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Promise

A publication of St. Jude Children's Research Hospital Spring 2003

Eagle's
Wings
page 12



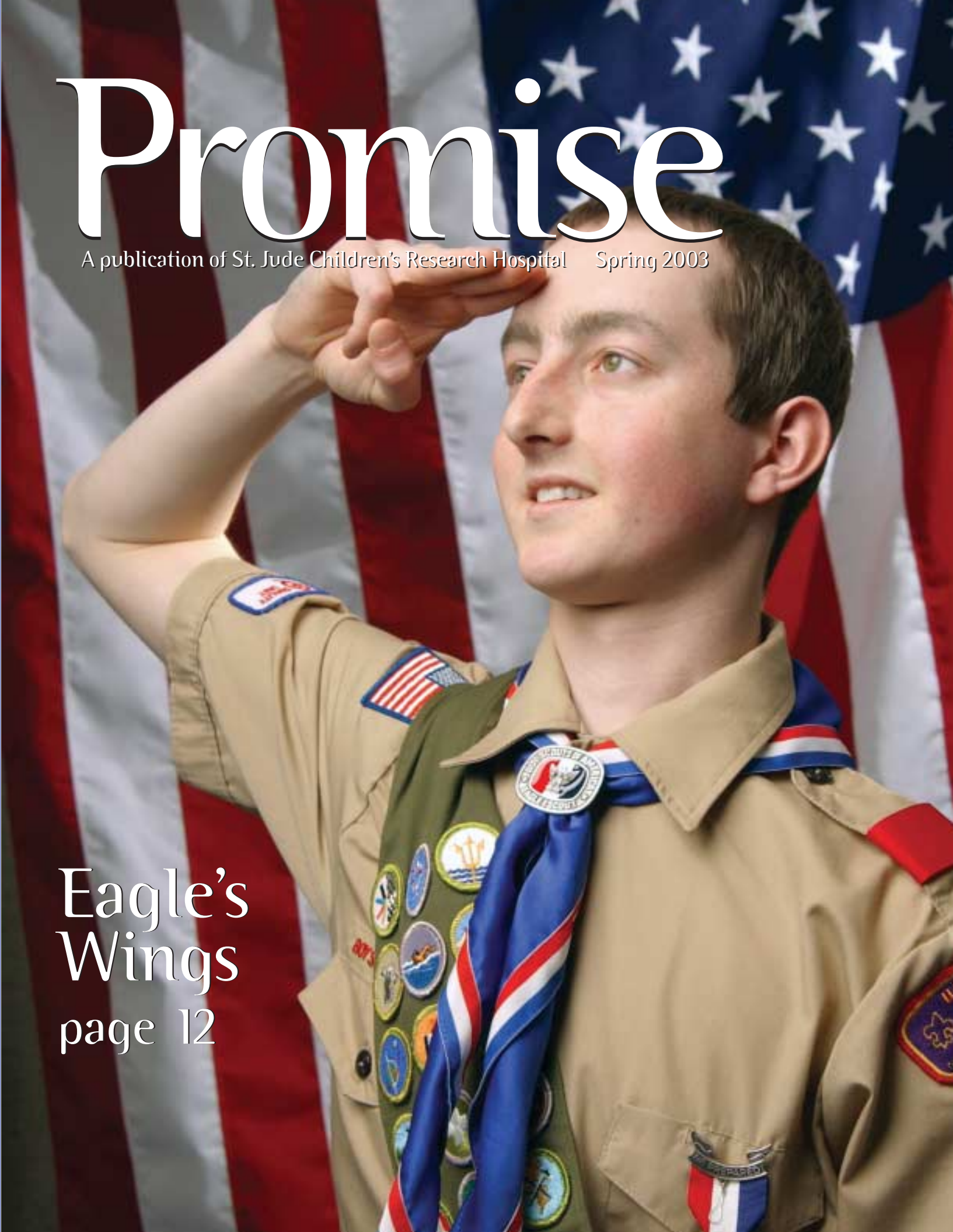
St. Jude Children's
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St. Jude Children's Research Hospital was founded by the late entertainer Danny Thomas. It opened February 4, 1962. The hospital was created because of a promise Danny made during the depression era to St. Jude Thaddeus, the patron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

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

Promise.



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

Promise

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

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Broadcasting the mission

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On the cover: St. Jude patient Jacob Littrell (see article, page 12). Many thanks to American Flag and Flagpole Co. for providing the flag used in this shot. Photo by Seth Dixon.

Highlights

Foiled again

St. Jude investigators have shown how cooperation between influenza virus and bacterial pneumonia infections can be foiled, even if treatment is delayed and flu virus levels in the lung have peaked.

Jonathan McCullers, MD, of St. Jude Infectious Diseases showed that the flu virus enzyme neuraminidase (NA) strips lung cells of molecules called sialic acid. The unprotected cells are then vulnerable to infection with bacterial pneumonia. But treatment with the drug oseltamivir blocked the activity of NA and offered protection against pneumonia. The findings appeared in the March 2003 issue of the *Journal of Infectious Diseases*.

The study is important because influenza and pneumonia together are the sixth leading cause of all deaths worldwide, and the top cause of death due to infection.

Brain power

Researchers have discovered a critical, early step in the embryo that is required for proper development of the human brain.

That step is controlled by the product of a gene called *Six3*, which guides the formation of the embryonic part of the brain called the forebrain. The forebrain is destined to contain the eyes, olfactory center, cerebrum and other structures. St. Jude scientists showed that the *Six3* gene ensures proper development of the forebrain by halting the activity of another gene that controls development of other more posterior parts of the brain. The discovery is an important step toward defining a critical regulatory pathway for normal brain development.

A team of scientists led by

Guillermo Oliver, PhD, and Oleg Lagutin, PhD, of Genetics published the study in the February 2003 edition of *Genes & Development*.

Bait and switch

A new immunologic “bait and switch” technique developed at St. Jude allows researchers to use a genetically engineered protein “bait” to lure rogue immune cells to their deaths.

The St. Jude strategy pitted the genetically engineered immune cells called T lymphocytes against a population of T cells that cause a brain disease. The genetically engineered cells reduced brain damage by destroying the T cells that caused the disease. The discovery offers hope for treating multiple sclerosis, rheumatoid arthritis and other autoimmune diseases caused by T cells. The technique also may be useful for slowing or preventing the body’s rejection of transplanted organs and tissues.

The research, led by Terrence Geiger, MD, PhD, of St. Jude Pathology, was featured in the December 2002 issue of *Nature Biotechnology*.

Primordial Genes

St. Jude researchers appear to have looked back in time. They have discovered that the *Arf* gene was once moderately effective in slowing down cellular reproduction until it linked up with a more efficient set of genes to create a powerful anti-cancer response.

Arf was already known to have cancer-suppressing activity. A St. Jude team found that *Arf* may have evolved to slow the cell’s metabolism and growth by limiting production of ribosomes, which guide production of all

other cellular proteins. The researchers showed that *Arf* interferes with production of the RNA components of ribosomes to control protein production and cell growth.

The discovery was made by Howard Hughes Medical Institute Investigator Charles Sherr, MD, PhD; Masataka Sugimoto; Mei-Ling Kuo, PhD; and Martine Roussel, PhD, all of St. Jude Genetics and Tumor Cell Biology. A report on the findings was published in the February 2003 issue of *Molecular Cell*.

Child’s play

Child magazine has named St. Jude as one of the top five children’s cancer hospitals in the United States. The rankings appeared in the February 2003 issue of *Child*.

To be considered for the *Child* magazine survey, a hospital must belong to the National Association of Children’s Hospitals and Related Institutions. *Child* narrowed the field, based on each hospital’s evaluation by the Joint Commission on Accreditation of Healthcare Organizations. St. Jude received an overall score of 98 out of a possible 100 points during the hospital’s last accreditation survey in 2000.

