolonged, immune suppression. Other survivors reported to be at elevated risk include those who had Hodgkin lymphoma and females who received pelvic irradiation.

Hudson, senior author of the Cancer report, said the evidence suggests even many high-risk survivors fail to take advantage of vaccine protection. “I tell parents this is a very prevalent virus,” she said. “Why take a chance?”

Physician of the Year

Ching-Hon Pui, MD, Oncology chair, was recently honored with the Clinical Excellence Award at the fifth annual National Physician of the Year Awards. The Clinical Excellence Award recognizes physicians who exemplify excellence in clinical medical practice. St. Jude National Outreach Director Marlo Thomas and her husband, Phil Donahue, joined Pui at the award ceremony held in New York.
Distinct origins found for immune cells

Different sub-classes of a type of white blood cell involved in autoimmune diseases such as multiple sclerosis (MS) arise independently within the immune system, according to a finding that provides new insight into how autoimmunity is controlled.

The St. Jude study answers a key question about the origin of two types of immune cells, known as regulatory and effector T lymphocytes. Effector T cells are important in clearing infections in our body, but when aberrantly directed against our own body’s tissues promote autoimmune diseases such as MS. Regulatory T cells protect against the immune system attack.

Investigators demonstrated that regulatory and effector T cells isolated from the central nervous system of laboratory models with an MS-like disease both recognize and respond to the same protein derived from the sheath surrounding nerves. But by analyzing the T cell receptors used by the responding cells, the researchers concluded that the T cell types arose from different populations involving the blood, bone marrow and immune system.

Model developed to help predict risk of complications

A model developed by St. Jude researchers is showing early promise as a tool to help physicians identify cancer patients with fever and low white cell counts who are at greatest risk for complications.

Currently all children with cancer who develop fever with neutropenia are hospitalized and treated with IV antibiotics. Neutropenia occurs when levels of infection-fighting white blood cells known as neutrophils fall to dangerously low levels.

“But not every patient with fever and neutropenia is at the same risk for developing infection and complications,” said Hana Hakim, MD, Infectious Diseases, first author of a report on this study that appeared in Pediatric Infectious Disease Journal. “If there were a way to identify those most likely to develop complications, perhaps the other patients could undergo an easier therapy on an outpatient basis.”

The study is one of three planned trials to develop, validate and test a tool to help doctors match treatment of fever and neutropenia with the likelihood that a young cancer patient will go on to develop widespread infection or serious clinical complications.

National mentoring award

Arthur Nienhuis, MD, Hematology, receives a 2009 Mentor Award from American Society of Hematology (ASH) President Nancy Berliner, MD, during the society’s recent annual meeting. The award recognizes hematologists who have excelled at mentoring trainees and colleagues. Nienhuis is a former director and chief executive officer of St. Jude as well as a researcher widely known for work involving gene therapy and related topics. ASH is the world’s largest professional organization focused on the causes, treatment and prevention of problems involving the blood, bone marrow and immune system.

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The study is one of three planned trials to develop, validate and test a tool to help doctors match treatment of fever and neutropenia with the likelihood that a young cancer patient will go on to develop widespread infection or serious clinical complications.
St. Jude researchers have developed a simple, effective method for identifying young cancer survivors who are most likely to start using tobacco and who might benefit most from prevention efforts. The new tool ranks the likelihood survivors will start smoking based on their answers to six questions designed to measure smoking intentions. Investigators reported that young cancer survivors whose responses suggested uncertainty in their commitment to abstain were almost three times more likely to become tobacco users than were survivors classified as committed nonsmokers based on their answers. The research was published in a recent issue of the *Journal of Clinical Oncology*.

“This has significant clinical implications,” said James Klosky, PhD, Behavioral Medicine, the paper’s lead author. “Smoking is associated with a range of health problems, including heart disease and cancer. We want to intervene with these young survivors before they start smoking. We can now use this tool to identify who is most likely to smoke and who needs to be targeted for tobacco prevention.”

St. Jude investigators have identified a new protein at work inside infection-fighting plasma cells that plays a critical role in quality control during antibody production. The protein, named pERp1, functions only in B lymphocytes and plasma cells, the immune cells where antibodies that fight infection and other threats are made. Without pERp1, plasma cells struggle to make the chemical bonds essential for proper antibody assembly and functioning, researchers reported.

But investigators said the predicted structure of pERp1 does not resemble any of the approximately 20 other enzymes at work in the protein-folding machinery that helps mammalian cells make the same chemical bonds, known as disulfide bonds. Writing in a recent edition of *Proceedings of the National Academy of Sciences*, the scientists noted that pERp1 might be a previously unidentified member of a completely different family of proteins, known as chaperone proteins.

Linda Hendershot, PhD, Genetics and Tumor Cell Biology, said pERp1 is critical for high-level antibody production. She is the study’s senior author. “If the cells don’t have it, they have trouble assembling the disulfide bonds that function like Velcro to help antibodies maintain their proper shapes,” she explained.

A new study led by St. Jude investigators disproves reports that well-fed children are more vulnerable to the dengue virus. Mosquitoes spread the virus, which can cause severe, flu-like symptoms and sometimes lethal complications. Health officials estimate about one-third of the world’s population is at risk for infection with one of the four dengue viruses. Researchers found that malnourished children are just as likely as their well-fed counterparts to develop life-threatening complications following repeated infections with the virus. Ernesto Pleites, MD (at left), treats patient Yesegia Rivera Lopez at Hospital Nacional de Ninos Benjamin Bloom in San Salvador, El Salvador. The St. Jude project involved patients hospitalized at the El Salvador hospital.
Chances are, you learned this simple concept on the playground: It’s fun to toss a ball into the air, but sharing that ball yields a more exciting and fulfilling experience. At St. Jude Children’s Research Hospital, that fundamental idea underlies the success of the institution’s state-of-the-art shared resources.

