

Solving for X
St. Jude saves the life of
COOPER WINTERS



Cover story

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St. Jude helps Cooper Winters beat a deadly, X-linked disease.

Features

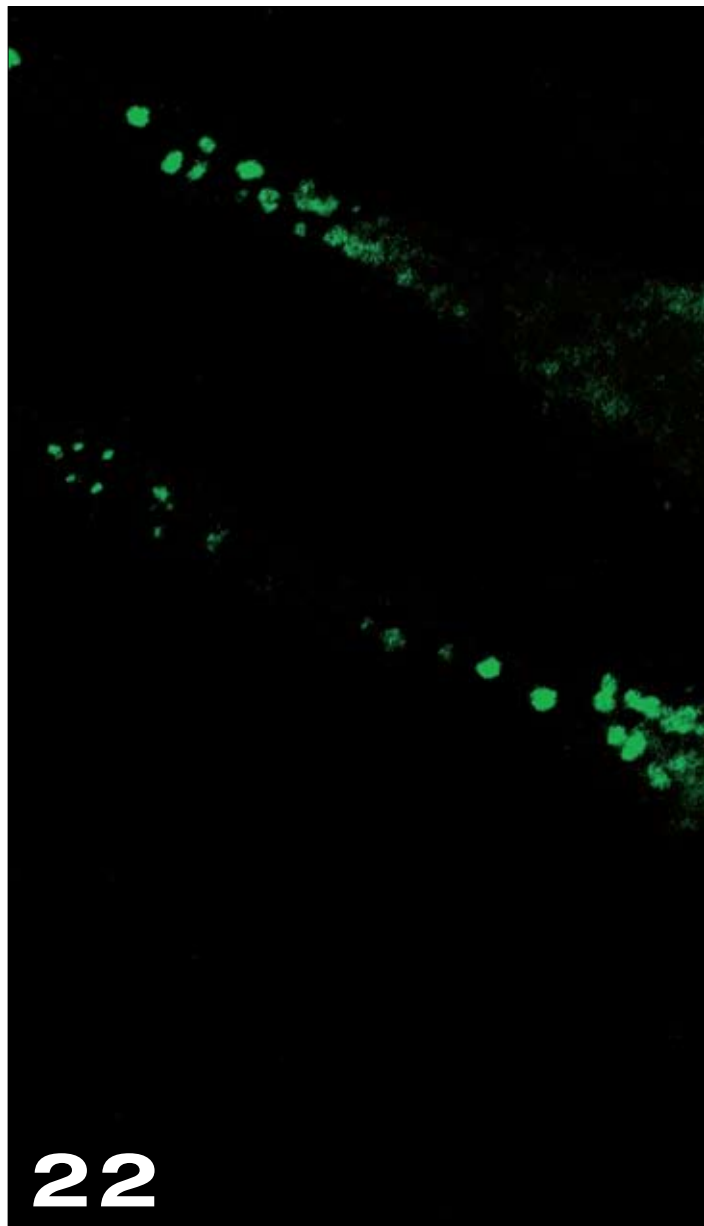
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Promise

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St. Jude has changed its mailing address to reflect the hospital's historical roots. The new address, 262 Danny Thomas Place, represents February 1962, the date St. Jude opened its doors.

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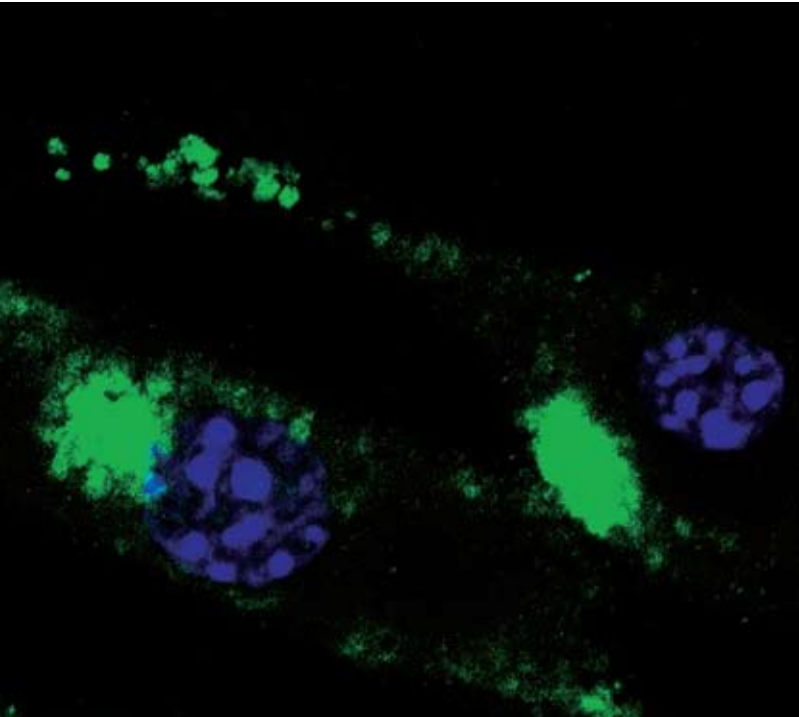
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Promise

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On the cover: photo by Peter Barta

Highlights

PETER BARTA



Shining a light on research

In August of 2008, St. Jude opened a 1,500-square-foot light microscopy facility containing high-tech tools to help researchers make lifesaving discoveries. Light Microscopy Director Samuel Connell (at right) and colleague Simon Moshiah, PhD, collaborate on a project in the new facility. Light microscopy includes confocal laser scanning microscopy, multiphoton microscopy, and live cell imaging and microinjection. "We are trying to develop techniques that are on the frontier of live and fixed cell imaging, and bring them directly to St. Jude researchers," Connell said. "This will shorten the timeline for development of new projects within the laboratories." The facility is part of the St. Jude Cell and Tissue Imaging Center, which also opened a separate facility for electron microscopy earlier this year.

Continued vigilance saves lives

Improved supportive care has greatly reduced early complications and death rates of children with acute myeloid leukemia (AML), according to a recent St. Jude study.

The study explored whether intensive supportive care of such children affected death rates. Supportive care includes careful monitoring of vital signs and mental status, cautious hydration and transfusion, correction of clotting abnormalities, better methods of pulmonary ventilation and protection, antibiotics and antifungal therapy, prevention and treatment of nausea and vomiting, and careful initiation of chemotherapy. Such supportive care also includes a treatment called leukapheresis, which reduces the levels of white blood cells.

The St. Jude analysis concentrated on children with newly diagnosed cases of AML who had hyperleukocytosis, an overabundance of white blood cells in circulation that can clog blood vessels. The researchers analyzed

St. Jude medical records of 106 AML patients with hyperleukocytosis. According to the study, the death rate among these children dropped from 26.2 percent before 1983 to 2.8 percent between 1983 and 2000, likely as a result of improved supportive care.

"These findings emphasize that patients with AML, especially those with high white blood cell counts, should be treated in an experienced tertiary center with a good supportive care team," said Ching-Hon Pui, MD, Oncology chair. "For example, at St. Jude, we have a dedicated team of clinicians taking care of AML patients, and they are more aware of the need to treat hyperleukocytosis, are more experienced and are more vigilant in patient care than is usually found at a less specialized hospital."

Hiroto Inaba, MD, PhD, Oncology, was first author of a report on this study, which appeared in the journal *Cancer* in June 2008.



Researchers explore mysteries of the brain

St. Jude scientists have identified one of the molecular mechanisms underlying the genetic brain malformation called holoprosencephaly (HPE). While the findings offer insights into HPE, they also help scientists understand the fetal brain formation process.

HPE occurs in about one in every 250 fetuses, frequently causing miscarriages and stillbirths or brain abnormalities and facial malformations such as cleft lip and cleft palate.

A team led by Guillermo Oliver, PhD, St. Jude Genetics and Tumor Cell Biology, investigated the role in HPE of a gene that codes for a protein called Six3. In previous studies, Oliver and his colleagues had identified the Six3 protein as critical to fetal brain formation. The researchers theorized that Six3 might trigger HPE by compromising the function of the Sonic Hedgehog pathway, a major regulator of fetal brain development. Oliver's team found that both Six3 and the Sonic Hedgehog pathway were active at the same time and place in the brain, important evidence that they could work together. The researchers also developed evidence that the two genes cooperate to cause HPE and to regulate normal brain development.

The team published their findings in *Developmental Cell* in August 2008.