National award

Robert Webster, PhD, of St. Jude Infectious Diseases recently received the Twelfth Annual Bristol-Myers Squibb Award for Distinguished Achievement in Infectious Diseases Research for his pivotal role in the understanding of the origins, evolution and approaches for control of epidemic influenza virus. Webster received the \$50,000 cash prize and a commemorative silver medallion at a dinner held in his honor in New York in December.

A Whole Lot of Lovin’ Goin’ On

BY ALICIA H. MATTHEWS

Elvis fans find much more than music in Memphis.



contributions to the hospital. When they decided it was time to plan their estate, they picked up the phone and called St. Jude. That call led to a meeting with a St. Jude representative in their region.

“When we met with the rep, she did not try to point us in one direction or another,” Anne says. “She just listened to what we had to say, gave us options and took our future needs into account. We have been pleased with every aspect of St. Jude.”

Because the Welshes don’t have children, they chose St. Jude as recipient of their estate. At every opportunity, they

Donald and Anne Welsh plan to bequeath their estate to St. Jude. They are pictured with Terre Thomas, daughter of St. Jude founder Danny Thomas, and St. Jude patients (from left) Brenan Rodgers and Nikki Orrell.

Twenty-five years ago, Donald and Anne Welsh of Drums, Pennsylvania, traveled to Memphis in search of a rock ‘n’ roll legend. In the process, they found a world-renowned hospital.

The Welshes came to Memphis in 1978 to visit Elvis Presley’s home, Graceland. As longtime Elvis fans, they fondly recall their visit that year as they tried to locate Elvis’ old school and the trauma center to which he donated money. In the process, they found St. Jude Children’s Research Hospital. After reviewing hospital publications and learning about the institution’s mission, the couple was impressed.

Today, the Welshes are still Elvis

“To see the work done at St. Jude just makes you want to do more.”

fans and zealous advocates for the work being done at St. Jude. “You can hear about the hospital, but you have to experience it,” Donald says. “To see the work done at St. Jude just makes you want to do more.”

“I don’t think there is another hospital on earth that does more,” adds Anne. “The love shows through in all the employees. Everyone is so caring. They make you feel like part of the family.”

Several years after that initial visit, the Welshes began making monthly

try to encourage others to consider donating to St. Jude as well.

“The first thing people want to know is don’t we have any family to leave our possessions to,” Donald says. “But the gift to St. Jude lets me make a mark in life. I wish we had the words to make people know how phenomenal the hospital is.”

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



ANN-MARGARET HEDGES

A rousing game of thumb wrestling between Torrey Sandlund, MD, and Ricky Mahar always has the same outcome: a victory for Ricky. Thanks to the A-T clinic at St. Jude, patients with ataxia-telangiectasia now have a better chance to vanquish cancer.

two thumbs up

BY ELIZABETH JANE WALKER

ST. JUDE OPENS THE WORLD'S FIRST CLINIC SPECIFICALLY DESIGNED FOR PATIENTS WHO HAVE CANCER AND A RARE GENETIC DISORDER CALLED ATAXIA-TELANGIECTASIA.

Every time Ricky Mahar goes to a checkup at St. Jude Children's Research Hospital, he challenges his doctor to a wrestling match.

And every time, Ricky wins.

Torrey Sandlund, MD, is quick to concede that 8-year-old Ricky is the undisputed thumb-wrestling champion. Each week, Ricky anticipates the moment when he can clasp hands with Sandlund for a game of dueling digits.

"Ricky loves to thumb-wrestle, and he has beaten me every time," Sandlund says. "But we have staring contests, too, where we stare at each other and see who laughs first. I win those; he always laughs first. So we are each undefeated in our respective areas of competition."

The camaraderie and affection between physician and patient have grown since September 2002, when Ricky traveled from New York to enroll in a new protocol, or scientific treatment plan, at St. Jude. Earlier that month, Ricky learned that he had non-Hodgkin lymphoma, a cancer of the lymphatic system. Because Ricky also has a disorder called ataxia-telangiectasia (A-T), his body would not tolerate traditional cancer treatment. So doctors at Johns Hopkins Hospital in Baltimore, Maryland, suggested that Ricky travel to St. Jude, which houses the world's only clinic specifically designed for A-T patients who have cancer.

The one-two punch

Children with ataxia-telangiectasia (pronounced A-TACK-see-uh Teh-LAN-jick-TAY-sha) have a rare, inherited neurological disorder. "Ataxia" refers to a loss of muscle control caused by degeneration of the cerebellum, the part of the brain that controls motor function. Children with this condition become increasingly clumsy, and their speech becomes slurred. Gradually, they lose their ability to write, talk and walk. Because their muscle control progressively diminishes, most A-T patients are wheelchair bound by age 10 and rarely live beyond their teens. Although they have normal intelligence, they have trouble reading because of jerky eye movements. Children with A-T also develop "telangiectasia," or tiny red spider veins in their eyes and on exposed areas of the skin.

Tim and Lisa Mahar vividly recall the day a doctor told them that Ricky had A-T, a disease that afflicts about 500 children in the United States. "The doctor had never had a patient with A-T before," Lisa says. "When he was giving us the diagnosis and telling us about it, he had a book in front of him, reading to us about it. He pretty much told us, 'This is what he has. There's no treatment; there's no cure; end of story.'"

The couple soon learned that their son's risk of developing a malignancy could be as high as 30 percent. Their worst fears were realized when

Ricky developed non-Hodgkin lymphoma. “We were completely shocked, because we knew that this could happen, but we didn’t think it would happen this soon,” recalls Tim.

Sandlund says a cancer diagnosis is the crowning blow to most parents of A-T patients. “These families are already stressed to the max, going through far more than most of us could ever imagine,” he says. “They’re watching their kids little by little losing ground. Then, on top of that, they find out that their kids have cancer. It’s like a one-two punch.”

Fighting back

Because children with A-T are extremely sensitive to radiation and cancer-fighting drugs, they do not respond well to traditional cancer therapy. Until recently, a diagnosis of cancer in a child with A-T meant a bleak prognosis.

“A lot of doctors thought that if A-T patients were sensitive to radiation, then they were also sensitive to everything else. So they wouldn’t treat the children, and they’d die of the cancer. Or they’d treat them very mildly,” says Michael Kastan, MD, PhD, chair of St. Jude Hematology-Oncology.

Kastan has been studying DNA damage in A-T patients for more than a decade. Using what he learned in the lab, he began designing treatment plans that he thought patients could tolerate. Physicians around the world began calling him for suggestions about treating their A-T patients who had cancer. “I would give them advice based on my experience with the few patients I had seen,” Kastan explains. “I would say, ‘please keep me informed about how they do—what toxicities you see, and what responses you get, so that I can continue to modify the advice I give.’” But the busy physicians rarely called back. The frustrated researcher then hit upon a solution. What if St. Jude created a cancer clinic just for A-T patients—a central location where research and treatment could occur simultaneously?

That’s exactly what happened in autumn of 2002. “We’re willing to take any patients in the world who have A-T and get cancer,” Kastan says. “St. Jude opened this clinic because there was a need for it. If we don’t do it, no one’s going to, and treatment would continue to go as it’s been going—a patient here, a patient there, and no one getting enough experience to know how to improve therapies.” The St. Jude specialists share what they learn with hospitals around the globe; that means children who have A-T and cancer can come to St. Jude for treatment or stay in their

hometowns. If they choose the latter option, their doctors will work closely with the investigators at St. Jude.

With a team of St. Jude researchers and clinicians united with a common goal, children who have A-T and cancer now have a better chance for survival, observes Kastan. “I can’t think of a disease that’s more devastating than A-T,” he says, “but we can cure the cancer in a significant number of these patients and hopefully let them live for many more years.”