St. Jude scientists have access to an impressive array of shared resources, also known as core facilities. Because they are centralized, these facilities help St. Jude make the best use of donor dollars and accelerate research —allowing scientists to make discoveries and find cures as quickly as possible.

The services offered range from genome sequencing and protein production to grants management.
and vector development. Most other research organizations outsource such services or charge high prices for investigators to use specialized equipment. Because of the convenience and the relatively low cost of St. Jude shared resources, the hospital’s core facilities have become an important draw for scientists who are looking for the best place to make a difference.

**Speeding up science**

When postdoctoral fellow Jason Rawlings, PhD, of Biochemistry arrived at St. Jude in 2005, he marveled at how quickly he could complete experiments, thanks to the hospital’s shared resources. “I was like a kid in a candy store,” he says. “Many research institutions offer nothing like these core facilities. At other places, if you wanted to sequence DNA, typically you’d prepare the sample, put it in the mail and send it off. It would arrive at the other facility in a day or two. They might run the sample several days later. Then it would take them a couple of days to get the data onto the Web where it could be downloaded. So typically it would take about a week from the time the sample is mailed until the time you can expect to receive the data. But at St. Jude, I just go downstairs and hand my sample to the people at the Hartwell Center for Bioinformatics and Biotechnology. I go back upstairs and continue my work; the next day, the data are available on my computer. That means I’m getting the results in one day as opposed to seven. “So,” he says, “you’re looking at a sevenfold increase in productivity.”

**Sharing expertise**

In recent years, St. Jude has enhanced its existing core facilities and developed new ones. For instance, an expanded flow cytometry facility is slated to open at St. Jude in the summer of 2010. Flow cytometry measures the amount of DNA and proteins on cells. The process is often used to identify different types of cancers and to determine how well those diseases will respond to particular types of therapy.

The hospital has also enhanced its cell and tissue imaging capabilities. In the past, microscopes and personnel were spread throughout

With nearly 40 shared resources at their disposal, St. Jude scientists can make discoveries quickly and economically.
the hospital. Now equipment and experts are in a central location convenient to researchers across campus. Investigators have access to services ranging from transmission electron microscopy and confocal laser scanning microscopy to image analysis, cell microinjection and live cell imaging. Researchers can either drop off their samples with the experts in the core facilities or undergo training so that they can perform the experiments themselves.

St. Jude investigators say the combination of staffing expertise and high-quality facilities bring a new level of excitement to their work. "The cell and tissue imaging facility not only provides laboratories like mine with the opportunity to use state-of-the-art equipment, but it also provides access to an experienced support staff to help plan, carry out and analyze experiments," observes Joseph Opferman, PhD, of Biochemistry. "By working closely with the facility’s staff, my laboratory has been able to incorporate cutting-edge methodology into our research. These studies have helped unveil important scientific discoveries and are helping to determine our future research directions."

Jian Zuo, PhD, of Developmental Neurobiology, is a vocal supporter of the hospital’s shared resources. "One of the main attractions of St. Jude is its core facilities; they’re marvelous," he says. "You name it—cell imaging, proteomics, sequencing, the transgenic core, genomics—it’s just outstanding. It’s hard to find any other place that offers such an amazing collection of top-notch equipment, short turnaround time and availability of experts."

One-stop shopping

Core facilities at many institutions are run by faculty members from specific departments, who bring their personal research interests and priorities to the tasks. But at St. Jude, the core facilities are shared by all researchers, meaning access to equipment is allocated in an unbiased fashion. "Other institutions may have pieces of equipment scattered throughout their facility, with different levels of access to the technology," says Michael Dyer, PhD, co-leader of the Developmental Therapeutics for Solid Malignancies Program. But at St. Jude, these services are very much integrated. That integration demands a lot of coordination.”

St. Jude has created a laboratory management system that allows scientists to use one single portal for requesting services, retrieving data and generating reports. If an investigator sends samples to several areas for testing, all details about those tests—including data generated—are available to the scientist at one location online. Known as Shared Resource Management, the system allows researchers to requisition services, retrieve data and generate reports quickly and easily.

“Shared Resource Management allows us to manage and track samples,” says Ron Smith, vice president of scientific operations. “It’s a great tool to manage workflow as well as utilization of the cores.”

Faculty members across the institution attribute the success of the hospital’s shared resources to the foresight of St. Jude Scientific Director James Downing, MD.

"Dr. Downing has an incredible vision of what he wants from the perspective of the shared resources," says Chris Calabrese, PhD, who oversees one of the hospital’s nearly 40 core facilities. "We’re small but perfectly formed. We have the correct technologies. We have investigators who ask the right scientific questions. We have the best laboratory models. We have state-of-the art facilities. "The one thing about science is that it never stands still," he explains. "Technology is always advancing. We will keep pushing the frontiers to help people answer their questions.”
“We did it!”

That’s the happy, confident shout of Dora when she and her friends wrap up an episode of Nick Jr.’s popular animated television series *Dora the Explorer*. But it also represents the can-do spirit of preschoolers who help St. Jude Children’s Research Hospital through the Trike-A-Thon program.

For more than 25 years, Trike-A-Thon has taught children how to safely ride their tricycles and riding toys, while promoting the importance of helping others. This year, Dora joins the fight against childhood cancer and other catastrophic childhood diseases as the spokesperson for Trike-A-Thon.

Through commercials that began airing on the Nick Jr. cable TV channel in January, Dora encourages parents and preschoolers to participate in this fun activity. Nick Jr. is also promoting the program on its Web site.

Traditionally, Trike-A-Thon events are held in preschools and childcare centers; more than 21,000 facilities use the program’s series of interactive stories to teach children important safety lessons such as the importance of always wearing helmets. This year, with the help of Dora, parents are also invited to host their own Trike-A-Thons as neighborhood or birthday party events. During the past three years, the program has averaged more than $8 million a year in fundraising support for St. Jude.

The Koziol family knows the value of that lesson in charitable giving. The day after their 5-year-old daughter, Katelyn, participated in her preschool’s Trike-A-Thon, she was admitted to St. Jude. Now in remission, Katelyn is still undergoing treatment for acute lymphoblastic leukemia, the most common form of childhood cancer.

