St. Jude Children's Research Hospital
ALSAC • Danny Thomas, Founder

Promise

Autumn 2007

Lessons in Living *page 6*

Promise

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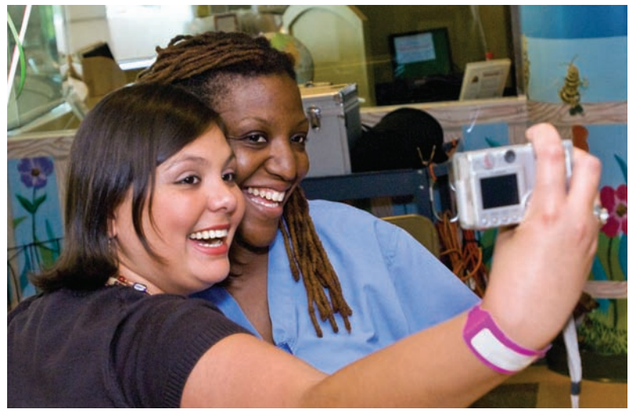

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On the cover: Stephan Boehme with his doctor, Carlos Rodriguez-Galindo, MD. Story on page 6; photo by Seth Dixon.

Highlights

California alliance

Treatment guidelines provided at St. Jude are now accessible to children in the southwest region of the country, thanks to a new alliance between St. Jude; Rady Children's Hospital, San Diego; and the University of California, San Diego (UCSD).

"The alliance is designed to encourage and facilitate collaborative research that is of great interest to St. Jude, while allowing patients in the San Diego area to continue to receive medical care close to their homes," said William E. Evans, PharmD, St. Jude director and CEO.

Making it possible for children in this region to receive the same treatment provided at St. Jude means children can stay near family and friends while undergoing treatment. The initial clinical study planned for this alliance is for children with acute lymphoblastic leukemia who have relapsed.

A sound discovery

Some children undergoing chemotherapy suffer hearing loss. This is a problem that researchers at St. Jude are trying to solve by studying some of the fine points of how the ear works.

Recently, these investigators settled a 30-year scientific debate that could explain why humans and other mammals have such sensitive hearing and the ability to discriminate among frequencies. The discovery centered on rod-shaped cells called outer hair cells, which are topped with tufts of hair-like projections called cilia.

Both mammals and non-mammals have these cilia-topped cells, and the cilia of both mammalian and non-mammalian outer hair cells vibrate in response to sound waves. But only mammalian outer hair cells contain a protein called prestin, which acts like a motor to make the cells contract and vibrate. The researchers showed that the prestin-driven movement of the mammalian outer hair cells rather than the movement of the cilia on top of those cells is the key to the hearing advantage of mammals. Key discoveries like this could help researchers learn how to prevent hearing loss in children while allowing them to benefit from chemotherapy, according to Jian Zuo, PhD, Developmental Neurobiology.

Zuo was senior author of a report on this work that appeared in the July 24, 2007, issue of *Proceedings of the National Academy of Science*.

Genes choosing helpers

Scientists at St. Jude discovered that a single protein called CREB uses different tools to trigger the activity of genes that help to control body activities as varied as the formation of memories and the production of glucose in the liver.

The St. Jude team showed that each gene that responds to CREB chooses which helper molecules CREB uses to activate that gene. This finding adds an important piece to the puzzle of how cells use CREB to activate different genes, said Paul Brindle, PhD, of Biochemistry. Brindle is senior author of a report on this work that appeared in the June 20, 2007, issue of *The EMBO Journal*. This finding is an example of how basic research conducted at St. Jude helps scientists understand how the body works at the level of molecules.

Such information is critical to understanding why certain diseases arise, and will guide researchers in their efforts to find new treatments for diseases as varied as memory loss and diabetes.

Circulation boosts chemo

St. Jude researchers have demonstrated a promising strategy for improving therapy for neuroblastoma, a pediatric solid tumor that arises from cells in the peripheral nervous system. The investigators used the drug bevacizumab to block a protein that stimulates blood vessel growth in tumors. The scientists found that the drug temporarily improves circulation in the tumor by first eliminating defective vessels. This brief improvement in circulation allows the chemotherapy drug topotecan to more effectively penetrate the tumor.

A report on this work appears in the July 1, 2007, issue of *Clinical Cancer Research*.

Results of the study are especially important because they will help scientists establish guidelines for the use of drugs like bevacizumab, said the report's senior author, Andrew Davidoff, MD, of Surgery.

Tiny tweezers twist DNA

A team of investigators at St. Jude and Delft University of Technology (The Netherlands) created a tiny model of how the anti-cancer drug topotecan works using microscopic "tweezers" that enabled them to manipulate a single molecule of DNA.

Normally, when a cell begins to divide it makes a copy of its DNA, so each newly formed daughter cell gets an identical set. During this process, the DNA gets twisted into supercoils much like the bulges in an over-wound telephone cord. The cell uses the enzyme DNA topoisomerase I to undo the coils so the DNA can be duplicated and cell division can continue. Topotecan blocks the enzyme, trapping the DNA in supercoils. This forces the cell to commit suicide.

The investigators used the microscopic tweezers—an example of nanotechnology—to twist a single molecule of DNA into supercoils. The researchers then monitored changes in the length of an individual DNA molecule caused by the action of a single topoisomerase I enzyme. Finally, they studied how the binding of a single topotecan molecule to this enzyme-DNA complex disrupts DNA uncoiling. A report on this work appeared in the July 12, 2007, issue of *Nature*.

"This model for how topotecan works is providing insights that could help scientists develop new drugs to treat cancer," said the report's co-author, Mary-Ann Bjornsti, PhD, of Molecular Pharmacology.

Back from the brink

St. Jude investigators have gained new insights into a strategy cancer cells use to survive and thrive. Researchers discovered how some abnormal cells can avoid a biochemical program of self-destruction by increasing their energy level and repairing the damage.

The finding offers an explanation of how abnormal cells that have cheated death once by disabling the main suicide pathway called apoptosis can also foil a backup self-destruct program called caspase-independent cell death. The process allows the cells to survive and become cancerous.

The St. Jude study also suggests that a drug that disrupts a cancer cell's ability to block this backup program would allow that program to kill the cell. Such a specifically targeted drug might be more effective and less toxic than standard chemotherapy. Douglas Green, PhD, Immunology chair, is senior author of a report on this work, which appeared in the June 1, 2007, issue of *Cell*.

Keeping it in the family

St. Jude investigators have learned more details about a process that is prevalent in cancer and can cause miscarriages or other diseases, such as Down syndrome.

Researchers used yeast cells to understand how a dividing human cell ensures that an identical set of chromosomes gets passed on to each new daughter cell. Errors in this critical part of cell division can cause one daughter cell to get extra copies of some chromosomes that should have moved into the other daughter cell, or no copies of other chromosomes. And those errors can have drastic consequences.

The St. Jude researchers tracked the activity of a small army of molecules that help maintain a specialized, tightly packaged form of DNA called heterochromatin at the part of the chromosome called the centromere. Investigators then and showed the order in which certain critical events occur in setting up and maintaining heterochromatin. A report on this work appeared in the May 25, 2007, issue of *Molecular Cell*. Janet Partridge, PhD, of Biochemistry is the report's senior author.

ANN-MARGARET HEDGES

Siblings had their moment in the limelight this year on St. Jude Sibling Star Day. This special event honors brothers and sisters for their contributions to the healing process of St. Jude children. The festivities included a red-carpet romp among cheering hospital staff, lunch, fun activities and a trophy presentation. Said one of the participants: "I don't know whose idea this day was, but this is awesome!"

PETER BARTA

Red clown noses were the key fashion accessory for St. Jude patients when Ringling Bros. and Barnum & Bailey® brought the big top to the hospital. Clowns, jugglers and acrobats dazzled and delighted children during a show filled with stunts, surprises and silliness. The event was offered as part of the St. Jude Child Life Program's Camp WAIT (wild, awesome, indoor time), a weeklong camp held on campus for patients.

Thanks and Giving 2007

The St. Jude *Thanks and Giving* campaign ensures that families find help when they need it most.

By Betsy Taylor

Susan Atkins (at left) and her mom, Patricia Barnes of CVS/pharmacy.

Even though CVS/pharmacy employee Patricia Barnes spends her days surrounded by medicine, none of it offered hope when her daughter, Susan, was found to have cancer. Then St. Jude Children's Research Hospital threw the desperate family a lifeline.

When Susan was 17, Patricia was a CVS assistant manager in a small town in Georgia. Her reason for working was to ensure that no matter what career path Susan decided to take, money would be there for her education.

But then something unexpected happened.

When Susan lay in bed at night, she had a catch in her lungs; drawing breath required willpower. The symptom seemed the aftermath of a particularly bad chest cold, but lingered.

"It got to the point where she was coughing blood," remembers Patricia.

The local doctor had no answers, and Patricia was beside herself. Without a diagnosis, how could they fight the problem?

Finally, an X-ray revealed a tumor covering 40 percent of Susan's chest, but local doctors still weren't sure of the diagnosis. A family friend in Florida, Gail Wynn, had heard of St. Jude and urged Patricia to obtain a physician's referral as soon as possible.