"These findings are important because, while genes that cause HPE have been identified, the interactions among those that produce HPE are not only complex, but poorly understood," Oliver said. "This represents a first step in understanding the mechanism of that interaction."



Protective "suicide protein" thwarted

St. Jude investigators have found that a protein called Puma, which normally protects the body by triggering cancer cells to commit suicide, is suppressed in Burkitt lymphoma. The discovery raises the possibility of treating the cancer using drugs that switch on the gene that makes the Puma protein.

Burkitt lymphoma is a cancer in which immune cells called B lymphocytes turn malignant and proliferate uncontrollably. It is the most widespread form of childhood cancer in Africa, but is rare in the United States.

The investigators explored whether production of the Puma protein was suppressed in Burkitt lymphoma, which would unleash B cell proliferation. When the researchers analyzed cells from humans with Burkitt lymphoma, they found that in most cases Puma expression had been lost.

"This finding represents a key extension of other studies on Puma, because such loss had never been shown before in human cancer," said Gerard Zambetti, PhD, Biochemistry, senior author of a study that appears in the September 2008 issue of *Molecular and Cellular Biology*.

"Such loss had never been shown before in human cancer."

Highlights

Small investment pays survivorship dividends

A small hike in funding for pediatric cancer care could significantly boost survival rates in low- and middle-income nations, according to an international team led by St. Jude.

Researchers analyzed data from 10 such nations and found no correlation between a country's pediatric cancer survival rate and its overall mortality rate for children under age 5.

International agencies consider under-5 mortality as an important indicator of child health within a nation. However, the study concluded that pediatric cancers are not a factor in under-5 mortality because they are uncommon and often underdiagnosed.

"This is a call to the global community that it is possible to increase pediatric cancer survival, even in countries that have high under-5 mortality rates for other causes, such as infectious diseases," said Raul Ribeiro, MD, International Outreach Program director and the paper's first author. "With a modest financial investment, we can improve survival very quickly."

Ribeiro and his colleagues reported their analysis of the data in the August 2008 issue of *The Lancet Oncology*, which is devoted to global health issues.



"I think this cooperation can help to make small changes, but small changes can be significant for those kids."

Improving nutrition around the world

Employees from the St. Jude International Outreach Program and Clinical Nutrition department have joined forces to take educational efforts around the world. In the past couple of years, St. Jude experts have traveled to locales such as Brazil, Central America and India to educate clinicians about the importance of proper nutrition for children receiving treatment in local hospitals, especially in lower-income populations.

Since malnutrition is a common problem for children with cancer in developing nations, Sara Day, RN, International Outreach nursing director, teamed with registered dietitian Terezie Mosby, Clinical Nutrition, to develop a plan for nursing nutritional interventions. This plan involved developing educational materials, providing Web-based nutritional lectures for nurses and designating a nurse to provide ongoing nutritional services.

"When you hear that the cure rate for leukemia in some of these countries is so low, you feel like you need to do something," Mosby said. "I think this cooperation can help to make small changes, but small changes can be significant for those kids."

St. Jude also created monthly, Web-based lectures for nurses in several countries to present new ideas and to field questions. Dietitians from Brazil, the Czech Republic and Mexico also visit St. Jude for training and observational sessions. They take what they learn at St. Jude and adjust it for their home hospitals and resources. *Turn to page 12 to learn more about the St. Jude Clinical Nutrition department.*

St. Jude helps kids affected by hurricane

During the days leading up to Hurricane Gustav's September landfall, employees across St. Jude finalized plans to take care of any children with cancer who might need assistance as a result of the storm. Hospital employees sprang into action, marshalling resources and carrying out detailed procedures that had been put in place after Hurricane Katrina struck in 2005.

St. Jude operates a clinical program for children with cancer at its Baton Rouge, Louisiana, affiliate at Our Lady of the Lake Regional Medical Center. Following the storm, St. Jude evacuated 14 children from its affiliate clinic and seven patients from other area hospitals.

All patients were treated in Memphis by St. Jude physicians at no cost to the families. St. Jude also assisted with transportation and provided free housing and meals until the families were able to return home.

St. Jude takes aim at worldwide killer

A few bacteria are especially adept at stealing genetic material from other bacterial species and incorporating those foreign genes into their own machinery. St. Jude researchers recently gained insight into how pneumococcus, the primary cause of pneumonia, uses a particular piece of stolen genetic material to render it more virulent.

The research is part of the hospital's ongoing effort to develop affordable and effective pneumonia vaccines for children in developing countries. This is an especially critical effort, given that pneumonia causes more than 2 million deaths a year in children worldwide—more than AIDS, malaria and measles combined.

Elaine Tuomanen, MD, Infectious Diseases chair, said that St. Jude and its collaborators aim to produce pneumococcal vaccines that will have a profound impact on the disease worldwide.

"Current vaccines used in the developed world cost more than \$100 a dose and are limited to protecting against perhaps 10 to 15 types of pneumococci," Tuomanen said. "But that price is far too high for developing countries, and there are 90 types of pneumococci out there."

St. Jude and its collaborators have already identified bacterial proteins that occur almost universally in pneumococci and that could be the basis for a vaccine inexpensive enough to be used in developing countries. Tuomanen was senior author of a report on this work that appeared in the July 2008 issue of *Infection and Immunity*.

Vaccines based on these proteins will be produced in the GMP facility, a sophisticated biomedical workshop for making vaccines, drugs, proteins, gene-based molecules and other biological products. St. Jude is the only pediatric cancer research center that has such an on-site facility.

New drug combo helps kids with sarcoma

A new combination of two anti-cancer drugs offers promise in treating recurrent and treatment-resistant bone cancer in children, according to a study conducted by researchers at St. Jude and Rady Children's Hospital at the University of California at San Diego.

The study is the first to analyze the effectiveness of the combination of the anti-cancer drugs gemcitabine and docetaxel in treating children with bone sarcomas that relapsed or had not responded to other treatments. Anti-tumor responses were seen in two types of bone sarcomas: osteosarcoma and malignant fibrous histiocytoma.

The two drugs attack cancers in different ways, said Najat Daw, MD, St. Jude Oncology. Gemcitabine interferes with the DNA synthesis critical for the rapid growth of cancer cells. Docetaxel jams the machinery of cell division that cancer cells need to proliferate.

"A major issue we face in managing patients with recurrent sarcomas is the paucity of active agents," Daw said. "A limited number of drugs are active against bone sarcomas, and these are usually used as front-line treatments. When the sarcomas recur, we have essentially no active agents."

Daw said the preliminary finding offers a promising option for treating drug-resistant sarcomas. Daw is senior author of a report on this work, which appeared in the journal *Cancer* in July 2008.

THE COMEBACK KID

BY SUMMER FREEMAN



PHOTOS BY PETER BARTA

WITH HELP FROM HER ST. JUDE TEAM, STANDOUT
SOFTBALL PHENOM CIARA GINET WINS THE MOST
DECISIVE GAME OF HER LIFE.



Ciara Ginnet's "fans" include friends, family, classmates and a large contingent of St. Jude supporters, such as Lisa McGregor, MD, PhD (at right), of St. Jude Oncology.

As third baseman for a competitive softball league, Ciara Ginnet was used to handling sharply hit line drives. Since her introduction to the sport at age 4, Ciara relished playing third base—a position known as the “hot corner” because of the high velocity of balls hit to that spot. Despite arduous training, nothing compared with what careened Ciara’s way not once, but twice in the past two years.

In late 2006, Ciara faced a rare cancer called ovarian dysgerminoma. After surgery and a year of remission, the softball star was thrown another curve when the cancer returned. With courage and resolve, Ciara battled the disease, winning the most important game of her life.

Strike one

“Ciara doesn’t play softball,” says her mother, Bobbi Ginnet. “Ciara breathes softball.”

It took crippling abdominal pain during a tournament in Cincinnati to get then-10-year-old Ciara off the field. At a local hospital, doctors diagnosed a viral infection. In days, the pain subsided and Ciara was ready to get back in the game.

During the next year, that scene occurred several more times. “Another hospital said it was diverticulitis (a digestive disease) and prescribed medicine,” Bobbi remembers. In November 2006, after two trips to the hospital in one

week, Bobbi demanded answers. “I thought that she was too young for diverticulitis and told them that I wasn’t leaving until they found out what was wrong with my child.”

An ultrasound revealed that Ciara’s left ovary had twisted. In the operating room, surgeons removed the unhealthy tissue, sparing a small piece of her left ovary. A pathology report found the tissue contained a germ cell tumor, identified as ovarian dysgerminoma.