“We had no idea it could happen to us,” said her mom, Michelle. “You don’t realize what a difference donating even a small amount of money makes. It’s good to have your children get involved with a program like Trike-A-Thon. They learn it’s important to help their friends.”

For more information on Trike-A-Thon, visit [www.stjude.org/trike](http://www.stjude.org/trike).
Sweet Relief

A new generation of pain management brings smiles to the faces of children with cancer.

BY LIN BALLEW

PAIN CONTROL is essential for a patient’s comfort and for healing. Just ask David and Wendy Goodman, whose son, Michael, underwent limb-sparing surgery in 2006 for Ewing sarcoma, a solid tumor that was located below his knee.

Doctors at St. Jude Children’s Research Hospital managed to save Michael’s leg, but the pain after the operation was excruciating. “All they could do was keep him on morphine,” David recalls. “Michael went to sleep in pain and woke up in pain. He was ornery, too.”

Cancer and its treatment almost always cause pain. Tumors press on nerves, bones and organs; radiation damages the skin and mucus membranes; chemotherapy agents inflict brutal side effects. In the past, medical professionals concentrated their efforts on eradicating disease. As cure rates increased, clinicians began exploring ways to eliminate suffering. They learned that by controlling pain they could actually speed recovery. That’s why St. Jude clinicians constantly seek better strategies for treating pain—and why they are excited when they make progress in alleviating it.

Michael underwent a second surgery this year. But in the past four years, technology had changed dramatically. This time, St. Jude clinicians were able to provide Michael with a portable pain pump that allowed him to take control of his pain.

“It was like night and day with the pump. He only had minimal pain, and he was able to quickly get around by himself,” David says.

The equipment that wrought such a dramatic transformation in Michael’s life is making a difference at St. Jude every day. Everything about the new generation of pump is better, says Roland Kaddoum, MD, of St. Jude Anesthesiology. The older pumps were large and bulky, heavy and expensive, and relatively fragile. The new generation of pain pump is much smaller—about the size of a grapefruit—sturdy and much less expensive. The chief appeal of this pump, however, is the freedom it offers children and their families.

Children who are at home or at one of the St. Jude housing facilities no longer have to travel to the hospital every time they need an adjustment to their IV pain medications. With the new pump, a patient leaves the hospital with a special key that dials a predetermined amount of pain medication. The pump is set by a pharmacist, and the patient can then dial medication delivery to meet individual pain needs.

The entire effort surrounding pain issues is multidisciplinary at St. Jude, according to Kaddoum. The Pain Management Service, Pharmacy, Nursing Education, Patient Education and the patient’s primary medical team all work together to reduce or eliminate the pain caused by cancer and its treatment. The final result is that children undergo less suffering and feel like they are in control. As 12-year-old Michael and his parents can attest, that’s sweet relief.

Roland Kaddoum, MD, of St. Jude Anesthesiology explains the workings of the portable pain pump to 12-year-old Michael Goodman.

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Mary Bird says she will never forget the first time she visited St. Jude Children’s Research Hospital. It was 1997, and she and a friend were passing through Memphis while on vacation.

Mary thought it would be interesting to see the hospital that she and her late husband, Robert, had supported as Partners In Hope for so many years, so she asked her friend if she wanted to stop for a tour.

“That visit was when I got serious about my support,” she says. “It was very emotional. You can feel the hope. You can see the wonderful things that are happening, and you want to be a part of them.”

Shortly after returning home, Mary decided to set up an endowment at St. Jude in memory of Robert, who had died of lymphoma the year before.

“It seemed like a good way to honor my husband, who was truly a wonderful man, so kind and loving,” she says. Robert had owned Modern Engineering and Acetylene Gas Co. (joint companies), and also served as president, chief operating officer and director of Atlas Redevelopment Corp. In his spare time he raised Missouri Fox Trot horses on their farm outside of St. Louis.

Mary has given generously toward the endowment each year, and has chosen to make her support unrestricted “so that it can be used where it is most needed.”

Last year, 12 years since her first visit, she returned to the hospital with her daughter, Lisa Waddell. “I saw so many advancements and additions from the time I had been there before,” she says.

In addition to seeing the hospital, they toured an infectious diseases lab with Richard Webby, PhD, and listened to him explain ongoing St. Jude research into H5N1 and H1N1 influenza viruses.

A highlight of their trip was seeing the plaque paying tribute to the Robert Bird Endowment, located outside the board room in the hospital.

As they stopped to view the plaque, Mary explained to Lisa why she continues to give so generously to St. Jude.

“Robert was very religious, and he always told me, ‘Don’t forget the church.’ It’s not that I don’t support the church, but St. Jude is doing the Lord’s work – the hospital has become my church,” she explains.

She adds that she hopes to return to St. Jude again with other members of her family. In addition to her two children, she has five grandchildren.

“Seeing St. Jude on television is one thing, but when you walk the halls and see it for yourself, you understand how wonderful a place it is,” she says.
Defying the Odds

St. Jude researchers expand the use of a rare immune cell to help patients like Jordan James thrive.

BY MARY POWERS

As the sun slants through the lobby of the Patient Care Center at St. Jude Children’s Research Hospital, a toddler with bright eyes and a ready smile stages an epic struggle between a stuffed, orange moose and a plastic giraffe. First the giraffe attacks; then the moose fights back. Within minutes both toys soar high into the air. “He loves wrestling,” explains Chancelly James, as she watches her 2-year-old son, Jordan, scoop the toys off the floor and offer high-fives to the lobby’s late-afternoon crowd. “Who is that?” Chancelly asks Jordan, pointing to the moose. “That’s robot,” he says, switching into the appropriate stiff-legged robot gait.

Not bad for a boy doctors had feared would die in infancy or would be profoundly disabled. “We had never had a tragedy like this in the family,” says Patricia James, Jordan’s grandmother. “We all just got together and prayed. As long as he was alive, we could deal with him not being able to see or walk or talk or whatever. We just wanted him alive.”