"By the time we got to St. Jude, she was breathing like Darth Vader," Patricia says. Susan had Hodgkin disease. "Her tumor was so big it pressed against everything, and it was as thick as cement."

At St. Jude, doctors couldn't risk removing the tumor surgically because of its close proximity to Susan's heart. They started Susan on chemotherapy. Once she recovered, they inserted a shunt to drain the fluids around her heart and began radiation therapy.

"The other doctors scared her to death. They didn't have any hope," Patricia says. "It was a total difference at St. Jude. They had all the hope in the world. It was like night and day."

> "It's the individual stories, like Susan's, that motivate us all."
>
> —*Eileen Howard Dunn, vice president of Corporate Communications and Community Relations, CVS/pharmacy*

Their CVS family allowed Patricia the time off to care for Susan and sent money so the family could have a fun outing together.

At 23, Susan has been cancer free for five years now.

This holiday season, CVS employees in Patricia's hometown will invite their checkout customers to contribute to a special fundraising campaign for St. Jude called *Thanks and Giving*.

They'll tell what they've learned about St. Jude—its groundbreaking research and survival rates, the fact that no child is ever turned away based on a family's ability to pay—and then they'll point out their personal incentive to support the hospital.

"See the woman behind the pharmacy counter?" they'll ask. "That's Patricia Barnes, and she almost lost her daughter, Susan, six years ago. Because of St. Jude, Susan is alive today."

Then they'll ask their customers for a donation to St. Jude—whatever they can afford is more than fine. And the good people of this small Georgia town will open their pocketbooks and give, just like they did six years ago when Patricia needed them most.

Companies That Care

Many generous organizations, including CVS/pharmacy, Domino's Pizza, Target, Williams-Sonoma Inc., Chili's Grill & Bar, Dollar General, Ann Taylor Brands, Kay Jewelers, Saks Fifth Avenue, the NFL, Gymboree, AutoZone, Nine West Stores and Kmart, have signed on as partners for this year's *Thanks and Giving* campaign.

"We are honored to be a part of the program that included some of the country's most respected brands and corporations," says David A. Brandon, chair and CEO of Domino's Pizza.

Retailers offer a variety of ways to give. Consumers may add a donation at checkout or purchase specialty items to benefit St. Jude.

The campaign is notable for its personal touches. For example, Target's Choxie Chocolates feature designs by St. Jude kids; Kay Jewelers has created a snuggly, limited-edition plush toy; and Christopher Radko glass ornaments are inspired by St. Jude patient artwork.

But what's most exciting about the campaign are the conversations taking place in checkout lines across the nation as employees and their customers talk about St. Jude and its work.

The words of St. Jude's National Outreach Director Marlo Thomas have become the theme of the fundraising campaign. "Give thanks for the healthy kids in your life, and give to those who are not," she says. It's a vital reminder of the most important thing in the world—a healthy child.

"Our employees wholeheartedly support the program, and our customers can sense that enthusiasm," says Terry Burman, executive chairman of Sterling Jewelers Inc., which retails under the brand names Kay Jewelers and Jared the Galleria of Jewelry.

"The campaign's grassroots approach fits perfectly with our philosophy of serving others in all communities we touch," says David Purdue, chair and CEO of Dollar General.

Thanks and Giving raises awareness for the hospital while it raises funds for St. Jude. Increased awareness means that more families hear about St. Jude and know where to turn when their children have cancer.

Visit *www.stjude.org* for a complete list of *Thanks and Giving* fundraising partners. You may also donate to St. Jude online at *www.stjude.org* or by phone at 1-800-4STJUDE. ●

PHOTOS BY BIOMEDICAL COMMUNICATIONS

This holiday season, St. Jude asks you to shop with retailers who display the green magnifying glass icon. Specialty items offered by participating retailers in the *Thanks and Giving* campaign include (clockwise, from left): St. Jude custom golf balls; Choxie Chocolates from Target; a limited-edition, plush bear from Kay Jewelers; and Christopher Radko glass ornaments.

SETH DIXON

Long before Stephan was found to have cancer, his uncle, Juan José Gutiérrez, supported St. Jude. The company Juan José heads is the primary corporate sponsor of the St. Jude International Outreach Program in Guatemala. Stephan's experiences have helped the family gain a new appreciation of their charitable work and of the St. Jude mission. "He is teaching us how to live," Juan José says.

Lessons in Living

Twelve-year-old Stephan Boehme inspires others through his illness.

By Mike O'Kelly

It's a hot, midsummer day—one most 12-year-old boys spend on a baseball diamond or swimming with friends. Instead, Stephan Boehme sits in the Solid Tumor Clinic at St. Jude Children's Research Hospital with his mother, Patty Gutiérrez. He could be complaining, but he's preoccupied with TV shows, frogs and bears.

"Did you watch *CSI* last night?" he asks a St. Jude staff member, in reference to the series set in Florida, his home state.

Unsatisfied with the "no" answer he receives, Stephan explains the show's plot before quickly moving to another subject. As he talks, he hangs onto his stuffed bear Rocky, who accompanies him everywhere. Adorned with a bracelet that bears the phrase "Go Steph Go," Rocky is as soft and cuddly as the day he was purchased nine years ago.

Stephan expresses concern over a few faded patches on Rocky's paws, but his mother reassures him the bear is fine.

"That's the way Stephan is," Patty says. "He worries about everybody."

First signs

On the evening of January 5, 2007, it was time to worry about Stephan. He suddenly felt pains in his abdomen during a trip to the movies with his mother, his fraternal twin brother, Christian, and his younger sister, Ivanna.

"I was feeling really weird, but I didn't want to say anything because I wanted to watch the movie," he says.

It didn't take long for Patty to notice her son sweating as he limped down the stairs of the theater. She immediately took Stephan to a local hospital.

Hours later, doctors found a mass in Stephan's stomach and checked him into the hospital for more tests. After five or six days, doctors still could not identify the tumor. Patty phoned her oldest brother, Juan José Gutiérrez. "I understood that his only opportunity to live was if he flew to Memphis and put his life in the St. Jude doctors' hands," says Juan José, who helped Stephan obtain a physician's referral to St. Jude.

Within 24 hours of his arrival at St. Jude, Stephan was found to have desmoplastic small round cell tumor, a rare, aggressive cancer with a low survival rate.

Charitable family

Stephan's uncle was no stranger to childhood cancer or to St. Jude. Juan José is president and CEO of Pollo Campero, which helps raise nearly $2 million annually for pediatric cancer research and treatment in Guatemala.

A chicken restaurant chain with more than 200 locations in seven Latin American nations as well as the United States, China, Indonesia and Spain, Pollo Campero is the primary corporate sponsor of the St. Jude International Outreach Program in Guatemala.

With Pollo Campero's support, St. Jude helped establish a pediatric cancer facility in Guatemala's lone public hospital, Unidad Nacional de Oncologia Pediátrica.

This charitable groundwork was laid long before Juan José learned that his nephew had cancer. Ironically, Juan José was already scheduled to present a

donation check to the cancer treatment program when Stephan first felt pains in his abdomen. Juan José says Stephan's cancer has helped the family gain a new appreciation of their charitable work and of the St. Jude mission.

"His diagnosis touched the whole family," Juan José says. "We understand from the bottom of our hearts what this really means."

Awesome kid

Doctors at St. Jude see one or two cases each year of desmoplastic small round cell tumor, which predominantly develops in young males. According to Carlos Rodriguez-Galindo, MD, of St. Jude Oncology, the cancer is usually advanced by the time it is diagnosed, as it was in Stephan's case.

"The current approach that we are using is very intensive chemotherapy," Rodriguez-Galindo says. "We escalate chemotherapy and try to remove as much of the tumor as possible."

Rodriguez-Galindo and Patty have talked to Stephan from the beginning about his cancer, his treatment and his prognosis.

"Stephan asks me a lot about his cancer, and he knows everything about it. He knows the big, long name. He knows it was 20 percent survival rate when we came, and that now it's maybe 30 percent," Patty says.

Stephan, who has received nine rounds of chemotherapy, has responded well to treatment. In April, he underwent successful surgery to remove several abdominal tumors, one of which was nearly 5 inches in diameter. Chemotherapy is scheduled to continue until he undergoes a bone marrow transplant later this year. His bone marrow was harvested in early March for the procedure.

"He is always ready for chemo. I've never heard him complain about anything—not about pain, about not feeling well or about being unhappy," Rodriguez-Galindo says. "He always says, 'Awesome.' Even after his surgery, when he could barely breathe, he would say that."

Occasionally, however, Patty wishes Stephan would be less stoic.

"Sometimes, I think, 'Stephan, complain. I need you to cry,'" Patty says. "I have to push him to react because he doesn't want me to be sad or upset."

It's not surprising to hear Stephan dispensing cheerful guidance to other St. Jude children to ease their concerns. "I would imagine it is quite easy for a near teenager to be upset and angry at what he has to endure, but not Stephan," says Candice Duffy, RN. "He has chosen to look at his journey through a different set of eyes."