Building on success

Long before the new clinic opened, Kastan and Sandlund began developing the protocol for children with A-T. They knew that the clinic’s patients would have unique problems that must be addressed. With a hypersensitivity to ionizing radiation, these patients must avoid radiation therapy and drugs that produce similar effects. Because A-T patients have trouble tolerating one of the cornerstone drugs used in lymphoma treatment, the investigators built in protective measures to eliminate those problems. As Kastan and Sandlund developed the protocol, they modified therapy to adjust for other challenges as well.

The A-T protocol combines several existing St. Jude treatment plans. Each is modified to account for the unique toxic effects experienced by A-T patients. The investigators included treatment plans for such diseases as high- and low-risk acute lymphoblastic leukemia, large-cell lymphoma, Burkitt’s lymphoma, lymphoblastic lymphoma, Hodgkin disease and non-Hodgkin lymphoma. Pooling their expertise, Kastan, Sandlund and colleagues from departments across the institution spent two years writing the protocol. “Basically, the best chance for curing cancer in children with A-T is based on strategies that we know work in children who don’t have this condition,” Sandlund says. “This multidisciplinary effort is for a very small number of patients, but why should they receive any less of an effort to cure their cancer than people who have much more common cancers?”

Sandlund says the investigators hope to learn much more about the kinds of cancers that children with A-T develop. The researchers also study blood samples from A-T patients for DNA breakage, in an effort to see if these patients are more sensitive than other people to chemotherapy.

“The academic questions are important,” says Sandlund, “but frankly, the most important purpose of this protocol is to provide the best therapy we can come up with for these kids.”



Michael Kastan, MD, PhD (at right), chair of St. Jude Hematology-Oncology, and Christopher Bakkenist, PhD, also of Hematology-Oncology, have discovered a process that helps cells in the body respond to DNA damage. The researchers expect that the discovery will lead to exciting new therapeutic approaches and prevention methods.

Scrutinizing genes

Scientists in Kastan’s laboratory at St. Jude investigate how cells respond to stresses such as DNA damage. Although some DNA-damaging agents can cause gene mutations, cell death or cancer, others—such as chemotherapy and radiation therapy—are used to cure cancer. So researchers are interested in understanding exactly how cells respond when their DNA is altered. If scientists can learn to manipulate the cell’s response to DNA damage, they might be able to create ways to prevent cancer or to make therapies more effective.

The gene that is mutated in ataxia-telangiectasia is called *ATM*. Children have a one-in-four chance of having A-T if both of their parents carry the faulty gene. Cells from children with ataxia-telangiectasia lack the ATM protein, which leaves them extremely sensitive to radiation. Kastan and his colleagues are trying to identify a drug that will inhibit that protein. By inhibiting ATM, they may be able to make all tumor cells more sensitive to radiation. If an ATM inhibitor were given during radiation therapy for a brain tumor, for instance, the radiation would be much more potent.

The ATM protein is a kinase, an enzyme that signals to other proteins by modifying them. ATM adds a phosphate molecule to the other proteins in a process called phosphorylation. Several years ago, Kastan discovered that the *ATM* gene phosphorylates the tumor-suppressor gene *p53*, the most commonly

mutated gene in human cancer. Scientists in Kastan’s lab have also identified eight other proteins that are modified by ATM. All eight play roles in causing different kinds of cancer.

Kastan and Christopher Bakkenist, PhD, of Hematology-Oncology recently discovered a process that helps cells in the body respond to DNA damage. The researchers found that such damage activates ATM almost immediately. The ATM enzyme leaps into action, phosphorylating other proteins that play important roles in cancer prevention. If this process does not occur, then the cell cannot respond to radiation; that is what happens to children with A-T, who lack the ATM protein.

Understanding this novel biochemical process lays the groundwork for learning how to manipulate it, Kastan says. “This is a really big breakthrough, because it’s

the first step in everything that happens to the cell when it’s been damaged,” he explains. “It’s a unique mechanism for an enzyme. Out of this research, we’re hoping to find a way to activate these pathways without damaging the DNA. We expect that this discovery will lead to new therapeutic approaches and prevention methods.”

Everyone’s a winner

Today, Sandlund is decked out in a jaunty Sponge Bob Square Pants necktie, a gift from Ricky, who is an aficionado of the underwater cartoon. Ricky dutifully admires the necktie, but his primary focus is on the inevitable thumb-wrestling match and an imminent homecoming. The boy has no idea that his departure marks the culmination of years of planning and research; he is unaware that his involvement in St. Jude research may help save the lives of other patients like himself. No, Ricky is much more concerned with chalk-ing up another victory against his arch-rival and best buddy.

“I’m really going to miss Ricky and his family when they go home,” Sandlund says, “but it’ll be nice to know that they’re going home because he has done well. If Ricky was the only kid we ever treated, I would still say this protocol—and all the time we have invested in it—would have been worth it.”

Ricky has won once again.●

FOLLOWING THE Clues

BY CARRIE L. STREHLAU

Why are children in southern Brazil more susceptible to a rare type of cancer than children in other parts of the world? St. Jude researchers and clinicians spend more than a decade unraveling the mystery.

In 1987, Raul Ribeiro, MD, finished his postdoctoral training at St. Jude Children's Research Hospital and returned to his home in Brazil. During his St. Jude fellowship, Ribeiro had treated children with many types of cancer. But when he returned to Curitiba, several of his young Brazilian patients had a kind of cancer he had not encountered during the years he spent in Memphis.

The Brazilian children had adrenocortical carcinoma (ACC), a rare tumor that grows on the adrenal gland located at the top of the kidneys. "Children with ACC were coming to me in large proportions," says Ribeiro, who has been director of the St. Jude International Outreach program since 1997. "In three years at St. Jude, I hadn't seen

any ACC cases. I was seeing six or seven in this small part of Brazil in just one year. I thought to myself, I know there is something abnormal here."

Possible culprits

In southern Brazil, the incidence of ACC is 10 to 15 times higher than in other parts of the world. At first, Ribeiro thought that the most likely explanation for the ACC prevalence was Li-Fraumeni syndrome. Members of families with this syndrome have an especially high risk of developing many kinds of cancer. But after conducting

careful clinical histories of Brazilian patients with ACC, Ribeiro found that the families did not

have histories of cancer. In 1990, he sent tumor and blood samples to St. Jude to test the function of a tumor suppressor gene called *p53*.

When cells grow, develop, complete their mission in the body and die, they are controlled by several proteins and genetically determined pathways. One of these regulators is the tumor suppressor gene *p53*, which regulates cell survival and death. "In general, *p53* is present in all cells controlling growth, development and cell fate," Ribeiro explains. A mutation in the *p53* gene increases the likelihood of having ACC. The tests at St. Jude showed the *p53* function was normal. "Nobody believed that we had a *p53* mutation," says Ribeiro.

"I had two strikes against me," he continues, "but we sequenced the *p53* gene in 1994 just to make sure." They subsequently discovered



St. Jude researchers have been working closely with Bonald Figueiredo, MD, PhD, of the Center for Molecular Genetics and Cancer Research in Brazil.

that a *p53* gene mutation had occurred after all, but that it had occurred on a new location on the DNA.

“Ninety percent of the mutations occur in the DNA binding domain, so people have not traditionally bothered to look at the outside areas,” says Gerard Zambetti, PhD, of Biochemistry. This mutation had occurred outside of that binding domain.

Gathering evidence

With the new information, Ribeiro and Zambetti called Richard Kriwacki, PhD, of Structural Biology. In 1999 the three men began collaborating to develop a genetic explanation for the specific type of ACC occurring in the children of Curitiba. Kriwacki identified a previously unknown defect in the structure of the *p53* protein that made it fall apart at certain pH levels, ultimately leading to the onset of ACC. The collaborators published their findings in the journal *Nature Structural Biology* in 2002, and are continuing to follow up with more studies of the *p53* protein.