With the cancer diagnosis, Ciara was referred to St. Jude Children’s Research Hospital.

“Germ cell tumors are rare,” says Lisa McGregor, MD, PhD, of St. Jude Oncology. “They occur at a rate of 2.4 tumors per million children and represent 1 percent of cancer diagnosed in people younger than 15 years old.”

While the type of cancer is rare, St. Jude has treatment plans for the disease and treats an average of five patients a year with different types of germ cell tumor in the chest and abdomen. For patients like Ciara, who have localized gonadal tumors, long-term survival rates are high.

“The cancer diagnosis was overwhelming, and we were in shock and terrified,” Bobbi says. “But once we got to St. Jude, the support was unbelievable. They helped us understand what we were facing. They gave us books, explained

treatments, told us cure rates—they basically gave us a crash course in oncology. It was an overnight relief.”

In addition to the emotional support, Ciara’s father, Ron Ginnet, remembers the relief of learning that they would never receive a bill for his daughter’s care. “When they told me I wouldn’t get a bill, I thought that I misheard,” Ron recalls. “I actually said, ‘Can you repeat that?’”

Back in the game

After St. Jude surgeons removed the remaining portion of Ciara’s left ovary, there was no sign of cancer. The Ginets were also thankful to learn that Ciara still had the chance to have children one day.

“We didn’t find any evidence of tumor remaining or any evidence that the tumor had spread in her body,” McGregor says. “At that point, she didn’t need any other therapy, and it was a case of monitoring.”

With the prognosis, Ciara threw herself back into the life she knew before the episodes of pain, returning to St. Jude for periodic checkups. Back up to speed, Ciara spent the next year following a rigorous schedule of school, practice and tournaments. Her skill on the field at 12 years old even earned her an invitation to play on a league with high school players.

“Ciara is a fighter and always bounces back,” Bobbi says.



Throughout her bouts with cancer, Ciara inspired her teammates and treatment team with her competitive spirit.

Strike two

Ciara showed no signs of illness in late 2007 when a routine checkup revealed unwelcome news. The cancer had returned in lymph nodes around one of Ciara's kidneys.

The Ginets were devastated. "I didn't know what to think," Bobbi says. "I didn't know what to say."

McGregor mapped out a treatment plan for Ciara that included chemotherapy and surgery.

With heavy hearts, the Ginets returned home. "I tried to stay strong as we were talking to Dr. McGregor," Bobbi says. "But when we got home, we had our cries. Ciara remembered the pain and the surgery from the first time and was so scared."

Ron, who had always been Ciara's loudest fan when she was on the field, tried to reassure her: "I wish I could take the pain for you, but I can't. This might make you feel sick, but it is going to make you better also," he told her.

The rally begins

Ciara started her treatment with six weeks of chemotherapy. As hair loss and nausea began to take their toll, she remained upbeat.

"I like to think that I'm the strong one, and I have to be that for her—but she always ends up showing me how much stronger she is than everyone else," Bobbi says. "She still tried to get out and play. She was losing her hair, wearing a mask to protect her weakened immune system and tossing the ball around in the backyard."

The operation to remove the

affected lymph nodes was successful, but recovery was tough. One post-surgery issue led to another. In less than two weeks, Ciara coped with a collapsed lung, a blood transfusion, a viral infection and debilitating blisters. But the athlete didn't remain on the bench for long.

"One day, she was in bed looking so pitiful," Ron recalls. "The next day, it was like she had decided that she was done lying in bed. I walked in the room and she said, 'Hi, Dad!' and was up and moving around on crutches."

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St. Jude Child Life specialist Cara Sisk recalls the day doctors gave Ciara permission to play softball again. "It was in mid-week when they told her, and that was it for Ciara," Sisk says. "By that Saturday, she was playing in an all-day tournament. She didn't just go out and play one game; she went out there and played with her team the whole day."

Cheering fans

On the softball field, Ciara had her share of supporters to cheer her on during games, but during treatment, that fan base grew. The group originated with Ciara's classmates; expanded to include friends of her older brother, Michael; and eventually spread throughout their entire hometown.

Ciara's teammates volunteered their time to clean out the air conditioner vents at the Ginets' home as well as to apply a fresh coat of paint to the interior rooms. A nearby university issued an invitation to the Ginets to visit its softball team—an especially thrilling treat for Ciara, who had been a longtime fan.

After Ciara finished her chemotherapy treatments in April 2008 and was told that she would only have to return for checkups, her hometown raised money to send the family on a surprise vacation—a Caribbean cruise. When the Ginets returned from the trip, they found their neighbors painting the exterior of their house. "There have been so many prayers, thoughtful acts," Bobbi says. "The support has been unimaginable."

Home run

Ciara is still sparkling on the softball diamond, as she has transitioned from the outfield to the infield, where she plays second base. She's returned to the game she loves and breathes and is still playing with passion—as illustrated by a broken arm she suffered in a recent game. Her spirit and her love for softball have not been broken—and despite having two strikes of cancer, she's still in the batter's box, eyeing that home run pitch. ●

The Right Call

One phone call. That's all it took to help save the lives of children.

BY JANICE HILL

Sometimes life-changing decisions are made in the most unlikely places, at the most improbable times. Just ask Mark and Wendy Wilson.

Late one night, Mark sat in an Oklahoma hotel room, contemplating an exciting business endeavor.

"At 1 a.m. I turned on the TV, and there was Marlo Thomas talking about St. Jude Children's Research Hospital," he recalls. "Because I was all fired up about our project, the last thing I wanted to watch was a show about sick kids, so I changed the channel. But Marlo was on the next station, too."

Another click of the remote; Thomas appeared again. Mark was preparing to change the channel one more time when Thomas looked into the camera and said, "Won't you help; won't *you* pick up the phone?"

Mark immediately dialed St. Jude and made a monthly pledge that he and Wendy continue today.

Last May, Mark was traveling back from Missouri where he had presented students with scholarships from The Reach Foundation, which he and his wife had established. On past trips, he had glimpsed St. Jude from the interstate. This time, he decided to stop and visit.

"I got out of the car, and the first thing I saw were children being pulled around in their little red wagons," he says. "I thought about my three healthy children, and how I couldn't imagine what it would be like to see one of them suffer. Wendy and I were given this blessing of healthy children. We feel there couldn't be a better organization to give to than one that does such a great job of caring for the entire family. When you give to St. Jude, you see how you are saving lives and saving families."

The Wilsons subsequently learned that their parents had been regular St. Jude contributors. Mark and Wendy funded a patient exam room in the new Chili's Care



ARTISTIC IMAGES OF CANTON, LLC

"When you give to St. Jude, you see how you are saving lives and saving families," Mark Wilson says. He and his wife, Wendy, are enthusiastic supporters of the hospital and its mission.

Center in his parents' honor and are currently sponsoring an additional room in honor of Wendy's parents.

Mark and Wendy are spearheading a "Harvest for Hope" Gala next year in Hartford, Connecticut, to benefit St. Jude. The couple also pledged profits from the sale of a home through the St. Jude Dream Home Program as well as 10 percent of all profits from their various businesses. Next summer, Mark plans to produce

"People say, 'Give until it hurts.' I say, 'Give until it feels good'—because it does."

KidStock, a concert benefiting children, including those at St. Jude.

Mark once heard a businessman asked why he had made a multimillion-dollar charitable donation. The philanthropist responded, "What do I need, a bigger boat?"

"That was such a profound statement because so many of us want that bigger boat," Mark says. "Of course, a boat would be nice. But that's a message too few of us hear, and Wendy and I are trying to live by that example.

"People say, 'Give until it hurts.' I say, 'Give until it feels good'—because it does." Our Reach Foundation's motto is 'If in only one life, make a difference.' Through St. Jude, we know we are."

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. ●

St. Jude mentoring opportunities inspire many high school and college students to consider careers in science and medicine.

The last thing most high school and college students want to do in the summer is more school work. But instead of non-stop texting, lounging by the pool or playing video games, some of the nation's brightest students spend each summer with some of the world's hardest working researchers in labs at St. Jude Children's Research Hospital.

Through two programs—The Summer for Sickle Cell Science Program and the Pediatric Oncology Education (POE) program—students experience mentoring opportunities beyond measure. The mentors act as advisers, guides and trusted counselors and gain dedicated student scientists in return.

Introducing teens to research

The Summer for Sickle Cell Science Program brings Memphis-area high school students into St. Jude science, research and medical environments for eight weeks. Funded by the National Institutes of Health, the program gives teens hands-on experience that could inspire them to pursue science or medical-related careers.