SETH DIXON

"I've never heard Stephan complain about anything—not about pain, about not feeling well or about being unhappy," says Carlos Rodriguez-Galindo, MD. "He always says, 'Awesome.' Even after his surgery, when he could barely breathe, he would say that."

A different person

Before his diagnosis, Stephan spent most of his time listening to his favorite band, Linkin Park; cheering the Miami Heat NBA team; or goofing off with his siblings and their miniature Schnauzer, Saskia. He still loves those things, but the cancer, chemotherapy and monthly visits to St. Jude have helped him grow into a more sensitive, intuitive person, according to his mom and uncle.

"He is teaching us how to live, and we have all experienced his transformation," Juan José says. "His understanding of life is 100 percent different than it was in the past."

It's not surprising to hear Stephan dispensing cheerful guidance to other St. Jude children to ease their concerns. His inquisitive and playful nature is revealed whether he's joking with Rodriguez-Galindo about his latest haircut or watching wild animals run across the TV screen in his hospital room.

"I would imagine it is quite easy for a near teenager to be upset and angry at what he has to endure, but not Stephan," says one of his favorite nurses at St. Jude, Candice Duffy. "He has chosen to look at his journey through a different set of eyes. He remains upbeat, drawing strength from his family, and most importantly, his faith."

Stephan's journey has brought inspiration to both friends and strangers. Two weeks after his surgery, he was greeted with applause and warm support as he stepped out of a car at a fundraising run in his home town. Stephan took the first lap around the park along with a host of cancer survivors, who were eager to take photos with him.

And there's the story of two of his classmates, who were moved enough by Stephan to begin attending church again.

"They found out I had cancer, and now they're going to church every Sunday, and all the kids are praying," Stephan says of his sixth-grade classmates. "I feel really good that I'm able to help change people."

Guest of honor

It didn't take long for others to realize how special Stephan was, as well. He and his family attended the fifth annual FedEx/St. Jude Angels and Stars Gala earlier this year. Stephan was the guest of honor at the event, which was chaired by entertainer Daisy Fuentes. He danced with Fuentes, won the silent auction prize of a basketball signed by the 2006 NBA champion Miami Heat, and played the drums on stage.

"Stephan was the star of the night, and all of the attention was for him," Patty says. "Everybody was in shock. They couldn't believe he was playing the drums."

By the end of the night, Stephan sympathized with celebrities who are hounded by the paparazzi, but he wasn't eluding any flash bulbs.

"It was really cool because I felt famous," Stephan says. "People came up to me and asked for pictures. I didn't want to say no because that would be rude."

PETER BARTA

Stephan dances with supermodel and TV personality Daisy Fuentes during the FedEx/St. Jude Angels and Stars Gala. As a special guest at the fundraiser, the 12-year-old reveled in the attention, even agreeing to play the drums onstage during the event. "It was really cool because I felt famous," Stephan says. "People just came up to me and asked for pictures. I didn't want to say no because that would be rude."

Graduation day

Few days will be as memorable as the one in early June when Stephan graduated from fifth grade alongside Christian. Stephan, an honor roll student since first grade, and Patty both arrived at the ceremony thinking he would not graduate because he had missed so much school during treatment.

Stephan sat with his classmates and even wore the Class of 2007 T-shirt, but he was nervous because he thought he was not going to receive a diploma. He awoke that morning unsure if his blood counts were high enough to allow him to attend, but he was assured midday that he could make the trip.

What happened next sent a wave of thunderous applause through the crowd.

"Our surprise was incredible when the principal called, 'Stephan Boehme Gutiérrez.' The entire school got up… parents started to applaud, and everyone was stomping their feet in joy," Patty wrote in a journal. "I got goose bumps all over my body, and tears were hard to hold. It was a memorable moment, and my angel, who wanted to cry, was containing himself with a great smile that I will never forget."

While Stephan and his family understand his prognosis, it has not affected their resolve, their faith or their ability to enjoy each day together. He understands that no one is guaranteed tomorrow, so he enjoys the daily nuances of life.

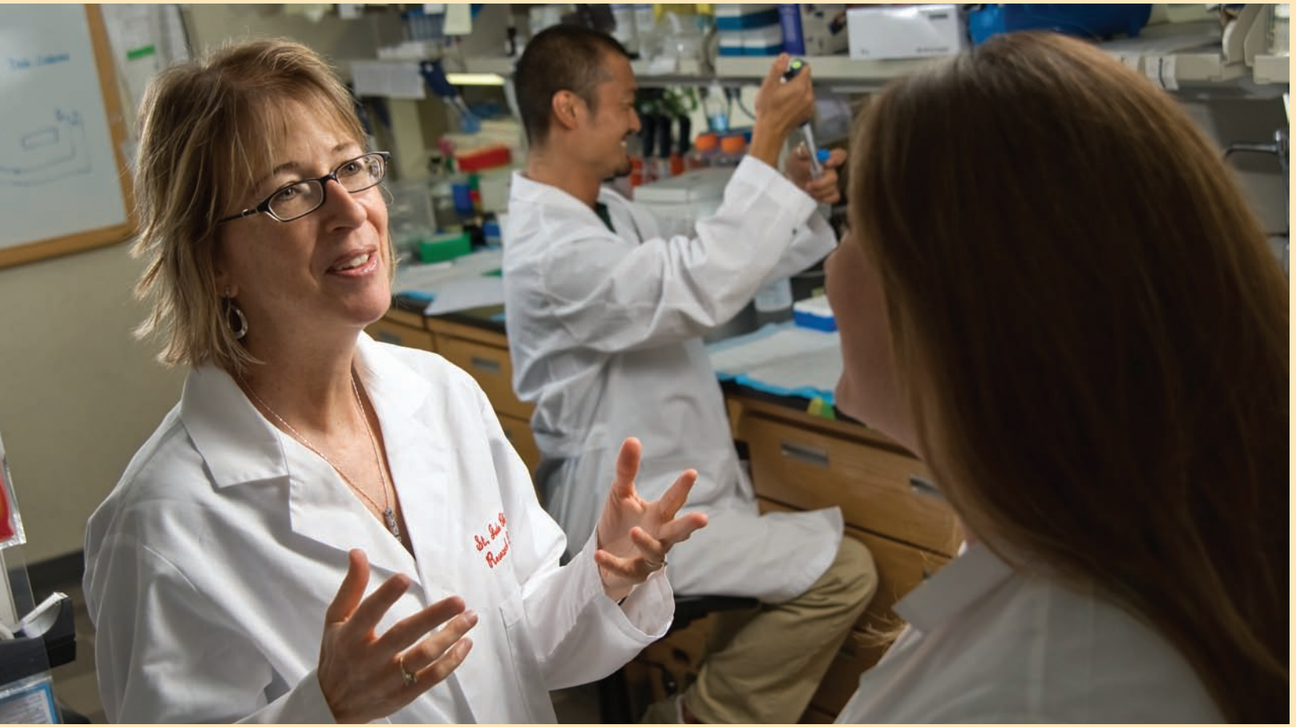
Stephan loves Miami Heat star Dwyane Wade. He drives his mom crazy by banging a pretend drum during car rides. He likes to tell embarrassing stories about his younger sister. And he just happens to make monthly visits to St. Jude.

"The people here are really nice," Stephan says of the hospital.

Patty sometimes refers to herself and her children as the Fantastic Four. The Fantastic Four know there will be tough days ahead, but this realization helps make the good times more special. ●

VITAMIN Deficiency

Kids undergoing certain kinds of chemotherapy can lose bone density because of a loss of vitamin D. Why does that happen? St. Jude scientists find answers.



PETER BARTA

Erin Schuetz, PhD, of Pharmaceutical Sciences (at left) and her colleagues work in the lab to understand the mechanism that causes bone loss in kids who undergo cancer treatment. "There is a lot of good work being done about this bone density topic that we could someday translate to the clinic for our kids," she says.

BY CARRIE L. STREHLAU

Drinking milk. Soaking up the sun. Eating salmon. Taking supplements. These are all ways to add vitamin D to the body. Children treated for cancer with certain chemotherapy drugs, however, can experience decreased bone density because of a loss of vitamin D. Scientists at St. Jude Children's Research Hospital recently discovered a mechanism in the body that connects the use of certain chemotherapy drugs to this vitamin deficiency. Ultimately, this discovery may lead to drugs that have fewer side effects.

"Loss of vitamin D is directly related to bone loss, and it is a debilitating side effect for our patients," says Erin Schuetz, PhD, of Pharmaceutical Sciences. "Some of our kids have had hip replacements even as teenagers. We want to prevent that, but first we had to understand the mechanism causing bone loss."

CYP3A: Bad to the bone

What researchers knew was that certain drugs being used to treat pediatric cancer activate a protein called PXR. This molecule acts like an "on" switch for the cell's garbage disposal system. It is a type of protein called a receptor, which means it catches certain molecules in the cell that should be eliminated. When such an unwanted molecule binds to PXR, this protein turns on a specific group of genes that break down the unwanted molecule.