“One of the unique features of this particular case is that very often when people have mutations to *p53*, they develop a wide variety of different cancers,” Kriwacki says. “In this particular case, the mutation is associated with one type of cancer. By looking at this mutation, we have an opportunity to get clearer insights into the molecular pathways leading to the development of cancer.”

Researchers at St. Jude are closing in on a probable explanation for the tumor development. “There is a pH-dependent defect in the mutant protein,” Kriwacki explains. “So, it suggests that in adrenal cells during early development, certain changes—best described as cellular remodeling—occur in the adrenal gland. This remodeling may cause the environment to be slightly basic or may elevate temperature slightly. There has to be something special about the adrenal gland to explain why only these cells

develop into tumors.”

“The *p53* protein consists of 393 amino acids,” Zambetti adds.

“Change just one and you get adrenal cancer. That’s what’s remarkable about this mutation.”

The *p53* mutation identified by the St. Jude team increases children’s chance of developing adrenal cancer—and only adrenal cancer—by 300,000 fold, according to Zambetti. “This is the first inherited *p53* mutation that gives rise to a specific tumor type,” he says. Zambetti and his colleagues are currently exploring the possibility that another *p53* mutation outside of the DNA binding domain may be responsible for a rare form of brain tumor that seems to have an inherited component. “We don’t have an answer yet to this specific case, but we’re working on it,” he says.

Early apprehension

The information gleaned from St. Jude researchers is helping clinicians already. Physicians in Curitiba are now more alert to the symptoms of ACC and can detect them earlier

than they could in the past. “Now that they know there’s a genetic link, they’re tracking all of the children in these families that have the mutation,” Kriwacki says. For the past two years, children at risk for adrenocortical carcinoma in Curitiba have been screened and monitored regularly for early symptoms of the disease.

Physicians have used the new information to develop treatment plans and a screening method. They closely observe ACC patients’ siblings to see if they exhibit signs of cancer; if symptoms occur, they begin treatment immediately. “We now have more than 70 patients we are following who have tested positive for a mutation but have not developed the cancer yet,” Ribeiro says. Staff members at the clinic in Curitiba have seen more than 100 patients with ACC.

The St. Jude researchers have been working closely with Bonald Figueiredo, MD, PhD, of the Center for Molecular Genetics and Cancer Research in Brazil. The discovery linking a *p53* mutation with ACC has helped Figueiredo and his staff identify the mutation in many relatives of ACC

“The *p53* protein consists of 393 amino acids. Change just one and you get adrenal cancer. That’s what’s remarkable about this mutation.”

patients. “The most important contribution of this research is the possibility of a cure we can now offer to children who test positive for the mutation but do not have ACC and who are enrolled in our surveillance program,” says Figueiredo, who has tested more than 600 individuals for the mutation. Figueiredo says he believes that ACC-related deaths will decrease because of the new surveillance program.

Figueiredo says the infrastructure of his institution has improved through association with St. Jude, and he cites numerous scientific and training opportunities that have resulted from the involvement. Videoconferencing has been one important window of research communication between St. Jude and Brazilian researchers. By using video technology, the colleagues can collaborate almost as easily as if they were sitting in a room together. Ribeiro also shares his expertise in person and on the phone. He travels to Curitiba twice a year to visit the center and give lectures. And physicians from around the world frequently call him for consults about their patients who have ACC.

Ribeiro says researchers are now exploring why ACC is prevalent in such a small area of the world. “The region in Brazil in which this is frequent is not the entire Brazilian area,” Ribeiro says. “We are trying to see if we can figure out if there are environmental or other reasons for the prevalence.”

Carlos Rodriguez-Galindo, MD, of St. Jude Hematology-Oncology is also leading an effort to create a multi-institutional protocol with the

Children’s Oncology Group for children in both the United States and Curitiba who have ACC. In addition to treating children with this rare tumor, researchers will study the biology of the tumors and the incidence of the different types of *p53* mutations, identifying any similarities or differences that appear in patients from each country. Rodriguez-Galindo predicts that the protocol will begin sometime in 2003, and may eventually expand to include children from other areas of southern Brazil, as well.

Joining forces, saving lives

A child in Paris, France, was recently found to have the mutated *p53* gene, so researchers suspect that the problem may extend far beyond the geographical boundaries of southern Brazil. As St. Jude researchers expand their focus to look outside the DNA binding domain, they may find that the mutation occurs more frequently than they had expected. To address this possibility, St. Jude has established an International Pediatric Adrenal Tumor Bank, which allows researchers to access samples from around the world and screen them for *p53* mutations and other genetic alterations.

By collaborating to attack a problem, researchers in the International Outreach program, the Hartwell Center for Bioinformatics and Biotechnology and other St. Jude departments are ensuring a brighter future for Brazilian children with adrenocortical carcinoma. Zambetti is pleased that interdisciplinary teamwork can have such far-reaching con-



Bonald Figueiredo, MD, PhD, of the Center for Molecular Genetics and Cancer Research in Brazil poses with patients who have benefited from the St. Jude research: Erick Quadra (top photo) and Kelly Felde and her daughter (bottom photo). Now 26 years old, Felde inherited the *p53* mutation from her father and passed it on to her daughter, who is now in the ACC surveillance program.

sequences. “Our work is making a difference,” he says. “All through my graduate training and postdoctoral work, my research has been focused on trying to figure out how things work using cell lines we can grow in the lab. Going from growing cell lines to actually helping kids...that’s the most rewarding part.”

Translational research—the ability to move discoveries from the laboratory to the bedside—is one of the hallmarks of St. Jude. In unraveling the *p53* mystery, researchers and clinicians have shown how collaborations can save the lives of children in other parts of the globe who may never even know about St. Jude Children’s Research Hospital.

“This project is sort of amazing not only in the scientific sense, but because it really exemplifies the mission of the hospital,” Kriwacki says. “The full resources of this institution have been brought to bear on the basic understanding of the origins of the disease and the effort on how to cure diseases better in the future. It’s really been an amazing opportunity.”



Stalking the gene that causes adrenocortical carcinoma in Brazilian children are three super-sleuths (from left): Gerard Zambetti, PhD, of Biochemistry; Raul Ribeiro, MD, of International Outreach; and Richard Kriwacki, PhD, of Structural Biology.

EAGLE'S WINGS

By Elizabeth Jane Waller



One St. Jude patient honors veterans while waging a war against cancer.

When

he's wearing his full Boy Scout regalia, Jacob Littrell's chest is covered with a kaleidoscopic array of badges. Each emblem represents a skill that Jacob has acquired or a challenge that he has surmounted. With every accomplishment, the 17-year-old from Iowa has exhibited grit and determination, leadership and selflessness.

But Jacob Littrell's most impressive badge of honor is not emblazoned on his uniform's sash. It's imprinted on his heart.

"Be Prepared" is the scout motto, and one that Jacob has embraced since kindergarten, when he joined the organization as a Tiger Cub. As he moved through the ranks of scouting—from Tenderfoot to Second Class, First Class to Star to Life—he learned to embody that motto, even earning a "Scholarship" honor badge for his academic preparedness. Jacob camped in the rain; hiked rocky trails; climbed high mountains. He mastered skills to help him safeguard the environment and enhance his community. But when the teen learned that he had cancer, "Be Prepared" assumed a new meaning. Although the diagnosis took him by surprise, Jacob kept his focus, marshaled his inner reserves and persevered.

On my honor...

Jacob, his parents and his 13-year-old sister, Lauren, live in a small town—the perfect place for a young man who loves to ride dirt bikes, work on car motors, canoe, fish, wage paintball wars and rappel off 300-foot cliffs. Bolstered by his family, friends, church and scouting involvement, the lanky, 6-foot-tall teen is a role model for his friends, acquaintances and other scouts.