St. Jude invites three highly qualified students with diverse backgrounds and interests into the program each summer.

"The recruitment and training of the next generation of scientists is a critical goal of the Summer for Sickle Cell Science Program," says Charlotte Hoyle, the program's coordinator. "Our program allows St. Jude to attract, encourage, and mentor talented scholars. These students are given the opportunity at age 18 to go into labs with PhDs, MDs and to work with other committed employees."

The program exposes students to researchers working in laboratories so they can gain experience that could

Passing the Torch

BY CARRIE L. STREHLAU



(From left) Sara Day, RN, and Elisabeth Chismark, RN, both of International Outreach, teach POE student Melissa Garcia how to conduct a Web-based nursing conference. The trio also created nutrition education materials for pediatric oncology caregivers in Central America.

cultivate continued interest in research related to sickle cell disease. The interns also develop altruistic projects with the goal of "giving back" to children with sickle cell disease. Such projects have included violin lessons, sickle cell soccer camps and blood drives to coincide with September's National Sickle Cell Awareness Month.

"Each student has had a phenomenal experience," says Russell Ware, MD, PhD, Hematology chair. "The laboratory mentors and staff also have enjoyed having these great students spend their summers working in the laboratory. My own personal interactions with the students have been highly positive. They are bright, motivated and eager to learn. In the laboratory setting, they demonstrate a keen intellect and quickly grasp ideas."

Other St. Jude faculty members say that they benefit from interacting with the students.

"Students coming into the sickle cell program bring great enthusiasm and energy to the projects," says Elaine Tuomanen, MD, Infectious Diseases chair. "They take on new directions and push the limits of existing dogma. The interaction in the lab is really dynamic."

Beyond the college campus

Funded by the National Institutes of Health and the National Cancer Institute, the POE Program allows students who are preparing for careers in biomedical sciences, medicine, dentistry, pharmacy, nursing and related areas to gain biomedical and oncology research experience.

"A number of outstanding institutions have summer internship programs, but ours is the only program focused on pediatric oncology," says Suzanne Gronemeyer, PhD, POE Program director.

POE students interact with St. Jude scientists, physicians and postdoctoral fellows. They are matched with faculty mentors who share their research interests, and they participate in the mentors' ongoing research projects. The 2008 class of 48 was selected from more than 300 applicants and represented 42 schools in 26 states and the District of Columbia.

"Experiences such as the POE Program can make a tremendous difference in a student's long-term career path," Gronemeyer says. "It can open a lot of doors from getting a better post-grad experience such as medical or graduate school to choosing a residency program." Historically, 85 to 90 percent of St. Jude POE students have earned doctoral degrees.

To qualify for the 11-week program, a student must be at least a sophomore in college and have excellent grades and recommendations. St. Jude faculty mentors then select students for their labs from the pool of qualified applicants.

POE and other summer students also attend a "Lunch and Learn" series, which offers networking and educational opportunities. Students can speak face-to-face with top researchers and with other students.

"I had the opportunity early in my career to do summer internships, and it made all the difference in my career path," Gronemeyer says. "I also had opportunities through the people I met during those internships. Former POEs frequently write to me saying they run into each other throughout the country, which is positive reinforcement of the program."

At the end of their appointments, participants give presentations on their research projects. They also submit reports on their research projects written in the style of specific journals in which their mentors publish.

The future of research

"We are grooming some of the next generation of pediatric oncologists, cancer researchers and cancer care providers," Gronemeyer says. "While most POEs have become physicians, others have obtained professional degrees such as nurse practitioner or medical physicist. They become highly accomplished people whom we need more of in this country."

Hoyle sees the same in her interns.

"These exciting summers are life changing for the interns, as well as for the employees who work with them," she says. "Everyone's a winner as they work together—fighting to cure children with catastrophic diseases." ●

PHOTOS BY ANN-MARGARET HEDGES



Aamir Khan (center) worked in the lab of Derek Persons, MD, PhD (at right), of Hematology during the Summer for Sickle Cell Science Program. "Within the lab, there existed an atmosphere of collaboration, which motivated me to work harder in understanding my research project," says Khan of the program, which was directed by Charlotte Hoyle (at left).

ADVICE FOR BUDDING SCIENTISTS

No magic formula applies to all students, but here are some initial steps for anyone who is considering a science or medical-related career. Russell Ware, MD, PhD, Hematology chair, offers the following tips:

- First, take several science classes to determine your interests and abilities.
- Second, apply yourself scholastically, since good grades provide evidence of your commitment to this kind of career.
- Third, show an interest—talk with your guidance counselor, science teachers and others who might help you later on with advice and letters of recommendation.
- Fourth, work on communication skills; these skills are critical in science and are often overlooked by students.
- Finally, get active in pursuing your dream.



Alaina Coleman proudly presents a pizza she created in the hospital's new Kay Kafe. The St. Jude Clinical Nutrition staff constantly come up with creative ways to encourage patients to eat healthy foods.

Well Done

BY JOYCE M. WEBB

It's a recipe for recovery: Mix one state-of-the-art cafeteria with a team of dedicated chefs and dietitians. Add a dash of innovation and a pinch of creativity. Voilà! Dinner is served.

For the past few weeks, food has had little appeal for 11-year-old Alaina Coleman. While undergoing her second bone marrow transplant for acute myeloid leukemia, she has spent many days as an inpatient at St. Jude Children's Research Hospital. Meanwhile, employees in the hospital's Clinical Nutrition department have been working diligently to ensure that Alaina obtains the nutrition she needs to help her regain her health.

Proper nutrition is important for all children, but especially for those undergoing treatment at St. Jude. During treatment, children's immune systems may be compromised. When their white blood counts are low, they are especially vulnerable to infection. During that time, the bacteria in many foods can be hazardous.

"When their counts are low, we have to make sure they stay away from rice, tea, strawberries, soft-serve ice cream from bulk machines, and other foods that do not harm you and me, but that could be very serious for the

patients," says Registered Dietitian Kathryn Alexander.

Early in her treatment, Alaina wanted a smoothie, but not just any smoothie. "She wanted a mango kiwi strawberry smoothie," Alexander recalls. "Because her counts were low, she couldn't have fresh strawberries, so we cooked them and then blended them with the mango and kiwi. We made the special smoothie that she wanted, and it worked out well."

Thanks to a \$16 million gift from Sterling Jewelers Inc., St. Jude has enhanced its ability to cater to kids like Alaina. The Kay Kafe, which opened in the summer of 2008, boosts the hospital's ability to provide variety and efficiency in meal preparations and delivery.

"Our primary goal is to get our kids to eat. It's the most natural thing for them to do," says Karen Smith of Clinical Nutrition. "The new cafeteria has given us a world of opportunity in enhancing our patients' oral intake with more options for healthy, nutritious and culturally diverse foods."

The Clinical Nutrition program at St. Jude participates in both daily patient care and research. The nutritional components of the hospital's protocols emphasizes the dietitian's role in the multidisciplinary team treating patients with catastrophic diseases.

Serving up smiles

When the hospital was constructed, St. Jude founder Danny Thomas decided the cafeteria would be the central gathering place where employees, patients, their families, researchers and clinicians could dine together under one roof. That model continues today, with a stellar kitchen and dining area that feels more like a chic restaurant than a hospital cafeteria.

Children come to St. Jude for treatment from every state and more than 70 countries. Hospital employees hail from more than 80 nations. Forgoing the one-size-fits-all approach to cafeteria food, St. Jude embraces its diverse population and caters to its hospital family by offering a wide variety of cuisines. If kids or staff are hungry for four types of southern barbecue on a smoker, Indian biryani rice or authentic Chinese dishes, specially trained chefs make it to order. In the new cafeteria, patients can also enjoy ethnic food choices such as Mediterranean salads or Italian pastas and gelato.

It is important that the St. Jude Clinical Nutrition staff understand different cultures and eating habits so that dietitians are prepared and knowledgeable about their patients.

"When patients say they don't like something, I know what they mean," says Terezie Mosby, a registered dietitian. "I have lived in several different countries, and the same food might taste totally different here than it does in another part of the world."

Children also participate in such fun activities as make-your-own-pizza and decorate-a-cupcake events.

"Our patients are constantly having someone running tests or giving them medications, which often leaves them feeling less comfortable than before," says Miles McMath, senior executive chef. "We have a chance to do something that the patient will enjoy and look forward to."