"PXR does that in a variety of tissues, but in particular in the liver and intestine, which are the major drug metabolizing tissues," Schuetz says. "It was already known that this is one mechanism by which drugs can increase the activity of these particular genes. One of the genes that PXR triggers is called *CYP3A*."

According to Schuetz, this link between PXR and *CYP3A* helps explain how many drugs interact with each other.

"When people take certain drugs, it will say on the package that the drug interacts with CYP3A because the enzyme this gene makes is responsible for converting many drugs to an inactive form," Schuetz says. "That's important because you don't want drugs hanging around in your body forever, or accumulating to dangerous levels when you take multiple doses. CYP3A recognizes these drugs and chemically modifies them so the body can excrete them more easily." That's good for keeping drug levels in the body from getting too high. But it can be bad if CYP3A inactivates vitamin D.

Decreased systemic vitamin D

In collaboration with researchers at the University of Washington in Seattle, St. Jude researchers showed that not only does CYP3A inactivate certain drugs, but in the intestine and liver it also inactivates the biologically active form of vitamin D.

"This form of vitamin D actually recirculates all the time between our liver and our intestine," Schuetz explains. "That active form is a major pool of vitamin D that is available in the systemic circulation, where it keeps calcium concentrations at healthy levels. Vitamin D in the intestine regulates absorption of calcium."

Researchers found that CYP3A and PXR are both active in the liver and intestine.

"So, now we have this unfortunate side effect," Schuetz says. "Drugs activate PXR, which turns on the CYP3A enzyme. Then CYP3A not only protects the body by getting rid of drugs, but in the liver and intestine, it can inactivate this pool of recirculating vitamin D. This decreases the amount of biologically active vitamin D in the intestine."

Vitamin D also goes to the bone, where it regulates calcium levels and bone growth. "With decreased amounts of vitamin D and decreased calcium, you get decreased bone mineralization and increased bone loss," Schuetz says. "That is just one way certain drugs are causing bone loss."

"If we can design drugs that do not interact with this PXR receptor, it will help prevent such high bone loss."

Avoiding interactions

Because most calcium comes from the diet and its absorption by the intestine is regulated by vitamin D, decreased vitamin D will lead to decreased calcium absorption.

"Inactivation of vitamin D in any compartment in the body is going to be bad, but we did not know about the role of CYP3A in breaking down vitamin D," Schuetz says. "It appears that activation of PXR by various drugs and the subsequent increase in the activity of this enzyme in the liver and intestine significantly contributes to loss of biologically active vitamin D."

For St. Jude children, this discovery is important.

"No one wants to see drug-drug interaction," Schuetz says. "At St. Jude, kids are going to take multiple drugs. If we can design drugs that do not interact with this PXR receptor, it will help prevent such high bone loss."

As researchers in the St. Jude Chemical Biology and Therapeutics department design new cancer drugs, they will test for PXR receptor interactions.

"In terms of treatment, this means that you would likely choose drugs that do not interact with this receptor," Schuetz says. "If there are cancer drugs that are equally effective and do not have that property, using them is one way to prevent that kind of drug-induced bone loss."

When a discovery like this is made in the lab, it is not instantly turned into a new, thoroughly tested drug that doctors can use. But Schuetz says the research may help scientists identify variations of existing drugs that do not cause bone loss and that can be immediately used in treatments.

"Doctors are also considering trying some other therapies in combination with the cancer drugs to try to prevent bone loss and supplements to restore bone density," Schuetz says. "There is a lot of good work being done about this bone density topic that we could someday translate to the clinic for our kids." ●

FREE to change the world

By Elizabeth Jane Walker

Reena Shah owes her life to St. Jude and a generous bone marrow donor. Now she embarks on an adventure to help others in turn.

Everyone has a birthday. But not everyone celebrates a "rebirth day."

Reena Kunvarji Shah does just that each July 4. As fireworks splay their multicolored fingers across the sky, Reena celebrates her personal Independence Day. In 2007, the thunderous blasts reminded her that exactly 10 years had passed since a transplant extinguished the pyrotechnics that raged within her own body.

Freed from the bonds of chronic myelogenous leukemia (CML), Reena now channels her energy into providing independence for others. She hopes to do that by improving global health—liberating poor and politically disenfranchised people from poverty, disease and oppression.

"I know I can't change the whole system," she says, "but you can cause a world of change just by helping one person."

PHOTOS BY PETER BARTA

Reena Shah (at right) shares a private moment with her bone marrow donor, Natalie, during a tour of St. Jude in July of 2007. "When I found out that I could be a match for someone," Natalie says, "I felt like I had won the lottery."

Ripple effect

That ripple effect began for Reena when the first life-giving drop of red liquid—bone marrow donated by a total stranger—slid through a tube and entered her body on July 4, 1997. Not only did the experience change Reena's blood type from O positive to A positive, but it changed the ebb and flow of her hopes and desires and interests.

As the daughter of a plastic surgeon and a nurse anesthetist, Reena was no stranger to the world of medicine when, at age 11, she began to suffer from headaches and lethargy. Jenny Shah took her daughter to several specialists in their Illinois hometown, including a pediatric neurologist who suggested that the young honor student was stressed from studying too much.

When Reena bumped her knee at school one day, the minor incident produced a nagging pain that radiated to her left hip. The pediatrician ordered a blood test to rule out rheumatoid arthritis. He was surprised at the results. Reena had a blood cancer called chronic myelogenous leukemia. "Her white blood cell count is about 233,000," the doctor said.

"But that's not even compatible with life!" Jenny responded. "Normal counts are between 5,000 and 10,000."

The pediatrician scheduled an appointment for Reena at St. Jude Children's Research Hospital's Midwest Affiliate in Peoria, Illinois. As she drove to the clinic with her parents, Reena was unaware of the diagnosis. But when they arrived at their destination, the 12-year-old quickly figured it out.

"Oh great," Reena muttered sarcastically to herself when she saw the St. Jude logo on the clinic's door. "I've got cancer in my knees."

After conducting further testing, the affiliate physician instructed Reena to leave for Memphis immediately. At 3 a.m., the family walked through the doors of St. Jude.

Needle in the haystack

According to Wing H. Leung, MD, PhD, director of St. Jude Bone Marrow Transplantation and Cellular Therapy, CML is a slow-growing cancer. Whereas acute leukemia may hit like a hurricane, CML moves in like a gentle breeze that sighs, murmurs then roars. Looking back, Reena realizes she probably had the disease for a year before she noticed the symptoms.

At St. Jude, the Shahs learned that the only cure for this disease was a bone marrow transplant. The procedure is risky, but it was Reena's only hope. "The transplant service has one of the highest mortality rates of any treatment area," Leung says. "But we have about 300 long-term survivors who have received allogeneic transplants (transplants of marrow or stem cells from other people). "St. Jude has the largest cohort in the world of pediatric bone marrow transplant survivors who have had allogeneic transplants."

Reena's parents and her brother were tested to see if they could donate marrow. When their marrow was not compatible, St. Jude turned to the National Marrow Donor Program (NMDP) to find a match.

Because Reena's father is Indian and her mother is Caucasian, physicians were concerned about her odds of finding a donor. In general, people of mixed racial heritage have problems finding donors. But Reena was fortunate. From their bank of 10 million volunteers, the NMDP identified several potential donors. St. Jude determined that one of those individuals was a perfect match: a woman named Natalie.

Lotto odds

Natalie was a college student in Virginia when she joined the NMDP during a campus bone marrow drive. Several years went by; she moved to Davis, California, for graduate school and forgot about the registry. Then she received a letter from the NMDP. Would she be interested in undergoing further testing to determine whether she would be a suitable donor for someone who needed a transplant?

"When I found out that I could be a match for someone, there was no question in my mind: 'I have to do this.' It meant saving a person's life," Natalie explains. "I felt like I had won the lottery."

"I know you can't change the whole system, but you can cause a world of change just by helping one person."

"If we had not been able to find a donor, Reena would have been left with no options," Leung says. "Unrelated bone marrow and stem cell donors are really heroes to me. They save another person's life out of kindness; they aren't blood relatives or even friends—they're strangers. It's pretty amazing."

While Natalie was preparing for the bone marrow harvest, Reena was in Memphis, undergoing radiation and brutal chemotherapy to kill the leukemic cells. "My hair fell out, I couldn't eat or drink; my gums and mouth turned into one big, raw sore," Reena recalls. "It felt like I had broken glass all the way down my throat. I couldn't even swallow for days. I couldn't talk, and it hurt to cry."

Kathleen Knowles, a graduate student at St. Jude during that time, remembers Reena's courage. "Her attitude was just remarkable," Knowles says. "Many days she obviously felt horrible, but she would still put a smile on her face and make an effort. I always felt uplifted when I left her room."

Finally the day arrived. In California, Natalie arose early and nervously drove to the hospital for the bone marrow

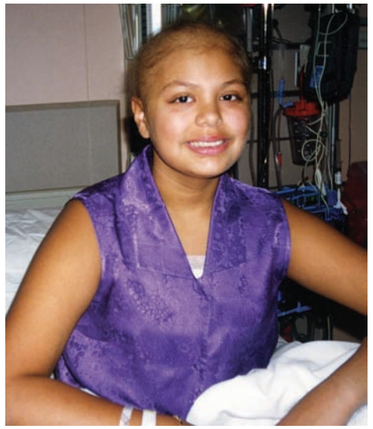
“St. Jude has the largest cohort in the world of pediatric bone marrow transplant survivors who have had allogeneic transplants.”

harvest. Because of privacy regulations, she knew only that the recipient would be “a 12-year-old girl” and that the marrow would be flown to the recipient.