One day in the spring of 2001, Jacob ran a mile in gym class. That evening, his right hip began to hurt. A few weeks later, his hip again ached after a run. When Jacob visited the doc-

tor, an X-ray revealed a tumor. A biopsy indicated that the high school freshman had osteosarcoma, a type of bone cancer. Jacob's aunt and uncle suggested that he visit the St. Jude Children's Research Hospital affiliate site in Peoria, Illinois. There, John McCallister, MD, sat down with Jacob and his parents, Jeff and Carol Littrell, and told them what to expect.

"He was very honest and truthful about what Jacob's treatment would probably be," recalls Carol. "He talked to Jacob like he was capable of understanding. The parents are important at St. Jude, but you can tell that the kids are the most important thing to the people who work there. I was impressed with that." Jacob was impressed, as well. "We found out about St. Jude, and it was the way we wanted to go right from the get-go," he says. Soon afterward, the family drove to Memphis so that Jacob could have a complete evaluation and begin chemotherapy. After undergoing three months of chemotherapy, doctors at St. Jude removed the tumor, as well as several inches of Jacob's femur and his hip joint.

"His hip is now made out of cobalt, chrome and titanium," explains Carol. "He's the bionic man. He even sets off alarms at the airport!"

I will do my best...

The young outdoorsman spent six grueling weeks trapped in a body cast. After removing the tumor in Jacob's leg, doctors decided to remove a nodule in Jacob's left lung. So on September 11, 2001, as a numbed nation quaked from terrorist attacks, Jacob—still in the body cast—traveled with his parents down the deserted highways to Tennessee. After that operation, Jacob continued chemotherapy at the St. Jude affiliate in Peoria for another eight months. Then, once again, the Littrells received disturbing news: more nodules had appeared in



Jacob's lung. A second operation in June of 2002 revealed malignant cells. That meant another six months of chemotherapy.

"A thoracotomy is tough," says his mother about the two lung operations. "Six months later, he was still sore from them. For the longest time, he couldn't give me a bear hug because it hurt too bad."

For the past two years, Jacob has endured multiple operations and countless infusions of chemotherapy drugs. How has he coped with the uncertainty and the pain and the sickness?

He has helped others.

Jacob Littrell has planned, executed and completed an ambitious service project that honors local Iowans who served in the U.S. armed forces.

To do my duty...

The highest rank a Boy Scout can achieve is the Eagle designation. Fewer than 4 percent of all scouts attain that rank. To become an Eagle Scout, a boy must exhibit leadership and citizenship skills, high ethics and a working knowledge of the outdoors. After progressing through the levels of scouting, Eagle candidates must have completed at least 21 merit badges. Before his illness, Jacob already had earned more than 30. The only obstacle blocking his way was the service project, which is intended to provide Eagle candidates with an

COURTESY OF THE QUAD-CITY TIMES



"We had a list of veterans' names, and I thought that we were going to go out there and see which ones had markers and which ones didn't; then we would just order the number of markers we needed." Wrong.

The project quickly assumed a life of its own. Armed with a list of veterans provided by the American Legion, Jacob and his dad visited the cemetery, which includes nearly 2,200 civilian and military graves. Jacob immediately realized that the cemetery had a chaotic record-keeping system. Vandals had moved or stolen many of the markers. Strolling through the grounds, the Littrells found markers for veterans who were not on the list. "We walked out into that cemetery and thought, 'Holy moly, there are so many stones!'" recalls Jeff. "And the plot maps they had were very outdated and hard to understand." Jacob told his father, "We've got to come up with our own map." So they divided the 25-acre cemetery into 49 sections and created a detailed map of the grounds. Realizing that the local veterans'

Jacob places a gleaming, new marker at a veteran's grave. Thanks to Jacob, members of the local American Legion post now have detailed and valuable information about their comrades who are buried in area cemeteries.

records were incomplete, Jacob asked his father to help him with research. While Jacob was in



school, his father scoured records in the local Veterans Affairs office. He pored over 22,557 entries, looking for veterans who were supposed to be buried in that cemetery. "It was overwhelming," recalls Jeff. "We found names that didn't coincide with anybody's records."

Jacob also called upon his friends and fellow scouts to help. He handed dimes to the workers, and instructed them to scrape the moss off cemetery stones so that they could read the inscriptions. Some of the stones only protruded a few inches out of the ground, so those had to be raised. "I bet we have walked through that cemetery 200 or 300 times," says Jeff. "Many of those times, Jake would be on crutches."

Gradually, Jacob and his team began to make progress. As a result, Jacob identified 80 veterans who had not been previously identified. Today, the cemetery and the American Legion have new maps showing where each veteran is buried, plus databanks containing detailed information about each person's service record. Jacob also expanded his efforts to encompass another small cemetery nearby.

To God and my country...

Because of Jacob's hard work, the members of the American Legion post have learned that the two cemeteries contain veterans of conflicts dating back to the Black Hawk wars of the 1830s, the Civil War and the Mexican-American War.

Tom Bloomingdale of the American Legion is amazed at the

Three days before he discovered that he had osteosarcoma, Jacob demonstrated his athletic prowess by leaping from a tower and rappelling to the ground. Rappelling is only one of the many skills Jacob mastered en route to earning his Eagle Scout designation.

scope of Jacob's achievement. "Jacob went further than we ever thought he would go," says Bloomingdale. "He put 800 to 1,000 hours into this project in between his cancer treatments. He has been an inspiration to everyone."

"Jacob carried it to completion under the most adverse conditions imaginable," Bloomingdale continues. "Now everything is updated and documented on the computer. Someone within the American Legion can carry it on from here."

Bloomingdale and his comrades wanted to find a way to thank the boy who had shown such courage and strength while waging his own war with cancer. So last November the veterans held a special ceremony to honor the young warrior who had been such an inspiration. As Jacob quietly accepted his award, every veteran in the room stood and saluted a fellow hero.

And to obey the Scout Law

Jacob does not perceive his project as heroic or extraordinary. He says he never considered the possibility of abandoning the Eagle project when he got sick. Fortunately, he had already completed the Eagle requirements that demanded outdoor skills and physical agility. "I knew I'd get the project done," says Jacob. "I just knew it would take a little bit longer than usual because I was dealing with other





Jacob (at far left) has been involved in scouting since the first grade. As he progressed through the ranks, he has participated in countless adventures, such as this journey down the Mississippi River, which occurred when he was in the eighth grade.

things that were more important at the time. I knew that the cancer was only a temporary thing and that this project would get finished.”

Jacob is pleased that his community has responded positively to his efforts, and he feels a sense of accomplishment at having helped others. “I think this project gives all the veterans their due,” he explains. “There were so many veterans buried in that cemetery who didn’t have markers, and it was an injustice to them. This project just kind of gives them the recognition they deserve.”

In earning the Eagle Scout designation, Jacob joins an elite group that includes former President Gerald Ford; William McCool,

pilot of the space shuttle *Columbia*; actor Jimmy Stewart; TV commentator Walter Cronkite; Togo West Jr., former secretary of the Army and secretary of Veteran’s Affairs; and director/producer Steven Spielberg. But Jacob says he’s not interested in fame; he’s more concerned about college and career. “Becoming an Eagle Scout finishes the scouting chapter in my life,” he observes. “I started out at the bottom and I pretty much worked my way up, learning a lot about organization and leadership and stuff like that. It will give me advan-



tages when I apply for college or jobs later in life.”

“I’m so proud of Jacob,” says Najat Daw, MD, the physician who treats Jacob at St. Jude. “He’s very bright and strong-willed.” Jacob’s parents concur with that description. They watched him plan the project, delegate authority and follow the task to completion. “He is our hero,” says his father. “A very brave young man. He doesn’t complain; he just gets it done.”

“Be Prepared.” According to the *Boy Scout Handbook*, this motto implies that scouts should be ready in body and mind to meet the struggles and challenges of life. In earning his wings, Jacob Littrell has shown us all how to fly. •

LAURA HAJAR

Untangling Sickle Cell

BY TANUJA COLETTA

A \$9 million federal grant may help St. Jude scientists reverse the effects of a tiny mutation that causes sickle cell disease.