A rough start

The first challenges surfaced in July 2007, when Jordan was less than 2 days old. Chancelly was recovering from a C-section delivery when Jordan, her only child, suffered a seizure. Within hours, both mother and child were in an ambulance speeding toward Memphis. Doctors at their Louisiana hospital had told Chancelly simply that there was something bad in Jordan’s blood and that St. Jude would take it out.

The next hurdle emerged shortly after their arrival at St. Jude. Scott Maurer, MD, a St. Jude oncology fellow, felt a bulging mass on top of Jordan’s head. Tests quickly revealed the problem. Jordan had suffered a bleed so severe that the back half of his brain—including regions responsible for vision, speech, hearing and movement—was obscured by blood. The same leukemia that threatened the newborn’s life was likely responsible for the hemorrhage and seizure.

Leukemia is a cancer of certain white blood cells. Jordan was born with a rare form of the disease known as transitional B-cell acute lymphoblastic leukemia (ALL). Normally, B cells make antibodies that help protect against bacteria, viruses and other germs. But Jordan’s B cells failed to mature properly and become fully functional. His blood stream was clogged with immature B cells, causing pressure to increase inside his blood vessels and probably triggering the bleed into his brain.

Jordan’s cancer complicated efforts to treat the hemorrhage. A neurosurgeon advised against a surgical procedure to ease the pressure inside his skull, fearing it might spread his cancer. The bleed also prompted doctors to delay the start of chemotherapy.

“It was a scary situation,” Chancelly recalls. Patricia adds, “Dr. Scott [Maurer] was trying to calm us down while telling us the truth. He and the other doctors would sit us down and tell us the possibility something would work and the possibility it wouldn’t work.”

Rare but mighty warriors

Jordan faced long odds. Infant leukemia is rare. Of the estimated 450 cancer patients who arrive at St. Jude annually, only two or three are infants with leukemia. Under the best circumstances, Maurer says, just 15 percent of patients like Jordan are cured.

But here Jordan’s story takes another turn, this time for the better. By late summer, he was out of intensive care. Separated from family and friends, Jordan’s mother and grandmother were building a St. Jude family. With chemotherapy, Jordan’s cancer had disappeared. But doctors warned that without further treatment his leukemia would eventually return.

For patients like Jordan, doctors often recommend a procedure called a hematopoietic stem cell transplant.
Jordan James was born with a rare form of the disease known as transitional B-cell acute lymphoblastic leukemia. He received transfusions of stem cells and natural killer cells from his mom, Chancelly. More than two years after the transplant, Jordan remains cancer free.
The treatment involves replacing the diseased stem cells in a patient’s bone marrow with cells from a healthy, matched donor. Siblings typically make the best donors because having the same parents increases the odds that two individuals will carry the same markers on their cells’ surface. Those markers help the immune system distinguish between normal cells and invaders to target for destruction. Mismatched markers raise the risk that a patient will develop a potentially fatal complication known as graft-versus-host disease.

As an only child, Jordan was not a candidate for that treatment. Instead, on February 14, 2008, he became one of the first infants with leukemia to join a St. Jude pilot study using immune cells known as natural killer, or NK, cells.

NK cells are the immune system’s warriors. The cells circulate widely in the body, armed with proteins that are capable of delivering a deadly one-two punch to viruses and cancer cells. Scientists recognized the cancer-fighting potential of NK cells more than 30 years ago, but until recently efforts to use them were hampered. There are few NK cells, and those that could be isolated from donors did not always target tumor cells. NK cells account for just 5 to 10 percent of lymphocytes, or white blood cells.

Pioneering new treatments

St. Jude has emerged as a leading center of research into using NK cells as a possible cancer treatment. Wing Leung, MD, PhD, director of Bone Marrow Transplantation and Cellular Therapy, is pioneering efforts to better match cancer patients like Jordan with the parent or sibling whose NK cells will provide the biggest anti-cancer punch. Meanwhile, work led by Dario Campana, MD, PhD, of Oncology and Pathology, is enhancing not only the supply of NK cells available to treat patients, but also those cells’ ability to more effectively target and kill a variety of cancer cells.

NK cells now play a role in at least four St. Jude treatment plans for children battling leukemia and sarcomas. Another St. Jude trial using NK cells is expected to open later this year. Investigators hope NK cells will extend cures by targeting cancer cells that survive chemotherapy.

“All immune therapies, including NK cells, promise to be able to treat patients who are resistant to chemotherapy because they work in a totally different way,” Campana explains. NK cells are also being tried against a variety of adult cancers, including multiple myeloma and cancers of the head and neck. Campana’s laboratory is collaborating in those efforts with centers in the United States and Japan.

His laboratory developed the patented techniques that helped fuel international interest in NK cells. The methods are designed to ensure an adequate supply of NK cells to treat patients. As a result, it now takes just one week for scientists to take donor NK cells and increase their number 100 times. Campana said the technology raises hope it might soon be possible to give patients multiple infusions of NK cells that can find and destroy cancer cells.

All or nothing

Campana’s team has also developed a strategy to modify donor NK cells to better target cancer cells. The resulting NK cells carry an artificial receptor on their surface. That receptor helps the NK cells recognize and link to a particular protein on the surface of the most common type of ALL cells. Once the two cells find each other, the NK cell works to destroy the leukemia cell. Campana said this research provides a platform to hone the anti-cancer properties of NK cells.

Leung has taken a different approach to developing NK cells as cancer weapons. About five years ago, he directed efforts that clarified the function of a family of genes that play a pivotal role in NK cells. Those genes carry instructions for making proteins called killer immunoglobulin-like receptors or KIRs. Carried on the surface of NK cells, KIRs help the immune cells recognize and kill cancer cells. Leung and his colleagues demonstrated the importance of checking for the KIR protein on the NK cells, instead of simply determining whether individuals carried the gene.