At 5 p.m. on July 4, Reena received the healthy bone marrow. Even Jenny’s medical training had not prepared her for the surprises that would occur afterward. “The last unit of platelets Reena got before her transplant were mine—O positive,” Jenny says. “Then they injected Natalie’s marrow. The next unit of platelets they hung on the pole was A positive.”

Family affair

Reena sailed through the recovery period with relative ease. Because of NMDP privacy regulations, bone marrow donors and recipients cannot divulge their identity until a year after transplant; then, if both people agree, they may meet or correspond directly. Soon after the transplant, Reena and Natalie began writing “Dear Donor” and “Dear Recipient” letters to one another. The NMDP served as intermediary, removing identifiers and forwarding the missives. The Shahs tried to imagine what Reena’s donor would be like. Would she be of Indian descent? Would she and Reena look alike or have similar personalities or interests?



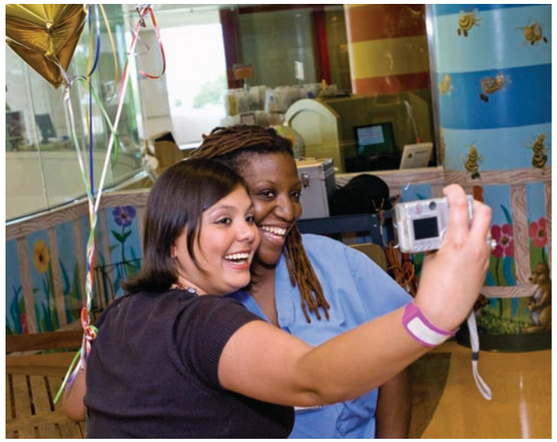
“My hair fell out...I felt like I had broken glass all the way down my throat,” says Reena, shown during her treatment.

Finally, NMDP allowed the two to meet. “As it turns out, Natalie is the absolute opposite of Reena,” Jenny says. Reena is gregarious; Natalie is more reserved. Reena’s hair and complexion reflect her Indian heritage, while Natalie’s fair skin, light brown hair and blue eyes display her Latvian and Polish-Irish background.

Although they share marrow, this donor and recipient are also linked at the heart. A Shah family photo includes Natalie, clad in a flowing Indian sari. And when Natalie married earlier this year, the Shahs traveled across the country to attend her wedding.

“There’s no way for other people to comprehend how much Natalie means to all of us,” Jenny says.

But Natalie says that she has also benefited from the relationship. “I’m so blessed and so overjoyed to know that I had this in my life and to know that I was able to help save Reena,” she says. “I feel like the Shahs are another branch of my family. When I have a bad day or I’m feeling down, I’ll think about it, and realize that I’m pretty lucky to have had this experience.”



On July 4, 2007—the 10-year anniversary of her transplant—Reena returned to St. Jude for her last regular checkup. She visited with old friends, such as her former line nurse, Kim Proctor, RN.

Search for meaning

Throughout her treatment, Reena also obtained another surrogate family, consisting of St. Jude children, parents and staff. Unfortunately, several of her close friends succumbed to disease. That loss forced Reena to ponder the vagaries of survival.

“Having cancer changed me a lot,” she admits. “You go to St. Jude and leave your home behind. That’s difficult. But then you form a community with people at the hospital. When that community begins to fade away, it’s really hard. As time went by and more of my friends died, I wondered, ‘Why is it not me?’

“So at a young age I developed a sense that there has to be a meaning for my life; otherwise it’s a waste. There are other people who didn’t make it and who were just as viable as I was as individuals, as human beings, but I’m the one who’s here. So I have to make my life worth it for them, if not for myself.”

That realization became the impetus for her personal and educational choices. At the University of San Francisco, she majored in politics and minored in French, in preparation for a career that uses politics to address important health care issues.

Inspired by the fact St. Jude accepts children without regard to their ability to pay, she raises funds for the hospital each year. “I understand more than anybody that it takes a lot of money to run the hospital every day,” Reena says. “Everybody there gets the same standard of care—regardless of their economic situation.”

World of change

Reena’s passion is searching for ways to make life better for people around the globe. She has traveled to Chile to study the educational system and poverty; she has spent time in Brazil, where she studied community-based responses to the issues of poverty and environmental destruction. And in the summer of 2007, she traveled to South Africa, where she worked with women and children who have become dehumanized by poverty, HIV/AIDS and the society in which they live.

“We spent time with a community of women who live on the rubbish dumps,” she says. “We got to play with their children and talk with the women about their hopes and dreams. It was a powerful experience.”

A 2007 honor graduate of the University of San Francisco, Reena plans to enter the Peace Corps Masters International Program, which will allow her to serve two years in the Peace Corps while pursuing a master’s degree in public health. Given her fluency in French, she hopes to work eventually in West Africa.

Reena knows that she owes her life to St. Jude and to Natalie. On July 4, 2007, Reena spent her 10th “rebirth day” touring her donor around the hospital. Now Reena wants to return the gift that has been given to her. Her generous spirit is evident in everything she does—whether she’s distributing socks and food to street people in San Francisco, raising money for a hospital in Memphis or embarking on a career to improve the health of people around the world. ●

Reena’s efforts to “give back” encompass raising money for St. Jude and pursuing a career that will enable her to improve conditions for people around the globe. In the summer of 2007, Reena (at left) worked with women and children in South Africa. She plans to enter the Peace Corps and pursue a master’s degree in public health.

Eradicating Ewing

Investigators throughout St. Jude attack one disease—Ewing sarcoma—from different directions.

ANN-MARGARET HEDGES

Nevada teenager Alexa Walker is grateful to Fariba Navid, MD, for the care she has received at St. Jude. Now Navid is investigating a new method for improving the survival statistics for Ewing sarcoma. Her approach incorporates a combination of drugs to kill off the blood supply to the tumor.

By Lin Ballew

Only a backache. What teenager hasn't had one? Carrying heavy books, slouching in bean-bag chairs and moving to the latest tunes can make muscles throb. But when mild discomfort suddenly becomes paralysis, something is definitely wrong.

That's how Nevada teenager Alexa Walker found out she had Ewing sarcoma, a rare tumor of the bone or soft tissues. The term "cancer" wasn't part of Alexa's consciousness in January 2005. She was getting ready to become a teenager, but even those happy plans were put on hold. "I received the diagnosis two days before my 13th birthday," Alexa recalls. "It's really hard to explain how I felt. It was scary—amazingly scary."

Melinda Walker, Alexa's mom, remembers the event as if it occurred yesterday. Alexa had experienced a range of symptoms from a back ache to tingling and pain in her legs and feet. Doctors were unable to identify the cause of her problems. "Then one morning she woke up and was paralyzed from the waist down," Melinda says. Even after an MRI identified a tumor, Melinda never considered cancer. "I guess I just didn't want to put that in my head," she says. "I'd never heard of Ewing sarcoma before. I was in denial."

Ewing sarcoma—also known as Ewing sarcoma family of tumors and primitive neuroectodermal tumor, or PNET—was first identified in 1921, but its mysteries are only now being solved. Some of the chief sleuths in that effort are conducting their investigations in the clinics and labs at St. Jude Children's Research Hospital.

Step by step

Scientists probing the genetic components of this disease have discovered that the cancer occurs when chromosomes swap places and cause two genes to fuse. One of the partners in this fusion is always the *EWS* gene; the other partner is *FLI-1*, or one of several closely related genes from the *ets* gene family. The result is a new gene that can transform a healthy cell into a malignant one.

Ewing sarcoma was one of the cancers treated in the early days of St. Jude. In 1962 the survival rate for Ewing was only 5 percent, but while diseases like acute lymphoblastic leukemia have improved from 4 percent to 94 percent, Ewing sarcoma has only improved to about 65 percent. St. Jude scientists have conducted several Ewing studies through the years that have added chemotherapy and drug-enhancing agents as well as other methods for reducing the number of cancer cells. This research has benefited children and helped international groups develop multi-institutional studies.

"We learned that adding ifosfamide and etoposide was helpful for children with previously untreated Ewing sarcoma, and that treatment intensification, with better support, was also beneficial," says Carlos Rodriguez-Galindo, MD, Oncology. "With these basic elements of treatment, we can now cure approximately 70 to 75 percent of children with localized Ewing sarcoma."

Questions to answer

With the news of cancer still swimming in her head, Melinda wasn't ready for 75 percent survival figures. "I was thinking that it should be 90 percent. I was looking up everything on the Internet I could find," she recalls.

The largest obstacle researchers have in tackling Ewing sarcoma is the tiny amount of tumor they can obtain during biopsy. Unlike leukemia, a blood cancer, where large samples can be obtained and stored for future testing, only small portions of Ewing sarcoma tumors can be removed. Surgeons attempt to spare as much surrounding tissue as possible, which leaves only a small amount of tissue for biological research.