Recipe for success

When children go to the hospital for treatment, they leave familiarity and predictability behind—along

with their toys, friends and pets. Dropped into an alien landscape, kids yearn for the comforts of home. Sure, they have access to the latest medical treatments, but what would really make them feel better is mom's chicken soup or grandma's special pot roast. At most hospitals, that craving goes unfulfilled. But not at St. Jude.

St. Jude clinicians recognize that children respond best to treatment when they have access to the foods they love. So, if dad's macaroni and cheese is what the patient craves, that's exactly what is served. The hospital's dietitians and chefs often replicate patients' favorite dishes by using recipes obtained from the children's families.

Dietitians may visit local grocery stores to purchase ingredients for special orders.

"Most hospitals are not going to do that," says Alaina's mother, Ginger Coleman. "I like the fact that they care about what the children want and do everything they can to get it for them."

In an area dedicated to preparing meals for inpatients, dietary technicians, chefs and cooks prepare creative meals while upholding the highest food safety and

sanitation standards. All staff in this area have undergone extensive training on preparing low-bacteria diets and meeting other specialized needs of patients with weakened immune systems.

"The treatments that St. Jude patients undergo can

cause appetite loss, nausea and mouth sores," says Chef John Gilbreath. "By catering to the children's cravings, we can help them stay well nourished, which is essential in helping them fight infection."

The inpatient room service food preparation area includes a Turbo chef oven, a commercial grade food steamer, a grilling station and a meal assembly area.

"The new cooking area in the kitchen has helped us ensure that we get meals out to our patients in a timely manner—usually 30 minutes from the time patients order to the time the meal is delivered to their rooms," says LaWanda Payne of the Food Services department.

Alaina and her family appreciate the effort that goes into providing her with appetizing, nutritious food. But she still longs for the day when she can eat supper in her own kitchen.

"I know it will take a little while," her mom says. "But we've been through this before and made it, and we'll get through it again." ●

"I like the fact that they care about what the children want and do everything they can to get it for them."

LEARNING MORE ABOUT DIFFUSE PONTINE GLIOMA

dpg

St. Jude study gives promise to young children with a brain tumor thought to be universally fatal.

BY MIKE O'KELLY



Erica Ely was 2 years old when doctors at another hospital diagnosed DPG and predicted that the toddler would not survive more than six months.

ERICA ELY was 2 years old when her mother, Jackie, first took her to the physician for eye-related problems. After several clinical visits for what was diagnosed as pink eye, a pediatrician noticed one side of Erica's face wasn't moving while she was crying and recommended that Erica visit a neuro-ophthalmologist.

"The neuro-ophthalmologist said she had Bell's palsy, and that it was nothing to really worry about," Jackie says. "I had a bad feeling and did some searching on the Internet and found out that 1 percent of the time Bell's can be misdiagnosed—and can actually be a tumor."

Weeks later, a brain magnetic resonance imaging (MRI), revealed

that Erica had an inoperable brain tumor, called diffuse pontine glioma (DPG). Jackie and her husband, Lincoln, were told there was a 99 percent chance Erica would not survive after six months, and that the 1 percent of children who did survive were actually misdiagnosed.

After visits to three medical institutions in her home state of North Carolina, Jackie sent a late-night e-mail to the St. Jude Children's Research Hospital Web site. Her message was answered with a quick reply of hope. Erica's pediatrician provided a referral and, two days later, the family flew to Memphis so that Erica could begin treatment.

Hope for toddlers with DPG

Physicians have long believed that DPG was universally fatal. Occurring in the brain stem, the tumor accounts for 10 percent of all pediatric brain cancers.

St. Jude scientists recently completed a study indicating that children under 3 years of age with DPG appear to have a better outcome than older children with the same tumor.

Alberto Broniscer, MD, of St. Jude Oncology and his team reviewed the medical records of 10 St. Jude children with DPG who

were younger than 3 years old. Each child received treatment—two with radiation, six with radiation plus chemotherapy and two with only chemotherapy. Six of the 10 children have survived for at least two years following these therapies, all of which are ineffective in older children with DPG.

Broniscer says the distinct biological characteristics of the tumor in children younger than 3 might account for their better response to radiation and chemotherapy.

Studying the future

Erica's story is one of the 10 cases Broniscer's team reported in their study, which reviewed cases of DPG at St. Jude dating back to 1996. The median age of these children was 2.2 years, and the median time between symptom development and actual diagnosis was two-and-a-half months.

Previous studies of DPG performed by other institutions were based on patients whose disease was not exclusively diagnosed by brain MRIs. Clinicians relied only on MRI scans to diagnose the disease in children at St. Jude.

"CT scans are not able to differentiate between DPG and other tumors, which originate in the brainstem with a better prognosis," Broniscer says. "These past studies, some in the 1980s and 1990s, had some children who were diagnosed with CT scans. Years later, patients were found to be alive and well, so one wonders, 'Did they have this tumor or did they have something else?'"

Results from the St. Jude study show that 45 percent of children younger than age 3 treated for DPG will survive for at least three years without experiencing tumor growth, and 69 percent of such children will survive.



Alberto Broniscer, MD, of St. Jude Oncology, confers with Pediatric Nurse Practitioner Lindsay Chapman of Neurology. A recent study led by Broniscer uncovers new information about a brain tumor called diffuse pontine glioma.

“I can’t describe the feeling when you are told that your child is going to die, and then somebody offers you a life preserver. You can’t even put that into words.”

No significant improvements in the treatment of DPG have occurred in the last 20 years, and the long-term survival of children older than 3 years with the tumor remains less than 10 percent, despite treatment with radiation and chemotherapy. DPG is also a rare exception to most types of brain cancer, since the diagnosis is based on brain MRIs, and a biopsy is rarely required to confirm the diagnosis.

“Since we don’t know the genetic make-up of the tumor, we don’t know the weaknesses of the tumor,” Broniscer says.

St. Jude researchers are now

collecting tumor samples as part of a collaborative protocol with other institutions. The team is performing molecular analyses on the samples to gain a better understanding of the biology of DPG in children.

“We believe that the more we learn about DPGs, the more likely we’ll be able to design more effective treatments for children of all ages with this tumor,” Broniscer says.

Life preserver

Erica received 18 months of chemotherapy treatment at St. Jude. During the treatment her hair never fell out and the tumor did not grow

larger. Three years after the initial diagnosis, Erica is off chemotherapy and is approaching her sixth birthday. The tumor remains the same size as the day it was discovered.

During chemotherapy, Erica’s smile returned, and her face no longer shows the signs of partial paralysis.

“I can’t describe the feeling when you are told that your child is going to die, and then somebody offers you a life preserver,” Jackie says. “You can’t even put that into words.”●

Thanks and Giving®: A Season of Hope

NOW IN ITS FIFTH YEAR, THIS FUNDRAISING CAMPAIGN HAS GENERATED VALUABLE AWARENESS FOR ST. JUDE RESEARCH AND CLINICAL CARE.

BY TARA MILLIGAN

November heralds the beginning of the holiday season, but it also brings the start of a campaign that creates extraordinary national awareness for the work of St. Jude Children's Research Hospital.

Thanks and Giving, the national fundraising campaign launched in 2004 by Marlo, Terre and Tony Thomas, will kick off November 24—the week of Thanksgiving and the start of the nation's busiest shopping season.

For the last four years, *Thanks and Giving* has cut through the season's barrage of consumer ads to spread the St. Jude message of hope. By urging consumers to "Give thanks for the healthy kids in your life, and give to those who are not," *Thanks and Giving* has struck a chord with millions of Americans eager to help St. Jude patients and their families.

This year, St. Jude will again be prominently featured on billboards; in newspaper, magazine and Internet ads; and in television spots featuring celebrities such as Robin Williams, Antonio Banderas and Jennifer Anniston. The campaign will be touted on network and cable television programs such as NBC's *TODAY* show and *Access Hollywood*. And for six weeks, *Thanks and Giving* will be visible in the stores of retail partners such as Target and Williams-Sonoma, where employees will encourage shoppers to buy special products that benefit the hospital or add money to their purchases for St. Jude.

St. Jude National Outreach Director Marlo Thomas and a few of her pals prepare for the 2008 kickoff of *Thanks and Giving*.

Reaching out to families

The *Thanks and Giving* campaign has also spread the mission of St. Jude research and clinical care to an important audience: families like the parents of 12-year-old Daniel Biljanoski of New York.

Last fall, Daniel's mom, Lisa, noticed he was often tired. In November, Daniel was hit in the head at school. He had begun having problems with double vision, and when the blow briefly made his eyes cross, Lisa took him to an ophthalmologist. A CT scan revealed a mass in the back of Daniel's brain.