“NK cells are all or nothing,” Leung explains. KIR proteins help determine whether NK cells attack cancer cells or ignore them. The proteins are the basis of the NK...
donor selection recommendations that Leung’s laboratory produces for St. Jude and the cooperative childhood cancer research organization known as the Children’s Oncology Group.

Leung and his colleagues are working to make NK donor selection even better. They recently published evidence suggesting tiny variations in the composition of KIR proteins either enhance or diminish the NK cells’ cancer-fighting ability. Investigators are now checking to see if the differences might better predict transplant outcomes.

**Breaking the mold**

Jordan’s family hoped NK cells could offer a cure. Both Chancelly and Jordan’s father were screened as potential NK cell donors. Tests indicated Chancelly’s cells offered the best hope.

In a process much like a blood donation, clinicians removed stem cells from Chancelly and treated them to remove other immune cells that might attack Jordan’s healthy tissue. The stem cells were then transfused into Jordan, who had received powerful anticancer drugs to eliminate his own diseased cells. A week later, Jordan received a second infusion, this time with NK cells isolated from Chancelly’s blood. Investigators hope the combination of stem cells and NK cells will be safer and more effective than a stem cell transplant alone.

During the month following the transplant, his doctors recognized that—despite the hemorrhage he had suffered in infancy—Jordan was behaving like a healthy baby.

Maurer entered Jordan’s room a day after transplant to find the child playing patty cake.

“Jordan was smiling. He could see the person he was playing with. He could make the complex movements needed to play the game,” Maurer recalls. “It was an epiphany moment. I thought to myself: ‘This kid is going to grow up, go to school and do great things with his life.’”

Now, more than two years after his transplant, Jordan remains cancer free. His health and development are closely monitored at St. Jude. Jordan’s speech has lagged a bit, but Maurer says the toddler who loves wrestling and dancing is an example of the infant brain’s resiliency. Following the bleed, undamaged regions of Jordan’s brain took on additional tasks. That helps explain why Jordan is now busy learning his letters and has such a good time singing and banging on the piano.

“This kid broke the mold,” Maurer says. “You hear stories about patients like this, but you never think you’ll meet one. He should not have survived either the cancer or the bleed.”

**Never give up**

Leung says Jordan exemplifies the hospital’s commitment to the dream of St. Jude founder Danny Thomas that no child should die in the dawn of life. “Jordan had all the high-risk features you don’t want in a patient,” Leung says. “But we never give up.”

Infants like Jordan are not the only cancer patients who may benefit from treatment with NK cells. Leung and his colleagues also conducted research involving 10 children with acute myeloid leukemia (AML) who received NK cells from parents. The children had completed standard therapy with anti-cancer drugs and were in remission when they received the donor NK cells. Nearly three years later, all participants remain cancer free.

An editorial that accompanied a report on this research in the *Journal of Clinical Oncology* praised the St. Jude approach, predicting it could have far-reaching implications for improving treatment of AML.

St. Jude oncologist Jeffrey Rubnitz, MD, PhD, says although it is too soon to credit the NK cell transplant for the continued remission of patients involved, the finding helped launch a nationwide study of NK cells as a possible alternative to stem cell transplant in some children with AML.

For Jordan’s family, St. Jude is a second home. An aunt makes an annual trip from Louisiana to Memphis to volunteer. Other relatives participated in the December marathon and 5-kilometer race held in Memphis to benefit St. Jude.

Chancelly still recalls her relief when she learned she would not have to pay for Jordan’s care. “They really do spend the funds they raise on the kids,” she says. “But I fell in love with this place when I arrived. The people at St. Jude really have a love for kids.”

“**This kid broke the mold. You hear stories about patients like this, but you never think you’ll meet one. He should not have survived either the cancer or the bleed.**”
In 1986, Eric Blumer’s life was spared. Now he “gives back” through his work as a police officer for the city of Memphis and through his involvement in the St. Jude Life program. “Sometimes when I’m in the hospital, I can tell that the kids are looking at my patient armband,” he says. “I hope that they have a chance to grow up to be as big and strong as I am, and that my presence gives them a little inspiration.”

St. Jude for LIFE

By Elizabeth Jane Walker

Thus far, nearly 900 adults have returned to St. Jude as participants in a unique follow-up study. These patients are continuing their relationship with St. Jude—for life.

In 1986, Eric Blumer’s life was spared. Now he puts it on the line every day.

“I love being a police officer,” says Blumer, who began treatment for acute lymphoblastic leukemia at St. Jude Children’s Research Hospital when he was 5 years old. “Being an officer is my way of giving back.”

Another way he shows his gratitude is through his participation in St. Jude LIFE. Three years ago, the hospital began one of the most ambitious follow-up projects ever conceived—an initiative that brings childhood cancer survivors back to campus to study the long-term effects of their disease and its treatment.

At first, employees, visitors and patient families were surprised by the sight of adult patients strolling the corridors. But now that nearly 900 former patients have returned for St. Jude LIFE evaluations, their presence has become commonplace. Participants even discover they are a source of inspiration to the families.

“A lot of the kids and their parents look at me with my armband, and they say, ‘You’re a survivor?’”
Then they want to know my story,” says Heidi Fowler, who received treatment for Wilms tumor (kidney cancer).

“Back in 1975, I had less than 30 percent chance of survival because my grapefruit-sized tumor had been ruptured during exploratory surgery at another hospital,” Fowler says. “I gladly tell families my story, and they say, ‘You’ve given us so much hope.’ That means the world to me.”

Welcome back

When St. Jude opened its doors 48 years ago, children with cancer faced a virtual death sentence. Today, more than 80 percent of those patients survive their disease. Unfortunately, health problems often occur as a result of cancer or its treatment. St. Jude investigators have found that adult survivors of pediatric cancer encounter significantly higher rates of health issues than their peers—problems such as second cancers, an increased incidence of heart and lung disease; and a variety of psychosocial and behavioral issues.