Scientists use the tissue they obtain to pinpoint a diagnosis and to study the tumor's cellular structure and genetic makeup. After those studies are conducted, little tissue is left for additional research. This lack of tissue for biological research probably contributed to the fact that the disease remains a mystery even though it has been studied for nearly a century.

Scientists have not reached a definite consensus on what type of normal cells allow for the formation of these tumor cells, or exactly how the *EWS/FLI-1* fusion gene contributes to tumor formation. Some of the basic science research conducted at St. Jude attempts to answer these questions.

New approaches

Suzanne Baker, PhD, of St. Jude Developmental Neurobiology conducted a laboratory study with a goal of understanding the function of the presumed culprit, *EWS/FLI-1*, by introducing it into all cells in the

SETH DIXON

Suzanne Baker, PhD, and Enrique Torchia, PhD, of Developmental Neurobiology discuss a project in the lab. Baker and her colleagues conducted a study that provided a new model for studying the cancer-promoting effects of ***EWS/FLI-1***, a gene that can transform a healthy cell into a malignant one. Baker's investigations may help scientists better understand the cell types that can bring about Ewing sarcoma.

PHOTOS BY SETH DIXON

EWING sarcoma was first identified in 1921, but its mysteries are only now being solved. Some of the chief sleuths in that effort are conducting their investigations in the clinics and labs at St. Jude Children's Research Hospital.

Peter Houghton, PhD, of St. Jude Molecular Pharmacology works with student intern Zachary Inman in the lab. Houghton's team is discovering in the laboratory the best way to use drugs in the clinic. The system was the model for a current nationwide system of such projects funded by the National Cancer Institute and led by St. Jude.

bone marrow compartment. In this experimental system, expression of the Ewing sarcoma-derived fusion gene quickly produced an extremely aggressive form of leukemia.

Baker and her team of researchers were surprised that this new model showed that *EWS/FLI-1* could promote leukemia so rapidly when the fusion gene has not been found in human leukemia. Although the experiment did not generate a Ewing sarcoma, it provided a new model for studying the cancer-promoting effects of *EWS/FLI-1*. Researchers hope to use this model in future experiments to fine-tune control of *EWS/FLI-1* by directing more selective expression of the gene only in specific cells. These investigations may help scientists better understand the cell types that can bring about Ewing sarcoma—and ultimately understand more about this devastating cancer.

Another research team led by Peter Houghton, PhD, of St. Jude Molecular Pharmacology approaches basic research with Ewing sarcoma differently. He and his colleagues use models to test drug functions against Ewing sarcoma with the ultimate goal of finding the most effective treatment with the fewest side effects. This pioneering program at St. Jude is eliminating the trial-and-error approach to finding the best drug and the right doses for children. In fact, it's so successful that it was the model for a current nationwide system of such projects funded by the National Cancer Institute and led by St. Jude.

The program is designed to address the unfortunate fact that virtually all new cancer drugs are designed for adult cancers. Physicians traditionally had to spend precious time juggling different combinations and doses of adult drugs to find the best way to use them in children. Houghton's team is overcoming this problem by discovering in the laboratory the best way to use drugs in the clinic.

Meanwhile, in the clinic

Alexa's doctor, Fariba Navid, MD, Oncology, is working to improve the survival statistics for Ewing sarcoma. Navid has developed a new protocol, or treatment study. Her approach takes aim at the blood supply that feeds the tumor.

Angiogenesis is the process by which cells are enabled to form blood vessels and feed tissue. Having a healthy blood supply is great for the body's muscles and organs, but that same process also helps tumors survive and grow. Scientists are interested in cells that will attack tumor vasculature, or tumor blood supply.

ANGIO1, a new Phase I study opening at St. Jude, is looking specifically at a combination of new drugs to kill off the blood supply to the tumor. Findings from ANGIO1 will be incorporated into the treatment study for Ewing sarcoma.

Targeted results

Contributing to those efforts are the work of Barry Shulkin, MD, Scott Snyder, PhD, and Elizabeth Butch, PhD, all of St. Jude Radiological Sciences. Since about 2002, St. Jude has been using its Positron Emission Tomography (PET) scanner to measure glucose as it is metabolized.

"Active tumors usually consume glucose, or sugar, and labeling a glucose molecule with a radioactive element allows researchers to map in more detail the location of the tumor and how it reacts to various treatments," Snyder explains. "A treatment can be given, the patient can get scanned again, and scientists can determine if the treatment is reaching the intended target."

The Radiological Sciences colleagues are taking a step into the future with this technology. Instead of using simple glucose forms that are presently commercially available, the scientists are planning to create "designer" radiolabeled agents that are much more targeted and yield greater results in the laboratory and the clinic. The consequences of such an approach are significant; this is the first step to creating an individualized treatment plan specific to a unique tumor, such as Ewing sarcoma, which will help doctors improve clinical trials.

St. Jude efforts to unravel the secrets of Ewing sarcoma extend across the country and around the world. Alexa received her chemotherapy treatments in Nevada. When it was time for radiation, she qualified for a St. Jude protocol.

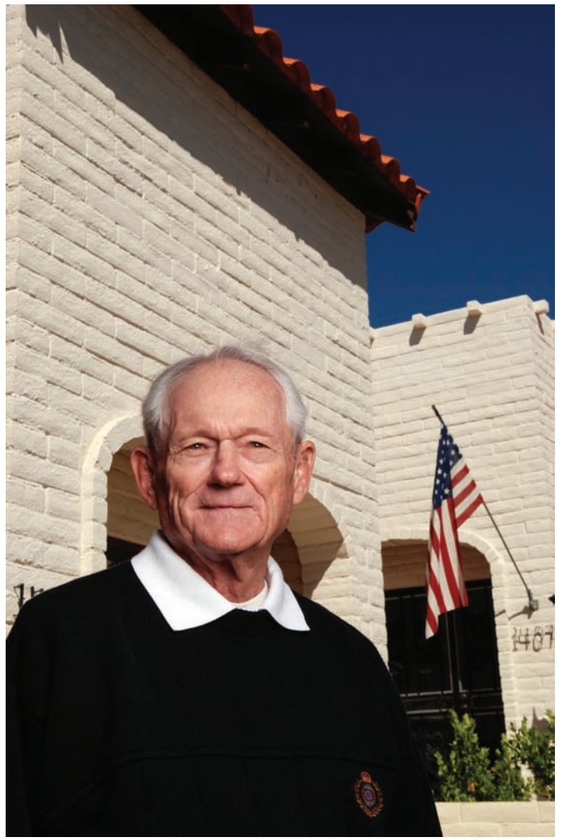
Thanks to the care she received in Memphis, the main things on Alexa's mind are hanging out with her friends, focusing on her studies and looking for concerts to attend. Being "amazingly scared" simply isn't part of her world anymore. ●

(From left) Barry Shulkin, MD, Elizabeth Butch, PhD, and Scott Snyder, PhD, all of St. Jude Radiological Sciences, are planning to create "designer" radiolabeled agents to map where tumors are located and how they react to specific treatments. This is the first step to creating an individualized treatment plan specific to a unique tumor, such as Ewing sarcoma, which will help doctors improve clinical trials.

A New Mission

By Janice Hill

His work ranged from B-52 bombers and lunar expeditions to secret laser projects. But Paul Sobolik's most important mission may lie in his ability to help children.



In his career, Paul Sobolik helped put Americans on the moon. In his retirement, he helps save children on Earth.

The former engineer for Boeing says his top priority is to help children in need. He does that by supporting St. Jude Children's Research Hospital and other charities that benefit young people.

"I guess I've always had a rapport with children, even though I've never had any children of my own," he says, "so helping them is important to me."

MEETING OBJECTIVES

For most of the last decade, Sobolik has set up a charitable gift annuity through St. Jude each year. He plans to continue to use retirement savings to create additional charitable gift annuities in the future.

"They help me achieve two objectives," he says. "They are good for St. Jude, and they pay me healthy dividends."

Paul also has chosen to include St. Jude in his will, as a percentage of his estate, with the goal of providing for his siblings and the causes he cares about.

MISSION TO THE MOON

Born and raised in the Midwest, Paul went to work for Boeing in Seattle immediately upon graduating from Purdue University in 1951. After initially working on the B-52 bomber, Paul was transferred to Huntsville, Alabama, in 1962. For the next five years he helped design and develop the first stage of the Saturn Moon Rocket. He was then sent to the Johnson Space Center in Houston, where he worked with astronauts and others in monitoring the moon missions. Later in his career, he was transferred to New Mexico to work on a secret airborne laser system. Paul liked the area and chose to make it his home when he retired in 1982.

Hiking all day in the nearby Sandia Mountains and playing golf were his favorite pastimes, but recent heart problems have caused him to curtail physical activity. However, he still enjoys short walks on some of his favorite trails.