Coincidentally, the Biljanoski family drama was playing out during the height of the 2007 *Thanks and Giving* campaign. That day, Daniel's grandmother had seen Marlo Thomas on the *TODAY* show, telling the



JOHN ZACHER



Daniel Biljanoski and his family learned about St. Jude through the *Thanks and Giving* campaign.

stories of some St. Jude patients, including a girl with atypical teratoid/rhabdoid tumor (ATRT), a rare, high-grade brain tumor.

"I called my mom from the hospital, and she said to me 'Lisa, Daniel has ATRT,'" Lisa says. "She knew because that child had the same symptoms as Daniel."

By the end of that day, a neurosurgeon told the family he suspected Daniel did, indeed, suffer from ATRT. Daniel underwent a five-and-a-half-hour surgery that confirmed the diagnosis. Then their

neurosurgeon showed them an article by Amar Gajjar, MD, director of the St. Jude Neuro-Oncology Division, and Larry Kun, MD, St. Jude Radiological Sciences chair. The authors stated that St. Jude research has shown that older children with ATRT have a chance of being cured. Daniel's doctor recommended that Daniel go to St. Jude.

St. Jude moments

At St. Jude, Daniel has received radiation therapy, chemotherapy and four autologous bone marrow transplants. The family is grateful for everything the hospital is doing for their son. "St. Jude is just amazing," Lisa says. "This is where Daniel needs to be."

Recently, Daniel had an opportunity to thank Marlo personally for her role in guiding him to St. Jude. John Remington, executive director of *Thanks and Giving*, introduced the two at the hospital.

"Everyone kept telling me about these 'St. Jude moments' that happen every day to reaffirm why we do what we do," Remington says. "When Daniel met Marlo and told her, 'You know, you're the reason I'm still here,' that was truly my St. Jude moment."

"Daniel's story is remarkable, and the impact of *Thanks and Giving* on the lives of children like him is immeasurable," said David McKee, chief operating officer of ALSAC, the fundraising organization of St. Jude. "We are so grateful to Marlo, Terre and Tony for creating this campaign. Not only does *Thanks and Giving* encourage shoppers to give to St. Jude so that patients can receive the lifesaving care they need, but the commercials, billboards and online ads all point to stjude.org, where anyone can learn about the huge strides that are being made in treating and curing childhood cancer."

A season of outreach

Building public awareness about the scientific and clinical discoveries at St. Jude is an important service of *Thanks and Giving*, according to Joseph Laver, MD, St. Jude clinical director and executive vice president.

"Despite extraordinary advances in diagnosis and treatment, cancer continues to kill more children in the United States than any other disease," Laver says. "Although the cure rate for the most common form of childhood cancer is close to 90 percent, many forms of childhood cancer are exceedingly rare and can be fatal. Families often don't know where to turn for information or help. That's why *Thanks and Giving* is such an important vehicle for communicating St. Jude's unique mission as a research center that has changed how the world treats childhood cancer."

With science and patient care under one roof, St. Jude is at the epicenter of pediatric cancer research. Its scientists and doctors are also researching new treatments for sickle cell disease, infectious diseases and genetic disorders. In 2007 alone, St. Jude researchers published more than 600 articles in academic journals, more than any other pediatric cancer research center in the United States.

"Every donation generated by *Thanks and Giving* helps support our mission," Laver says. "And the awareness created by *Thanks and Giving* about the work of St. Jude is a blessing for families in search of hope." ●



How can I help?

Look for the *Thanks and Giving* magnifying glass this holiday season wherever you shop to support the patients at St. Jude. Thanks and Giving partners include Target, Kay Jewelers, Williams-Sonoma, Kmart, CVS/pharmacy, AutoZone, Dick's Sporting Goods, Dollar General and Domino's Pizza, plus many more. St. Jude warmly welcomes our newest Thanks and Giving partners: RadioShack, New York & Co. and Crayola.

To learn more about *Thanks and Giving*, visit www.stjude.org. There, you'll find a full list of *Thanks and Giving* partners, with details about where to shop and how to donate, as well as inspirational stories about St. Jude patients and information about the hospital.

Solving for

BY ELIZABETH JANE WALKER

“There’s nothing we can do,” his physicians said, when they discovered that Cooper Winters had an extremely rare disease carried on the X chromosome. Then Cooper came to St. Jude.

If he lives to be 100, Jeremy Winters will never forget the quiet joy of holding his newborn son in the predawn hours of August 2, 2006. Grinning with pride, Jeremy kissed Cooper’s soft head and felt the baby’s perfect fist close around his finger.

If she lives to be 100, Shanna Winters will recall with heartbreaking clarity the day she planned Cooper’s funeral. Picking out a coffin for her 4-month-old. Feeling hot tears course down her face. “There’s nothing we can do for him,” doctors had said, as, tethered to a respirator, Cooper labored for every breath.



PETER BARTIA



➤ **Baffled by Cooper's symptoms, doctors at another institution sought the expertise of St. Jude immunologist Mary Ellen Conley, MD. After scrutinizing Cooper's family history, Conley made a diagnosis and subsequently assisted the St. Jude transplant team in developing a treatment plan.**

But Shanna and Jeremy Winters prefer to remember the day they took their son to St. Jude Children's Research Hospital. There, clinicians and researchers would perform a truly memorable feat—saving Cooper's life.

X points to IPEX

A couple of weeks after Cooper's birth, a rash appeared on his downy head. The doctor proclaimed it to be a minor ailment called cradle cap. But instead of improving, the rash worsened, spreading across Cooper's body and causing his skin to peel. When the baby also began to lose weight from frequent vomiting, the pediatrician referred him to a local children's hospital.

Cooper spent the next few months in the hospital, while clinicians sought ever-elusive answers.

For Shanna and Jeremy, concern turned to despair as they watched their son's condition deteriorate. Clinicians bandaged Cooper's cracked skin and provided nourishment through a tube. When his lungs filled with fluid, a respirator helped him breathe. The future looked so bleak that Shanna and her father made funeral arrangements. "How are we even going to pay for his funeral?" Shanna asked her dad, as she considered the medical expenses the family had already incurred.

Baffled by Cooper's symptoms, the doctors consulted Mary Ellen Conley, MD, an immunologist at St. Jude Children's Research Hospital.

Cooper's doctors told Conley that several baby

boys in Shanna's family had died in previous generations. "That was the clue for me," Conley says. "It was inherited in a pattern, so it had to be on the X chromosome."

As she considered disorders carried on the X chromosome, Conley realized that Cooper's symptoms most resembled those of immunodysregulation polyendocrinopathy enteropathy X-linked (IPEX) syndrome. This rare disease is carried by mothers and passed on to sons, who rarely live beyond infancy. Genetic tests confirmed Conley's suspicions: Cooper had IPEX.

Doctors still have much to learn about IPEX, as only seven years have passed since scientists associated a specific genetic mutation with the disease.

"Before the gene was identified, a lot of babies probably died without a diagnosis," says Conley, who estimates that between one and four children per million are born with the disorder.

Shanna and Jeremy were not comforted when they learned the diagnosis.

"It's scary when the doctors say, 'Well, your baby's got this rare disease that nobody's ever heard of, and we really don't know what to do,'" Shanna says.

Experts unite

A bone marrow transplant offered Cooper his only hope for survival. In December of 2006, St. Jude accepted Cooper as the hospital's first IPEX patient.

Jeremy and Shanna were amazed by the reception they received at St. Jude. "It was such a happy environment," Jeremy says. "The nurses, the doctors, the janitors—every single person we met told us that they would help us any way that they could. And when we found out that St. Jude was going to pay for everything, I

➤ **Cooper Winters is the first child to be treated at St. Jude for a rare and deadly genetic disease called immunodysregulation polyendocrinopathy enteropathy X-linked (IPEX) syndrome.**

Researchers and clinicians in the St. Jude Immunology, Molecular Pathology, and Bone Marrow Transplantation and Cellular Therapy departments pooled their expertise to determine how to save Cooper's life.



Kim Kasow, MD (at left), and Nurse Practitioner Jennifer Ferree were members of Cooper's transplant team. "Cooper has taught us a lot," Kasow says. "It has been a nice collaboration. The clinical transplant team and Dr. Conley worked together to create a plan, and then Dr. Riberdy helped us better understand what is going on with the T regulatory cells."

can't explain how wonderful it was. It took a big load off, and it was one less thing we had to think about."