Winfred Wang, MD, director of the St. Jude Hematology division, has been giving hydroxyurea to 6-year-old Lokia Baldwin, with great results. “Lokia used to feel sick all the time,” says her mother. “Now she doesn’t even get a headache.”

Krista Mills is obsessed with baby dolls. She has scores of them sitting in bookcases and crowding her bed, many tumbling onto the floor. “Whenever I get my allowance, the first thing I want to get is a new doll,” says the grinning 14-year-old. “I love to hold them.”

As a collectors’ catalog featuring a new line of realistic dolls seizes Krista’s attention—she has her heart set on a newborn wrapped in a soft, pink blanket—her mother stares at her from across their kitchen. Wendy Mills’ wish is simply for her own baby to grow into a healthy woman, free of the sickle cell disease that has plagued Krista since birth.

She has reason to be optimistic.

St. Jude Children’s Research Hospital, where Krista is a patient, has been awarded a \$9 million federal grant that may help scientists discover sickle cell’s elusive cure.





LAURA HAJAR

After suffering two strokes because of sickle cell disease, Krista Mills had to cope with the loss of some cognitive skills. She is making progress through an expanded resource program at her school. Because teachers are often unaware of sickle cell disease's effects on learning, St. Jude has hired a teacher to work with school officials and parents on issues relating to the disease. The position is one of the first of its kind in the nation. St. Jude is also one of the largest publishers of sickle cell education literature, with a national and international distribution of more than 9,000 items annually.

A five-pronged approach

Although St. Jude is best known for its advances in research and treatment of pediatric cancer, the first grant ever awarded at the hospital went to a sickle cell researcher. That was in 1962, the year the hospital opened its doors. Today, St. Jude is one of 10 Comprehensive Sickle Cell Centers in the country to receive a multi-million-dollar, competitive five-year grant from the National Heart, Lung and Blood Institute. St. Jude is already home to one of the nation's largest sickle cell research centers. The grant will allow expansion of the institution's research and outreach efforts and collaboration with other sickle cell centers.

"This will be our first attempt to

build a national clinical trials network among the Comprehensive Sickle Cell Centers," says Winfred Wang, MD, director of the St. Jude Hematology division and the hospital's sickle cell program. "This approach has been successful in improving outcomes for childhood cancers but has not been established for sickle cell disease." A national clinical trials network will give researchers access to a much larger pool of patients and information than ever before, as large numbers of children and adults with sickle cell disease are treated uniformly across the country.

St. Jude researchers plan to target sickle cell disease with studies in five main areas: combination drug thera-

py, bacterial infection, stem cell transplantation, gene therapy and the molecular biology of hemoglobin development. "If we have success in any or all of these areas, there is potential for tremendous benefit for all sickle cell patients, children and adults," says Wang.

Tragic typo

An inherited disorder of the red blood cells, sickle cell disease is like a typo with tragic results. The disorder arises from a single incorrect letter in the 60,000-letter gene for hemoglobin, the oxygen-carrying protein that gives red blood cells their color. Normally round and soft, cells affected by this mutation resemble micro-

scopic boomerangs. The misshapen cells hook together, forming long rods that clog small blood vessels and deprive organs and tissues of oxygen-carrying blood. The bottleneck leads to episodes of severe pain, organ damage and even death. Regular blood transfusions are the oldest form of therapy, but they mainly combat symptoms, not the underlying disease. Bone marrow transplants have cured sickle cell disease in about 200 patients, but the procedure is not a universal option due to a lack of suitable donors.

About half of the patients with sickle cell disease live beyond age 50, and Krista plans to be a member of that group. She is one of 72,000 Americans with the disease, which disproportionately affects people of African, Hispanic, Middle Eastern, Mediterranean and Indian descent. She inherited one copy of the mutated gene from her mother and one from her father. When both parents carry the trait—a single copy of the mutated gene—each of their children has a one-in-four chance of developing the disorder. Krista's younger sister Katlyn was born with the trait, meaning that she will likely never have sickle cell symptoms but could pass the trait to her children.

Early detection is important because treatment could ward off the painful symptoms. More than 40 states now have a sickle cell screening test for newborns. Wendy Mills wishes Krista had been tested when she was born. The couple didn't find out Krista had sickle cell disease until she had her first crisis at 2 years of age. "She was getting very sick and lethargic," says Wendy. "She would scream in her sleep. The pain was excruciating."

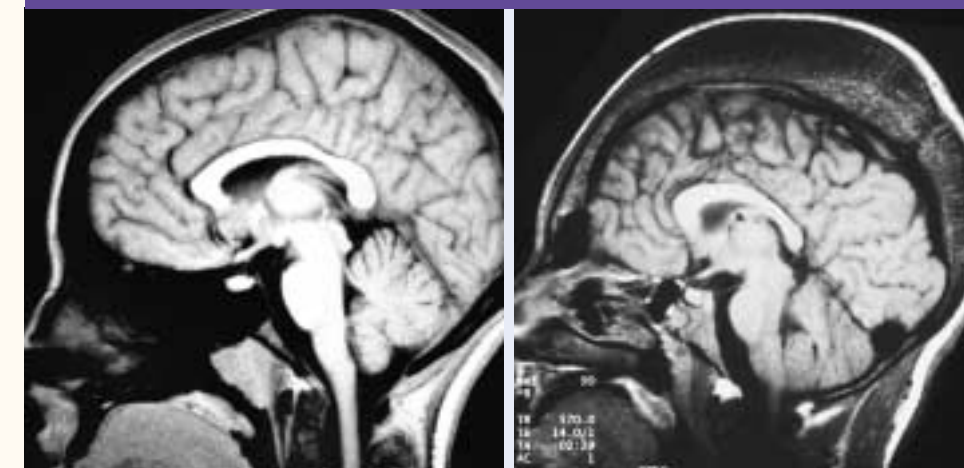
Krista had one or two pain episodes a year. Then, just before her eighth birthday, she suffered her first stroke, a devastating complication of

sickle cell disease. The stroke weakened the left side of Krista's body, causing her to lean to one side and limp. A couple of months later, a second stroke left Krista weak on both sides. The strokes caused seizures, damage to her eye muscles and some

loss of cognitive abilities. Krista began wearing braces on her legs for support.

The Millses were referred to the St. Jude Sickle Cell Program. After much discussion—the family had serious concerns about blood transfu-

Battling Brain Damage



Grant Steen, PhD, obtained these MRI images during a study of young patients with sickle cell disease. The one at left shows the brain of a healthy child. The image at right offers a glimpse of a severe compensation for sickle cell disease: the bone marrow of the skull has proliferated to produce more red blood cells, and this may be squeezing the patient's brain.

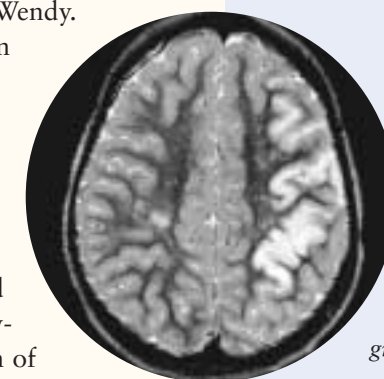
Grant Steen, PhD, of St. Jude Diagnostic Imaging is studying the brains of hundreds of healthy people, from newborns to octogenarians. He hopes that by examining normal brains, he may better understand the brains of children with sickle cell disease.

Sickle cell patients have a 250-fold higher risk than normal of having strokes. Steen is using a form of magnetic resonance imaging (MRI) to demonstrate subtle changes in the brains of many young

sickle cell patients with damaged blood vessels. The damage may be caused by the high rate of blood flow through the brain as the body tries to compensate for a lack of oxygen-carrying red blood cells. Sometimes the body adapts by dilating arteries or expanding bone marrow around the brain. Often, the adjustments still do not allow enough oxygen to reach the brain.