Other institutions have attempted to conduct follow-up studies, but their success has been impeded by their need to rely on surveys and questionnaires to gather data. St. Jude is the world’s first institution to embark on an initiative that provides a uniform clinical assessment for such a large group of childhood cancer survivors.

Researchers expect that results garnered from St. Jude LIFE will help in the development of safer therapies for new cancer patients and will help identify survivors who may be at risk for specific health problems during adulthood. That’s why Jackie Jerry agreed to participate in the study, 30 years after a diagnosis of ovarian germ cell tumor.

“I’ve had no secondary problems as a result of my treatment, but I think St. Jude LIFE is going to be wonderful for a lot of other patients,” says Jerry, who has worked as a nursing care assistant at St. Jude for 16 years.

Unlike Jerry, who has watched the hospital’s growth firsthand, many participants are overwhelmed by changes that have occurred since their departure.

“It was kind of surreal to come back to the hospital. I didn’t know what to expect,” observes Doug Hostetler, a Maryland resident who received treatment for non-Hodgkin lymphoma when he was 11 years old. “I enrolled in St. Jude LIFE for my own benefit—to find out if I had any health problems—and for the benefit of children who will come after me.”

All participants in St. Jude LIFE undergo risk-based assessments based on the specific treatment they received as children. For instance, clinicians evaluated how the therapy Hostetler received in 1983 has affected his heart, bones and neurological system. His testing ranged from a thorough eye exam and bone density analysis to dietary counseling, an echocardiogram and a session with an exercise physiologist.

The frequency of follow-up visits depends on each survivor’s risk profile. Most St. Jude LIFE participants will return to the hospital once every couple of years.

Survivors at risk

The study’s first three years have yielded some startling results, says Melissa Hudson, MD, principal investigator for St. Jude LIFE.

“Of 70 women who were at risk because of chest radiation, we identified nine who had breast cancer,” Hudson says. “This group is considered to have a risk comparable to that of women who have the breast cancer gene. I’m not surprised that they have a high incidence of breast cancer, but I’m shocked that they were either unaware of their health risk or that they simply failed to

After Doug Hostetler (center) visited campus for his St. Jude LIFE checkup last fall, he and his family decided to forego Christmas presents and instead provide DVDs for the children of St. Jude. Doug; his wife, Sheri; his sister-in-law, Becki; and six children drove from Maryland to Tennessee to deliver the gifts in person.
undergo suggested screenings, which should begin at age 25, or eight years after radiation. Many times, doctors in their communities were not advising the screening, either.”

Hudson admits that community physicians generally encounter few, if any, childhood cancer survivors.

“It’s much more common to see survivors of adult malignancies,” Hudson says. “Childhood cancer survivors have unique health issues. We have to figure out the best ways to communicate that information to health care providers.”

St. Jude investigators are also discovering many cases of heart disease in the study’s participants.

“They have health problems that we typically see in populations that are aging,” Hudson says.

Many survivors are overweight, inactive and have high cholesterol or diabetes—conditions that can exacerbate cancer-related problems such as heart disease.

“We’re seeing these conditions in younger people who generally are not practicing health behaviors that can help reduce or control their risks,” Hudson says. “They need to know how important it is to make lifestyle changes to maintain their health.”

As a result of these issues, St. Jude LIFE investigators are looking at ways to ensure that more survivors receive regular health screenings in their communities, practice healthy behaviors and understand their health risks. Based on data obtained through St. Jude LIFE, researchers are already planning intervention studies.

Heidi Fowler still deals with the effects of treatments that saved her life back in 1975. In addition to affecting her colon and ovaries, the radiation she received greatly increases her risk of skin cancer. Fowler agreed to participate in St. Jude LIFE in spite of anxiety caused by memories of childhood medical procedures. “I was nervous at first, I must admit, but I said yes because I want to do anything I can to help the children of St. Jude,” she says. “I’m truly blessed and happy to be a part of this study.”

Jackie Jerry undergoes testing in the Human Performance Lab under the watchful eye of Clinical Exercise Specialist Webb Smith. Unlike most St. Jude LIFE participants, Jerry did not have to travel far for her exam—she works at St. Jude as a nursing care assistant in Nursing Surgical Services and Sedation. “This study is all about helping people who will come after us,” she says. “If St. Jude can use what they learn from us to help other patients, that will be great.”

Helping tomorrow’s survivors

Eric Blumer considers himself a lucky man. With a broad smile, he counts his blessings: He is healthy and has a great job and family. His 4-year-old stepdaughter views him as a superhero who “catches bad guys.”

But Eric is not just helping citizens by keeping the streets safe. He’s also helping scientists improve treatment for today’s children and for other adult cancer survivors.

“St. Jude did so much for me,” Eric says. “I figured I could do my part to help them find out what long-term effects may be happening to me and to others. Hopefully, those studies will also help future survivors.”
For most cross country runners, those attributes are an outgrowth of training.

As eighth grader Broox Middleton anticipated a high school running career, he figured he already knew a little about perseverance. Years before, he had survived a brain tumor. Then, as a middle school athlete, he had run through rain and mud and suffocating heat. He had inhaled the acrid scent of dust and desire. He had grown stronger, tougher, faster.

Perseverance? Yeah, Broox knew a lot about that. And then he got cancer. Again.
For a competitive athlete, one faltering step can mean the difference between victory and defeat. For a 5-year-old boy, one rogue cancer cell can have the same outcome.

In 1995, Broox was more interested in rounding the bases on a T-ball field than in running a 5K. When he began suffering from headaches and nausea, his parents, Fara and Alvin Middleton, suspected the culprit might be migraines. During a subsequent checkup, the physician prescribed a pain reliever, and then said, “I don’t really have a reason to order an MRI, but let’s just go ahead and do one to be on the safe side.”

That intuitive move may have saved Broox’s life.

The MRI revealed a large brain tumor situated near the center of his brain. Immediately, the neurologist sent the scans to several cancer centers.