Meanwhile, researchers and clinicians in the hospital's Immunology, Molecular Pathology, and Bone Marrow Transplantation and Cellular Therapy departments pooled their expertise to determine how to save Cooper's life.

Several children had undergone traditional bone marrow transplants for IPEX at other institutions. As part of that process, the kids received aggressive conditioning regimens—chemotherapy or irradiation given before the transplant to eradicate the disease and prevent transplant rejection. But because IPEX patients already suffer from severe medical problems, most of the children did not survive that treatment.

"We decided to reduce the intensity of the conditioning regimen for Cooper," explains Kimberly Kasow, DO, Oncology. "Because his digestive system was already torn up, we used a specific drug to protect

it against the chemotherapy agents that break it down. Cooper didn't receive big blasts of chemotherapy, but a more gentle treatment—enough to wipe out his immune system, allow his body to accept the graft and avoid the toxic side effects of a traditional transplant."

St. Jude also obtained FDA approval to use special equipment to deplete the bone marrow graft of T cells and B cells. Clinicians then gave Cooper enough cells to permit engraftment yet prevent graft-versus-host disease, a complication in which transplanted immune cells recognize the child's body as "foreign" and attack it.

Examining the cells

Cooper was fortunate to come to an institution that houses an expert on regulatory T cells, a population of white blood cells that typically put the brakes on the immune response. In a child with IPEX, these cells do not function, causing the immune system to run amok. When the immune system becomes overactive, the children develop a host of autoimmune diseases and life-threatening infections.

Janice Riberdy, PhD, of Immunology helped the St. Jude treatment team better understand the role regulatory T cells played in Cooper's case. Riberdy came to St. Jude 12 years ago to work with Nobel Laureate Peter Doherty, PhD. Currently, her lab studies the function of regulatory T cells. Only within the past few years have scientists begun to uncover the secrets of these elusive cells. Researchers ultimately want to be able to harness the power of regulatory T cells and develop



PETER BARTA

superior therapeutic strategies. Such knowledge would not only help children with autoimmune problems, but also individuals with infections, cancer and other diseases.

IPEX results from a mutation in the FOXP3 gene, which prevents the normal development of regulatory T cells. Riberdy and her colleagues examined Cooper's cells before transplant and have continued to study his cells as his immune system has reconstituted.

"Cooper's case afforded us a unique opportunity to try and understand how the FOXP3 mutation affects the function of regulatory T cells and what this population of cells does in individuals to keep them healthy," Riberdy says.

Because of the mild conditioning regimen, Cooper's immune system was not completely replaced by donor cells, as is the case in many transplants. The new regulatory T cells in Cooper's system came from an anonymous, unrelated donor, while the other cells in his immune system are ones that were present before the transplant.

"What happened was rather unexpected," Riberdy says. "We found that engraftment of only a few donor stem cells was able to correct IPEX. Selective growth of regulatory T cells that contain the correct FOXP3 gene is so strong that an entire population of regulatory T cells can develop from a tiny number of donor-derived stem cells. That's good news, because not requiring full donor engraftment suggests that the mild conditioning strategy may offer hope to other kids."

"We had never known that before," Riberdy says.

"Cooper has taught us a lot," Kasow says. "It has been a nice collaboration in which the clinical transplant team and Dr. Conley worked together to create a plan and then Dr. Riberdy helped us better understand what is going on with the T regulatory cells."

Exaltation and relief

As Shanna sat by Cooper's hospital bed during his transplant, she was filled with cautious optimism. "It was exciting," she recalls. "I was thinking, 'This is our new beginning.' To me it was more significant than the day he was born, because hopefully it was the event that was going to keep him here."

Not only did Cooper survive the transplant, but he thrived. "Even with all that he went through, he remained a happy little boy," Jeremy says. "He's so much fun to be around. Cooper can make anybody smile."

Cooper's nurses agree. During his long hospitalization, they put a sign on his hospital room door that read, "We love Cooper!"

If she lives to be 100, Shanna will remember the last day she donned a gown and mask to enter her son's St. Jude hospital room. For months, Cooper had been in isolation to protect him from acquiring a life-threatening infection. As Shanna put on her protective garb, a nurse said, "You don't have to wear that anymore."

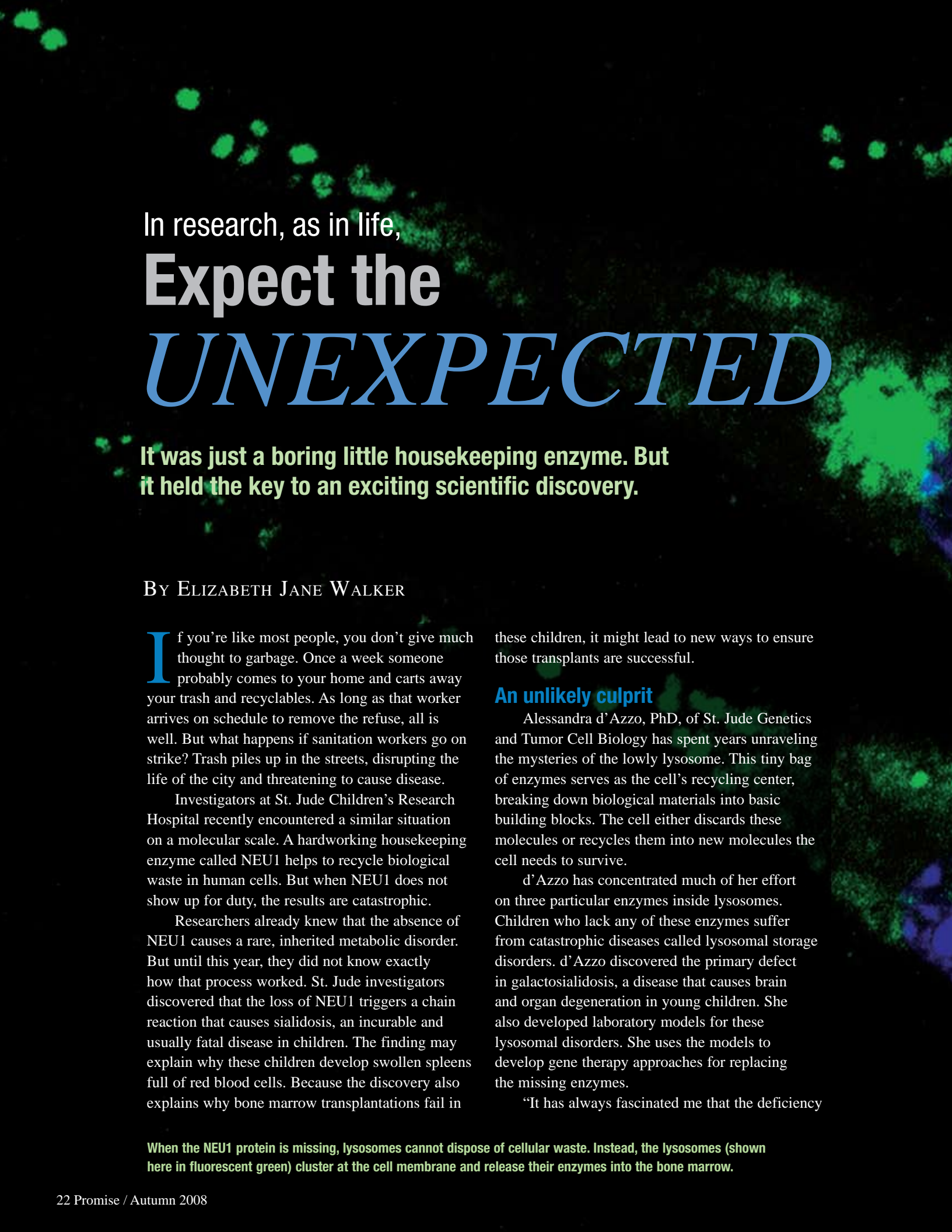
"I was so relieved," Shanna says. "That's the day I realized that everything was going to be OK." ●

(At right) Janice Riberdy, PhD, and Research Laboratory Specialist David Wichlan work together in the lab. Riberdy helped the St. Jude treatment team better understand the role regulatory T cells played in Cooper Winters' case. Riberdy says the mild pretreatment strategy used in Cooper's transplant may offer hope to other children.

(Facing page) A couple of months before Cooper came to St. Jude, the infant's skin began to crack and peel. The condition became life threatening, necessitating the use of a respirator. Cooper is the first child to be treated at St. Jude for this rare and deadly genetic disease, called immunodysregulation polyendocrinopathy enteropathy X-linked (IPEX) syndrome.