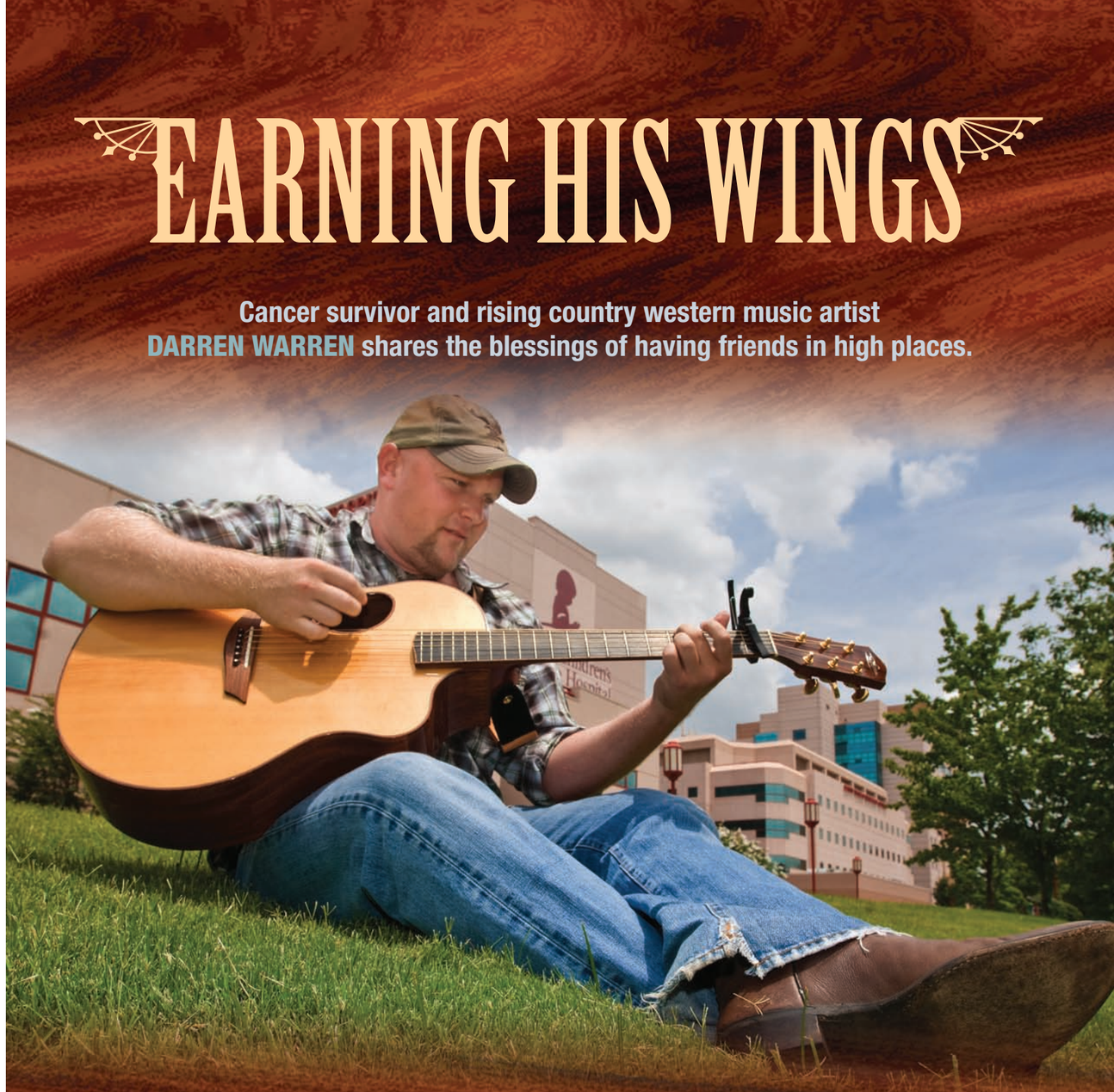
Paul has never toured St. Jude, and now does little traveling. But he says the information he receives as a donor strengthens his commitment to support the hospital's research and treatment of children with cancer and other catastrophic diseases.

"Learning about the children who are helped—and those who don't make it—makes me even more interested in helping St. Jude," he says. ●

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

EARNING HIS WINGS

Cancer survivor and rising country western music artist DARREN WARREN shares the blessings of having friends in high places.



By Ruth Ann Hensley

His jeans are Wranglers, his boots are worn and his shirt is top-stitched, country western plaid with pearly snaps. While it may not sound like typical angel attire, the only thing that appears to be missing from Darren Warren's wardrobe are his wings—but they are there; you just can't see them.

ANN-MARGARET HEDGES

A survivor of non-Hodgkin lymphoma (NHL), Darren Warren regards the diagnosis he received when he was 16 as a gift. It hardly seems heaven-sent, but Darren has transformed that life-threatening experience into the pursuit of a dream.

The amazingly talented, up-and-coming country western singer, songwriter and musician has cut two CDs and opened for Travis Tritt; but one of Darren's greatest passions is giving back to St. Jude Children's Research Hospital, the institution he credits for saving his life.

This unpretentious, self-proclaimed country boy with a voice as big as his heart takes major detours to perform benefit concerts, gets up with the chickens to promote the hospital on morning radio shows and goes the extra mile to bring his manager and crew to St. Jude so they can see it for themselves. He gives of himself with a tireless, refreshing, it's-*not*-all-about-me attitude.

Maybe it's his zest for life, his humility or the way he is firmly grounded in his faith, but Darren is so busy seeing beauty in the world that he wouldn't dream of looking for it in himself. "If it wasn't meant for me to stay on this earth, well… I'm not very good looking, but I would make a pretty angel," he says with a hearty laugh, never realizing that he already is.

Friends in high places

A typical teenage boy, Darren enjoyed all the things his rural Kentucky hometown had to offer: playing ball with his friends, riding four-wheelers, working at his dad's construction company and singing in the church where his father preached. One autumn afternoon in 1998, Darren was imagining how it would feel to hold the keys to the brand-new, Chevrolet pick-up he had been eyeing when he reached up and felt something else—a pronounced lump under his chin.

Doctors thought it was a cyst until they surgically removed it. "It was inflamed and irritated, and they realized that something wasn't right," Darren recalls. Tissue samples were immediately sent off for testing.

Darren went ahead and bought that truck, and like a rusty nail in a new tire, the cancer diagnosis caught up with him a few days later.

"That's a shocking place to be when you're 16 years old," Darren says. "It's shocking at any age, but at 16, you think you're invincible."

Even bullet-proof boys have to allow themselves a moment to "do what anybody would do," as Darren says. So he retreated to his room, stretched across his bed and cried.

When just enough time had passed, his mom quietly entered the room and sat down beside him.

"She said, 'Look at me,'" Darren recalls, with an intensity that strikes a chord. "So I looked at her and she said, 'We are going to beat this. We are going to do it. And we've got a friend who is going to help us.' And she pointed up to heaven."

Then he stood up, walked outside and climbed back in his new truck—determined never to play that sad, broken record again.

Giving denial the boot

But first, Darren had to wrestle the demon of denial.

"I didn't feel a bit sick," Darren says, remembering the day he arrived at the hospital. "I looked straight up at that statue of St. Jude, and I knew it was for my own good to be there; at the same time, it felt like hell on earth because I kept thinking, 'This can't be right. Just a few days ago, I was hanging out with my friends, and everything was fine.'"

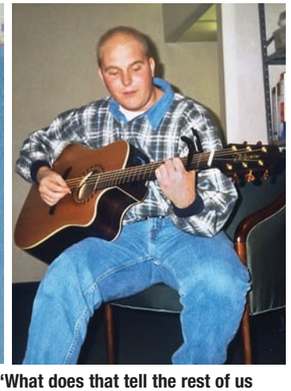
"Darren was still in shock, and he really wanted to think through things, to pray through things and to make a decision about his treatment that he felt good about—both intellectually and in his heart," explains John Sandlund, MD, of St. Jude Oncology. "He approached the situation in an extremely mature way and always kept a positive attitude."

When Darren came to terms with the diagnosis of NHL, a cancer of the lymphoid tissues and the third most common malignancy in children, he was treated with a regimen similar to the institutional protocol for acute lymphoblastic leukemia, which calls for more than two years of chemotherapy.

He responded well to the therapy, went into remission at the expected time and has been cancer free for eight years, according to Sandlund, who Darren describes as "the best guy that God has pretty much put together."

Darren also formed a close connection with Gwendolyn Anthony, RN, of the hospital's Ambulatory Care Unit.

"When I first met Darren, I realized what a special patient he was," Anthony says. "He was, and is, a great encourager to other patients and their families as well as to the staff. Darren shared with everyone that his strength to endure this trial came from his love and faith. He was thinking of how he could help others. I consider myself blessed to have been a part of Darren's care."



"The way Darren has handled his situation so positively makes me ask, 'What does that tell the rest of us about how to face our problems?" says John Sandlund, MD, Oncology. "You learn a lot about life from the kids who come through here. They come here for help from us, and sometimes I think we get more out of the relationship than they do. Actually, I think that's the case most of the time."

Stepping stones

In addition to the support of St. Jude staff, family and his friend upstairs, Darren found solace in music.