“All of the hospitals said that they could remove part of the tumor, but probably couldn’t get all of it because it was in such a dangerous area. They said he would also have to undergo radiation and maybe have a shunt in his head,” recalls Fara.

In the midst of the decision-making process, the Middletons received advice from a parent whose child had been treated at one of those hospitals: “If I had it to do over again,” she said, “I would go to St. Jude.”

The Middletons’ neurologist sent Broox’s scans to Amar Gajjar, MD, director of the Neuro-Oncology Division at St. Jude Children’s Research Hospital. “When we saw the films, we knew that this was a juvenile pilocytic astrocytoma and that we could take it out,” Gajjar says.

According to Gajjar, each year about 500 children in the United States are found to have this type of tumor, which arises from star-shaped brain cells called astrocytes. Broox had a low-grade astrocytoma, which is a localized, slow-growing tumor.

The Middletons arrived at St. Jude just in time. The night before the operation, Broox permanently lost his vision on the right side.

**Stepping out in faith**

The day of Broox’s brain surgery, Alvin and Fara prayed and paced, their hearts beating like feet on pavement. “I was terrified,” Fara says. “The only thing that gave me comfort that day was reading the book of Psalms and knowing that God had placed us in the hands of the best doctors in the world.”

St. Jude surgeon Robert Sanford, MD, was able to remove the entire tumor. In addition, the 5-year-old did not have to undergo the radiation therapy that had been a standard treatment offered by other hospitals.

Broox has clear memories of the days following the operation. “I remember when they moved me from ICU to a room, I felt pretty good,” Broox recalls. “But the first time I tried to walk, I had no feeling in my right leg.”

Broox regained the ability to walk within a couple of weeks and soon returned home. For the next few years, he visited St. Jude for regular checkups with Gajjar and eventually transferred to the hospital’s After Completion of Therapy (ACT) Clinic, which provides long-term follow-up for patients whose disease has been in remission for five years.

“At that point, I thought, “Wow. I can put this behind me. I never have to deal with this again,” Broox says.

**A different course**

During middle school, Broox discovered that he had a gift for
running. By Christmas of his 8th grade year, he was already anticipating an exciting athletic career.

“He had high hopes of making the cross country team as a high school freshman,” Fara says. Then—thanks to the education he had received in the ACT clinic—the 14-year-old identified a suspicious lump. Surgeons at a local hospital opted to remove the mass. Before the operation, a physician tried to reassure Fara. “I’ve consulted with about 10 of my colleagues, and we don’t think it’s cancer,” she said. “There’s just no way that a child could have two unrelated cancers.”

“Dr. Gajjar had always told us that you never really know for sure until you do a biopsy,” Fara says. “So I just thanked her. But when the doctor came out of the ER, she was crying. She said, ‘I’m so sorry. I am just so sorry. It’s cancer. What can I do?’”

“I was shocked,” Broox recalls. “I thought I was through with being the ‘cancer kid,’ and then out of nowhere I found out that I had it again.”

Fara and Alvin called Gajjar, who advised the family to return to St. Jude, where Broox could undergo treatment under the guidance of Sheri Spunt, MD, who specializes in solid tumors.

“Dr. Spunt is another angel in our lives,” Fara says. “She was so calm and was such an inspiration to Broox.”

Spunt explained that Broox was, indeed, facing a totally different type of cancer. This time, he had an embryonal carcinoma, a malignant tumor that develops when germ cells divide rapidly and erratically. Since the local hospital had removed the mass and had identified no metastases, the physicians decided to monitor Broox’s condition closely.

“OK, I’m back to my old self,” Broox thought. But a few months later, the cancer returned. “They said it was mostly in my lymph nodes,” Broox recalls. “Once again, I was totally shocked.”

**Running toward recovery**

In the film *Chariots of Fire*, runner Eric Liddell muses, “Then where does the power come from, to see the race to its end? From within.” Like Liddell, Broox quickly learned to lean upon his faith and to draw on inner reserves of strength. Chemotherapy treatment, he discovered, would not be a sprint, but an endurance race.

The grueling cycles of chemotherapy seemed to drag on forever.

“When he was hospitalized for chemo, there were times he was too weak to even brush his teeth,” Fara says. Between each cycle of chemotherapy, Broox would return home to recuperate. “A few days after we’d get home, Broox would try to run,” Fara recalls. “His dad and I would walk alongside for a mile, and Broox would huff and puff and try his best to make it.”
Thus Broox began his slow run toward recovery.

“When I was in the hospital, all I could think about was getting out and making more of my life,” he says. “During middle school I had not been serious about running track. But after I had cancer, I needed to do it. I wanted to prove that I could do it after having chemo and cancer.”

Gradually, Broox regained his stamina and, when he tried out for track during spring semester of his freshman year, he made the team.

“That spring, I wasn’t very good,” Broox admits. “I came in last place in several races, but I was just so happy to be out there.”

As his strength returned, his times improved, eventually allowing him to make varsity and twice compete in the state’s cross country championships.

**Finishing the race**

Although Broox hung up his cross country spikes when he enrolled in his university’s industrial engineering program, he still enjoys a daily run and frequently participates in area road races. But running is no longer his sole passion.

“Because of my experiences, I have a whole new outlook on life,” he explains. “Nobody can really understand what it’s like unless they have gone through it.”

That’s why Broox spends time counseling young cancer survivors at summer camps. He helps construct houses for the poor. He serves meals to the homeless. He raises money for St. Jude.

“If other people hadn’t helped St. Jude,” he says, “I wouldn’t have been able to go there for treatment.”

Altruism has even played a role in Broox’s career choice, which he says combines his aptitude for math with an interest in helping others.

“Industrial engineering will help me do both,” he says.

That attitude of gratitude runs in the family. Fara recently co-chaired a new St. Jude fundraising relay from Memphis to Mobile, Alabama. (Visit www.stjudeonthebay.com for more details.) Unfortunately, because of final exams at college, Broox was unable to participate in this year’s event, but he hopes to do so next year.