Sickle cell disease provides a good model for studying stroke, which often kills adults.

"The problem with studying stroke in adults is that by the time we reach old age, we have a host of other ailments that mask what's happening with the disease," Steen explains. "We can better understand the idiosyncrasies of pediatric stroke, which is essentially the same process as in adults, since stroke is likely the only brain illness they have."



This MRI image shows the brain of a 3-year-old sickle cell patient who had a stroke. The pale areas at right show damage to the brain. The brightness indicates that there is too much water in this part of the brain, probably because cells in the gray matter have died.

sions—Krista was placed on hydroxyurea, an anti-cancer drug recently approved by the Food and Drug Administration for use in adults with sickle cell disease and frequent pain crises. Trials with children and infants are showing promise, too. “We knew it was experimental, but we were hopeful,” says Wendy. “So far, it has been a miracle for us.” Krista has not suffered any major pain crises or strokes since starting her daily dose of pills.

Hydroxyurea increases the body’s production of a type of so-called fetal hemoglobin, which counteracts the effects of sickle hemoglobin within the red blood cells and reduces the disease’s severity. Wang, who has led St. Jude studies on hydroxyurea, is interested in combining the drug with magnesium. He hopes the combination will further ease symptoms and delay or prevent organ damage to the spleen, kidneys and brain. By age 3, most children with sickle cell disease do not have functioning spleens to help fight infection. The consequence may be a fatal bacterial infection, which in the past has been the leading cause of death in children with sickle cell disease.

Looking deeper

“Sickle cell patients are a curiosity,” says Elaine Tuomanen, MD, chair of St. Jude Infections Diseases. “They are at a 300-fold increased risk of dying of pneumococcal disease, yet no one knows exactly why.”

Tuomanen is studying the antibiotic tolerance level of sickle cell patients, who are often on the infection-fighting drugs for many years. Long-term antibiotic use may eventually lead patients to resist the drugs’ benefits and succumb to bacterial invaders, especially pneumococcus. Because sickle cell patients are on antibiotics for so long, the deadly bacteria learn to out-fox the drugs.

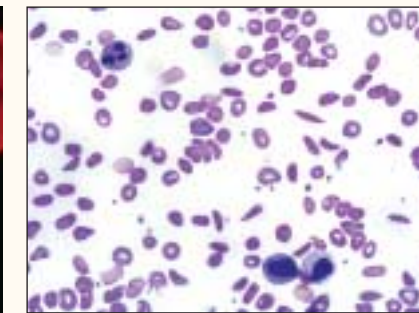
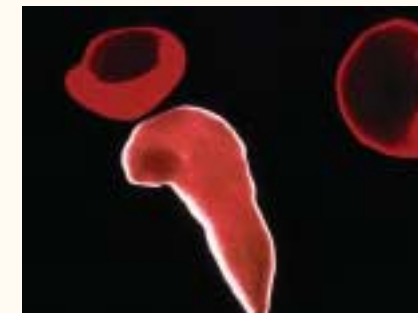
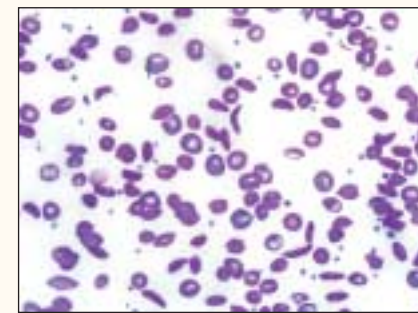
“Bacteria divide every 20 minutes, so they can rethink their game plan every time they launch a new attack,” says Tuomanen. “If you give them long enough, they will certainly figure out a method that works. Unfortunately for sickle cell patients, it’s like they are wearing a red flag telling the bacteria to come take advantage of them.”

Tuomanen models the scenario in her laboratory to help understand why sickle cell patients are at a higher risk for infection than healthy people. Other St. Jude researchers are studying hemoglobin development at the molecular level. Sickle cell disease

was the first disease for which scientists knew the exact genetic defect that caused the malady, but scientists have been unable to translate that knowledge into a cure. John Cunningham, MD, of St. Jude Hematology-Oncology, predicts that new advances, especially in the study of globin genes, will have great impact on sickle cell treatment during the coming decade. “Specifically, the long-term interest of my lab is to understand the switch of gamma globin to beta globin,” he says. During normal development, the genes coding for gamma globin, the kind produced by fetuses, are switched off



St. Jude patient Khadi Toure, 11, pictured with her father, Abdoulaye, was the first child in the country to receive umbilical cord blood from a sibling to treat sickle cell disease.



Instead of being round and soft, sickle cells look like microscopic boomerangs. The misshapen cells can cause severe pain crises, organ damage and even death.

soon after birth, and the body begins producing adult beta globin. “In people with sickle cell disease, with this switch, the sickle cell protein becomes predominant. We are testing approaches to reverse this switch.” The answer could provide clues for the cure of the related blood disease, beta-thalassemia.

Transplants to the rescue

For now, bone marrow transplants offer the best hope for a cure. The first bone marrow transplant to cure sickle cell occurred at St. Jude in 1982 when a leukemia patient underwent the procedure and was cured of both diseases. During a transplant, a patient’s bone marrow—the spongy tissue in the center of bones—is destroyed and replaced with healthy donor tissue. But often, perfectly matched donors are not available. Even if donors are available, transplants are risky: patients may develop graft-versus-host disease, in which the transplanted tissue attacks the patient’s cells.

St. Jude scientists are experimenting with a way to sidestep those complications and allow unmatched donors to supply stem cells for transplants. Produced by bone marrow, stem cells are undeveloped cells that mature into immune and blood cells, including, in some cases, mutated

sickle cells. A technique pioneered by Rupert Handgretinger, MD, PhD, director of Stem Cell Transplantation, isolates healthy stem cells from the cells that can trigger graft-versus-host disease. The method allows patients to receive a higher concentration of stem cells and better tolerate the transplant than they would with traditional bone marrow transplantation.

Sickle cell patients may also benefit from new transplant methods using stem cells in blood from the umbilical cord and placentas of newborns. In 2000, St. Jude patient Khadi Toure was the first child in the country to receive umbilical cord blood from a sibling to treat sickle cell disease.

However, researchers are already looking beyond these therapies to a technique that could rival all others for a cure: gene therapy.

New hope for cures

Still highly experimental, gene therapy is designed to replace the defective gene for hemoglobin. Gene therapy may one day allow doctors to insert a normal gene into a cell to eradicate the disease. One possible gene therapy approach is to permanently increase the level of “good” hemoglobin in the body to overpower the sickling type. “A possibility we

are studying is to take the patient’s own blood stem cells, to correct them and to place them back into the body,” says Derek Persons, MD, PhD, Hematology-Oncology. Viruses are adept at injecting their own genes into cells, so Person and his colleagues are using viruses as “carriers” to insert a healthy hemoglobin gene. The viruses are gutted of their harmful genetic codes and are replaced with the healthy gene. Instead of attacking the cell and causing harm, the virus instead injects the healthy gene into the diseased cell.

“It would still have its risks so it’s not the first thing you try out of the box,” says Persons, “but it’s an option, especially for those without any other recourse.”

Persons is encouraged by the collaboration among St. Jude departments and the new networks growing between the hospital and other sickle cell centers. “We’re coming at this from different aspects,” he says. “You never know where the answer will come from. At the end of the day, it might very well be that the answer lies in a combination of these approaches.”

Krista Mills is counting on it. “I’ve always had a strong sense of faith from my parents and my grandmother that I can do anything,” she says. “I choose to look at that side of the rainbow and focus on what I can do, not on what I can’t. For me, the greatest thing would be to grow up into a good girl like my mother.”●

SETH DIXON

GOPAL MURTHI

Country music fan clubs are competing to raise money for St. Jude kids.