"You can take the bad things in your life, and you can make them a stumbling block or a stepping stone," says Darren, who began creating song lyrics at age 5. "There were times when I sat down and told my guitar how I felt, and I realized I had created a song—and there are times I realized I had just created something that needed to be left in that little room."

Darren never lacked for inspiration at St. Jude. In fact, he wrote every song on his *Tears are a Language* CD during treatment. "Go Get My Angel," one song that deals with love and loss, has already touched thousands of people.

"I was doing a morning radio show, and after the song aired, every line lit up. People were calling in—people who had been touched by the song and people who had ties to St. Jude," Darren says. "When we stepped outside, my manager said, 'What do you think about that?' and I just broke down crying."

"It's been a dream of his ever since his treatment to give back to St. Jude in some way," says Darren's mom, Sharon Warren.

That dream has kept Darren's feet firmly planted on those stepping stones, even as his music career begins to soar. "If your goal is to be a star and have money and fame, you are looking at it for the wrong reasons," Darren explains. "But if you become someone who is well known, the hope is that you can use that to try and make a difference. I wouldn't take anything—not a thing in the world—for going through what I went through. It makes you appreciate life, and it makes you treat others better. That's what we're here for, to reach a hand out to somebody else."

The youngest of three boys, Darren attributes his strong faith to his parents. He says that virtually every aspect of his music career is built around what he and his crew can do for St. Jude.

What drives his commitment?

"I tell people it's like God put a bunch of angels that he hand-picked to work at St. Jude," Darren says. "From the doctors to the nurses to the people who mop the halls, everybody was so sweet and caring. You don't find that anywhere else."

No, you don't —unless you're Darren Warren looking in a mirror at one of the prettiest angels there ever was.

To hear Darren Warren's music, visit www.darrenwarren.com. ●

GENE LEEPER

Although he has cut two CDs and opened for Travis Tritt, St. Jude patient Darren Warren (shown here in concert) says one of his greatest passions is giving back to the hospital he credits for saving his life.

Perspective

Closer Than You Think

"St. Jude research doesn't just benefit the children who walk through the doors of the hospital, but kids everywhere—in the United States and around the world. I'm a direct beneficiary of that research."

By Kevin Sharp

When I was a teenager living in California, I thought Memphis, Tennessee, was very far away. I had heard of St. Jude Children's Research Hospital because of watching the TV programs from time to time, but I didn't dream that their work would ever affect me or anyone I knew.

Then I got cancer.

It was Ewing sarcoma that had spread from my leg to my lungs. I was treated in a California hospital—on a protocol from St. Jude.

Memphis suddenly seemed a lot closer.

Since that time, I've learned that St. Jude shares its discoveries freely. Their research doesn't just benefit the children who walk through the doors of the hospital, but kids everywhere—in the United States and around the world. I'm a direct beneficiary of that research.

I'd be surprised if there is anybody who hasn't been affected by cancer on some level, whether a friend or family member or themselves. I think a lot of people are under the impression that, wherever they live in the country, Memphis is far away. They might wonder why they would ever benefit from donating to St. Jude. The answer to me is obvious. Since I have been affected by cancer, I want to be a part of trying to find the answers that will eliminate this disease.

And what a blessing it is that St. Jude treats children regardless of their ability to pay. I was fortunate, because my family had insurance when I got cancer as a teen. If we had not had that coverage, it would have destroyed my family financially. It's hard enough to deal with the fact that you may lose a loved one or a child; on top of that to be worried about financial needs is just way too much. St. Jude realizes that.

JERE PAROBEK

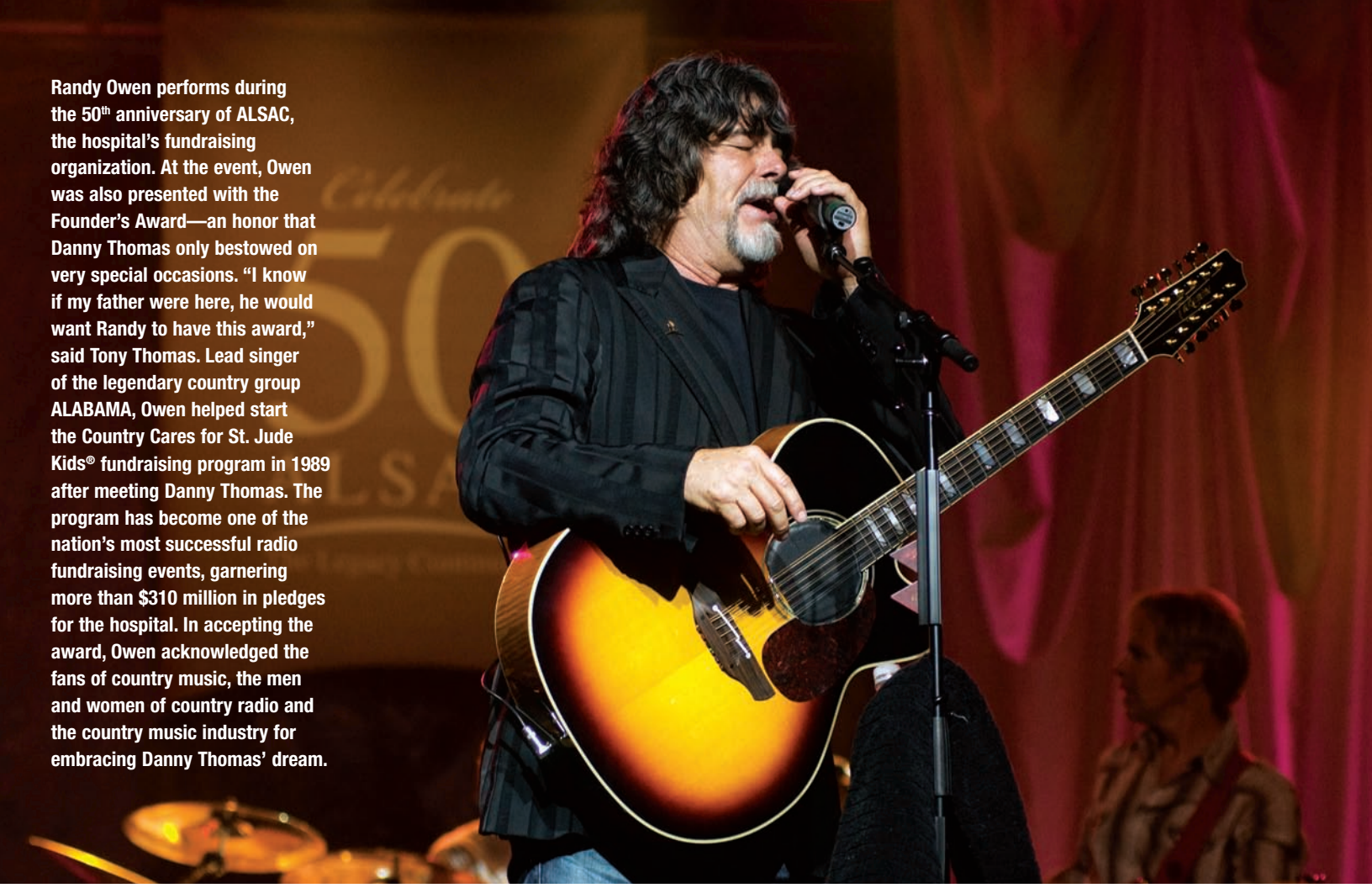
Cancer survivor Kevin Sharp visits St. Jude, extending hope to a young patient and his family.

I've had the opportunity to visit St. Jude numerous times, even sharing my experiences with families at the hospital's Survivor Day celebration. As a patient, it's beneficial to hear that there is life after cancer—that you can continue and that you can succeed. Sometimes situations are far more difficult than we seem to be able to handle. We all have our cross to bear and our different tragedies and trials in life, and it's important that people know that they can see it through to the other side—that it's tough, but it's worth it. Spreading that message is just a part of who I am.

I've also had opportunities to support St. Jude through my role as part of the country music community. It's a way to thank the hospital for what they did, not just for me individually, but what they do for childhood diseases and cancer treatment around the world.

St. Jude definitely will always be a part of my life. So many people and organizations played a role in saving my life. I can't imagine going through those experiences without helping to make opportunities available to others. ●

Kevin Sharp is an award-winning country music artist, entertainer, author and motivational speaker. He recently published Tragedy's Gift: A Cancer Survival Story, *a chronicle of his battle with cancer and the lessons he learned from that experience. To learn more about his work, visit* www.kevinsharp.com.



Randy Owen performs during the 50th anniversary of ALSAC, the hospital's fundraising organization. At the event, Owen was also presented with the Founder's Award—an honor that Danny Thomas only bestowed on very special occasions. "I know if my father were here, he would want Randy to have this award," said Tony Thomas. Lead singer of the legendary country group ALABAMA, Owen helped start the Country Cares for St. Jude Kids® fundraising program in 1989 after meeting Danny Thomas. The program has become one of the nation's most successful radio fundraising events, garnering more than $310 million in pledges for the hospital. In accepting the award, Owen acknowledged the fans of country music, the men and women of country radio and the country music industry for embracing Danny Thomas' dream.

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