“When Broox got cancer, I would have sold all my worldly possessions to get the best treatment for him,” Fara says. “But thanks to St. Jude, I didn’t have to do that. I do the fundraising work because I have benefited. I also do it for friends we made at St. Jude who lost their lives. I want to see cures; I want other children to benefit like Broox did.”

**Strength. Endurance. Perseverance.** Broox and his parents are experts on those topics.

And cures? Yeah, Broox knows a little bit about that, too.
They have glue on their fingers and smiles on their faces; crayons spread before them and kids crowded around them. They’re the Volunteens of St. Jude Children’s Research Hospital. The enthusiasm these fresh-faced teenagers bring to the hospital energizes the children undergoing treatment for cancer and other catastrophic diseases.

The St. Jude Volunteens program enables teens to explore career paths and develop leadership skills while helping children. Each year, the highly competitive program seeks 30 participants between the ages of 16 and 18 with strong character and high spirits. Each applicant must write an essay as part of the stringent application process.

Volunteers visit the hospital two days a week for six weeks. To plan activities for both patients and siblings, the teams begin by perusing scrapbooks that previous cohorts of teens have created. Each new team, in turn, leaves a scrapbook for future groups. Many Volunteer projects have included arts-and-crafts or game themes. In addition, participants assist other volunteers with story time or with the Happy Cart—a game distribution system on wheels.

In addition to helping the children of St. Jude, Volunteens also explore possible career paths, develop leadership and team-building skills, improve their interpersonal skills, increase their self-awareness and interact with a diverse population of people.

“It’s more than an opportunity to give back your time,” says Kathryn Berry Carter, Volunteer Services director. “It’s a learning experience where teens learn about our mission and one day, hopefully, become more involved as donors, adult volunteers or even employees.”

Mary Greer Simonton has a special perspective on her experience in the program. She first came to St. Jude at the age of 4, suffering from rhabdomyosarcoma, a soft tissue tumor. Years later, she returned to the hospital as a Volunteer.

“I remember there wasn’t much to do when I was here as a patient,” she says. “It’s so nice to provide such an outlet to the patients.”

As part of the program, Volunteens learn about possible career paths in research, child life, social work and many other areas. The participants meet clinicians, scientists and hospital staff who serve as role models.

“Listening to professionals share their jobs and backgrounds with us helped,” Mary Greer says. “Now that I’m in college, I’m using a lot of what I learned about organization and leadership through the Volunteens program. It was a great experience.”

If you know teens who might be interested in participating in the 2011 Volunteer program, encourage them to plan ahead. Applications generally open in January, and space is limited. For more information, visit www.stjude.org/hospitalvolunteers.
Hope Is a Remedy

“St. Jude is the greatest place in the world—where hope lives every day.”

My battle with cancer started in March of 2001. About two weeks before that time, I was sitting at my kitchen table with my family, directly across from my aunt. She looked at me and commented that my neck had a knot on it. My family and I observed the knot and feared it could be serious. The next day, my mother took me to my family physician, who ran a series of tests. The doctor couldn’t find out what the problem was, so she referred me to an ear, nose and throat (ENT) specialist who did a biopsy the next week.

When the results from the biopsy came in, the ENT told us to go into his office and sit down. I was 8 years old when he told my family that I had cancer and that he was going to send me to St. Jude Children’s Research Hospital in Memphis, Tennessee. He told us that I had nasal cancer and that it was very rare.

The next week, my family drove to Memphis. When I walked into the hospital, I could feel the love in the atmosphere. I was amazed at how big the hospital was.

I had the greatest doctors and nurses. I was not nervous, because when I would come into the hospital, the doctors would embrace me with love. I received seven weeks of radiation and six rounds of chemotherapy. The next year, I was cancer free. I am now 17 and have been in remission for eight years.

St. Jude is the greatest place in the world—where hope lives every day. The doctors and nurses there have inspired me to do better in life. They gave me love when I needed it most. By inspiring me to work hard on anything or any problem I’m faced with, they made me the strong and determined person I am today.

St. Jude saved my life. They never asked me to pay a dollar, thanks to the generous donations of partners. I am now in the eleventh grade, and I’m president of my class. Because of St. Jude, I am a straight-A student. After I graduate in 2011, I will go to college and major in vocal music education and eventually receive my doctorate in music composition.

I will never forget what St. Jude did for me, and I will continue to support them in every way that I can—believing and living the promise that Danny Thomas made, that “No child should die in the dawn of life.”

High school junior Keyone Docher is a St. Jude cancer survivor. One day he hopes to become a famous composer and pianist. He enjoys playing his piano and riding his horses.
You can play a vital role in helping secure a healthy future for children battling cancer with a gift to St. Jude Children’s Research Hospital® through your will. Join others who share the desire to leave a legacy of hope to catastrophically ill children by considering a bequest gift to St. Jude. To learn more about these special gifts and the Danny Thomas – St. Jude Society recognizing these contributions, please call us at 800-395-1087, visit www.stjudelegacy.org or complete the enclosed postage paid envelope today.

*Tess, 4 years old, neuroblastoma*

Your legacy can be her future.

You can play a vital role in helping secure a healthy future for children battling cancer with a gift to St. Jude Children’s Research Hospital® through your will. Join others who share the desire to leave a legacy of hope to catastrophically ill children by considering a bequest gift to St. Jude. To learn more about these special gifts and the Danny Thomas – St. Jude Society recognizing these contributions, please call us at 800-395-1087, visit www.stjudelegacy.org or complete the enclosed postage paid envelope today.

*Ensure that our research continues until the day we have conquered childhood cancer. The promise of your charitable legacy helps make it possible.*

The St. Jude Child Life department presented “All About the Body” week in March 2010. The week included a series of events focused on different body parts or systems. Interactive activities helped patients and siblings learn more about how the body functions. Pictured, Amy Scott of Child Life instructs patient James Richmond on how a stethoscope works. During the activity, patients and siblings created their own stethoscopes, blood pressure cuffs and medical collages out of the provided materials.