Fan-tastic CHALLENGE

BY JOE HANNA

Country Cares for St. Jude Kids radiothons have become one of the biggest fund-raising programs for St. Jude Children's Research Hospital. Through Country Cares, the fans of country music have raised more than \$181 million in pledges in the program's 14-year history.

But country music star Keith Urban thought they could do much more.

The challenge

The day before the 2002 Fan Fair, an annual gathering where country music stars mingle and greet with fans, Urban invited members of his and other fan clubs to a reception. There he issued what is now known as the "Fan Club Challenge."

Oklaboman Caitlyn Garner benefits from the dedication of country music fans.

Wynonna Judd connects with St. Jude patient Annalisa Burrow, who is in isolation at the hospital. Wynonna's fans are helping raise funds for St. Jude.



JERE PAROBER



LAURA HAJAR

Keith Urban listens intently to St. Jude patient Ishmael Lawrence during a visit to the hospital. Urban has challenged members of country music fan clubs to compete against one another in a St. Jude fund-raising effort.

Urban asked all in attendance to do what they could to raise money for St. Jude through a friendly competition among fan clubs.

This Australian singer/guitarist burst on the country music scene in 2000. Urban's performance earned him the Top New Male Vocalist Award at the 2001 Academy of Country Music Awards and established him as a rising star. The year 2000 also marked Urban's first visit to St. Jude. He toured the hospital as part of the 2000 Country Cares seminar along with other artists and hundreds of representatives from country radio stations around the country. The mission of Danny Thomas, to ensure that "no child should die in the dawn of life," touched Urban's heart.

"One trip to St. Jude will leave you with no doubt that progress is being made," Urban says. "There is no greater contribution to make in our lives than to our children, the future. In sharing their findings with hospitals all around the world, St. Jude continues to help not just the kids who are there but children and their families everywhere. This is why we initiated the Fan Club Challenge. Awareness is the key to continue and grow the support we all have for St. Jude."

Enthusiastic warriors

Country entertainer Toby Keith's fans, or "warriors" as he calls them, threw down the first gauntlet in the Fan Club Challenge. The day after Urban made his challenge, Keith's fans raised \$2,705 through an auction of the singer's memorabilia at the opening day of Fan Fair.

A flurry of activity followed. Fan club Web sites began carrying the challenge to all corners of the country music world. Ideas on how to meet the challenge poured in. Calendar and T-shirt sales, silent auctions, sales of food by individuals and businesses—even collections of aluminum cans—were all ways that groups rallied around the cause.

Fans of country artists Tracy Lawrence, Tommy Shane Steiner, Billy Ray Cyrus, Andy Griggs, Bryan White, Gary Allan, Wynonna Judd and more have joined in the challenge to see whose fan club can raise the most funds.

Urban fans respond

One of Urban's fans opted to sell Keith Urban calendars that featured concert photos submitted by the fans. Response was tremendous, not just in

terms of the photographs, but in individuals wishing to help defray production costs so the total profit from the calendar sales would go to St. Jude.

So far, the Urban calendar has raised \$6,165 for the hospital. That puts Urban's fan club in the lead with more than \$21,000 raised, including a \$10,000 donation from an anonymous fan.

"I am very proud of how the fans have responded; how giving they have all been," says Bettina Tangman, a Web master for keithurbanfans.com. "I am proud of the other fan clubs and I am proud to be a fan of Keith's."

Patients are the winners

Toby Keith's "warriors" followed up their opening salvo with a silent auction through the fan club newsletter, which raised \$2,135. Kay Johnson, who oversees the fan club newsletter for the club, expressed her respect and admiration for the country music fans who have supported the hospital year after year and have taken on this additional challenge.

Until the anonymous \$10,000 donation through Urban's fan club, both his and Keith's groups were running neck and neck. But winning the Fan Club Challenge is not at the forefront of everyone's minds.

"I'm not real worried about winning the challenge," says Johnson. "I'm just worried about raising as much money as we possibly can for St. Jude ... for the kids."

"Since we began Country Cares we have known that country music fans have a special place in their hearts for St. Jude," says David L. McKee, ALSAC's chief operating officer. "The response to the Fan Club Challenge has again shown the generosity that this musical genre and its fans have for our children." •

Perspective

Broadcasting the mission

By Ron Seggi

A nationally syndicated radio personality explains his passion for the work of St. Jude.

Like most children growing up in the 1950s, television played an important role in my life. One of my favorite programs was *Make Room For Daddy*, starring Danny Thomas. I remember the day and time it aired: Mondays at 9 p.m.

When I was 7, I built a little radio station in the basement of our family's home. Throughout junior and senior high school and college, I was a disc jockey at a local radio station. When I was 19, I was asked to serve as Teenage March captain for the annual

an excellent choice, since I was the station's top-rated disc jockey among the teen audience. I was honored by the offer, but I really knew little about the cause.

During the weeks leading up to the event, I learned how Danny Thomas had promised he would build a shrine to honor St. Jude. I was told Elvis had donated a yacht, once owned by President Roosevelt, to the hospital. But most important, I learned that St. Jude was dedicated to curing children stricken with cancer.

Although I was a hot-shot radio personality with a fancy sports car and a "flower power" wardrobe, I worked endlessly to make that fund drive succeed.

Afterward, I attended the national convention in Cincinnati, Ohio. Danny Thomas was present.

A photo was taken to memorialize my meeting with Mr. Thomas. Talking to the man I had watched on TV was

cool. But having him thank

me for the efforts I had put forth on behalf of St. Jude was even better—an experience I will always remember. In

fact, I recall the exact words he said, even though it was more than 30 years ago.

Throughout my career, I have kept in mind the promise that Danny Thomas made to St. Jude. I am not a strongly religious person; however, not a day goes by that I do not pray to St. Jude. The reason I honor him is twofold. First, he has given me strength when I was tired and forlorn. But more important, he is watching over those helpless, beautiful and precious children who find comfort, hope and love at St. Jude Children's Research Hospital. Thank you, St. Jude and the staff at ALSAC, for allowing me to tell my story. I hope it will inspire others to get involved.

The recipient of two Grammy nominations, Ron Seggi has owned radio stations, an advertising agency and is currently CEO and president of a production company at Universal Studios Florida. He also produces a radio show for his partner, Ed McMahon. In 2003, Seggi will be producing and hosting a weekly national television show based on the legends of rock 'n' roll. In addition, Seggi hosts a nationally syndicated talk show, where Marlo Thomas recently discussed her book, The Right Words at the Right Time. All proceeds from the sale of that book go to St. Jude.



Danny Thomas and Ron Seggi

fund drive for ALSAC, the fund-raising arm of St. Jude Children's Research Hospital. My boss thought I would be



LAURA HALJAR

Many a little boy has dreamed of being a cowboy, riding the range and sleeping beneath the stars. Edwin Kennedy and some of his friends did just that recently—and they did it so that little boys and girls could continue to have dreams of their own. Kennedy and five friends hitched up a couple of covered wagons to some mules in Louisiana and rode them north toward Memphis in an effort to raise funds and awareness for St. Jude. Three weeks later, they pulled up to St. Jude.

For Kennedy, a retired rodeo clown, the trip was an emotional apex. Last August, doctors told him his oldest daughter had a tumor. He prayed that the doctors were wrong. He added a vow, much like St. Jude founder Danny Thomas, that if his little girl would be all right, he would devote himself to St. Jude and the hospital that bears the saint's name.

Some time later, doctors told the family the original diagnosis was in error and that Kennedy's oldest daughter did not have a tumor. Amid the feelings of relief, Kennedy remembered his promise and began to put together what would be called Cowboys Against Childhood Cancer Tour the United States (CACCTUS).

The donations Kennedy and his group raised have yet to be tallied. But the feeling of accomplishment he felt and the smiles he saw of the patients who came out to greet him have reaffirmed his dedication and his desire to take three weeks again next year and follow his little-boy dream of being a cowboy and doing it to help children fighting cancer.