PETER BARTA





In research, as in life,
Expect the

UNEXPECTED

It was just a boring little housekeeping enzyme. But it held the key to an exciting scientific discovery.

BY ELIZABETH JANE WALKER

If you're like most people, you don't give much thought to garbage. Once a week someone probably comes to your home and carts away your trash and recyclables. As long as that worker arrives on schedule to remove the refuse, all is well. But what happens if sanitation workers go on strike? Trash piles up in the streets, disrupting the life of the city and threatening to cause disease.

Investigators at St. Jude Children's Research Hospital recently encountered a similar situation on a molecular scale. A hardworking housekeeping enzyme called NEU1 helps to recycle biological waste in human cells. But when NEU1 does not show up for duty, the results are catastrophic.

Researchers already knew that the absence of NEU1 causes a rare, inherited metabolic disorder. But until this year, they did not know exactly how that process worked. St. Jude investigators discovered that the loss of NEU1 triggers a chain reaction that causes sialidosis, an incurable and usually fatal disease in children. The finding may explain why these children develop swollen spleens full of red blood cells. Because the discovery also explains why bone marrow transplantations fail in

these children, it might lead to new ways to ensure those transplants are successful.

An unlikely culprit

Alessandra d'Azzo, PhD, of St. Jude Genetics and Tumor Cell Biology has spent years unraveling the mysteries of the lowly lysosome. This tiny bag of enzymes serves as the cell's recycling center, breaking down biological materials into basic building blocks. The cell either discards these molecules or recycles them into new molecules the cell needs to survive.

d'Azzo has concentrated much of her effort on three particular enzymes inside lysosomes. Children who lack any of these enzymes suffer from catastrophic diseases called lysosomal storage disorders. d'Azzo discovered the primary defect in galactosialidosis, a disease that causes brain and organ degeneration in young children. She also developed laboratory models for these lysosomal disorders. She uses the models to develop gene therapy approaches for replacing the missing enzymes.

"It has always fascinated me that the deficiency

When the NEU1 protein is missing, lysosomes cannot dispose of cellular waste. Instead, the lysosomes (shown here in fluorescent green) cluster at the cell membrane and release their enzymes into the bone marrow.

of one single enzyme can have such a devastating consequence and cause such serious defects,” d’Azzo says. “I was particularly interested in NEU1, because it is such a basic yet complex enzyme, and I have always had the feeling that we were touching the tip of the iceberg as far as its actual functions went.”

Taking out the trash

Kids with sialidosis often have spleens that are two or three times their normal size, and sialidosis laboratory models develop the same problem. “Looking at the spleen in the sialidosis model, we noticed that over time it became increasingly enriched with blood stem cells, while simultaneously the bone marrow was depleted of those cells,” d’Azzo says.

That symptom was the first clue that led to her recent discovery. The second clue came when she attempted treatment of the disease with bone marrow transplantation: The donor bone marrow did not engraft in the sialidosis model.

Thinking that these two phenomena could be linked, d’Azzo asked a postdoctoral fellow in her lab to find out why these perplexing changes in the bone marrow occurred. After a long series of studies, d’Azzo and her team figured out that the lack of NEU1 caused a complex chain of events that forced the stem cells to leave the bone marrow and migrate to the spleen.

The NEU1 protein controls how lysosomes dispose of cellular “waste.” Usually, lysosomes digest or process molecules and either recycle them into building blocks for new molecules or dispose of them. But when NEU1 is missing, lysosomes lose these capacities. Instead, these bags of enzymes become prone to dock at their cell’s membrane and dump their enzymes into the bone marrow environment. The accumulation of these enzymes creates a hostile bone marrow environment for the retention of blood stem cells in the bone marrow cavity, where they are needed to perform their task of giving rise to new blood cells. Instead, the stem cells flee the neighborhood, crowding into the spleen, which becomes enlarged in a child who suffers from sialidosis.

Eyes wide open

A couple of years ago, d’Azzo organized an

international scientific meeting about lysosomal storage diseases. There, she met the mother of a child with sialidosis. “You know, I went to the hospital and they transplanted my child, but it doesn’t seem the marrow engrafted,” the woman told d’Azzo.

“I immediately connected our findings with what this mother was telling me, and I decided to investigate why NEU1 is important for bone marrow engraftment,” d’Azzo says.

In a transplant, donor stem cells must remain in the bone marrow until they mature and create healthy, new cells. But d’Azzo found that, if *NEU1* is missing, the donor cells desert the hostile bone marrow environment and the transplant fails.

These discoveries, in turn, create more questions for d’Azzo and her team to investigate. “For kids with sialidosis, we now have a way to explain why they don’t engraft,” she says. “But I think our findings could have a much, much broader significance than that.

“I really think that we might have the possibility to improve bone marrow engraftment,” she continues. “We may be able to pretreat the child to create the correct environment for the marrow to engraft. This is super exciting and gives us a better understanding of the aspects of cell biology that apply to many other fields of medical research.”

Who would have dreamed that studying a lowly housekeeping enzyme would yield such exciting scientific advances?

“I think that no matter what you study, you should keep your eyes wide open,” d’Azzo says. “Everything is interconnected, and it’s often the most unexpected finding that’s important.” ●

Alessandra d’Azzo, PhD, and Erik Bonten, PhD, of Genetics and Tumor Cell Biology discovered why children with sialidosis develop swollen spleens and why bone marrow transplants fail in these children. Their finding may lead to new ways to ensure that transplants are successful.

ANN-MARGARET HEDGES



Perspective

BY JUSTIN LEONARD

Supporting St. Jude: Everybody Wins

“Giving to St. Jude is important because it helps families who might not otherwise have a chance to obtain world-class treatment.”

The 2008 Stanford St. Jude Championship marked the 10th year that I’ve competed in the PGA TOUR tournament that benefits St. Jude Children’s Research Hospital. Winning this year’s tournament in a playoff against world-class players Robert Allenby and Trevor Immelman was truly a special feeling.

I remember a few years ago at the tournament, several of the patients were seated near the 18th green at the Tournament Players Club at Southwind. When players got finished with their rounds, they could go over there and have lunch. That was a pretty special afternoon—seeing those kids get the chance to attend the golf tournament and get away from everything they were going through, to escape for a little bit.

After winning the event in 2005, I commented to tournament director Phil Cannon that it would be great if the PGA TOUR golfers could interact more with the children of St. Jude. Such a personal experience would not only allow players to see the hospital and meet some of the kids and their families, but it would help the golfers realize how important the tournament is for St. Jude.

In June of 2008, I participated in the fulfillment of my request from three years ago. I had the opportunity to visit with patients and families during the PGA TOUR Wives Association picnic at Target House. It was a special night to be able to interact with so many of the patients and their families. The golfers got to see a small part of what St. Jude is about—how they take care of these children. It was also a way to give these families a fun night so that they could forget for a little while about why they are there.

Golfer Justin Leonard holds up the champion’s trophy after capturing the 2008 Stanford St. Jude Championship. The tournament has raised more than \$19 million for St. Jude since 1970, when the hospital was named the event’s sole charity.

The tournament staff made this a personal experience for the players.

Giving to St. Jude is important because it helps families who might not otherwise have a chance to obtain world-class treatment. St. Jude helps people who aren’t able to help themselves when it comes to financial needs. This method of caring for each other is something we should all strive to do.

My wife, Amanda, and I are fortunate to have three healthy, young children. I know that if something did happen and we needed to seek out serious medical advice, St. Jude is the first place we would go because of what I’ve witnessed and heard from the families of patients who seek treatment there. ●

A 12-time winner on the PGA TOUR, Justin Leonard won the British Open in 1997 and the Stanford St. Jude Championship in the summer of 2008. The recent win marked the second time that Leonard has prevailed at the tournament to benefit St. Jude.



PETER BARTA



ELLIE VS. BRAIN TUMOR

LET'S
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SHE WINS.

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Ellie suffers from a supratentorial primitive neuroectodermal tumor, a life-threatening form of childhood cancer. But your donation helps. In fact, 85 cents of every dollar received supports the research and treatment at St. Jude Children's Research Hospital®. Thanks to you, we're finding breakthroughs and cures for kids with catastrophic diseases in communities everywhere.

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ANN-MARGARET HEDGES



Sarah Ferguson, the Duchess of York, toured St. Jude June 24. The duchess visited with patients such as McKaylee Borklund (at left) and learned how St. Jude shares protocols internationally.


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